



EHS Core Centers

2013 Meeting, Seattle



Science Symposia

- *Implications of the ENCODE Project for the Future of Gene-Environment Interactions Research*
- *Emerging Issues in Global Environmental Health*

**April 17th
through
April 19th
2013**



Center for
ecogenetics
& Environmental Health

BLOG: www.ecogenetix.org
TWITTER: @ecogenetix, @phcafe
FACEBOOK: Public Health Café



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Map of South Lake Union Neighborhood



Agenda for Directors and Investigators

DIRECTORS • Wednesday, April 17th, 2013

2:00 pm Registration opens (2nd floor foyer)

4:30 pm Science Highlight and COEC Posters go up (Cascade A, Gateway)

5:00 pm Reception and Poster Session (Pre-Function, Gateway, Cascade A)

Pan Pacific Hotel
Conference Rooms
2nd Floor

6:15 pm Directors' Welcome (Lakefront)

6:30 pm **BUFFET DINNER** (Directors and Dr. Birnbaum in Cascade B, others in Lakefront room)

Meals and Breaks
All Attendee Sessions
Special Events

DIRECTORS • Thursday, April 18th, 2013

7:30 am	Late Registration and CONTINENTAL BREAKFAST	SLU, Room 123
8:15 am	Welcome • Howard Frumkin, Dean, UW School of Public Health	
8:30 am	<p>Science Symposium 1: Implications of the ENCODE Project for the Future of Gene-Environment Interactions Research (Session Chair: Dave Eaton, University of WA)</p> <p>Keynote: <i>Genes, Chromatin, and Common Disease</i> • John Stamatoyannopoulos, University of WA</p>	UW School of Medicine, South Lake Union (SLU) 850 Republican Street
9:15 am	<p>PANEL DISCUSSION (10 minutes commentary by each panelist, followed by Q&A) Panelists:</p> <ul style="list-style-type: none"> • <i>Environmental impact on gender-specific DNA methylation in autoimmunity</i> • Bruce Richardson, University of Michigan • Mario Medvedovic, University of Cincinnati • David Hawkins, University of WA 	Orin Smith Auditorium
10:15 am	NIEHS Director's Welcome and Updates • Linda Birnbaum, NIEHS	
11:00 am	BREAK	
11:15 am	<p>Working Group Breakout Sessions:</p> <p>A. Inter-Center Working Group on Fracking (Orin Smith Auditorium)</p> <p>B. Preparing the Next Generation of EH Scientists and Building a Diverse Workforce (Room 123) • <u>Panelists:</u> Neasha Graves, Dave Eaton, Clark Lance</p>	SLU
12:30 pm	LUNCH (Provided)	SLU, Room 123
1:30 pm	<p>Working Group Breakout Sessions:</p> <p>C. Inter-Center Working Group on Fracking, cont. (Orin Smith Auditorium)</p> <p>D. Strategies to Build Bi-Directional Communication (Room 123)</p>	SLU
2:45 pm	BREAK	
3:00 pm	EHS Core Centers Long-Range Evaluation & Strategic Planning	
4:00 pm	NIEHS Directors' Update: Future Steps for the EHS CC Program • Linda Birnbaum, Gwen Collman, Les Reinlib	SLU, Orin Smith Auditorium
4:45 pm	Meeting Adjourns	
5:30 pm	Public Forum: The Duwamish River Cleanup	Portage Bay Café
7:30 pm	Dinner on your own	

DIRECTORS • Friday, April 19^h, 2013

7:30 am	Late Registration and CONTINENTAL BREAKFAST	UW SLU, Room 123
8:30 am	Working Groups Report Back • Les Reinlib and Liam O'Fallon, NIEHS	SLU, Orin Smith Auditorium
9:15 am	NIEHS Disaster Research and Training Update • Chip Hughes & Aubrey Miller, NIEHS	SLU, Orin Smith Auditorium
10:00 am	BREAK	
	Young Investigator Talks	
10:15 am	Introductory Remarks • Claudia Thompson, NIEHS	
10:30 am	<i>Health Concerns Related to Unregulated Electronic-Waste Recycling</i> • Aimin Chen, University of Cincinnati	
10:45 am	<i>A New Study to Evaluate Persistent Organic Pollutants and Vaccine Efficacy</i> • Parveen Bhatti, University of WA	
11:00 am	<i>Phasing Out Residual Oil: A Community-based Participatory Research Project on the NYC Clean Heat Initiative in Northern Manhattan</i> • Diana Hernandez, Columbia University	SLU, Orin Smith Auditorium
11:15 am	<i>Bioinformatics Tools for Genome-Wide Epigenomic Studies</i> • Maureen Sartor, University of Michigan	SLU, Orin Smith Auditorium
11:30 am	<i>Neurodevelopmental Impacts of Air Pollution Exposure</i> • Heather Volk, University of Southern CA	
11:45 am	<i>Potential role of adipose-derived mesenchymal stem cell migration in promoting prostate tumorigenesis</i> • Marxa Figueiredo, UTMB Galveston	
12:00 pm	<i>Effects of Phthalates on Neonatal Inflammatory Responses</i> • Anna Vetrano, Rutgers	
12:15 pm	LUNCH (Provided)	SLU, Room 123
1:00 pm	Science Symposium 2: Emerging Issues in Global Environmental Health (Session Chair: Claudia Thompson, NIEHS) Keynote: Title TBD • Theo Vos, University of WA	
1:45 pm	PANEL DISCUSSION (10 minutes commentary by each panelist, followed by Q&A) Panelists: <ul style="list-style-type: none"> • John Balbus, NIEHS • Laura Rozek, University of Michigan • Mollie Kile, Oregon State University 	SLU, Orin Smith Auditorium

DIRECTORS • Friday, April 19^h, 2013

2:45 pm	BREAK	
Young Investigator Talks, continued		
3:00 pm	<i>Formaldehyde-induced Airway Hyperresponsiveness</i> • Joseph Jude, University of Pennsylvania	SLU, Orin Smith Auditorium
3:15 pm	<i>Effects of Acrolein on histone modifications</i> • Chunyuan Jin, New York University	
3:30 pm	<i>Environmental Metabolomics: An opportunity for biomarker development</i> • Alex Lu, Harvard University	
4:00 pm	Meeting Adjourns	
5:00 pm	Buses Depart from Hotels for Pier 55	
6:00 pm	Boat Tour of Puget Sound aboard the Lady Mary (dinner provided)	
9:00 pm	Return to Pier 55, Buses Depart for Hotels	

Agenda for Administrators

ADMINISTRATORS • Wednesday, April 17th, 2013

2:00 pm Registration opens (2nd floor foyer)

4:30 pm Science Highlight and COEC Posters go up (Cascade A, Gateway)

5:00 pm Reception and Poster Session (Pre-Function, Gateway, Cascade A)

6:15 pm Director's Welcome (Lakefront)

6:30 pm **BUFFET DINNER** (Directors and Dr. Birnbaum in Cascade B, others in Lakefront room)

Pan Pacific Hotel
Conference
Rooms
2nd Floor

Meals and Breaks
All Attendee Sessions
ADMIN Only Sessions
Special Events

ADMINISTRATORS • Thursday, April 18th, 2013

7:30 am	Late Registration and CONTINENTAL BREAKFAST	UW SLU, Room 123
8:15 am	Welcome • Howard Frumkin, Dean, UW School of Public Health	
8:30 am	<p>Science Symposium 1: Implications of the ENCODE Project for the Future of Gene-Environment Interactions Research (Session Chair: Dave Eaton, University of WA)</p> <p>Keynote: Genes, Chromatin, and Common Disease • John Stamatoyannopoulos, University of WA</p>	<p>UW School of Medicine, South Lake Union (SLU) 850 Republican Street</p> <p>Orin Smith Auditorium</p>
9:15 am	<p>PANEL DISCUSSION (10 minutes commentary by each panelist, followed by Q&A)</p> <p>Panelists:</p> <ul style="list-style-type: none"> • <i>Environmental impact on gender-specific DNA methylation in autoimmunity</i> • Bruce Richardson, University of Michigan • Mario Medvedovic, University of Cincinnati • David Hawkins, University of WA 	
10:15 am	NIEHS Director's Welcome and Updates • Linda Birnbaum, NIEHS	
11:15 am	Move to Pan Pacific Hotel for Afternoon ADMINISTRATORS ONLY Sessions	
Noon	LUNCH (Provided)	Pan Pacific Hotel, Cascade Room
1:00 pm	Administrators Session 1: NIEHS P30 Updates (Les Reinlib and Dorothy Duke)	Pan Pacific Hotel, Cascade Room
2:45 pm	BREAK	
3:00 pm	Administrators Session 2: ASSIST System, Promises & Perils (Linda Bass)	Pan Pacific Hotel, Cascade Room
4:45 pm	Meeting Adjourns	
5:30 pm	Public Forum: The Duwamish River Cleanup	Portage Bay Café
7:30 pm	Dinner on your own	

ADMINISTRATORS • Friday, April 19^h, 2013

7:30 am	Late Registration and CONTINENTAL BREAKFAST	SLU, Room 123
8:30 am	Working Groups Report Back • Les Reinlib and Liam O'Fallon, NIEHS	SLU, Orin Smith Auditorium
9:15 am	NIEHS Disaster Research and Training Update • Chip Hughes & Aubrey Miller, NIEHS	
10:00 am	BREAK & Move to Pan Pacific Hotel for Afternoon ADMINISTRATORS ONLY Sessions	
10:45 am	Administrators Session 3: Use of Social Media, General Discussion, and 2014 Meeting Planning Brainstorm	Pan Pacific Hotel, Cascade Room
12:15 pm	LUNCH (Provided at the Pan Pacific)	
1:00 pm – 2:15 pm	Administrators Session 4 (OPTIONAL session for those not wishing to attend Science Symposium 2): Pilot Project Program, Planning for the future with the new RFA, Sequestration, etc.	Pan Pacific Hotel, Cascade Room
1:00 pm	Science Symposium 2: Emerging Issues in Global Environmental Health (Session Chair: Claudia Thompson, NIEHS) Keynote: Title TBD • Theo Vos, University of WA	
1:45 pm	PANEL DISCUSSION (10 minutes commentary by each panelist, followed by Q&A) Panelists: <ul style="list-style-type: none"> • John Balbus, NIEHS • Laura Rozek, University of Michigan • Mollie Kile, Oregon State University 	SLU, Orin Smith Auditorium
2:45 pm	BREAK	
	Young Investigator Talks, continued	
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3:15 pm	<i>Effects of Acrolein on histone modifications</i> • Chunyuan Jin, New York University	
3:30 pm	<i>Environmental Metabolomics: An opportunity for biomarker development</i> • Alex Lu, Harvard University	
4:00 pm	Meeting Adjourns	
5:00 pm	Buses Depart from Hotels for Pier 55	
6:00 pm	Boat Tour of Puget Sound aboard the Lady Mary (dinner provided)	
9:00 pm	Return to Pier 55, Buses Depart for Hotels	

Agenda for COECs

COECs • Wednesday, April 17th, 2013

2:00 pm Registration opens (2nd floor foyer)

3:00 pm COEC Session 1: The History Wall (Cascade Room B)

4:30 pm Science Highlight and COEC Posters go up (Cascade A, Gateway)

5:00 pm Reception and Poster Session (Pre-Function, Gateway, Cascade A)

6:15 pm Director's Welcome (Lakefront)

6:30 pm **BUFFET DINNER** (Directors and Dr. Birnbaum in Cascade B, others in Lakefront room)

Pan Pacific Hotel
Conference Rooms
2nd Floor

Meals and Breaks

All Attendee Sessions

COEC Only Sessions

Special Events

COECs • Thursday, April 18th, 2013

7:30 am	Late Registration and CONTINENTAL BREAKFAST	UW SLU, Room 123
8:15 am	Welcome • Howard Frumkin, Dean, UW School of Public Health	
8:30 am	<p>Science Symposium 1: Implications of the ENCODE Project for the Future of Gene-Environment Interactions Research (Session Chair: Dave Eaton, University of WA)</p> <p>Keynote: Genes, Chromatin, and Common Disease • John Stamatoyannopoulos, University of WA</p>	UW School of Medicine, South Lake Union (SLU) 850 Republican Street
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10:15 am	NIEHS Director's Welcome & Updates • Linda Birnbaum, NIEHS	
11:00 am	BREAK	
	Working Group Breakout Sessions:	
11:15 am	A. Inter-Center Working Group on Fracking (Orin Smith Auditorium) B. Preparing the Next Generation of EH Scientists and Building a Diverse Workforce (Room 123) • <u>Panelists</u> : Neasha Graves, Dave Eaton, Clark Lance.	SLU
12:30 pm	LUNCH (Provided)	SLU, Room 123
	Working Group Breakout Sessions:	
1:30 pm	C. Inter-Center Working Group on Fracking, cont. (Orin Smith Auditorium) D. Strategies to Build Bi-Directional Communication (Room 123)	SLU
2:45 pm	BREAK	
3:00 pm	COEC Session 2: Small Group Un-Conferences: 1. EH Literacy 2. Fracking 3. Health Impact Assessments 4. Using the CAB Effectively 5. Healthy Homes	SLU, Room 123
4:45 pm	Meeting Adjourns	
5:30 pm	Public Forum: The Duwamish River Cleanup	Portage Bay Café
7:30 pm	Dinner on your own	

COECs • Friday, April 19^h, 2013

7:30 am	Late Registration and CONTINENTAL BREAKFAST	SLU, Room 123
8:30 am	Working Groups Report Back • Les Reinlib and Liam O’Fallon, NIEHS	SLU, Orin Smith Auditorium
9:15 am	NIEHS Disaster Research and Training Update • Chip Hughes & Aubrey Miller, NIEHS	
10:00 am	BREAK	
10:15 am	COEC Session 3: Evaluation	SLU, Room 123
12:15 pm	LUNCH (Provided)	
1:00 pm	<p>Science Symposium 2: Emerging Issues in Global Environmental Health (Session Chair: Claudia Thompson, NIEHS)</p> <p>Keynote: Title TBD • Theo Vos, University of WA</p>	
1:45 pm	<p>PANEL DISCUSSION (10 minutes commentary by each panelist, followed by Q&A)</p> <p>Panelists:</p> <ul style="list-style-type: none"> • John Balbus, NIEHS • Laura Rozek, University of Michigan • Mollie Kile, Oregon State University 	SLU, Orin Smith Auditorium
2:45 pm	BREAK	
3:00 pm	COEC Session 4: Tools to Communicate Science Online	SLU, Room 123
4:00 pm	Meeting Adjourns	
5:00 pm	Buses Depart from Hotels for Pier 55	
6:00 pm	Boat Tour of Puget Sound aboard the Lady Mary (dinner provided)	
9:00 pm	Return to Pier 55, Buses Depart for Hotels	

Session Descriptions

Preparing the Next Generation of EH Scientists and Building a Diverse Workforce

(Working Group B, Thursday, 11:15 am, South Lake Union, Orin Smith Auditorium)

In this session, participants will explore how Centers can enhance their work to prepare and promote diversity among the next generation of researchers, particularly from the perspectives of research, administration and outreach. In addition, participants will have an open exchange of ideas to address specific challenges and opportunities for partnerships and other resources that help Centers match the need for a more diverse workforce with their overall mission, goals and activities. The session will begin with a panel discussion of professionals describing how they use existing tools within the Center structure to engage the next generation of researchers and promote diversity in their Centers. The other half of the session will involve small group discussions between participants who have interests in defining diversity for their Centers, recruiting and retaining a diverse pool of faculty, staff and students, and addressing the needs of underserved communities. By the end of the breakout session, participants will be able to determine actions they can take to prepare the next generation of environmental health scientists and build a more diverse workforce in their Centers.

Bidirectional Communication

(Working Group D, Thursday, 1:30 pm, South Lake Union, Orin Smith Auditorium)

Bi/multi-directional communication is an essential component of the EHS Core Centers carried out by their Community Outreach and Engagement Cores. Bi/multi-directional communication enables the Center to engage with their various audiences including, community groups, healthcare professionals, and decision makers to ensure research translates into action and that issues of importance to the audience are reflected within the science agenda at the Center. A challenge Centers face is deciding how to respond to emerging issues identified by their audience while continuing to engage in their current research. Adapting to the changing needs of the research and the current conditions and concerns presented by communities is a necessity.

This workshop will highlight three perspectives on the importance of bi/multi-directional communication: a Center Director, a COEC Director, and a Community stakeholder. The panel will provide examples of how bi/multi-directional communication has helped the Center advance their environmental health science research agenda as well as meet the needs of its defined audience. In addition, the interactive workshop will include small group discussions to share different bi/multi-directional communication strategies employed for engaging a wide range of audiences, discuss challenges, and highlight opportunities to strengthen this approach within the EHS Core Center program.

Learning Objectives

1. Participants will understand and utilize the approaches of **bidirectional** and **multidirectional** communication in their everyday work
2. Identify examples and tools to engage their Center's audience (e.g. researchers, policy makers, community members) more effectively.
3. Leave with a next step for creating additional opportunities for bi/multidirectional communication in your Center

NIEHS Disaster Research and Training Update

(Friday, 9:15 am, South Lake Union, Orin Smith Auditorium)

NIEHS Worker Education and Training Program (WETP), which part of the US Department of Health and Human Services (HHS) in the National Institutes of Health (NIH), has activated and mobilized its network of worker education and training resources to support response and cleanup activities from Super Storm Sandy in order to assure safe work practices and high levels of worker protection during the cleanup process.

Since early November 2012, NIEHS has been working to build safety and health training partnerships in both of the severely impacted zones of New York and New Jersey. Through multiple interagency outreach strategies, NIEHS has been able to leverage its existing training capacity in both states. Many of our key partners in academia, with labor and community organizations are already working with targeted at-risk populations who are on front-lines of the cleanup and recovery process.

Based on the requirements of the Hurricane Sandy Health and Safety Plan and the accompanying job hazard analysis, safety and health training has been tailored to the specific exposure and job tasks of numerous target group of volunteers, homeowners, day laborers and cleanup workers. Building a field safety training capacity during this disaster has resulted in numerous lessons learned for field response to emerging environmental health hazards during disasters.

Current national disaster response plans (National Response Framework and National Contingency Plan) do not have a formal mechanism to include science research into the response effort. As a result of this gap a critical health component is lacking that could assist the incident commander, policy makers, and public health officials in making decisions that impact responders and the affected population's health and safety.

NIEHS currently possesses scientific resources that could be brought to and integrated into a disaster response with a goal to improve public health during, and after, a disaster. Such activities could include: Assessment and identification of research resources available; identifying a research participation process; identifying resources needed (material and financial); identifying data collection protocols and mechanisms for the incorporation of local resources (public health, community, and academia). There is currently a Trans-NIH disaster interest group that is looking at how to improve the NIH's disaster response efforts as well as interest from DHHS/ASPR. We will update the group on these ongoing efforts.

COEC Evaluation Session

(Friday, 10:15 am, South Lake Union, Room 123)

The purpose of the session is to discuss evaluation in the context of community outreach and engagement. Drs. Drew and Pettibone will provide assistance for identifying outcomes from activities that are difficult to capture. The session may lead to the development of new logic models on common issues that have been raised from the COEC webinar on evaluation, the COEC Lightning Talk Webinars and the COEC History Wall. An additional goal is to strengthen COEC ability to communicate to different audiences (Center Directors, NIEHS Program Staff, Reviewers, and community groups) what they are doing and achieving.

Session Outline

Introduction – Liam O'Fallon

Liam will re-iterate the importance of capturing and communicating outcomes from COEC to different audiences. Audiences include NIEHS program staff and reviewers.

Review of the common themes – Kristi Pettibone

These themes will be captured from the Lightning Talks and the COEC History wall. The group will winnow the list to just 3 or 4.

Breakout into small groups – Christie Drew

These breakouts will be determined by the discussion above.

1. Topic A (Drew)
2. Topic B (Pettibone)
3. Topic C (O'Fallon)
4. Topic D and/or Evaluation 101 - for newer COEC members (if needed)

Report Backs – Kelly Edwards

Attendee Roster (sorted by affiliation)

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CENTER **Center for Ecogenetics and Environmental Health (U WA)**

LOCATION University of Washington, Seattle, WA

PI Dave Eaton

COEC DIRECTOR Kelly Edwards

ADMINISTRATOR Jon Sharpe

WEB SITE <http://depts.washington.edu/ceeh/>

THEME

The Center for Ecogenetics and Environmental Health (CEEH) is dedicated to contributing to science-based changes in regulatory policy and public health or medical practice that result in a reduction in the burden of environmentally induced diseases.

RECENT SCIENCE HIGHLIGHTS

In a series of high profile articles, CEEH Investigator Dr. John Stamatoyannopoulos and colleagues recently published their ground breaking work on the Encyclopedia of DNA Elements (ENCODE), a multicenter project that seeks to map euchromatin and heterochromatin domains together with transcription factor binding sites, and the roles they play in cellular differentiation, proliferative potential, gene-gene and gene-environment interactions, human evolution and the transcriptional bases of human disease. This forward-looking and data-rich project has revolutionized our view of the human genome and will yield many exciting insights on the role of gene-environment interaction in disease and the role of epigenetics in human susceptibility to toxicants.

CEEH Investigator Dr. Joel Kaufman and colleagues examined the hypothesis that alterations in blood pressure (BP) are a mode of action through which inhaled pollutants can increase both acute and chronic risk of cardiovascular events. In double-blinded, crossover exposure studies, they measured the effects of diesel exhaust (DE) exposure on BP in young adults. Compared with filtered air, systolic BP consistently increased after DE exposure with no significant effect on heart rate or diastolic pressure. This study helps to clarify how exposure to DE can elevate risk for both acute and chronic cardiovascular outcomes.

CEEH Investigator Dr. Sheela Sathyanarayana and co-workers together with collaborators from the Study for Future Families tested whether 24 common SNPs in eight genes that influence male genital development were associated with intermediate phenotypes in healthy male infants. They found that a variant in the coding region of estrogen receptor alpha (ESR1) was associated with a shorter anogenital distance. Another variant in the 3' untranslated region of ATF3, approached significance for a shorter anoscrotal distance ASD after controlling for multiple comparisons, as were two SNPs in genes that regulate estrogen signaling during male genital development. Their findings suggest that AGD and ASD are influenced by heritable factors in genes known to be associated with frank male genital abnormalities such as hypospadias and cryptorchidism. They did not observe a statistically significant interaction between prenatal phthalate exposure, genetic variants and the measures they examined, although the sample size was small in this pilot study.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

In 2012, the Community Outreach and Ethics Core worked to enhance partnerships with community groups and strengthened relationships with local tribal members. We expanded our network by increasing our Social Media presence using Twitter, Facebook, blogging, and a video series, *People Matter*. Here we highlight two current COEC activities: Our partnership with the Duwamish River Cleanup Coalition, and building our network through

Social Media.

The Duwamish River Cleanup Coalition (DRCC) is EPA's Community Advisory Group for Seattle's Duwamish River Superfund site. The mission of DRCC is to ensure a Duwamish River cleanup that is accepted by and benefits the community and protects fish, wildlife and human health.

In 2012, the COEC was a sponsor of the 7th annual Duwamish River Festival that provides a summer afternoon of entertainment, boat tours, and cleanup information to the Georgetown and South Park neighborhoods that abut the Superfund site. Georgetown and South Park have many low-income, non-English speaking, and non-white residents. The Festival drew several hundred community members, including Native Americans, Hispanics and Southeast Asians. The COEC sponsored a bike tour/DRCC fundraiser and staffed a popular table about environmental health.

Along with a Center member researcher, the DRCC Program Manager was a presenter at our quarterly Public Health Café, *Seafood: It's Healthy, But Is It Safe to Eat?* The Program Manager focused on environmental justice issues such as the effects of river and seafood contamination on the local community, especially Native Americans and subsistence fishermen whose traditional diets include lots of seafood.

In anticipation of the EPA cleanup proposal to be announced in February 2013, DRCC has conducted the Duwamish Valley Healthy Communities Initiative and Community Health Impacts Analysis (CHIA). COEC partnered with DRCC to produce the published report of the CHIA study.

Building our network through social media was another 2012 COEC focus. We created a blog (www.ecogenetix.org) on which we post upcoming events, research highlights, event highlights on local presentations pertaining to environmental health, and Center member news. We actively post on two Twitter accounts and have created a Facebook page to promote the Public Health Café as well as inform our audience about other Science Cafés.

HIGHLIGHTED PUBLICATIONS

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Sathyanarayana S, Swan SH, Farin FM, Wilkerson HW, Bamshad M, Grady R, Zhou C, Schwartz SM (2012). A pilot study of the association between genetic polymorphisms involved in estrogen signaling and infant male genital phenotypes. *Asian J. Androl*. 14:766-72.

RESEARCH HIGHLIGHT POSTER

Modification of neurobehavioral effects of mercury by a genetic polymorphism of coproporphyrinogen oxidase in children

Woods JS, Heyer NJ, Echeverria D, Russo JE, Martin MD, Bernardo MF, Luis HS, Vaz L, Farin FM

ABSTRACT: Mercury (Hg) is neurotoxic, and children may be particularly susceptible to this effect. A current major challenge is the identification of children who may be uniquely susceptible to Hg toxicity because of genetic disposition. We examined the hypothesis that CPOX4, a genetic variant of the heme pathway enzyme coproporphyrinogen oxidase

(CPOX) that affects susceptibility to mercury toxicity in adults, also modifies the neurotoxic effects of Hg in children. Five hundred seven children, 8-12 years of age at baseline, participated in a clinical trial to evaluate the neurobehavioral effects of Hg from dental amalgam tooth fillings in children. Subjects were evaluated at baseline and at 7 subsequent annual intervals for neurobehavioral performance and urinary mercury levels. Following the completion of the clinical trial, genotyping assays for CPOX4 allelic status were performed on biological samples provided by 330 of the trial participants. Regression modeling strategies were employed to evaluate associations between CPOX4 status, Hg exposure, and neurobehavioral test outcomes. Among girls, few significant CPOX4-Hg interactions or independent main effects for Hg or CPOX4 were observed. In contrast, among boys, numerous significant interaction effects between CPOX4 and Hg were observed spanning all 5 domains of neurobehavioral performance. All underlying dose-response associations between Hg exposure and test performance were restricted to boys with the CPOX4 variant, and all of these associations were in the expected direction where increased exposure to Hg decreased performance. These findings are the first to demonstrate genetic susceptibility to the adverse neurobehavioral effects of Hg exposure in children. The paucity of responses among same-age girls with comparable Hg exposure provides evidence of sexual dimorphism in genetic susceptibility to the adverse neurobehavioral effects of Hg in children and adolescents.

OUTREACH HIGHLIGHT POSTER

Tribal and Community Partnership Highlights

Kelly Edwards, PhD, Marilyn Hair, MPH, Jon Sharpe, MEd

ABSTRACT: The UW CEEH further developed our partnerships with community and tribal members in 2012.

We continued the 2008 Native Tradition, Environment And Community Health (TEACH) Project, collaborative research with Northwest Indian College that collected data that identified 3 core themes of Native Environmental Health Science: Community, Wellness and Inter-Relationship. To return research results to participants, we created a traditional story, *The Return*. In 2012 we partnered with a Native Senior Fellow at UW to create a comic book version of *The Return*. A student at the Institute of American Indian Arts was commissioned to illustrate the story. The comic book was distributed at the 2013 American Indian in Higher Education Consortium (AIHEC) Student Conference.

We also partnered with the Duwamish River Cleanup Coalition (DRCC), EPA's Community Advisory Group for the Lower Duwamish Waterway Superfund Site to help sponsor the Duwamish River Festival, including a fundraiser bike tour and CEEH table, and the DRCC Community Health Impact Assessment (CHIA). One Public Health Café topic was Safe Seafood; EJ issues in the Duwamish were presented. We created a role play, *Seafood from Puget Sound: How Much Can We Safely Eat?* with fictional characters that hold various perspective toward seafood contamination and cleanup of Puget Sound.

CENTER **Center for Environmental Genetics (UC)**

LOCATION University of Cincinnati, Cincinnati, OH

PI Shuk-Mei Ho

COEC DIRECTOR Erin Haynes

ADMINISTRATOR Deena Watson

WEB SITE <http://eh.uc.edu/ceg/>

THEME

The theme of the Center for Environmental Genetics is to elucidate how gene and environment interaction through epigenetics influences disease risks and health outcome. Ohioans are exposed to exceptionally bad air quality due to dated power plants and the fact that it is situated in the nation's main artery of the north-south transportation route. These unique geographical/economic features put the residents in the state at high risk of the following diseases: (a) endocrine disruption and cancer; (b) immune and allergic diseases; (c) cardiovascular and lipid disorders; and (d) neurology and behavior disorders. Our environmental health center focuses on understanding how genes and environment affect our health, serving the residents, communities of Ohio, the nation and the globe by generating knowledge that is applicable to the general public and policymakers for healthier living.

RECENT SCIENCE HIGHLIGHTS

Epigenetic epidemiology and biomarkers of exposure and disease: The role of epigenetic modifications due to environmental toxicants has been an exciting area of research, but there has been limited translation of research results to human health outcomes. CEG members are developing epigenetic biomarkers of exposure and disease. Advances in this new field, epigenetic epidemiology, include modeling maternal exposures to polycyclic aromatic hydrocarbons (PAHs), asthma and atopy in children exposed to diesel particulate matter (DPM), and occupational exposure and risk of developing prostate cancer in firefighters. Interdisciplinary and inter-Center collaborations have made exciting new inroads into this area.

Shuk-Mei Ho, Glenn Talaska, and alumnus Wan-ye Tang joined with Frederica Perera of the Columbia Center for Children's Environmental Health to study maternal exposure to PAHs. They found that maternal PAH exposure was related to the methylation status of IFN γ in cord blood. These findings support a potential role of epigenetics in fetal reprogramming by PAH-induced environmental diseases.

Yeut-Kin Leung, Patrick Ryan, Gurjit K. Khurana Hershey, Grace LeMasters, and Ho mentored Kelly Brunst and Hong Ji found that children exposed to DPM have hypermethylation of Forkhead box proteins 3 (FOXP3). They have three times the risk of wheezing, and twice the likelihood of developing asthma. Firefighters are also exposed to mixtures of environmental toxicants. A team led by Ho discovered that methylation status of DUSP22 could distinguish firefighters from non-firefighters, and was also correlated with years of service. The motivation for this study came from results published by the LeMasters team, which had completed a meta-analysis, and found that firefighters are at a higher risk for developing prostate cancer. Ho's team was able to take advantage of samples gathered by Haynes through a CEG 2009 Pilot. This proof-of-concept study indicates that epigenetic changes occur in an exposed population, and may aid in developing new strategies for exposure surveillance and disease prevention. Taken together, CEG scientists have identified epigenetic biomarkers of exposure and disease prediction that provide insights into earlier diagnosis of disease.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Over the past two years, the University of Cincinnati Center of Environmental Genetics (CEG) COEC has worked to establish bi-directional communication between Investigators and our target audiences of community members and key opinion leaders, health care professionals, and public health policy makers. A few of these are described herein.

1. Through a partnership with the Cincinnati Health Department we provided environmental health expertise and community communication for several Health Impact Assessments (HIAs) related to traffic and bridge demolition. In coordination with the 6th Street Viaduct Demolition HIA, we created and implemented a lead education outreach program. Through this program fact sheets, magnets, and tacky mats were distributed to the community.
2. With the growing rate of oil and gas drilling in Ohio, the CEG COEC provided environmental health expertise to the Ohio Board of Health Commissions on hydraulic fracturing and developed a fact sheet for environmental groups. We received a supplement award to conduct a comparative assessment of community information needs related to health and hydraulic fracturing along with the University of Rochester and the University of North Carolina - Chapel Hill. Through conducting a series of interviews with a variety of Ohio perspectives, our results will lend to an overall community information needs assessment that spans these three states.
3. In a CEG-funded pilot research study to explore a community's exposure to metals, the COEC engaged residents in stakeholder advisory board meetings, translated research summary findings for the community, and created graphics to explain individual study results.
4. A tri-state symposium addressing the impact of traffic exhaust on children's health for the Greater Cincinnati region was organized and executed by the COEC, and generated diverse conversation and networking. Topics of presentation included air particle size and the effect on children's health, updates on the City of Cincinnati transportation, and air monitoring.
5. We also developed a science communication curriculum for graduate students in partnership with the Stony Brook University in New York. And, our social media networks being only a year old have grown to over 150 followers on both Twitter and Facebook.

HIGHLIGHTED PUBLICATIONS

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Hypomethylation of dual specificity phosphatase 22 promoter correlates with duration of service in firefighters and is inducible by low-dose benzo[a]pyrene. *J Occup Environ Med.* 2012 Jul;54(7):774-80. doi: 10.1097/JOM.0b013e31825296bc. PubMed PMID: 22796920; PubMed Central PMCID: PMC3398512.

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Walker CL, Ho SM. Developmental reprogramming of cancer susceptibility. *Nat Rev Cancer.* 2012 Jun 14;12(7):479-86. doi: 10.1038/nrc3220. Review. Erratum in: *Nat Rev Cancer.*

RESEARCH HIGHLIGHT POSTER

Uranium exposure to a community population: renal proximal tubule damage and other biomarkers of renal function

Susan M. Pinney, PhD Department of Environmental Health University of Cincinnati
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Background: We evaluated urine uranium levels and biomarkers of renal function in the Fernald Community Cohort (FCC), a volunteer population who lived within 5 miles of a uranium processing plant in Fernald, OH during plant operation (1951-1989) and followed 1990-2008 in a medical monitoring program.

Materials and Methods: Releases of soluble and insoluble uranium particulates from this plant were used by the US Centers for Disease Control in uranium dose estimation models, which we applied to 8770 persons in the FCC. We measured urine uranium samples of 201 persons, collected in the early 1990's.

Results: Urine uranium levels for most were within the 1999-2000 NHANES population 95% reference interval (0.006-0.009 $\mu\text{g}/\text{gr Cr}$); 12% were above the 95th% value. Geometric mean concentrations were highest for those using a well (0.010 $\mu\text{g}/\text{gCr}$) or cistern (0.009 $\mu\text{g}/\text{gCr}$) as a drinking water source compared to those living far from the plant (0.007 $\mu\text{g}/\text{gCr}$). A strong correlation existed between urine U and urine β -2-microglobulin (a biomarker of renal proximal tubule function) ($R=0.664$ -Spearman). Serum creatinine, blood urea nitrogen and urinary microglobulin also were associated with urine U.

Conclusions: Chronic, low dose uranium exposure is reflected by urine U concentration and associated with renal health effects.

OUTREACH HIGHLIGHT POSTER

Collaboration with Cincinnati Health Department HIA on 6th St. Viaduct Demolition

Sarah Elam, Erin Haynes, DrPH University of Cincinnati, Department of Environmental Health, Cincinnati, OH

ABSTRACT: The University of Cincinnati (UC) Center for Environmental Genetics (CEG) Community Outreach and Engagement Core (COEC) partnered with the Cincinnati Health Department (CHD) to produce community outreach and education for their Health Impact Assessment (HIA) called "Demolition of a Lead Painted Bridge Adjacent to a Residential Area" on the Waldvogel/6th Street Viaduct Demolition. We connected key partners for the HIA resulting in air sampling by the EPA and lead reduction expertise from UC. We created outreach materials such as informational magnets, distributed tacky door mats to reduce lead exposure in homes, wrote a demolition update for the Lower Price Hill newsletter, and developed a fact sheet on the demolition and ways to keep homes lead-free. The COEC provided educational sessions on lead exposure and how to use the tacky mats during community meetings. Educational materials, tacky mats and a brief survey were distributed to 86 affected residents. Over 90% found the educational materials and information meetings useful. When asked if the fact sheet clearly explained the potential lead exposure in the home and explained the dangers of demolition, over 80% agreed. Almost 300 informational magnets featuring ways to keep homes lead-free were distributed to affected residents.

SUPPLEMENT PROJECT POSTER

Health and Hydrofracking: Comparative Assessment of Community Information Needs

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ABSTRACT: Communities have expressed concerns surrounding hydraulic fracturing (HF) on potential health and environmental risks from air emissions, water pollution, and other changes. Community Outreach and Engagement Cores (COECs) in three Environmental Health Science Centers in New York, North Carolina, and Ohio are collaborating to better understand these concerns. These states are geographically, politically, economically, and culturally different, but are in similar phases (initiation/early expansion) of HF. This project responds to community information needs by compiling existing resources, creating new outreach materials, and sharing community concerns with agencies and investigators planning future research on the health effects of HF. Each COEC conducted 12 to 15 key informant interviews with selected community groups, health professionals, and local government officials to obtain diverse perspectives on health concerns and information needs. Interviews explored concerns about potential community health effects, sources of information on health effects, and additional research needs. The process of interviewing was integrated with the collection of additional data (e.g., reports, news articles, etc.) to provide the geographic, political, and economic context for each case study. Initial analysis suggests that communities in all three states identified a common set of environmental and human health concerns, as well as some regional differences.

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THEME

The theme of the Center for Environmental Health and Susceptibility (CEHS) at the University of North Carolina – Chapel Hill is to promote interdisciplinary research that improves our understanding and ability to modulate gene-environment interactions that shape an individual's susceptibility to disease.

RECENT SCIENCE HIGHLIGHTS

A vibrant research environment within the CEHS utilizes Flexible Interdisciplinary Research Groups (FIRG) to identify critical research issues and pair them with basic, clinical and population scientists. State-of-the-art CEHS facility cores provide cutting-edge expertise and equipment that meet the broad and exacting needs of our researchers. These consist of an Integrated Health Sciences Facility Core, a Systems Biology Facility Core and a Biostatistics and Bioinformatics Facility Core. We disseminate our results to the scientific community, the citizens of North Carolina, the United States and the world through publication in peer-reviewed literature, presentations at scientific meetings and strong interactions with our Community Outreach and Education Core. Currently, the FIRGs are organized around several major areas associated with environmental disease: Cancer, Pulmonary Disease, Reproductive and Developmental Disease, Obesity and Metabolic Disease, Metal-Induced Disease, and Superfund Hazardous Waste Sites. We strongly support a Pilot Project Program focused on early investigators that has yielded a 29.6-fold return on investment, as well as FIRG Pilot Projects that support interdisciplinary research teams.

CEHS Highlights

- The Biomarker Mass Spectrometry Facility received an NIH Instrumentation grant that is enhancing Drs. Swenberg, Nakamura and Rusyn's research to developed very sensitive and specific mass spectrometry-based assays for the quantitation of biomarkers resulting from exposure to environmental agents. The sensitivity of this new instrumentation will enable significant reductions in the amounts of biological specimens required and accurate measurements of extremely low amounts of metabolites and endogenous/exogenous DNA adducts.
- Drs. Rebecca Fry and Miroslav Styblo studied residents in Mexico with high levels of iAs in drinking water. Analysis of urine allowed determination of consumption of iAs as well as metabolism of inorganic arsenic to organic metabolites. Their research revealed dramatic differences in DNA methylation profiles in promoters of genes associated diabetes.
- CEHS investigators developed a Children's Health Center grant proposal.
- Our COEC worked with local and state agencies to lead healthy homes and lead poisoning prevention efforts.
- The CEHS held a public symposium on hydraulic fracturing and health, featuring Dr. Trevor Penning (U of Penn), which was attended by over 80 people and had an additional 82 online viewers.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

In the past year, COEC staff significantly influenced statewide healthy homes and lead poisoning prevention efforts, including policy processes. Staff led the year-long strategic planning process for the NC Healthy Homes initiative, convening state and local health and housing agencies to develop a plan for 2012-2015 to address environmental health hazards in homes. In the resulting plan, the COEC is taking the lead or partnering in activities focused on increasing awareness among residents, providing tools for home assessments, fostering partnerships with state and local agencies, and using emerging research to improve outreach and education. COEC staff also convened a workgroup of state and local health agencies to develop an implementation plan for the CDC's Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women. The COEC partnered with the Women's Health Branch (WHB) in the NC Division of Public Health (NCDPH) to develop and pilot an educational brochure and assessment tool for clinicians and health educators on lead and pregnancy. As a result, WHB added a requirement for assessment for lead exposure and patient education to the agreement addendums with all local health departments serving pregnant women, effective July 1, 2012. The COEC also assisted WHB in training 250 clinical staff and environmental health professionals. Additionally, the COEC assisted the NCDPH Childhood Lead Poisoning Prevention Program in revising the NC Childhood Lead Testing and Follow-Up Manual to reflect the CDC's revised lead reference value for public health action.

The COEC is collaborating with COECs at the University of Rochester and the University of Cincinnati, to assess community information needs related to the potential health effects of hydraulic fracturing. After interviewing up to 15 key informants and comparing findings with the New York and Ohio COECs, we will jointly develop responsive educational materials. The CEHS also sponsored a public symposium on hydraulic fracturing and health, featuring Dr. Trevor Penning of the University of Pennsylvania's Center of Excellence in Environmental Toxicology. This important event was attended by over 80 persons and also had an additional 82 online views.

HIGHLIGHTED PUBLICATIONS

Swenberg JA, Moeller BC, Lu K, Rager JE, Fry RC, Starr TB. Formaldehyde Carcinogenicity Research: 30 Years and Counting for Mode of Action, Epidemiology, and Cancer Risk Assessment. *Toxicologic Pathology*. 2013; 41(2):181-9. Epub 2012 Nov 16. PMID: 23160431.

Xu X, Gammon MD, Hernandez-Vargas H, Herceg Z, Wetmur JG, Teitelbaum SL, et al. DNA methylation in peripheral blood measured by LUMA is associated with breast cancer in a population-based study. *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*. 2012 Jun;26(6):2657-66. PMC3360146.

Carson C, Omolo B, Simpson DA, Thomas NE, Ibrahim JG, Kaufmann WK, et al. A prognostic signature of defective p53-dependent G1 checkpoint function in melanoma cell lines. *Pigment Cell & Melanoma Research*. 2012 Jul;25(4):514-26. PMC3397470.

Hoffman K, Adgent M, Goldman BD, Sjodin A, Daniels JL. Lactational Exposure to Polybrominated Diphenyl Ethers and Its Relation to Social and Emotional Development among Toddlers. *Environmental Health Perspectives*. 2012 Oct;120(10):1438-42. PMC3491946.

RESEARCH HIGHLIGHT POSTER

The "Exposome": What we are learning about low dose exposures to mutagens and how it improves the scientific basis of risk assessment?

J. Swenberg, J. Nakamura, B. Moeller, X. Tian, V. Sharma, R. Yu, W. Bodnar and L. Collins

ABSTRACT: The “Exposome” was first described by Dr. Chris Wild in 2005. This concept proposes that we should consider our total external and internal exposures, including endogenous chemicals, oxidative stress, inflammation, etc. In addition, laboratory tools have undergone major improvements in sensitivity and accuracy. The CEHS Systems Biology Facility Core has provided outstanding mass spectrometry, NMR and DNA damage analysis. We have been able to compare endogenous and exogenous DNA damage through the use of stable isotope exposures. Our DNA Damage facility has developed new mutagenesis assays and utilized DT40 cells to identify critical DNA repair pathways. These studies and many others in the literature have clearly demonstrated that while metabolites and DNA adducts are often linear at low doses, mutations always have a non-zero background. We and others have demonstrated that our DNA is not pristine. In fact, it has ~60,000 lesions in every cell. These lesions are likely to be responsible for background mutations. With the help of our Biostatistics Core, strong data are now available for the nonlinear responses of numerous mutagens, including MMS, MNU, EMS, H2O2, formaldehyde, acetaldehyde, and radiation. This new information offers a tremendous opportunity to apply this knowledge to science-based low dose risk assessment.

OUTREACH HIGHLIGHT POSTER

Integrating Environmental Health into Public Health Practice in North Carolina

Kathleen Gray, MSPH; Carolyn Crump, PhD; Neasha Graves, MA; Amy MacDonald, MS; Kelly Robinson. Community Outreach and Engagement Core, UNC Center for Environmental Health and Susceptibility

ABSTRACT: In 2012-13, the UNC CEHS COEC built the capacity of local public health programs to engage constituents on environmental health issues, supported the implementation of a statewide healthy homes strategic plan and assisted the NC Division of Public Health (DPH) in putting into practice new guidelines for lead and pregnancy.

Staff trained over 150 public health professionals and lay health advisors on CEHS research related to healthy homes and breast cancer, providing hands-on educational materials for use with clients in small group settings and during home visits. After leading the year-long NC Healthy Homes strategic planning process, with participation from health and housing agencies, the COEC is now addressing the identified outreach needs, such as providing introductory training for community audiences and in-depth training and assessment tools for professionals. COEC staff also partnered with NCDPH to convene a workgroup to develop an implementation plan for CDC’s Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women, resulting in NCDPH adding a requirement for lead exposure assessment and patient education to the local health department agreements, effective July 1, 2012. The COEC also assisted in training 250 clinical and environmental health staff on compliance with the Guidelines.

CENTER Center for Environmental Health in Northern Manhattan
(Columbia)
LOCATION Columbia University, New York, NY
PI Regina Santella
COEC DIRECTOR David Evans
ADMINISTRATOR Gail Garbowski
WEB SITE <http://www.mailman.columbia.edu/academic-departments/centers/niehs-center-environmental-health>

THEME

The NIEHS Center for Environmental Health in Northern Manhattan (CEHNM) brings together basic scientists, physicians, epidemiologists, biostatisticians and citizens in a partnership focusing on a central theme that stresses understanding and preventing environmental components of disease. Most of the work of the 32 Center investigators is focused in three main disease areas: cancer, respiratory diseases and neurotoxicology/neurodegenerative diseases.

RECENT SCIENCE HIGHLIGHTS

Exposure to several phthalates, widely used in commercial products, has been associated with respiratory symptoms and decreased lung function. Associations between levels of urinary phthalate metabolites in 244 urban children and fractional exhaled nitric oxide (FENO), a biomarker of airway inflammation, were examined. Independent associations between exposures to DEP and BBzP and FENO were observed. These results suggest that these two ubiquitous phthalates, previously shown to have substantial contributions from inhalation, are positively associated with airway inflammation in children (Just AC et al, 2012).

Exposure to naphthalene, a possible carcinogen, and polycyclic aromatic hydrocarbon (PAH), is widespread, though resulting health effects are poorly understood. Metabolites of naphthalene (1- and 2-naphthol) and PAH in urine and chromosomal aberrations (CA), including translocations, in blood were measured in 113 five-year-old urban minority children. Increased levels of urinary naphthols were associated with increased CA in children in a dose-related manner (Orjuela MA et al, 2012).

Early-life arsenic (As) exposure may influence the trajectory of health outcomes later in life. The influence of prenatal As exposure on global methylation of cord blood DNA was evaluated in a study of mother/newborn pairs in Bangladesh. Increasing maternal urinary As was associated with an increase in means of newborn global DNA methylation. Sex-specific analyses suggested that the associations were positive among male newborns but negative among female newborns. These results suggest that As-induced epigenetic modifications in utero may potentially influence disease outcomes later in life (Pilsner JR et al., 2012).

Global decreases in DNA methylation, particularly in repetitive elements, have been associated with genomic instability and human cancer. Methylation levels of three repetitive elements (Sat2, LINE-1 and Alu) were measured in white blood cells of a total of 282 breast cancer cases and 347 unaffected sisters from the New York site of the Breast Cancer Family Registry (BCFR). Sat2 methylation was statistically significantly associated with increased breast cancer risk. There was no association for LINE-1 and Alu methylation. These findings support that selected markers of epigenetic changes measured in blood may be potential biomarkers of breast cancer risk (Wu HC et al., 2012).

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Last year our COEC was involved in four projects to engage middle and high school students in environmental learning and careers. (1) David Evans and graduate students Maya Kappil and Maria Rosa took part in a Science Career Day sponsored by Columbia's Double Discovery Program for Manhattan public school students to enable them to ask scientists and health professionals about their careers. (2) Steve Chillrud will lead middle school students from the Lang Youth Medical Program in a learning activity on air pollution, and WE ACT and a Center laboratory will each host a Lang summer intern. (3) David Evans and Ogonnaya Dotson-Newman from WE ACT met with New York City teachers hosted by New Visions, Inc, a non-profit company that develops new schools and curriculum, to help the teachers develop a six-week biology curriculum focused on the biology and control of pests. In May, we will make classroom presentations on IPM as part of this project. (4) The CARE II initiative on composting, led by Ogonnaya Dotson-Newman, has blossomed in the WHEELS Academy charter school. Nine high school biology students are comparing two methods of composting waste from the school lunchroom: regular compost heaps vs. the quicker, more labor intensive Bokashi method. The students teach middle school students about composting and collect waste, which is composted and used in their school garden. The students and their teacher are working with Cornell to test samples for soil quality to evaluate the two composting methods. WE ACT is leading a partnership with COEC, NYC, Con Ed Energy, and EDF to promote conversion from #6 heating oil to #2 or gas under NYC Local Law 43. The Clean Heat Council is focusing on 50-75 properties in Northern Manhattan, educating tenants and owners and linking them to NYC facilitated low cost loans. Drs. Matt Perzanowski, Diana Hernandez, Pat Kinney, Steve Chillrud and Dave Evans are involved, and Drs. Hernandez and Chillrud are leading a pilot project to assess air quality before and after conversion.

HIGHLIGHTED PUBLICATIONS

Just AC, Whyatt RM, Miller RL, Rundle AG, Chen Q, Calafat AM, Divjan A, Rosa MJ, Zhang H, Perera FP, Goldstein IF, Perzanowski MS. Children's urinary phthalate metabolites and fractional exhaled nitric oxide in an urban cohort. *Am J Respir Crit Care Med.* 2012; 186 (9), 830-837. PMID:PMC3530221.

Orjuela MA, Liu X, Miller RL, Warburton D, Tang D, Jobanputra V, Hoepner L, Suen IH, Diaz-Carreno S, Li Z, Sjodin A, Perera FP. Urinary naphthol metabolites and chromosomal aberrations in 5-year-old children. *Cancer Epidemiol Biomarkers Prev.* 2012; 21(7):1191-202. PMID: PMC3392422.

Pilsner JR, Hall MH, Liu X, Ilievski V, Slavkovich V, Levy D, Factor-Litvak P, Yunus M, Rahman M, Graziano JH, Gamble MV. Influence of Prenatal Arsenic Exposure and Newborn Sex on Global Methylation of Cord Blood DNA. *PLoS ONE.* 2012; 7(5): e37147. PMID:PMC3360698.

Wu HC, Wang Q, Delgado-Cruzata L, Flom JD, Perrin M, Liao Y, Ferris JS, Santella RM, Terry MB. Repetitive element DNA methylation levels in white blood cell DNA from sisters discordant for breast cancer from the New York site of the Breast Cancer Family Registry. *Carcinogenesis.* 2012; 33: 1946-1952. PMID:PMC3499042.

RESEARCH HIGHLIGHT POSTER

Children's urinary phthalate metabolites and fractional exhaled nitric oxide in an urban cohort.

Just AC, Whyatt RM, Miller RL, Rundle AG, Chen Q, Calafat AM, Divjan A, Rosa MJ, Zhang H, Perera FP, Goldstein IF, Perzanowski MS.

ABSTRACT: Phthalates are used widely in consumer products and exposure has been associated with respiratory symptoms and decreased lung function. Associations between

children's phthalate exposures and fractional exhaled nitric oxide (FENO), a biomarker of airway inflammation, were examined. We hypothesized that urinary concentrations of four phthalate metabolites would be positively associated with FENO and would be stronger among children with seroatopy or wheeze. In an urban birth cohort, 244 children 4.9-9.1 years old had urine collected and FENO measured the same day. Seroatopy was assessed by specific IgE and wheeze in the past year by validated questionnaire. Log-unit increases in urinary concentrations of metabolites of diethyl phthalate (DEP) and butylbenzyl phthalate (BBzP) were associated with a 6.6% (95%CI= 0.5–13.1%) and 8.7% (95%CI=1.9–16.0%) increase in FENO, respectively, adjusting for other phthalate metabolites and potential covariates/confounders. There was no association between concentrations of metabolites of di(2-ethylhexyl) phthalate or di-n-butyl phthalate and FENO, and no significant interaction by seroatopy. The BBzP metabolite association was stronger among children who wheeze (P=0.016). Independent associations between exposures to DEP and BBzP and FENO suggest that these two ubiquitous phthalates, previously shown to have substantial contributions from inhalation, are positively associated with airway inflammation in children.

OUTREACH HIGHLIGHT POSTER

Engaging public school students in environmental learning and career exploration.

David Evans¹, Ogonnaya Dotson-Newman², Peggy Shepard², and Matt Perzanowski¹.

1) Columbia University Center for Environmental Action in Northern Manhattan

2) We Act for Environmental Justice, Inc (WE ACT)

Last year our COEC was involved in four projects to engage middle and high school students in environmental learning and career exploration.

(1) Columbia's Double Discovery Program recruits talented, low-income students from Manhattan public schools to help prepare them for college and professional careers. David Evans and graduate students Maya Kappil and Maria Rosa took part in a Science Career Day sponsored by Double Discovery.

(2) The Lang Youth Medical Program at Columbia's Medical Center also recruits talented students in middle school and exposes them to work in health care settings through high school. WE ACT and a Center laboratory will each host a Lang summer intern.

(3) David Evans and Ogonnaya Dotson-Newman from WE ACT met with a group of New York City teachers hosted by New Visions, Inc, to help the teachers develop a six-week biology curriculum focused on the biology and control of pests.

(4) The CARE II initiative on composting, led by Ogonnaya Dotson-Newman, has blossomed in the WHEELS Academy charter school. Nine high school biology students are comparing two methods of composting waste from the school lunchroom: regular compost heaps vs. the quicker, more labor intensive Bokashi method.

CENTER	Center for Environmental Health Sciences (MIT)
LOCATION	MIT, Boston, MA
PI	John M Essigmann
COEC DIRECTOR	Kathleen Vandiver
ADMINISTRATOR	Amanda Tat
WEB SITE	http://cehs.mit.edu/

THEME

The Massachusetts Institute of Technology (MIT) Center for Environmental Health Science (CEHS) has as its overall mission the study the biological effects of, and processes of exposure to environmental agents. Our goals are to understand and predict how such exposures affect human health. Three areas represent the pillars of our program: studies of the nature of exposure to environmental agents, the duration of that exposure, and how well the exposed organism is equipped to deal with the exposure -- in other words, the organism's genetic susceptibility.

RECENT SCIENCE HIGHLIGHTS

The following accomplishments are noteworthy from the MIT CEHS: (1) B. Engelward developed a single cell trapping and DNA damage analysis system, using microwell arrays, to automate the COMET assay. This assay has been commercialized and is now being widely used to probe strand breaks in vivo. (2) She also discovered lower level genotoxicity thresholds in animals that provide a measure of defense against ionizing radiation. (3) J. Essigmann established the substrate specificities of the alpha-ketoglutaratedioxygenase DNA repair enzymes, which protect cells against oxidative stress. (4) P. Dedon and L. Samson led multi-investigator collaborative teams that provided insight into the mechanisms of colon cancer induction by (a) chemical inflammation and (b) bacterial infection. They discovered that the AlkB and AAG repair systems are of critical importance to survive chemical inflammation stress and that 5-chlorocytosine is a biomarker of bacterial inflammation leading to colon cancer. (5) Direct evidence was obtained by S. Tannenbaum and J. Fox that arsenic exposure perturbs the gut microbiome, and they demonstrated that the biotransformation of inorganic arsenic was impacted by gut microbiome phenotypes. Their data suggest that perturbation of the gut microbiome may serve as a new mode of action of arsenic-induced disease, including diabetes, cardiovascular disease and impaired immune functions. (6) Finally, E. Alm and S. Erdman published a high profile paper showing that the lactobacilli present in yogurt trigger in mice an epithelial follicular anagen-phase shift with sebocytogenesis resulting in thick lustrous fur due to a bacteria-triggered interleukin-10-dependent mechanism. These data are part of a developing program on the health benefits of probiotic administration via manipulation of the immune system.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Cited by the MIT Museum as exemplar collaboration with a research center, the exhibit and classroom space called "Learning Lab: the Cell" has reached thousands of museum visitors in a four year span as well as classroom groups on fieldtrips. The curricular materials attracted the attention of Boston Public Schools and as result, COE2C is currently in year three of a grant to provide LEGO® molecular biology sets, the curriculum, and teacher professional development workshops to schools in Boston. During the calendar year 2012, COE2C organized and led community volunteers who provided 10 man-months of labor (1,600 hours of time) assembling the science kits for delivery. In another key accomplishment, MIT COE2C helped to support other universities' high school science partnerships. We responded to an invitation in December 2012 from the Emergent Behaviors of Integrated Cellular Systems (EBICS) NSF program to lead a teacher workshop

in environmental health science for the University of Illinois and Georgia Tech in Atlanta.

Another key COE2C achievement happened closer to home, a weekend event in downtown Boston for the general public called Science Family Days, sponsored by the American Association for the Advancement of Science (AAAS) in February 2013. Over the two days, about 250 people enjoyed learning about climate change and air pollution at our booth called "Understanding Air." Finally the most recent milestone we mention is the growing recognition, evidenced by nursing faculty and NIH related requests in recent months, that our LEGO-based genetic teaching tools are well suited to meet the nation's call for increased genetics and genomic instruction for nurses. Nurse professional development workshops present the ideal opportunity to deliver key concepts about gene-environment interactions. Environmental concerns have been heightened in recent years by basic research elucidating the role that epigenetic mechanisms play in human health. Thus genetics provides many teachable moments for environmental health instruction.

HIGHLIGHTED PUBLICATIONS

Olipitz W, Wiktor-Brown D, Shuga J, Pang B, McFaline J, Lonkar P, Thomas A, Mutamba JT, Greenberger JS, Samson LD, Dedon PC, Yanch JC, Engelward BP. (2012) Integrated Molecular Analysis Indicates Undetectable Change in DNA Damage in Mice after Continuous Irradiation at ~ 400-fold Natural Background Radiation. *Environ Health Perspect.* 120(8):1130-1136. doi: 10.1289/ehp.1104294. PMID: PMC3440074

Calvo JA, Meira LB, Lee CY, Moroski-Erkul CA, Abolhassani N, Taghizadeh K, Eichinger LN, Muthupalani S, Klungland A, Samson, LD. (2012) DNA Repair is Indispensable for Survival After Acute Inflammation in Mice. *J of Clinical Investigation.* 122(7):2680-2689. PMID: PMC3386829

Mangerich A, Knutson CG, Parry NM, Muthupalani S, Ye W, Prestwich E, Cui L, McFaline JL, Mobley M, Ge Z, Taghizadeh K, Wishnok JS, Wogan GN, Fox JG, Tannenbaum SR, Dedon PC. (2012) Infection-induced Colitis in Mice Causes Dynamic and Tissue-specific Changes in Stress Response and DNA Damage Leading to Colon Cancer. *Proc Natl Acad Sci USA.* 109(27):E1820-E1829. doi: 10.1073/pnas.1207829109. PMID: PMC3390855

Li D, Delaney JC, Page CM, Yang X, Chen AS, Wong C, Drennan CL, Essigmann JM. (2012) Exocyclic carbons adjacent to the N6 of adenine are targets for oxidation by the *Escherichia coli* adaptive response protein AlkB. *J Am Chem Soc.* 134(21):8896-8901. doi: 10.1021/ja3010094. PMID: PMC3363417

OUTREACH HIGHLIGHT POSTER

"Understanding Air" a booth for teaching about climate change and air pollution

Kelsey Boulanger, Eben Cross, Amy Fitzgerald, Jessica Garrett, Amanda Gruhl, Jesse Kroll, and Kathleen M. Vandiver

ABSTRACT: Often people do not take a stand on environmental health issues because they feel uncertain about the basics. Thus educational activities on climate change and air pollution were developed, working with the LEGO® Atoms & Molecules Set where each brick represents an atom. Molecules can be constructed according to specifications both didactic and enjoyable for the visualization of the basic molecular composition and chemical reactions occurring in air. Students in teams construct the tiny lumps of matter which make up air, creating visualizations of the invisible molecules. Eighth graders in Revere, MA (n=137) responded positively by 100% to "Did you learn something?" With a 4.0 Likert scale, "Liked this activity" averaged 3.4; "Learned from this activity" averaged 3.3; and "Would like to learn more" averaged 3.2. Since outreach audiences are informal, COE2C is perfecting the delivery to the general public. In Feb 2013, "Understanding Air" at AAAS Family Days event in Boston had these results (n=88): "Liked this activity" averaged 3.8;

“learned from this activity” averaged 3.3; and “would like to learn more” averaged 3.5. The COE2C with the MIT Kroll Lab and MIT Edgerton Center look forward to creating a turn-key booth package, making it freely available online.

CENTER **Center in Molecular Toxicology (Vanderbilt)**
LOCATION Vanderbilt University, Nashville, TN
PI Dan Liebler
COEC DIRECTOR Barbara Clinton
ADMINISTRATOR Kakie Mashburn
WEB SITE <http://www.toxicology.mc.vanderbilt.edu>

THEME

The molecular mechanisms by which environmental agents affect human health form the core research theme of the Center in Molecular Toxicology at Vanderbilt. Major goals of research in the Center include (1) understanding fundamental chemical and biological mechanisms of chemical toxicity, (2) identifying biochemical and cellular responses to chemicals that govern susceptibility and resistance to disease, (3) the development of new analytical methods to study chemical exposures and their roles in disease processes, and (4) translating fundamental knowledge and emerging analytical technologies to study the contribution of environment to human disease.

RECENT SCIENCE HIGHLIGHTS

A major research focus is the role of oxidative stress in diseases linked to environment. The application of isoprostane measurements, an oxidative stress biomarker discovered at Vanderbilt, is provided through the Integrative Health Sciences Facility Core and has been used by Judy Aschner and colleagues to describe oxidant and nitric oxide tone in regulating ductus arteriosus closure in newborns. Michael Aschner linked lipid electrophiles to manganese activation of stress signaling pathways in astrocytes. Nancy Brown and Alp Ikizler used isoprostane analyses to establish in part the role of oxidative stress in mediating cardiac surgery-induced acute kidney injury associated with obesity. Center Investigators have employed new technologies to explore the molecular basis of chemical toxicity and host-pathogen-environment interactions that contribute to environmental disease. Richard Caprioli and Eric Skaar applied mass spectrometry-based imaging methods to study pathogen infection-associated inflammatory protein expression. This innovative study combined imaging mass spectrometry and magnetic resonance imaging to produce a spatially-resolved map of protein expression changes in mice infected with *Staphylococcus aureus*, thus demonstrating new opportunities to study host-pathogen interactions that influence environmental disease. Larry Marnett and Ned Porter and colleagues used mass spectrometry-based proteomics and an alkynyl-tagged analog of the lipid electrophile 4-hydroxynonenal (HNE) to identify peptidyl-prolyl cis/trans-isomerase A1 (PIN1) as a target of covalent modification by HNE. Because PIN1 is a target of dietary chemopreventive agents that reduce cancer risk, this study suggests PIN1 as a potentially important target for both environmental agents and oxidative stress. Mechanisms of DNA damage recognition and repair are a key focus in the Center. Martin Egli, Fred Guengerich, and Carmelo Rizzo reported a structural characterization of the interaction of N2,3-ethenoguanine-containing DNA with human Y-family DNA polymerases. The adduct is a potentially important mediator of environment-induced cancers. The study, which was featured on the cover of the October 15, 2012 issue of the *Journal of Biological Chemistry*, reported the first crystal structures of these labile DNA adducts and revealed the base-pairing features that drive preferential misincorporation during replication past the adducted guanine residue.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

The Community Outreach and Engagement Core (COEC) for the Center in Molecular Toxicology recently has been initiated with developmental funding from Vanderbilt. (The current Vanderbilt P30 grant was awarded when NIEHS did not require a COEC, and thus no funds from the P30 are available.) With guidance and input from NIEHS staff and internal and external advisors the following initial steps have been taken: In April 2011, Jennifer Dix was hired as COEC Program Coordinator. She has focused on communication infrastructure development for the new program, including website development, development of community friendly materials, and coordination of community presentations. Later in 2011 the Center's External Advisory Board recommended hiring of a COEC Director at a modest effort percentage. Barbara Clinton, MSW, Director of the Vanderbilt University Center for Community Health Solutions (CHS), became Director of our developing COEC in early 2012. As Director of the CHS, Ms. Clinton has designed, implemented, and evaluated community development and health services for low-income families in Tennessee, Kentucky, Virginia, Mississippi, and West Virginia. In addition to serving as an Adjunct Assistant Professor in the Vanderbilt University Schools of Medicine and Nursing and at Meharry Medical College, Ms. Clinton is a Commissioner of the Nashville Metro Action Commission and has been an advisor to the Tennessee Commission on Aging, the National Center for Children in Poverty at Columbia University, the Appalachian Rural Science Initiative of the National Science Foundation, former Vice President Al Gore, and several private foundations. Ms. Clinton and Ms. Dix have expanded contacts in the community in part through a series of interviews with community leaders concerned about asthma, pesticide contamination in the home, environmental risk factors for cancer, and health risks of lead exposure. The COEC has convened an advisory board (including school nurses, public health advocates, and representatives of non-profit organizations) and has hosted community forums, developed fact sheets, and created web-based videos and other materials.

HIGHLIGHTED PUBLICATIONS

Lee E, Yin Z, Sidoryk-Węgrzynowicz M, Jiang H, Aschner M. 15-Deoxy- Δ 12,14-prostaglandin J₂ modulates manganese-induced activation of the NF- κ B, Nrf2, and PI3K pathways in astrocytes. *Free Radic Biol Med*. 2012 Mar 15;52(6):1067-74. doi: 10.1016/j.freeradbiomed.2011.12.016. Epub 2011 Dec 29. PMID: PMC3439999.

Aluise CD, Rose K, Boiani M, Reyzer ML, Manna JD, Tallman K, Porter NA, Marnett LJ. Peptidyl-prolyl cis/trans-Isomerase A1 (Pin1) Is a Target for Modification by Lipid Electrophiles. *Chem Res Toxicol*. 2012 Dec 24. [Epub ahead of print] PMID: PMC3579456.

Attia AS, Schroeder KA, Seeley EH, Wilson KJ, Hammer ND, Colvin DC, Manier ML, Nicklay JJ, Rose KL, Gore JC, Caprioli RM, Skaar EP. Monitoring the inflammatory response to infection through the integration of MALDI IMS and MRI. *Cell Host Microbe*. 2012 Jun 14;11(6):664-73. doi: 10.1016/j.chom.2012.04.018. PMID: 22704626. PMID: PMC3377982 [Available on 2013/6/14].

Zhao L, Pence MG, Christov PP, Wawrzak Z, Choi JY, Rizzo CJ, Egli M, Guengerich FP. Basis of miscoding of the DNA adduct N2,3-ethenoguanine by human Y-family DNA polymerases. *J Biol Chem*. 2012 Oct 12;287(42):35516-26. doi: 10.1074/jbc.M112.403253. Epub 2012 Aug 21. PMID: 22910910. PMID: PMC3471744 [Available on 2013/10/12].

RESEARCH HIGHLIGHT POSTER

Basis of Miscoding of the DNA Adduct N2,3-Ethenoguanine by Human Y-Family DNA Polymerases

Zhao L, Pence MG, Christov PP, Wawrzak Z, Choi JY, Rizzo CJ, Egli M, Guengerich FP

ABSTRACT: N(2),3- ϵ G is an exocyclic DNA adduct produced by endogenous processes and exposure to bioactivated vinyl monomers like vinyl chloride. Due to the lability of the glycosidic bond, we utilized a 2'-fluoro isostere approach to stabilize this lesion and synthesized oligonucleotides containing 2'-fluoro-N(2),3- ϵ -2'-deoxyarabinoguanosine to investigate miscoding potential of N(2),3- ϵ G by Y-family human DNA polymerases (pols). In primer extension assays, pol η and pol κ replicated through N(2),3- ϵ G, whereas pol ι and REV1 yielded only 1-base incorporation. Steady-state kinetics revealed that dCTP incorporation is preferred opposite N(2),3- ϵ G with relative efficiencies in the order of pol κ > REV1 > pol η \approx pol ι , and dTTP misincorporation is the major miscoding event. Pol ι had the highest dTTP misincorporation frequency followed by pol η . REV1 misincorporated dTTP and dGTP with lower frequencies. Crystal structures of pol ι with N(2),3- ϵ G paired to dCTP and dTTP revealed Hoogsteen-like base pairing mechanisms. Two hydrogen bonds were observed in the N(2),3- ϵ G:dCTP base pair, whereas only one appears to be present in the N(2),3- ϵ G:dTTP pair. Base pairing mechanisms derived from crystal structures explain the favored dCTP insertion for pol ι in steady-state kinetic analysis. These results provide a basis for the mutagenic potential of N(2),3- ϵ G.

OUTREACH HIGHLIGHT POSTER

Community Forum on Fluoride, Plastics, and Vaccines: What Parents Should Know

Dix J, Clinton B

ABSTRACT: The Vanderbilt University Community Outreach and Engagement Core held a community forum on August 30, 2012, at the 100 Oaks conference facility. This forum focused on three issues affecting healthcare, especially in young children: "Fluoride, Plastics, and Vaccines: What Parents Should Know." These three topics were chosen due to (1) recent media attention, (2) the perpetuation of misinformation and/or conflicting information in the community, often among new parents, and (3) relevant expertise within the Center in Molecular Toxicology and other Vanderbilt research programs and their affiliated colleagues. Speakers included Dr. James Pace, Jr., DDS of Belle Meade Dentistry (fluoride), Dr. Nathalie Maitre, M.D./Ph.D. of the Vanderbilt Division of Neonatology (plastics), and Dr. Elizabeth Williams, M.D. of the Vanderbilt Vaccine Research Program (vaccines). Fact sheets were developed on all three topics, and the three talks were recorded to be posted on the Center's web site (currently under construction).

CENTER	Center in Urban Environmental Health (Johns Hopkins)
LOCATION	Johns Hopkins, Baltimore, MD
PI	John Groopman
COEC DIRECTOR	Michael Trush
ADMINISTRATOR	Theresa Daniel
WEB SITE	http://www.jhsph.edu/departments/environmental-health-sciences/research_centers/Urban_Environmental_Health/index.html

THEME

The goal of the Johns Hopkins Center in Urban Environmental Health is to protect vulnerable at-risk people living in urban environments from the deleterious health consequences unique and insidious to these complex environmental settings. This goal is achieved through multi-disciplinary strategies aimed at identifying the critical environmental exposures, their mechanisms of action, and their biological consequences that increase the health risk for people living in cities, and translation of these findings into prevention and intervention strategies to improve urban environmental health locally, nationally, and internationally.

RECENT SCIENCE HIGHLIGHTS

The JH Center for Urban Environmental Health has made significant progress in its mission to discover and apply new knowledge critical to understanding and mitigating the impact of the urban environment on human health. Notable findings by Center members this year include: 1) identification of a key role for exposures to various metals including arsenic and cadmium (Tellez-Plaza, *Epidemiology*, 2013) in incident cardiovascular disease; 2) identification of genetic determinants of variation in urine arsenic metabolites (Tellez-Plaza, *Environ Health Perspect*, 2013); and 3) detection of urinary free Bisphenol A concentrations in newborns (Nachman, *J Pediatr.*, 2013). In the area of air pollution, we have made several significant observations: 1) that indoor air pollution is linked to respiratory morbidity in former smokers with COPD patients (Hansel, *Am J Respir Crit Care Med.*, 2013); 2) that being overweight enhances susceptibility to indoor pollutants among urban children with asthma (Lu, *J Allergy*, 2013); and 3) that a dose-response relationship exists between mouse allergen exposure and asthma morbidity among urban children and adolescents (Torjusen, *Indoor Air*, 2012). We have recently extended these studies of indoor pollution to Bangladesh. We show that young children are exposed to indoor PM 2.5 concentrations that are 7 times greater than current standards (Gurley, *Environ Res.*, 2013). These exposures are likely due to use of biomass fuels for cooking in the homes suggesting that interventions aimed at reducing biomass fuels may provide significant benefit for respiratory health. Translating our previous work showing that diets rich in cruciferous vegetables reduces the risk of cancer, we examined the effects of broccoli sprout-derived beverages [sulforaphane-rich (SFR), glucoraphanin-rich (GRR)], in a cross-over design of individuals with high exposures to airborne pollutants, recruited from a community in Qidong, China (Kensler, *Carcinogenesis*, 2012). These results suggest that urinary excretion of mercapturic acids of acrolein, crotonaldehyde, ethylene oxide and benzene were significantly increased in individuals receiving either SFR or GRR or both as compared to baseline levels. These results suggest that intervention with broccoli sprouts may enhance detoxification of airborne pollutants and attenuate their health-associated risks. Another notable mechanistic observation made this year is that Cu/Zn superoxide dismutase integrates signals from oxygen and glucose to repress respiration (Reddi, *Cell*, 2013).

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

COEC seeks to establish partnerships with credible community agencies so as to create the opportunity to respond to specific concerns identified by community leaders and residents. These types of effective partnerships generate mutually beneficial relationships and assure positive outcomes through the translation of information and outcomes from the Center's Research and Facility Cores into educational programs, into knowledge applied to public health and environmental health policy. Accordingly, COEC functions as a Center core resource and strives to meet the following goals and aims: 1) to continue to serve as the conduit between the Center and community organizations in identifying environmental agents and issues which affect the health of the community; 2) to continue to facilitate community based research in partnership with diverse community groups and organizations to address local needs as defined by community leaders and residents; 3) to design educational materials and implement programs concerning the risks and effects of environmental agents that are of concern to the diverse groups with which we interact; 4) to develop interactions with organizations, both within and outside of Johns Hopkins who will help facilitate translation of the Center's research and public health goals. COEC continues to offer a four-quarter course special studies course on Environmental Health Community Outreach which includes community outreach and engagement seminars and the opportunity for students to do independent community projects. The two hour seminar component is open to all and consists of presentations by faculty, students and representatives of community groups, mainly organizations with whom COEC partners. With the Environmental Justice Partnership, COEC participates in organizing and participating in EPA's Student Environmental Development Program (SEDP) for seventh grade students (rising eighth graders). COEC and EJP are continuing our 'Day at the Market' engagement event that engages residents, disseminates materials, obtains feedback from the community, and promotes interactions between residents and researchers. We have provided information about research in environmental health and justice including how to safeguard against environmental hazards such as lead poisoning, mold, community demolition hazards, cancer, smoking and COPD and asthma. COEC continues to interact with residents of Turner Station regarding chromium exposure and other toxicants in their area.

HIGHLIGHTED PUBLICATIONS

Reddi AR, Culotta VC. SOD1 integrates signals from oxygen and glucose to repress respiration. *Cell* 2013, 152:224-35.

Nachman RM, Fox SD, Golden WC, Sibinga E, Veenstra TD, Groopman JD, Lees PS. Urinary free bisphenol a and bisphenol a-glucuronide concentrations in newborns. *J Pediatr*. 2013 Apr;162(4):870-2.

Lu KD, Breyse PN, Diette GB, Curtin-Brosnan J, Aloe C, Williams DL, Peng RD, McCormack MC, Matsui EC. Being overweight increases susceptibility to indoor pollutants among urban children with asthma. *J Allergy Clin Immunol*. 2013 Apr;131(4):1017-1023.

Hansel NN, McCormack MC, Belli A, Matsui EC, Peng RD, Aloe C, Paulin L, Williams DL, Diette GB, Breyse PN. In-home air pollution is linked to respiratory morbidity in former smokers with COPD. *Am J Respir Crit Care Med*. 2013 Mar 22.[EPub ahead of print]

RESEARCH HIGHLIGHT POSTER

Low to Moderate Arsenic Exposure & Incident Cardiovascular Disease: The Strong Heart Study.

Katherine Moon, Eliseo Guallar, Jason Umans, Richard Devereux, Lyle Best, Kevin Francesconi, Walter Goessler, Jonathan Pollak, Ellen Silbergeld, Barbara Howard, Ana

Navas-Acien.

ABSTRACT: Inorganic arsenic in water and food are major global health problems. In the US, arsenic in drinking water disproportionately affects rural and suburban populations, including American Indian communities. The NIEHS Center funded a pilot study to assess exposure to arsenic in American Indian adults from Arizona, Oklahoma and North/South Dakota. The study showed that moderate to high levels of arsenic exposure in Arizona, intermediate in North and South Dakota, and low in Arizona. Subsequently, we conducted a prospective cohort study to characterize the cardiometabolic effects of low-moderate arsenic exposure in American Indian communities (<50 ug arsenic/L in drinking water) (R01HL090863). Our results support the hypothesis that low-moderate arsenic exposure is associated with increased incidence and mortality of cardiovascular disease. In additional analyses, we have also confirmed that arsenic is associated with increased prevalence of diabetes, increased prevalence of albuminuria, and increased mortality for cancers of the lung, prostate and pancreas. We are currently evaluating gene-arsenic interactions for cardio-metabolic disease (R01ES021367). By investigating the contribution of arsenic exposure to CVD development, this study can inform risk assessment with implications for the prevention and control of arsenic exposure in drinking water and food in the US and abroad.

OUTREACH HIGHLIGHT POSTER

Engaging East Baltimore Residents Through a “Day at the Market” Event

Michael A. Trush, Barbara Bates-Hopkins, and Patricia J. Tracey

ABSTRACT: One of the mechanisms by which the NIEHS Johns Hopkins Center in Urban Environment Health has engaged community members is by holding a “Health Day at the Market” at 6 Baltimore City run food markets. It is a joint Environmental Justice Partnership and COEC program that has been ongoing for the past 6 years. This informal event engages Baltimore residents, disseminates materials, obtains feedback from the community and promotes interactions between residents and researchers. “Day at the Market” is used to discuss environmental health issues relevant to the community; to disseminate materials; to introduce researchers and their research project to the community; and to assist investigators in the recruitment of community residents for Community Advisory Boards, focus groups and participation in translation-oriented research. We have provided information about research in environmental health and justice issues to residents including how to safeguard against environmental hazards such as lead poisoning, mold, community demolition hazards, cancer, smoking, COPD and asthma. In 2013, we have expanded this event to two days a month through a grant from the Maryland Cigarette Restitution Fund. Accordingly, COEC is working closely with the community outreach committee of the Sidney Kimmel Comprehensive Cancer Center to assure that this event is supplied with appropriate materials.

CENTER Center of Excellence in Environmental Toxicology (Penn)

LOCATION University of Pennsylvania, Philadelphia, P

PI Trevor Penning

COEC DIRECTOR Marilyn Howarth

ADMINISTRATOR Mary Webster

WEB SITE <http://www.med.upenn.edu/ceet/>

THEME

The CEET elucidates the mechanistic links between environmental exposures and human disease and translates its findings into action to improve the health of vulnerable individuals, and local, national and global communities.

RECENT SCIENCE HIGHLIGHTS

The research agenda of the CEET is driven by elucidating how environmental exposures adversely affect health and cause disease. Exposure to allergens causes airway hyper-responsiveness a hallmark of asthma. Inhaled glucocorticoids are the mainstay therapy for chronic asthma yet a significant number of patients are non-responders. CEET investigators showed that a novel class of agents (histone deacetylase (HDAC) inhibitors) e.g. trichostatin was able to block allergen induced airway hyper-responsiveness in mice and inhibit the carbachol-induced contraction of human precision-cut lung slices by a mechanism that was independent of an anti-inflammatory effect. It was found that trichostatin blocked the intracellular release of Ca²⁺ which would abrogate smooth muscle contraction. Thus, HDAC inhibitors demonstrate a mechanism of action distinct from that of anti-inflammatory agents such as steroids, and represent a promising therapeutic agent for airway disease. CEET investigators used high-coverage whole-genome sequencing to identify 13.4 million variants in African hunter-gatherers that heretofore were unidentified. This study used distinct phenotypes characterized by height to determine an archaic admixture that was associated with taste perception, metabolism and immunity. Specifically, genetic associations with height were found in specific cohorts located on chromosome 3. Importantly, these are the first studies to characterize archaic introgression in three populations to common ancestors in European cohorts. The identification of such genomic regions will be insightful in the characterization of disease disparity and personal responses to therapy in African American ancestry in the US. Children are especially vulnerable to lead toxicity, and exposure to lead has been linked to poor school performance and delinquency in children and adolescents. Even blood lead levels (BLLs) <10 µg/dL can cause an intellectual deficit. CEET investigators examined the socio-demographic factors associated with BLLs above 10 µg/dL by examining BLLs of 1344 preschool children (3-5 years old) from the China Jintan Child Cohort Study. Regression models were used to explore the association between log-transformed BLLs and socio-demographic factors with the risk of BLL ≥10 µg/dL. This study showed that children in this province still have high BLLs even after the phasing out of leaded gasoline which were related to community conditions and parental smoking.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Our COEC engages a number of audiences to improve environmental health, communities, decision makers, and health care professionals. Drs. Emmett and Francis Barg were awarded a \$1.2 million Science Education Partnership Award (SEPA) from the NIH to develop an educational program using the Ambler communities' history of asbestos products manufacturing, and resulting asbestos exposure. The goals of the REACH Project—Resources for Education and Action for Community Health—are to develop a storehouse of information online and at the Chemical Heritage Foundation in Center City

Philadelphia about asbestos-related health risks, profile people who were affected by living or working near the asbestos materials, and provide an opportunity for community members and scientists to learn about each other's experiences. COEC is an active and long-time partner with the environmental justice community in Chester City and is a member of the Chester Environmental Partnership, a broad-based organization which was founded in 2005 by Reverend Horace Strand in order to improve health and the environment through cooperative action. Dr. Emmett helps guide, zoning and planning in Chester in order to reduce health impacts on the residents. For example, in May Dr. Emmett participated in a Community Meeting at Chester City Hall on the I-95/I-476 Interchange Improvement Feasibility Study hosted by the Delaware Valley Regional Planning Commission & Delaware County Planning Department. We also offered our course for fourth year medical students entitled "Frontiers in Environmental Health Sciences" for a third year. This course aims to develop an understanding of environmental health in medical students and how this may affect their practice of medicine and areas of clinical research. The course covers human health impacts of physical, biological, and chemical agents in the environment and workplace. The mode-of-action of these agents, how they cause disease, and how exposures can be identified and prevented are discussed. Students are also exposed to Community Based Environmental Health through field trips to Ambler and Chester. Students gave rave reviews: "I found the course fantastic and interesting"; "I am seriously considering focusing my career more on public health issues because of this course".

HIGHLIGHTED PUBLICATIONS

Banerjee A, Trivedi CM, Damera G, Jiang M, Jester W, Hoshi T, Epstein JA, and Panettieri RA Jr. Trichostatin A abrogates airway constriction, but not inflammation, in murine and human asthma models. *Am J Respir Cell Mol Biol*. 2012 Feb;46(2):132-8. doi: 10.1165/rcmb.2010-0276OC PMCID: PMC 3297166.

Patnaik SK, Yendamuri S, Kannisto E, Kucharczuk JC, Singhal S, Vachani A, MicroRNA expression profiles of whole blood in lung adenocarcinoma. *PLoS ONE* 2012; 7(9): e46045, PMCID: PMC3460960.

Lachance J, Vernot B, Elbers CC, Ferwerda B, Froment A, Bodo JM, Lema G, Fu W, Nyambo TB, Rebbeck TR, Zhang K, Akey JM, Tishkoff SA. Evolutionary history and adaptation from high-coverage whole-genome sequences of diverse African hunter-gatherers. *Cell*. 2012 Aug 3;150(3):457-69. PMCID: PMC3426505.

Liu J, Ai Y, McCauley L, Pinto-Martin J, Yan C, Shen X, Needleman H. Blood lead levels and associated sociodemographic factors among preschool children in the South Eastern region of China. *Paediatr Perinat Epidemiol*. 2012 Jan;26(1):61-9. doi: 10.1111/j.1365-3016.2011.01234.x. PMCID: PMC3241210.

OUTREACH HIGHLIGHT POSTER

Resources for Education and Action in Community Health-Ambler

Frances, K. Barg, Edward Emmett, Lisa Marie Jacobs

ABSTRACT: Asbestos exposures in Ambler, PA began in the late 1800s when the Keasbey & Mattison Company began using asbestos to manufacture asbestos cement products. Asbestos-containing waste from the plant was dumped in several surrounding areas through the 1980s. These sites continue to present remediation challenges that are being evaluated by the EPA. Residents have many questions about how to understand the consequences of their exposure. The University of Pennsylvania's Center for Excellence in Environmental Toxicology funded a pilot ethnographic study designed to identify community perceptions about their environmental and occupational exposure to asbestos. Researchers identified a range of themes, including significant uncertainty about risk and remediation mechanisms and the effects of asbestos exposure on community identity. This pilot work informed the team's successful application for an NIH Science Education Partnership Award (SEPA). The

SEPA study will 1) Document the historical and current experience of living and working in a contaminated site 2) provide residents with data so that they have information to help shape the future of their community 3) Develop and evaluate a science education program that will elaborate on the history of asbestos manufacturing and resulting asbestos exposure in the communities of West and South Ambler.

CENTER	Children's Environmental Health Sciences Core Center (U WI)
LOCATION	University of Milwaukee, Milwaukee, WI
PI	David Petering
COEC DIRECTOR	Jeanne Hewitt
ADMINISTRATOR	Randall Schmidt
WEB SITE	http://www.uwm.edu/cehsc

THEME

The Center's theme is children's environmental health. Its mission is to contribute powerfully to the prevention of environmentally related diseases and disorders that affect development during the period from conception to maturation. Human development beginning with embryogenesis and continuing through adolescence is a particularly sensitive period during which environmental factors play a pivotal role in immediate health status and lifetime health outcomes. Of particular concern are health inequities that children suffer in families with lower socio-economic status, typically, racial/ethnic minorities. Milwaukee mirrors the health problems and inequities that children face in urban centers across the country. In this context, the Center stimulates and sustains the regional community of scientists who carry out significant and innovative research to understand the burden of environmentally related childhood diseases and engage communities locally to find effective ways to reduce them.

RECENT SCIENCE HIGHLIGHTS

Center research focuses on developmental toxicology. Exposure of zebrafish embryos to nM Methylmercury (MeHg), lead, or bis-phenol A causes pronounced behavioral deficits in adults without compromising overt development (1-3). Laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) shows that Hg concentrates in the eye. Aberrant visual startle responses in adults resulted from defective functioning of retinal bipolar cells. Subsequent generations not exposed to MeHg retain similar behavioral and physiological deficits, signaling a profound epigenetic component in the organismic response to this chemical.

Gene-environment interaction studies constitute a significant segment of members' research. Having demonstrated the extensive similarity between the gene regulatory Ah receptor system in mammals and zebrafish as well as the disruption of cranial-facial and cardiac development in zebrafish by TCDD, Center investigators have shown that there is an epigenetic component to its (4). To facilitate epigenomic/transcriptomic research, the first workflow computational system for Next Generation Sequencing data analysis for zebrafish is under construction.

Center investigators are devising methods to measure exposure and outcomes of exposure to environmental chemicals. Using a new gel electrophoresis method that provides excellent protein band resolution and maintains relatively native protein structure, the distribution of toxic metals and metalloids among proteins can be defined by LA-ICP-MS and relevant proteins identified by mass spectrometry (5). Another group is designing next generation nano-sensors that selectively measure gaseous and aqueous pollutants with high sensitivity and selectivity (6,7). A cutting-edge finding is that two-dimensional graphene (carbon) surfaces have favorable properties to serve as such sensors.

Research also focuses on the consequences of environmentally induced premature birth and other neonatal risks. In mice, prematurity limits the number of nephrons that develop in the kidney (8). In turn this puts the host at risk during aging. For example, Cd²⁺ causes nephrotoxicity by targeting sites such as Zn-Sp1 in its role as a key transcription factor of glucose transporter synthesis (9). In another study examining the interaction of

environmental factors with infectious disease, toll receptor variants were linked with the severity of bronchopulmonary dysplasia a leading cause of morbidity and mortality in premature infants.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Three 2012 initiatives are highlighted. Annually, a NIEHS-funded Science Education Partnership Award facilitates COEC's involvement of more than 30 faculty and 800 Milwaukee Public and area-wide high school students' engagement in an enrichment of high school biology/science curriculum with live animal model classroom experiments that help youth link environmental exposures to their own health. A unique feature of this program is the development of science communication skills. In April, 2012, COEC sponsored a scientific conference that drew more than 300 students and faculty featuring students' posters and competitively selected paper presentations.

Since 2011, COEC has been a core member of the Cleaner Valley Coalition comprised of 20 organizations that asked We Energies to bring one of two remaining coal-burning power plants in Milwaukee into compliance with the Clean Air and Clean Water Acts. In joining, our specific role was to bring the Center's research and expertise in air and water quality and the effect of contaminants (e.g., mercury, PAHs, particulates) on children's health to help undergird decisions made by the coalition. At the July 2012 meeting, We Energies reaffirmed its commitment to convert to natural gas and offered to move the timeline up 2-3 years—to December 2015—in response to the coalition's persistence. For this feat, the Wisconsin Asthma Coalition gave the CVC the 2012 'WAC Award' at their annual fall meeting in 2012.

In 2012, Lisbon Avenue Neighborhood Development (LAND), on Milwaukee's near north side sought the COEC's help to evaluate the safety of vegetable gardens. With Center funding, a UW-Milwaukee geology team conducted an evaluation of the levels of lead and other contaminants in urban gardens. Initial soil samples indicated very high levels of lead in soil and elevated lead in some vegetable samples. COEC, LAND, and the scientists are in the process of disseminating the findings to the homeowners, landlords, and tenants, and are working on partnerships and additional funding to mitigate the hazard. This project is ongoing, Together with the discontinuation of federal funding to support state lead surveillance programs and substantial reduction of housing remediation funding, it was the impetus for a state-wide coalition led by COEC to reinvigorate lead prevention efforts including through policy initiatives.

HIGHLIGHTED PUBLICATIONS

Myers CR (2012) The effects of chromium(VI) on the thioredoxin system: implications for redox regulation. *Free Radic. Biol. Med.* 2012 52:2091–2107. PMID: 22542445.

Crago J, Klaper R (2012) A mixture of an environmentally realistic concentration of a phthalate and herbicide reduces testosterone in male fathead minnow (*Pimephales promelas*) through a novel mechanism of action. *Aquatic Toxicology*, 110-111:74-83. PMID:22277248

Rush T, Liu XQ, Nowakowski AB, Petering DH, Lobner D (2012) Glutathione-mediated neuroprotection against methylmercury neurotoxicity in cortical culture is dependent on MRP1. *Neurotoxicology*. 33:476-481. PMID: 22464990

Weber, DN, Hesselbach, R, Kane, A, Petering, DH, Petering, L, Berg, CA (2013) Minnows as a classroom model for human environmental health. *American Biology Teacher* (in press).

RESEARCH HIGHLIGHT POSTER

Children's Environmental Health Sciences Core Center: Highlights of Research and Center Support

David Petering and Paula North

ABSTRACT: The Children's Environmental Health Sciences Core Center supports a range of basic through translational research focused on chemicals that may alter development. A constellation of studies on metals toxicology utilize cutting edge approaches, including EPR spectroscopy to investigate the reaction of Cr (VI) with thioredoxin, laser ablation inductively coupled plasma mass spectrometry to reveal the distribution of CH₃Hg in larval zebrafish, and Zn-sensors to follow the reaction of Cd²⁺ with the Zn-proteome. The Center's emphasis on freshwater toxicology is exemplified by research on the impact of the pharmaceutical fluoxetine (serotonin reuptake inhibitor) on the behavior and related gene expression of fathead minnows. A major emphasis is on embryological development. Recent experiments in zebrafish and mouse show that nicotine exposure alters neural crest differentiation, resulting in cranial-facial defects. Two new initiatives are underway. In one, a pediatric environmental genomics group has formed, involving scientists working with children as well as zebrafish as a companion model organism. In the other, researchers are focused on children's environmental health inequities and their origin in Milwaukee. In order to support this broad range of research, the Center has greatly expanded its facility core infrastructure and staff in the areas of exposure assessment and genomics.

OUTREACH HIGHLIGHT POSTER

Center Resources for Community-Driven Engagement in Milwaukee

Jeanne B. Hewitt

ABSTRACT: The Lisbon Avenue Initiative began when a business owner asked about 'noise pollution.' His café is located on this highway through the city's north side, which experiences heavy traffic and sirens from two ambulance companies and a nearby fire department. Community Outreach and Engagement Core (COEC) conducted key informant interviews with local fire, police, business, and community organizations to identify stakeholders' perceptions about the challenges and assets in this neighborhood. Both ambulance company owners offered 'noise' as a key issue. They also noted that many of their 'runs' did not require ambulance transportation, but clients needed or wanted transportation to health care (i.e., hospitals) despite a federally qualified health center located in the neighborhood. COEC recruited a community noise specialist and President of Industrial Design, Inc., from the Madison area, Gonzalo Sanchez, who is volunteering as our acoustics expert. An after-school/summer youth organization, Our Next Generation, offered to have their youth be key team members. These high school-aged youth are learning from Mr. Sanchez and COEC about the science of noise; how it is measured and mitigated; and health effects including hypertension, stress, and violence. We describe the plans for how this initiative will proceed over the next two years.

CENTER Environmental Agents as Modulators of Disease Processes (Rochester)

LOCATION University of Rochester, Rochester, NY

PI Thomas A. Gasiewicz

COEC DIRECTOR Katrina Korfmacher

ADMINISTRATOR Patricia Noonan-Sullivan

WEB SITE <http://www2.envmed.rochester.edu/envmed/index.html>

THEME

The underlying THEME that guides and integrates the interdisciplinary research efforts of the Rochester EHSC is the modulation of disease processes by environmental and occupational agents.

RECENT SCIENCE HIGHLIGHTS

Investigations within the Neurodegeneration & Neurodevelopmental Disease Program observed that the outcome of developmental lead (Pb) exposure is dependent on the presence and type of behavioral experience during the perinatal period. Additional collaborative studies of this group and those within the Musculoskeletal Disease Program found that developmental Pb exposure in rats results in an osteoporotic-like phenotype and that this is related to a depression in Wnt signaling and disruption of the TGF β signaling pathway. Notably, the exposure paradigm represents one that is relevant to current environmental human exposure in the United States, and suggests that Pb may have a detrimental impact on human bone at levels previously thought safe. Studies by investigators in the Pulmonary & Cardiovascular Disease Program (PCDP) and the Program in Early Life Antecedents of Adult Disease found that maternal BPA exposure slightly modified innate immunity in adult offspring, but does not impair the anti-viral adaptive immune response that is critical for virus clearance and survival following influenza infection. However, additional studies by these groups found that neonatal exposure to hyperoxia alters susceptibility to the development of lung disease mediated by influenza virus A later in adult life. These findings also demonstrated that novel epithelial expression of Ear1 functions to limit influenza A virus infection, and its loss contributes to associated epithelial injury and fibrosis after infection. This may have implications for other toxicant-associated injury to lungs, as well as potential therapeutic measures. Studies by a new Center member, in collaboration with scientists in the PCDP, suggest that nanoparticle (NP) skin penetration and translocation may depend on the specific barrier insult and inflammatory status of the skin, and that the differentiation state plays an important role in keratinocyte response to UVB exposure and exposure to NPs. Other investigations within the PCDP found that SIRT1 is a potential therapeutic target in COPD. A reduction in SIRT1 expression was associated with chronic inflammatory response in the lung. Finally, other investigations found that exposure to ambient ultrafine and fine particles is associated with adverse cardiac responses in patients undergoing cardiac rehabilitation and in patients with Type 2 diabetes.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Our COEC has developed strong connections with local government and community organizations in the Rochester area and across New York State. In 2012, we built on our strong foundations in lead and healthy homes, significantly expanded our efforts in hydrofracking and health impact assessments, and made new contributions in several additional issue areas related to Center research.

1. Lead Poisoning Prevention: We completed a major effort to evaluate the Rochester lead law in a comparative analysis of seven recent local lead laws from across the

- country and plan to disseminate the findings in 2013.
2. **Healthy Homes:** We coordinate Rochester's Healthy Home Program Partnership, which includes over 20 local groups and conducted Healthy Homes trainings in the community.
 3. **Hydrofracking:** Local interest in hydrofracking continues to rise as the state considers regulations that would allow high volume horizontal hydrofracking in New York State. We received an administrative supplement to partner with UNC and UC to identify information gaps and education needs of communities in New York, North Carolina, and Ohio.
 4. **Health Impact Assessment (HIA):** We initiated a community learning group on HIA in 2011 and continue to support it. We are conducting upstate New York's first full HIA, which will be complete in June 2013.
 5. **Perinatal Environmental Health Literacy (EHL):** We explored how educating pregnant women can help them protect their children's environmental health. We received an administrative supplement to partner with University of Arizona to develop concepts of EHL; our focus was on EHL during pregnancy.
 6. **Additional issue areas:** We leveraged EHSC research expertise to support community, health, and government groups in addressing issues including toxins in locally-caught fish, pesticides, obesogens, stress, BPA, and air quality. School-based outreach programs provided opportunities for nearly 1000 primary school students to learn about water and air quality monitoring.

Our Community Advisory Board (CAB) informs our priority issue areas, reviews new outreach topics, and leverages our efforts by networking with their members. In addition, our membership in a number of key local boards and partnerships provides input about topics of local concern and priority outreach needs.

HIGHLIGHTED PUBLICATIONS

Cory-Slechta DA, Merchant-Borna K, Allen JL, Liu S, Weston D, Conrad K. Variations in the nature of behavioral experience can differentially alter the consequences of developmental exposures to lead, prenatal stress, and the combination. *Toxicol. Sci.* 131: 194-205, 2012. PMID: 22930682.

Beier EE, Maher JR, Sheu T-J, Cory-Slechta DA, Berger AJ, Zuscik MJ, Puzas JE. Heavy metal lead exposure, osteoporotic-like phenotype in an animal model, and depression of Wnt signaling. *Environ. Health Perspect.* 121: 97-104, 2013. PMID: 23086611.

Yao H, Chung S, Hwang JR, Rajendrasozhan S, Sundar IK, Dean DA, McBurney MW, Guarente L, Gu W, Ronty M, Kinnula VL, Rahman I. SIRT1 protects against emphysema via FOXO3-mediated regulation of premature senescence in mice. *J. Clin. Invest.* 122: 2032-2045, 2012. PMID: 22546858.

Rich DQ, Zareba W, Beckett W, Hopke PK, Oakes D, Frampton MW, Bisognano J, Chalupa D, Bausch J, O'Shea K, Wang Y, Utell MJ. Are ambient ultrafine, accumulation mode, and fine particles associated with adverse cardiac responses in patients undergoing cardiac rehabilitation? *Env. Health Perspect.* 120: 1162-1169, 2012. PMID: 22542955.

RESEARCH HIGHLIGHT POSTER

CNS Consequences of Developmental Exposure to Ultrafine Air Particles

Joshua L. Allen and Deborah A. Cory-Slechta, PhD

ABSTRACT: Increasing evidence suggests that the central nervous system (CNS) exhibits vulnerability to the consequences of air pollutants. Early development is a period of enhanced vulnerability of CNS to insults. Thus we profiled CNS effects of developmental and adult concentrated ambient particulate matter (CAPS) exposure. C57Bl6 mice were exposed to CAPS during early postnatal life with or without adult challenge. CAPS mass

concentrations averaged 100-200 $\mu\text{g}/\text{m}^3$. Multiple behavioral deficits, including impaired ability to learn in a repeated learning paradigm and impulsivity or choice of immediate reward on an FR waiting-for-reward paradigm, were observed in a sex-dependent manner in postnatal CAPS-exposed mice. Further, histopathological hallmarks of CNS perturbation, namely astrogliosis and increased microglial presence, along with altered neurochemistry, were observed in multiple brain regions, and appear to be highly persistent. being seen as long as at least one year post exposure. A time course study underway to examine earliest effects of CAPS has revealed notable CNS structural changes including what appears to be significant white matter loss, particularly in males at 24 hr post-termination of exposure. Collectively, these findings suggest that air pollutants may represent an underappreciated contribution to developmental and/or neurodegenerative CNS disease and disorders. Supported by T32ES007026, R21ES019105 and P30ES01247.

OUTREACH HIGHLIGHT POSTER

Health Impact Assessment in Rochester

Katrina Korfmacher, PhD and Valerie Garrison

Five years ago, Community Advisory Board chair Dr. Andrew Doniger, Director of the Monroe County Department of Public Health, asked for help in exploring the potential for Health Impact Assessment to shape decisions that might impact health through environmental change in our community. In January 2011, we started a local "HIA Learning Group," involving members from several government and non-profit organizations to learn more about the practice of HIA and explore its potential in Rochester. Now led by a local health agency, the group has hosted speakers, developed proposals, and discussed how HIA could be integrated in various decision-making settings. In 2012, our COEC was awarded a grant by the Health Impact Project (a collaboration of the Robert Wood Johnson Foundation and the Pew Charitable Trusts) to conduct an HIA of the Local Waterfront Revitalization Program. Regular updates on our project have enhanced the Learning Group's experience, and we have benefitted from the group's input. Our poster will summarize the Learning Group's experiences, progress on our HIA, and "lessons learned" for the practice of HIA in Rochester. In particular, we will discuss questions raised about appropriate COEC roles in HIA as a foundation for the HIA "unconference" session.

CENTER	Environmental Exposures, Host Factors and Human Disease (USC)
LOCATION	University of Southern California, Los Angeles, CA
PI	Frank Gilliland
COEC DIRECTOR	Andrea Hricko
ADMINISTRATOR	Tracy Bastain
WEB SITE	http://hydra.usc.edu/scehsc/index.html
THEME	Environmental Exposures, Host Factors and Human Disease

RECENT SCIENCE HIGHLIGHTS

In the past year, Center investigators have produced several important research findings. Dr. Towhid Salam has used an integrative genetics approach to examine the relationship between particulate matter exposure and airway inflammation and the role that DNA methylation and sequence variation may play in this process. Dr. Salam's research utilizes the wealth of health and exposure data available in a subset of the Children's Health Study (CHS), and ongoing cohort study of 11,000 children investigating both genetic and environmental factors related to respiratory disease. The results from this research will contribute to the rapidly evolving field of environmental epigenomics by investigating novel associations between air pollutants and DNA methylation, both of which may be important to early life onset diseases. We have also made further progress in cardiovascular disease (CVD) research as Dr. Carrie Breton has reported that small differences in CIMT may translate into clinically relevant CVD later in life – a leading cause of morbidity and mortality in the U.S. Dr. Jim Zhang also reported in JAMA that changes in air pollution levels during the Beijing Olympics were associated with changes in biomarkers of inflammation and thrombosis in healthy young adults.

Both Dr. Zhang's paper on the Beijing Olympics and Center Deputy Director Rob McConnell's paper on the costs of asthma in Long Beach and Riverside were named two of the NIEHS Top Papers of the Year. Dr. McConnell's paper was designed to help policymakers understand the significant burden caused by traffic-related pollution.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

We presented Center research findings on health effects of air pollution at 30+ public meetings and conferences, harbor commission hearings, journalist and health department inspector training programs, and government policy-making proceedings. One of our objectives this year was leadership development of community-based groups in Boyle Heights, Long Beach and other communities impacted by truck traffic along the I-710 (Long Beach) Freeway. COEC staff and Center members Avol, Froines, Fruin and McConnell all made presentations about potential health impacts of plans to expand this 20-mile long freeway, which include: 1) adding more lanes and elevating a truck-only section as the highway passes through 18 lower-income, Latino communities; and 2) extending the freeway north by building twin tunnels. The California Department of Transportation issued a Draft Environmental Impact Report (DEIR) for the first part of the expansion. The I-710 carries 35,000 trucks a day; the plan is to double or triple that capacity.

Schools and homes are located in close proximity to the I-710. A major challenge has been moving Caltrans to consider near-roadway health impacts in its environmental reviews. One recent success was agreement to conduct a Health Impact Assessment (HIA); but Caltrans' chose to exclude the completed HIA in its published DEIR. We have urged U.S. EPA to work more closely with U.S. DOT in requiring state transportation agencies to examine the latest research findings when building new highways.

Awards in 2012 went to:

- Andrea Hricko, from Physicians for Social Responsibility (PSR-LA) for bridging the gap between scientists and the public;
- John Froines, from PSR-LA for “courageous commitment to scientific integrity and for increasing understanding of the impacts of toxic chemicals on the health of workers and communities.”
- Rob McConnell, whose paper on understanding the asthma burden caused by traffic-related pollution was selected by NIEHS as one of the Best 30 NIEHS-supported Papers of 2012; and
- Junfeng (Jim) Zhang, who received the Jerome Wesolowski award from the International Society of Exposure Science. His paper on the Beijing Olympics also was an NIEHS Top Paper of the Year.

HIGHLIGHTED PUBLICATIONS

Breton, C.V., Wang, X., Mack, W.J., Berhane, K., Lopez, M., Islam, T.S., Feng, M., Lurmann, F., McConnell, R., Hodis, H.N., et al. (2012). Childhood air pollutant exposure and carotid artery intima-media thickness in young adults. *Circulation* 126, 1614-1620.

Rich DQ, Kipen HM, Huang W, Wang G, Wang Y, Zhu P, Ohman-Strickland P, Hu M, Philipp C, Diehl SR, Lu SE, Tong J, Gong J, Thomas D, Zhu T, Zhang JJ. Association between changes in air pollution levels during the Beijing Olympics and biomarkers of inflammation and thrombosis in healthy young adults. *JAMA* 2012; 307: 2068-78
PMID:22665106

Salam, M.T., Byun, H.M., Lurmann, F., Breton, C.V., Wang, X., Eckel, S.P., and Gilliland, F.D. (2012). Genetic and epigenetic variations in inducible nitric oxide synthase promoter, particulate pollution, and exhaled nitric oxide levels in children. *J Allergy Clin Immunol* 129, 232-239 e231-237.

Brandt SJ, Perez L, Künzli N, Lurmann F, McConnell R. Costs of childhood asthma due to traffic-related pollution in two California communities. *Eur Respir J.* 2012 Aug;40(2):363-70. doi: 10.1183/09031936.00157811. Epub 2012 Jan 20. PMID: 22267764.

RESEARCH HIGHLIGHT POSTER

Non-linear models for multiple flow exhaled nitric oxide data

S. Eckel, K. Berhane, W. Linn, M. Salam, Y. Zhang, E. Rappaport, F. Gilliland

ABSTRACT: The fractional concentration of exhaled nitric oxide (FeNO) is thought to be a marker for airway inflammation and has been associated with air pollution exposure. A deterministic non-linear two-compartment model describes the physiology of NO production in the respiratory system. Regression models approximating the two-compartment model can be estimated using a small number of repeated FeNO measurements at multiple exhalation flow rates. The coefficients are interpreted as parameters governing NO production in different anatomical locations and may provide insight into the mechanisms of airway inflammation, particularly related to air pollution exposure. Multiple flow data originated in small experimental studies, but is now available in a large cohort of children in the Southern California Children’s Health Study (CHS) which also has extensive data on air pollution exposures. Methods for effectively modeling such data have not been developed. We develop and evaluate methods to: estimate physiologic parameters, either separately for each participant or by pooling across participants using a mixed-effect model (Stage I) and relate estimated parameters to environmental exposures (Stage II). Methodological challenges include producing parameter estimates within a biologically plausible range of values and non-linear mixed-effect models with non-normal random effects.

OUTREACH HIGHLIGHT POSTER

Environmental Sustainability Activities Combining COEC and Center Resources. Southern California Environmental Health Sciences Center

Andrea Hricko, Carla Truax, Ed Avol, Rob McConnell, John Froines

ABSTRACT: A highlight during 2012-2013 for our COEC and Center was involvement in environmental sustainability activities at both USC and UCLA. At USC, a new Environmental Sustainability Research Network (ESRN) has been formed, providing valuable links between the Center and USC faculty in engineering, business, public policy, sociology, history and environmental studies. COEC director Andrea Hricko and IHSFC Core Director Ed Avol were featured speakers at the ESRN's first workshop in February 2013 on "Industry, Transportation & Health." Center Associate Director John Froines co-directs UCLA's Sustainable Technology & Policy Program at UCLA, for which he is writing a report on California's pesticide approval process in highlighting methyl iodide. The COEC poster highlights new environmental sustainability activities of our Center, including new teaching programs in environmental health at the undergraduate and graduate levels, directed by Ed Avol and Center Deputy Director Rob McConnell, respectively. These efforts are already bringing in new students to the COEC for conducting independent research and the MPH practicum. Our poster also highlights the COEC's leadership in developing a nationwide network to link organizations working on health impacts of ports and goods movement throughout the U.S., which held its latest meeting in Kansas City, Missouri in February 2013.

CENTER Environmental Health Sciences Research Center (Iowa)
LOCATION University of Iowa, Iowa City, IA
PI Peter S. Thorne
COEC DIRECTOR Edith Parker
ADMINISTRATOR Mindy Sickels
WEB SITE <http://www.ehsr.org>

THEME

The overarching theme of the Environmental Health Sciences Research Center is research and outreach on the adverse health effects of current and emerging environmental contaminants among rural and agricultural populations.

RECENT SCIENCE HIGHLIGHTS

None provided.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

A fourth Midwest Environmental Health Summit was held at the State Capitol in Des Moines, IA January 24-25, 2013. There were 30 participants from the states of IA, IL, IN, KS, MN, MO, WI. The program featured a tour of a biodiesel plant, a radon presentation to the Senate State Government Committee, and invited speaker Trevor Penning on hydraulic fracturing. Additional topics included PCBs and the Farm Bill/Agriculture and EH. Edith Parker and Nancy Wyland attended the Indian Health Service Tribal and Federal Sanitarians Meeting in Aberdeen, SD in February 2012, where they conducted a focus group meeting on EH issues; in addition, Dr. Parker delivered an invited presentation on Community Assessment in Environmental Health. 50 sanitarians were present. Through our partnership with the Iowa Radon Coalition, a Radon Bill was submitted to the state legislature in 2012-2013 and recently passed the Senate. The bill requires school testing statewide and radon-resistant new construction.

There was much activity around Community Engagement, Outreach, and Education on Radon through the EHSRC in 2012. The Iowa Radon Coalition produced an educational video for physicians which has been widely distributed. In addition, we have continued distribution of radon education brochures to parents of newborns in Iowa. Finally, Bill Field was featured on The Today Show in a story about radon in schools.

HIGHLIGHTED PUBLICATIONS

None provided.

RESEARCH HIGHLIGHT POSTER

Chlordane is enantioselectively metabolized by hepatic microsomes

Korwel, I.

ABSTRACT: The persistent environmental pollutant chlordane has been implicated as a factor contributing to the epidemic of obesity and diabetes. Major components of technical chlordane (trans -chlordane, cis-chlordane and heptachlor) and their metabolites are chiral. This study investigated the enantioselective metabolism of those chemicals by liver microsomes prepared from rats treated with corn oil (CO) or inducers of CYP2B (PB; Phenobarbital) and CYP3A enzymes (DX; dexamethasone). The extent of the metabolism of all three chemicals was dependent on microsomal preparation used, and followed the rank order PB > DX > CO. Both cis- and trans-chlordane were enantioselectively metabolized to oxychlordane and another, currently unknown metabolite. Heptachlor was metabolized enantioselectively to heptachlor epoxide. Interestingly, the direction on the enrichment for

oxychlordane, heptachlor epoxide and the unknown metabolite differed depending on the microsomal preparation. Overall, our results suggest that components of chlordane are enantioselectively metabolized by different cytochrome P450 isoforms.

OUTREACH HIGHLIGHT POSTER

Preparing the Next Generation of Interdisciplinary Environmental Health Workers: Two Graduate Student Projects – EHSRC COEC, 2012

Meagan Schorr and Joanna Krajewski

ABSTRACT: In 2012, the EHSRC COEC implemented two projects to engage Community and Behavioral Health graduate students in the environmental health (EH) sciences. One student researched the EH aspects of the 2012 Farm Bill, with the goal of producing an accessible fact sheet. It features livestock production; food supply, access, and assistance programs; and sustainability concerns. Because the Farm Bill has been under perpetual legislative review without resolution in 2012, the information presented is from the 2008 Farm Bill and will be revised upon the final passage of Farm Bill 2012.

Another student worked with the Iowa Flood Center to incorporate public health entities and tips into the Iowa Flood Information System (IFIS), an interactive web-based system developed after the Midwestern Floods of 2008. IFIS provides access to community-based flood conditions, forecasts, inundation maps and flood-related information. Once completed, it will include the locations of trauma centers and county public health offices, sewage treatment plants, and livestock operations within Iowa. Additionally, mold clean-up instructions, sandbag pick-up locations, and health protection measures will be made available on the site. The poster presentation will highlight the process of recruiting students from disciplines outside of environmental health to participate in COEC activities.

CENTER Cellular Response Mechanisms to Environmental Challenge (UTMB)

LOCATION University of Texas Medical Branch at Galveston, TX

PI Cornelis J. Elferink

COEC DIRECTOR Sharon Croisant

ADMINISTRATOR Tracie Anne Albritton

WEB SITE <http://www.utmb.edu/cet/>

THEME

The mission of the UTMB Center in Environmental Toxicology (UTMB-CET) is to explore the environmental basis of human diseases by fostering collaborative interactions amongst multidisciplinary basic and clinical investigators pursuing both fundamental and translational research pertinent to the effects of environmental factors on human health. The UTMB-CET is housed at the University of Texas Medical Branch in Galveston, and is the only NIEHS environmental health center located on the Gulf of Mexico coast, near the nation's busiest shipping port (Port of Houston) and an expansive petrochemical refining and manufacturing infrastructure. Our proximity to sources of many significant environmental problems makes UTMB a compelling site for such an environmental health sciences center. The underlying causes of these problems include the composition of the natural environment, meteorological conditions (namely hurricanes), population density, personal and commercial transportation patterns, and the endemic petrochemical industry. Some of the most serious environmental issues are ozone pollution, emissions of fine particulates, hazardous chemical releases, hazardous waste sites, and PCB/dioxin contamination of the marine biota. The UTMB-CET investigators concentrate their efforts in three disease categories: 1) asthma pathogenesis; 2) environmentally-linked carcinogenesis; and 3) disease states induced by reactive oxygen stress.

RECENT SCIENCE HIGHLIGHTS

The environmental basis for the increasing prevalence in childhood asthma may be related to exposures affecting prenatal development of the immune system. Center investigators have focused on the potential effects of bisphenol A (BPA) on the development of childhood asthma. Using a mouse model, the study identified a critical period of BPA exposure. Prenatal exposures that produce environmentally relevant burdens of BPA, followed by postnatal allergic sensitization and challenges, promote the development of experimental allergic asthma. Delayed expression of BPA-metabolizing enzymes may explain, at least in part, the enhanced fetal susceptibility to this common environmental contaminant. Specific subgroups of asthma patients have severe disease leading to increased healthcare costs and socioeconomic burden. Asthmatics present with common clinical signs and symptoms but therapeutic responses differ with some patients at increased risk of morbidity. Approaches to asthma phenotyping can be partitioned into 2 essential groups; clinical phenotyping and molecular phenotyping. Molecular phenotyping distinguished patient clusters with significantly different pulmonary functions using cytokine values in bronchoalveolar lavage samples. These results suggest that a molecular-based classification of asthma patients could improve the diagnosis and treatment of this disease. 8-Oxo-7,8-dihydroguanine (8-oxoG), a prevalent base lesion induced by ROS, is repaired via the base excision repair pathway that is initiated with the excision of 8-oxoG by OGG1. Center members showed that OGG1 binds the 8-oxoG base with high affinity and that the complex then interacts with canonical Ras family GTPases to catalyze replacement of GDP with GTP, thus serving as a guanine nuclear exchange factor. OGG1-mediated activation of

Ras leads to phosphorylation of the mitogen-activated kinases MEK1,2/ERK1,2 and increasing downstream gene expression. These studies document for the first time that in addition to its role in repairing oxidized purines, OGG1 has an independent guanine nuclear exchange factor activity when bound to 8-oxoG.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

The Community Outreach and Engagement Core (COEC) divisions are; I) Education (secondary, undergraduate/graduate/health professionals); II) Children's Environmental Health; III) Toxics Assistance and Public Forum; and IV) Environmental Health Policy Outreach and Education. The COEC partnered with the Galveston Historical Foundation to promote healthy homes and neighborhoods, sustainable living, and green lifestyles. The COEC members also participated in CBPR education at the Community-Engaged Research Conference in Houston sponsored by the Hobby Center for Public Policy, University of Houston, and Community-Campus Partnerships for Health. The COEC developed new course material addressing the concepts of translational science is offered for 1st and 4th year School of Medicine students.

The Children's Environmental Health division participated in a national meeting in Galveston seeking to form a nationwide disease-based research network that will educate the community about a new strain of hypervirulent *C. difficile* infections. The COEC authored a report for the EPA and the NIMHHD contributing to the development of new Centers of Excellence in the Environment and Health Disparities. Dr. Croisant was selected as a member of the national EPA Science Advisory Board, Environmental Justice Technical Panel. The COEC also organized and carried out Hurricane Isaac relief efforts for communities in Mississippi and south Louisiana, by providing financial aid from donations and environmental public health education.

The Toxics Assistance and Public Forum division conducted community science workshops in Louisiana, Alabama, Mississippi, and Texas to bring scientists and clinicians together with community members to discuss implications of the Gulf Oil Spill, probable and possible health effects, and potential collaborative relationships and projects. This division also supported environmental justice (EJ) initiatives in Port Arthur— designated by EPA's Region 6 as one of ten EJ Showcase Communities in the country.

The Environmental Health Policy Outreach and Education division maintained active involvement with the National Conversation on Public Health and Chemical Exposures Network to develop a multidirectional communication model for government agency use, and improve public availability and clarity of chemical information on products throughout the supply chain. These initiatives will build a stronger foundation with local and state policy leaders to inform environmental health policy.

HIGHLIGHTED PUBLICATIONS

Pillai, R.R., et al., Strategies for molecular classification of asthma using bipartite network analysis of cytokine expression. *Curr Allergy Asthma Rep*, 2012. 12(5): p. 388-95.

Nakajima, Y., R.M. Goldblum, and T. Midoro-Horiuti, Fetal exposure to bisphenol A as a risk factor for the development of childhood asthma: an animal model study. *Environ Health*, 2012. 11: p. 8.

Boldogh, I., et al., Activation of ras signaling pathway by 8-oxoguanine DNA glycosylase bound to its excision product, 8-oxoguanine. *J Biol Chem*, 2012. 287(25): p. 20769-73.

Sullivan J, Croisant S, Bambas-Nolen A, Prochaska J, Parras B, & Elferink C. (2012). Building community-researcher CBPR capacity and incubating partnerships through an Environmental Justice Network/Community Science Workshop. *International Journal of Community Based Research*. 10:12-14.

RESEARCH HIGHLIGHT POSTER

The Tumor Suppressor Kruppel-Like Factor 6 is a Novel Aryl Hydrocarbon Receptor DNA Binding Partner

Shelly R. Wilson, Aditya D. Joshi, and Cornelis J. Elferink

ABSTRACT: The Aryl Hydrocarbon Receptor (AhR) is a ligand mediated basic helix-loop-helix transcription factor of Per/Arnt/Sim family that regulates adaptive and toxic responses to variety of chemical pollutants including 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Ligand activation leads to AhR nuclear translocation and binding to a xenobiotic response element (XRE) in association with the aryl receptor nuclear translocator (Arnt) to regulate gene expression. Several recent genome-wide transcriptional studies identified numerous AhR target genes that lack the canonical XRE recognition site in the promoter regions. Characterization of one such target gene, the Plasminogen Activator Inhibitor 1 (PAI-1) identified a novel non-consensus XRE (NC-XRE) that confers TCDD responsiveness independently of the Arnt protein. Studies reported here show that the NC-XRE is a recognition site for the AhR and a new binding partner, the Kruppel-like Factor (KLF) family member KLF6. In vivo chromatin immunoprecipitations and in vitro DNA binding studies demonstrate that the AhR and KLF6 proteins form an obligatory heterodimer necessary for NC-XRE binding. Mutational analyzes show that the protein-protein interactions involve the AhR C-terminus and KLF6 N-terminus, respectively. Collectively, the results unmask a novel AhR signaling mechanism distinct from the canonical XRE-driven process that will enrich our future understanding of AhR biology.

OUTREACH HIGHLIGHT POSTER

Transforming Community Outreach and Engagement: Development of a Gulf Coast Regional Network

Sharon A. Croisant, MS, PhD, John Sullivan, MA, Lauren E. Scott, MSW, Amber Anthony, B.S, & Michele K. Cravey

ABSTRACT: The UTMB CET mission is to translate environmental health science for the communities we serve through establishment of bidirectional communications among scientists, clinicians, trainees, and the public to foster the exchange of information and, in conjunction with the IHSFC, to promote research which addresses community-identified EHS needs. COEC audiences include broad-based stakeholders: Center investigators, health care practitioners, those engaged in public health and in policy-making related to EH, and the lay public. Our iterative process includes meaningful dialogues that frequently lead to progressively intensive activities—EJ *Encuentros* for networking, Community Science Workshops to incubate potential CBPR projects, followed by research (via the IHSFC), and dissemination of findings—which jump starts the next project. We have repeated this engagement process across the Gulf Coast region, resulting in a series of overlapping networks with emphases on: EJ, coastal heritage, Healthy Ports Communities, educational initiatives, and communities affected by the Macondo Oil Spill and other natural and manmade disasters that impact community resiliency. To maximize not only the scope but the impact of our efforts, we are now in the process of developing a more integrated Gulf Coast Regional Environmental Health Science Network. We believe this network will enhance future EH research, and outreach and engagement projects originated by the NIEHS CET and other NIEHS Centers of Excellence.

SUPPLEMENT PROJECT HIGHLIGHT POSTER

Synthesis of Petrogenic PAH Metabolites For Analyte Identification

Linda C. Hackfeld, Richard P. Hodge, Meng Huang, Trevor M. Penning and Kees Elferink

ABSTRACT: The EHSCCs at UTMB and UPenn are involved in The Gulf Coast Health Alliance: health Risks related to the Macondo Spill (GC-HARMS)-U19-ES020676 which

includes an assessment of the toxicology of petrogenic polycyclic aromatic hydrocarbons (PAHs) in the gulf-oil spill. Petrogenic PAH differ from the pyrogenic PAH (e.g benzo[a]pyrene) since they are heavily alkylated and oxygenated, and little information exists regarding their metabolism which may determine their toxicity. The parent grant has elucidated the metabolic profiles of 5-methyl chrysene [C1-chrysene] and 1-methyl-7-isopropyl phenanthrene [C4-phenanthrene(retene)] in human hepatoma (HepG2) cells using HPLC-UV/Fluorescence and LC-MS/MS. C1-Chrysene forms tetraols, mono- and bis-phenols, o-quinones and catechol-conjugates, indicative of P450 and AKR activation. By contrast C4-phenanthrene forms dihydrodiols, mono-phenols, o-quinones and catechol-conjugates indicative of AKR activation only. Since regio- and /or stereoisomers are possible for these metabolites authentic standards are required to validate analyte identity. Analyte identity could lead to rapid deployment of a biomarker assay to determine human exposure to petrogenic PAH. The Synthetic Core at UTMB is synthesizing a library of authentic petrogenic PAH metabolites identified in HepG2 cells. The Translational Biomarker Core at UPenn will compare the LC-MS/MS properties of the authentic standards with those observed for the metabolites identified in HepG2 cells.

CENTER **Lifestage Exposures and Adult Disease (UM)**

LOCATION University of Michigan, Ann Arbor, MI

PI Rita Loch-Caruso

COEC DIRECTOR Amy Schultz

ADMINISTRATOR Rachel L. McDuffie

WEB SITE <http://www.sph.umich.edu/niehs/>

THEME

The UM EHS Core Center is a relatively new entity that brings together basic and translational scientists into a partnership focused on the theme of "Lifestage Exposures and Adult Disease". Our mission is to promote translational research using novel multi-disciplinary approaches to understand the impact of environmental exposures on adult chronic disease through mechanisms involving epigenetic modifications during vulnerable stages of life.

RECENT SCIENCE HIGHLIGHTS

- In a life course analysis of mouse offspring exposed perinatally to bisphenol A (BPA) through maternal diet, a team led by Dana Dolinoy found that female mice were more likely to exhibit hyperactivity and increased spontaneous activity, as well as leaner body mass, than those not exposed to the chemical, and that, overall, perinatally exposed females and males exhibited increased energy expenditure throughout the life course (Anderson, 2013). These findings suggest that BPA exerts specific effects in the critical perinatal period of life.
- A bottleneck in epigenetic analysis is bridging the gap between identification of a list of genomic regions or genes of interest, and making biological conclusions or discoveries based on those results. To facilitate this step, LRpath (<http://lrpath.ncibi.org>), recently highlighted on epibeat.com, is a logistic-regression based gene set enrichment testing method developed in the lab of Maureen Sartor (Kim et al., 2012). LRpath allows researchers to compare and visualize DNA methylation and/or gene expression results across multiple experiments at the level of cellular pathways, biological processes/functions, and other biologically-related gene sets such as genes related to a specific disease.
- Hearing loss is the third leading disabling condition among older adults. A team of scientists led by Sung Kyun Park demonstrated that environmental exposure to cadmium and lead are associated with increased risk of hearing loss in a representative sample of U.S. adults who participated in NHANES 1999-2004 (Choi et al., 2012). This is the first epidemiologic study showing a significant dose-response relationship between hearing loss and cadmium exposure in adults.
- Preterm birth is associated with increased risk for infant death and chronic health conditions. Projects led by John Meeker, Marie O'Neill and Rita Loch-Caruso are evaluating associations between specific environmental contaminants – including phthalates and air pollutants – with preterm birth. Using multi-disciplinary approaches that span cell biology to molecular epidemiology, these projects are linking exposure to pollutants with inflammation and oxidative stress as potential mechanisms of preterm birth (Ferguson et al., 2012; Manzano-León et al., 2013; Tetz et al., 2013).

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

- In order to reach a broader audience, the COEC worked with students through the course "Material and Methods in Health Education Programs" in the Department of Health Behavior and Health Education, University of Michigan School of Public

Health, to develop a short health video. The video, Oxidative Stress in Your Everyday Life, features a definition of oxidative stress, links to environmental exposures, and implications for health outcomes. It is now available online via YouTube, the EHS Core Center website and the PEPH Resource Center.

- Acting on the principle of community partnership and bidirectionality, COEC members participated with community partners in several public presentations. At the Soot Air Pollution: TAKE Action Event on August 28, 2012 in Detroit, COEC Coordinator Myra Tetteh presented information on particulate matter and its impact on health. The event also featured COEC Leader Amy Schulz who co-presented with community Stakeholders Advisory Board Angela Reyes, Executive Director of Detroit Hispanic Development Corporation, on findings on health effects of airborne particulate matter from research conducted by the Detroit Healthy Environments Partnership. Ms. Tetteh and community Stakeholders Advisory Board member Sheryl Shellman Weir, Director of Minority Health and Health Disparities with the Michigan Department of Community Health, co-presented a poster at the Michigan Premier Public Health Conference titled, "Methods to Improve Environmental Public Health in Underserved Communities" in October 2012. Additionally, Ms. Tetteh, along with Dr. Schulz (COEC Co-leader) and community Stakeholders Advisory Board member Sherita Smith, who is a lifelong Detroit resident, Detroit Community-Academic Urban Research Center Policy Trainer, and community activist, gave a webinar for other COEC members as part of the NIEHS Partnerships in Public Health (PEPH) series in November 2012, to share our work.
- Preparations are underway for a community tour and forum with NIEHS Director, Linda Birnbaum, on June 18, 2013. The Stakeholders Advisory Board identified air pollution and health-related effects as the focal topic for the tour and forum.

HIGHLIGHTED PUBLICATIONS

Anderson OS, Peterson KE, Sanchez BN, Zhang Z, Mancuso PE, Dolinoy DC. Perinatal Bisphenol A Exposure Promotes Hyperactivity, Lean Body Composition, and Hormonal Responses Across the Murine Life-Course. *FASEB J.* 2013 Jan 23. [Epub ahead of print] PMID: PMC Journal - In Process

Kim JH, Karnovksy A, Mahavisno V, Weymouth T, Pande M, Dolinoy DC, Rozek LS, Sartor MA. LRpath analysis reveals common pathways dysregulated via DNA methylation across cancer types. *BMC Genomics.* 2012 Oct 4;13:526. PMID: PMC3505188

Choi YH, Hu H, Mukherjee B, Miller J, Park SK. Environmental cadmium and lead exposures and hearing loss in u.s. Adults: the national health and nutrition examination survey, 1999 to 2004. *Environ Health Perspect.* 2012 Nov;120(11):1544-50. PMID: PMC3556613

Manzano-León N, Quintana R, Sánchez BN, Serrano J, Vega E, Vázquez-López I, Rojas-Bracho L, López-Villegas T, O'Neill MS, Vadillo-Ortega F, de Vizcaya A, Rosa I, Osornio-Vargas AR. 2013. Variation in the composition and in vitro pro-inflammatory effect of urban particulate matter from different sites. *J Biochem Molec Toxicol.* Forthcoming 2013. PMID: PMC Journal - In Process

RESEARCH HIGHLIGHT POSTER

Oxidative Stress and Lupus

Gabriela Gorelik, YePeng Li, Donna Ray, Faith Strickland and Bruce Richardson

ABSTRACT: Systemic lupus erythematosus is an autoimmune disease that flares when genetically predisposed people encounter certain environmental agents. The genetic predisposition is evidenced by validation of 38 susceptibility loci, and epidemiologic studies have found that agents causing oxidative stress, including sunlight, silica and smoking, are

associated with lupus. How oxidative stress causes flares is unclear. Human lupus is also associated with impaired T cell DNA methylation, due to decreased ERK pathway signaling causing a failure to upregulate DNA methyltransferase 1 (Dnmt1) during mitosis, impairing replication of DNA methylation patterns. More recent work shows that oxidative damage contributes to the impaired signaling. Specifically, PKC δ is inactivated by oxidative damage in T cells from patients with active lupus, decreasing ERK signaling and preventing Dnmt1 upregulation during mitosis. Further, human and mouse T cells treated with oxidizers exhibit similar PKC δ inactivation and epigenetic modifications, and the treated murine cells cause a lupus-like disease when injected into syngeneic mice. Finally, selectively inducing expression of a dominant negative PKC δ in mouse T cells using a tet-on system is sufficient to cause lupus in genetically predisposed mice. These studies strongly implicate oxidative stress as a mechanism by which environmental agents can contribute to lupus flares. (Protein kinase C δ oxidation contributes to ERK inactivation in lupus T cells. *Arthritis Rheum* 2012, 64; 2964-74).

OUTREACH HIGHLIGHT POSTER

Community Outreach and Education Core (COEC): Increasing Capacity of Environmental Public Health Issues and Policy Strategies

Niladri Basu, Jaye I. Clement, Paul Harbin, Barbara Israel, Alisha Opperman, Erminia Ramirez, Angela Reyes, Amy Schulz, Sheryl Shellman-Weir, Robert Sills, Sherita Smith, Myra Marie Tetteh, Donele Wilkins, Guy Williams

ABSTRACT: The Community Outreach and Education Core is part of the NIEHS-funded University of Michigan Environmental Health Science Lifestage Exposure and Adult Disease Center. The COEC fosters enhanced understanding among community members, policymakers and public health decision-makers concerning the role of environmental exposures in adult disease. The Center specifically focuses on how environmental exposures over the lifecourse are linked to asthma, early life development, diabetes, and cancer through three pathways (epigenetic regulation, oxidative stress, and endocrine disruptors). Detroit and Southeast Michigan are disproportionately impacted by environmental exposures (e.g. air pollution) and have reduced access to potentially protective resources (e.g., access to foods rich in antioxidants), thus increasing vulnerability to negative effects of those exposures. Over the lifecourse, these increased environmental exposures and vulnerabilities contribute to racial, ethnic and socioeconomic health disparities.

We will describe activities used to increase awareness among community and policymakers. and to build policy advocacy skills for improved environmental decision making in Detroit and Southeast Michigan. The activities include policy fact sheets and community policy advocacy training. We will also describe activities to increase awareness and understanding among community members with recent scientific findings associating environmental exposures across the lifecourse and adult disease. These include development of the *Oxidative Stress in Your Everyday Life* video and fact sheets.

CENTER NIEHS Center for Environmental Health (Harvard)

LOCATION Harvard, Boston, MA

PI Douglas Dockery

COEC DIRECTOR Ann Backus

ADMINISTRATOR Julie Goodman

WEB SITE <http://www.hsph.harvard.edu/niehs/>

THEME

Populations to Pathways: At the Harvard-NIEHS Center, we study the effects of real world environmental exposures on human populations. Our population-based studies inform and guide our laboratory investigations of the mechanisms by which these exposures impact human health. In turn evidence from the laboratory refines our questions about environmental toxicants and human risk. This “Populations to Pathways” approach allows us to effectively translate research findings to inform public health policy and improve clinical practice.

RECENT SCIENCE HIGHLIGHTS

Our focus is on the impact of three major environmental exposures, Metals, Organic Chemicals and Particles, on human health. Our studies are multidisciplinary and span all levels of investigation from “Populations to Pathways”. Below are highlights from each Research Core.

Particles: Studies of exposures to fine particles (PM_{2.5}) have been hindered by insufficient monitoring capabilities. Researchers from our Particles, IHFSC and Biostatistics cores developed an innovative method for comprehensive, fine-scale estimation of air pollution exposures. They used Satellite-derived Aerosol Optical Depth (AOD) measurements, which provide spatio-temporally resolved estimates of long and short-term exposures to PM_{2.5}, coupled with land use regression, meteorological variables, and a rotating network of community monitors, to create substantially improved hybrid estimates of PM_{2.5} exposure that can be mapped onto residential locations of participants in epidemiologic studies. For example, using this method, estimated PM_{2.5} exposure during the last month of pregnancy was associated with increased risk of lower birth weight and preterm birth. In elderly patients, these estimates were associated with increased hospital admissions for respiratory, cardiovascular disease (CVD), stroke and diabetes.

Organic Chemicals: Through a collaborative pilot project, Organics Core members and researchers at Brigham & Women’s Hospital (BWH) examined the impact of environmental exposure to endocrine disrupting chemicals on human fertility. In-vitro immature human oocytes were exposed to BPA to explore its effect on meiotic maturation. The study showed that as BPA dose increased, the likelihood of full oocyte maturation decreased significantly. This project initiated a growing collaboration between our Center and clinical researchers at the BWH-IVF Center, providing new opportunities to translate research from bench to bedside.

Metals: A goal of our Center is to bring modern tools of genomics, epigenomics, and proteomics to our population and pathways studies. Metals Core researchers are examining ways that airborne particulate matter (PM) might alter the epigenetic profile and influence gene expression. In a study of steel workers, metals in PM were associated with the quantity of specific histone modifications in blood and DNA methylation levels in certain cancer genes, suggesting that DNA methylation effects may mediate processes related to metal-induced lung carcinogenesis.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Outreach and Engagement in Dorchester and Boston - The neighborhoods of Dorchester, MA, our partner community, have high asthma and obesity rates. The asthma rate in North Dorchester is 7% higher than the 11% rate in Boston, and the obesity rate is statistically significantly higher than that of Boston with 31% of the population obese. South Dorchester rates are somewhat less problematic than those of North Dorchester. Our COEC has been involved with a variety of activities intended to raise awareness of these issues. After our NIEHS Community Forum on Asthma in March 2012, we were a co-sponsor with the Boston Public Health Commission at Dorchester House of a Health of Boston Forum (June 2012) which addressed the asthma and obesity issues. At the June forum we provided Peak Expiratory Flow (PEF) measurements for attendees and discussion about protecting airway health. This year, back by popular demand, we will provide PEF measurements at the Winter Farmers' Market at the Codman Community Health Center, at a Dorchester House Health Fair for Latinos, and again at the 2013 Health of Boston Forum in June. At the conclusion of these events and the collection of PEF values, we will have created a large community chart of airway health that we will convert to a poster and informational brochure about asthma and airway health.

We have recently partnered with an NSF-funded project at Boston College which will deploy a number of stationary air quality instruments, Air Quality Eggs (AQE), outside of Dorchester homes and businesses of volunteers and at Boston City Hall. These eggs will record NO₂, CO, time, temperature, and humidity. After data is transmitted by radio frequency to a base egg and then via Ethernet to Cosm, the data can be viewed on the Cosm website along with data from AQEs from around the world. Students will map the Dorchester data on the Harvard WorldMap.

The PEF and Air Quality Egg activities are designed to engage citizens in data collection and in the visualization of health and exposure data to expand their interest, knowledge and motivation for policy and behavior change.

HIGHLIGHTED PUBLICATIONS

Kloog I, Melly SJ, Ridgway WL, Coull BA, Schwartz J. Using new satellite based exposure methods to study the association between pregnancy PM_{2.5} exposure, premature birth and birth weight in Massachusetts. *Environ Health*. 2012 Jun 18;11:40. PMID: 22709681; PMCID: PMC3464884

Humblet O, Korrick SA, Williams PL, Sergeev O, Emond C, Birnbaum LS, Burns JS, Altshul LM, Patterson DG Jr, Turner WE, Lee MM, Revich B, Hauser R. Genetic modification of the association between peripubertal dioxin exposure and pubertal onset in a cohort of Russian boys. *Environ Health Perspect*. 2013 Jan;121(1):111-7. PMID: 23060366; PMCID: PMC3546349

Lepeule J, Laden F, Dockery D, Schwartz J. Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. *Environ Health Perspect*. 2012 Jul;120(7):965-70. PMID: 22456598; PMCID: PMC3404667.

Hou L, Wang S, Dou C, Zhang X, Yu Y, Zheng Y, Avula U, Hoxha M, Díaz A, McCracken J, Barretta F, Marinelli B, Bertazzi PA, Schwartz J, Baccarelli AA. Air pollution exposure and telomere length in highly exposed subjects in Beijing, China: a repeated-measure study. *Environ Int*. 2012 Nov 1;48:71-7. PMID: 22871507.

RESEARCH HIGHLIGHT POSTER

Effect of Air Pollution Control on Life Expectancy in the United States: An Analysis of 545 U.S. Counties for the Period from 2000 to 2007

Andrew W. Correia,^a C. Arden Pope III,^b Douglas W. Dockery,^c Yun Wang,^a Majid Ezzati,^d and Francesca Dominica ^aDepartment of Biostatistics, Harvard School of Public Health, Boston, MA; ^bDepartment of Economics, Brigham Young University, Provo, UT; ^cDepartments of Environmental Health and Epidemiology, Harvard School of Public Health, Boston, MA; ^dMRC-HPA Centre for Environment and Health and Department of Epidemiology and Biostatistics, Imperial College London.

ABSTRACT: Background: In recent years (2000–2007), ambient levels of fine particulate matter (PM_{2.5}) have continued to decline as a result of interventions, but the decline has been at a slower rate than previous years (1980–2000). Whether these more recent and slower declines of PM_{2.5} levels continue to improve life expectancy and whether they benefit all populations equally is unknown.

Methods: We assembled a data set for 545 U.S. counties consisting of yearly county-specific average PM_{2.5}, yearly county-specific life expectancy, and several potentially confounding variables measuring socioeconomic status, smoking prevalence, and demographic characteristics for the years 2000 and 2007. We used regression models to estimate the association between reductions in PM_{2.5} and changes in life expectancy for the period from 2000 to 2007.

Results: A decrease of 10 µg/m³ in the concentration of PM_{2.5} was associated with an increase in mean life expectancy of 0.35 years (SD = 0.16 years, P = 0.033). This association was stronger in more urban and densely populated counties.

Conclusions: Reductions in PM_{2.5} were associated with improvements in life expectancy for the period from 2000 to 2007. Air pollution control in the last decade has continued to have a positive impact on public health.

OUTREACH HIGHLIGHT POSTER

The Harvard WorldMap – A New Tool for Research, Engagement, and Outreach

Ann Backus, MS; Matthew Tumpney, SM; Steven J. Melly, MS

ABSTRACT: The Harvard WorldMap (HWM) was launched in July 2011 by the Harvard Center for Geographic Analysis as a public domain, open source tool for the sharing and visualization of spatial-temporal data. It was expressly designed for collaboration among researchers and for use with the community.

Research: As a tool for research collaboration and to illustrate the use of multi-discipline and multi-source data we will show a Fracking Map that depicts the current unconventional drilling permits in Pennsylvania and oil and gas wells in the US overlaid on the geological shale formations and demonstrate the Frack Map using the computer. We will show that GIS maps can be used to explore spatial patterns in data collected and analyzed in an epidemiologic study, to generate new hypotheses, and for field/university collaboration.

Engagement and Outreach: The HWM was used as a tool for community engagement in a PM_{2.5} study organized by Matt Tumpney that involved bikers, runners, and walkers from the HSPH neighborhoods, and a map of asthma hospitalizations was used in an HSPH outreach program to focus attention on asthma in Dorchester.

We will describe a Multi-Center collaboration through HWM training and raise some ethical and quality control issues.

CENTER **Reducing Susceptibility to Environmental Stress Throughout the Life Span (OSU)**

LOCATION Oregon State University, Corvallis, OR

PI Joe Beckman

COEC DIRECTOR Laurel Kincl

ADMINISTRATOR Lisa Shepard

WEB SITE <http://ehsc.oregonstate.edu/about>

THEME

The Environmental Health Science Center at Oregon State University focuses on discovering ways to improve human health and prevent disease through:

- assessing exposures in our homes, at work and in our community
- understanding the biological responses to these environmental stressors,
- clarifying the risks associated with exposures to environmental stressors, and modifying susceptibility to diseases caused by environmental stressors.

RECENT SCIENCE HIGHLIGHTS

New Methods of Immunosuppression: By elucidating the mechanisms of immune suppression induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), Dr. Kerkvleit's laboratory described how AhR-mediated immune suppression can be developed from a toxicological response to environmental exposure to the real possibility that the AHR pathway can be harnessed for the treatment of immune-mediated diseases. Dr. Kerkvleit's group showed TCDD prevents the rejection of allogeneic cell transplants and suppresses the induction of allergic asthma in animal models of human disease. TCDD also blocked the development of type I diabetes in NOD mice and suppressed the development of experimental autoimmune encephalomyelitis (EAE) in a murine model of multiple sclerosis. The induction of Tregs by TCDD was consistent with all of these outcomes.

Proving causality in oxidative stress: Using mass spectrometry, certain sites on particular proteins are known to be particularly vulnerable to tyrosine nitration. HSP90beta, the master chaperone in cells, was vulnerable to nitration in ALS and treatment of purified HSP90 with peroxyxynitrite causes HSP90 to activate a complex death cascade selectively in motor neurons. Using the capabilities of the Unnatural Amino Acid Core at OSU, we were able to genetically encode nitrotyrosine in HSP90. The ability to encode "oxidative damage" such as nitrotyrosine opens enormous possibilities to understand pathological mechanisms involving inflammation.

Bridging environmental mixtures and toxic effects: Biological Response Indicator Devices Gauging Environmental Stressors (BRIDGES) is a bioanalytical tool that combines passive sampling with the embryonic zebrafish developmental toxicity bioassay to provide a quantitative measure of the toxicity of bioavailable complex mixtures for 1,201 chemicals of concern. The developmental toxicity of the extracts was analyzed using the embryonic zebrafish bioassay. The BRIDGES tool provided site-specific, temporally resolved information about environmental contaminant mixtures and their toxicity. Multivariate modeling approaches can pair chemical and toxic effects data sets to help unravel chemistry-toxicity associations. Modeling elucidated spatial and temporal trends in PAH concentrations and the toxicity of the samples and identified a subset of PAH analytes that were the most highly correlated with observed toxicity.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

We have several COEC highlights to report from our past year. We have a new COEC Director, Laurel Kincl, as well as a new Outreach and Engagement Coordinator, Isabela Mackey. We have continued to support EHSC scientists and graduate students with web communication technologies. COEC partnered with the Superfund Research Program to develop videos in English, Spanish and Vietnamese for communities affected by the Gulf Coast Oil Spill entitled, "How do Scientists Study Contaminants in the Environments?" and "Contaminants in the Environment: How Can I be Exposed?". These described novel passive sampling devices used by EHSC researchers to measure PAHs in the environment, where such contaminants go in the environment and how communities are exposed to them. Also, we are taking advantage of the new OSU College of Public Health and Human Sciences and having a bilingual coordinator to foster community-based projects with EHSC investigators. COEC is involved in two interdisciplinary pilot projects with EHSC investigators. One project started this year, Environmental Determinants of gains in school readiness for children aged 3-5, is using novel passive sampling devices to measure flame retardants and neurodevelopmental outcomes. This project is working with two communities in Oregon and COEC will support the investigators in reporting out and communication with the families of the study results and implications. Another pilot project that began this past year, Mobile Exposure Device: Tool and Method Development, involves another community in Oregon to develop and test a device that integrates environmental exposure, location and lung function measures. This project is collaborating with an environmental justice group that has studied incidence of self-reported asthma cases in a low-income neighborhood located in an industrial corridor. COEC will work with this community, which has both Spanish- and English-speaking residents, to develop a practical device and a protocol to collect and share the data to be used in future larger studies. Additionally, the COEC has continued to support K-12, community and professional development with ongoing environmental health presentations and activities in the region. Finally, a COEC Stakeholder Advisory Board was assembled to help inform our outreach and engagement activities.

HIGHLIGHTED PUBLICATIONS

Allan SE, Smith BW, Tanguay RL, Anderson KA. Bridging environmental mixtures and toxic effects. *Environ Toxicol Chem.* 2012 Dec;31(12):2877-87. doi: 10.1002/etc.2018. Epub 2012 Nov 7. PMC3502726

Tal TL, Tanguay RL. Non-coding RNAs--novel targets in neurotoxicity. *Neurotoxicology.* 2012 Jun;33(3):530-44. doi: 10.1016/j.neuro.2012.02.013. Epub 2012 Feb 27. PMC3462486.

Franco MC, Ye Y, Refakis CA, Feldman JL, Stokes AL, Basso M, Melero Fernández de Mera RM, Sparrow NA, Calingasan NY, Kiaei M, Rhoads TW, Ma TC, Grumet M, Barnes S, Beal MF, Beckman JS, Mehl R, Estévez AG. Nitration of Hsp90 induces cell death. *Proc Natl Acad Sci U S A.* 2013 Mar 19;110(12):E1102-11. Epub 2013 Mar 4. PMID: 23487751

Kerkvliet, N.I. (2012) TCDD: An environmental immunotoxicant reveals a novel pathway of immunoregulation – a 30-year odyssey. *Toxicol. Pathol.* 40, 138-42. PMID: 22089840

RESEARCH HIGHLIGHT POSTER

Bridging Exposure with Biological Responses and Susceptibility at OSU

Joe Beckman, Kim Anderson, Robert Tanguay

ABSTRACT: Multiple efforts to develop new technologies and core facilities at the OSU EHSC are enabling new approaches to assessing what we are exposed to and what are the potential biological targets. Dr. Anderson has developed "Biological Response Indicator

Devices Gauging Environmental Stressors” (BRIDGES), which is a bioanalytical tool that combines passive sampling in the environment with the embryonic zebrafish developmental toxicity bioassay to provide a quantitative measure of the toxicity of bioavailable complex mixtures for 1,201 chemicals of concern. BRIDGES provides site-specific, temporally resolved information about environmental contaminant mixtures and their toxicity. Multivariate modeling approaches pair chemical and toxicity data sets. As agents of particular are revealed, approaches with zebrafish can probe more deeply into what are the underlying causal mechanism and parallel experiments in mammalian cells and computational modeling are conducted for further validation.

OUTREACH HIGHLIGHT POSTER

Fostering Inter-Disciplinary Research Utilizing Novel Technologies to Empower Communities and Promote Change

Laurel Kincl, Kim Anderson, Naomi Hirsch, Isabela Mackey

ABSTRACT: To foster community engagement in EHSC research, COEC is involved in the pilot project, “Mobile Exposure Device: Tool Method and Development”. An inter-disciplinary team led by EHSC investigator, Kim Anderson, is developing a mobile exposure device (MED) to capture uniquely linked environmental-health information. Three data streams from spirometer measurements, GPS, and a chemical absorbing wristband will be integrated in order to discover statistical relationships among air pollutants, locations, and asthma conditions. COEC’s involvement is to facilitate the development of the MED with input and testing with our community partner, Beyond Toxics, an environmental justice (EJ) organization that recently completed an EJ project partnering with the Centro Latino Americano organization in West Eugene, Oregon, an industrial corridor. Their project found high rates of self-reported asthma related to proximity to point sources of emissions from industries in the area, leading them to our Center and this successful collaboration to develop an MED to help answer their environmental health concerns. The integrated data from the MED and exposure-health outcome relationships will be made available to our partner community through cloud-based data visualization. Our community collaborators will help inform the format and how the visualization is disseminated as well as future studies.

CENTER	Research Center in Environmental Health Science (Rutgers)
LOCATION	Rutgers, Piscataway, NJ
PI	Helmut Zarbl
COEC DIRECTOR	Laura Liang
ADMINISTRATOR	Kimi Nakata
WEB SITE	https://eohsi.rutgers.edu/ceed/ceed

THEME

The mission of CEED is to improve human health by performing translational research using emerging science, engineering, and technology to determine how the total environment, the genome and the epigenome interact to modulate the risk of disease. To achieve this mission, CEED forms a hub of transdisciplinary research that focuses on: 1) Assessing and modeling exposures; 2) Discovering and applying biological response indicators which link exposures to mechanisms of pathogenesis; 3) Developing and implementing targeted prevention, intervention, and treatment strategies; 4) Reducing exposures by influencing public policy, planning and regulation; and 5) Engaging and informing stakeholders.

RECENT SCIENCE HIGHLIGHTS

- New technologies: Shalat developed the Pre-toddler Inhalation Particulate Environmental Robot to mimic child activities while measuring exposures. Mainelis developed bio-aerosol samplers and robotics to characterize nanoparticle exposures from consumer products. With Boise State University, Wiesel developed a battery-operated exposure monitor with telemetry, providing real-time data on meteorological variables, in-home noise, particulate matter, CO and CO₂.
- Effects of air pollution: Zhang, Kipen, Rich, Ohman-Strickland and Lu conducted studies designed to analyze the health effects of drastic reductions in air pollution during the Beijing Olympics. Results showed reductions in biomarkers of oxidative stress, inflammation, and thrombosis.
- Susceptible populations:
 - The Jersey Girl Study, a cohort of pre-pubertal girls examines effects of diet on development and growth. Pilot studies discovered endocrine disrupting effects of mycoestrogens on puberty and body mass (E. Bandera, Buckley, Zarbl).
 - Using Pilot funds, Schwander studied acute effects of diesel PM on the macrophage response to TB. This research led to NIEHS R21 and R01 grants for translational studies of vulnerable populations.
- Transport: Guo identified transporters that control hepatic uptake of polybrominated diphenyl ethers. Aleksunes and Richardson showed that MDR1 limits brain accumulation of paraquat, explaining the association between MDR1 variants, pesticide exposure and Parkinson's disease.
- Cellular injury and inflammation: Vetrano, Weinberger and D. Laskin linked phthalate exposure and inflammation in neonates. NIEHS funded studies are testing the hypothesis that PPAR- γ agonists, ω -3 fatty acids and nitrated fatty acids, can ameliorate toxicity.
- Epigenetic mechanisms: Kong demonstrated epigenetic regulation of Nrf2 signaling, and inhibition of CpG methylation by mixed tocopherols. M. Uzumcu found that developmental exposure to methoxychlor causes epigenetic alterations in ovarian genes.
- Inflammation: D. Laskin, J. Laskin, Gow and Hussain identified distinct subpopulations of activated lung macrophages and showed that these subpopulations release different inflammatory mediators to regulate injury and repair.

- Human studies: Kipen, Fang, and Zarbl conduct an occupationally-based randomized trial w methylselenocysteine to mitigate increased risk of cancer from disruption of circadian rhythm during shift work. Yang completed a phase 0 trial on mixed tocopherols in prostate cancer patients Administered prior to prostatectomy increased blood and prostate levels of tocopherols and metabolites.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

Emergency Response to Hurricane Sandy: CEED investigators immediately became involved in the response to Hurricane Sandy. K. Reuhl and P. Liroy contacted local mayors and legislators with offers of assistance, including discussions regarding immediate responses, and the long-term strategy for clean-up, repair and restoration. CEED joined the NY/NJ consortium of universities (Columbia, Mount Sinai School of Medicine, Hunter College and New York University) to assess local conditions and needs. One of the first joint outreach efforts was the distribution of 18,000 N95 respirators to local community groups involved with the recovery. Simultaneously, A. Gotsch and G. Rhoads used their NIEHS Training Center to develop Webinars on aspects of clean-up hazards and protection for volunteers and workers. B. Buckley, P. Liroy, G. Mainelis, J. Bennett, H. Kipen, M. Gochfeld and J. Burger participated in and assessed the safety clean-up recovery efforts in highly affected communities. CEED members tested homes that had not been cleaned or were in the process of being cleaned for mold growth, bacteria, volatile chemicals, and disinfectant residuals. Recognizing the complexity of the problems and the need for swift action, CEED provided Pilot grants to C. Weisel, S. Shalat and J. Burger for studies on electric generator use, prevalence of respiratory illness, and information sources in communities. CEED is working with the NJ Governor's office and NJDEP on long-term initiatives to minimize residual risks, and improve response planning.

Enhance dialog between stakeholders and CEED researchers: As part of an EPA STAR grant, R. Laumbach, Z. Fan, and Q. Meng conduct studies on asthma exacerbation among children residing near diesel truck routes in the Ironbound Community of Newark, NJ. These communities represent a densely populated urban environment crisscrossed by transportation corridors, and experiencing multiple types of exposure (e.g., air quality, water and soil contaminants, industrial pollutants, noise). With other EPA funding, Z. Fan engaged community groups in Newark to develop citizen science projects. COEC worked with these CEED investigators to align its activities with ongoing environmental research within the Ironbound and South Ward of Newark, Elizabeth and Port Newark communities.

HIGHLIGHTED PUBLICATIONS

Gibson CJ, Hossain M, Richardson JR, Aleksunes LM. Inflammatory Regulation of ABC Efflux Transporter Expression and Function in Microglia. *The Journal of pharmacology and experimental therapeutics*. 2012. Epub 2012/09/04. doi: 10.1124/jpet.112.196543. PMID: 22942241; PMCID: PMC3500534.

Nazarenko Y, Zhen H, Han T, Liroy PJ, Mainelis G. Potential for inhalation exposure to engineered nanoparticles from nanotechnology-based cosmetic powders. *Environmental health perspectives*. 2012;120(6):885-92. Epub 2012/03/08. doi: 10.1289/ehp.1104350. PMID: 22394622; PMCID: PMC3385434.

Rich DQ, Kipen HM, Huang W, Wang G, Wang Y, Zhu P, et al. Association between changes in air pollution levels during the Beijing Olympics and biomarkers of inflammation and thrombosis in healthy young adults. *JAMA : the journal of the American Medical Association*. 2012;307(19):2068-78. Epub 2012/06/06. doi: 10.1001/jama.2012.3488. PMID: 22665106; PMCID: PMCN/A.

Dragomir AC, Sun R, Choi H, Laskin JD, Laskin DL. Role of Galectin-3 in Classical and Alternative Macrophage Activation in the Liver following Acetaminophen Intoxication. *J Immunol*. 2012. Epub 2012/11/24. doi: 10.4049/jimmunol.1201851. PMC3518653

RESEARCH HIGHLIGHT POSTER

Methylselenocysteine Enhances NAD⁺-Dependent Sirt 1 Activity to Reset Epigenetic Regulation of Circadian Gene Expression in Mammary Epithelial Cells Exposed to Carcinogen

Ming Zhu Fang, Guo Wei Len, Christal Lewis, Ben Crabtree and Howard Kipen

ABSTRACT: Our previous studies demonstrated that exposing rats to a carcinogenic dose of N-methyl-N-nitrosourea (NMU) ablates circadian rhythm in mammary cells. We further showed that a chemopreventive regimen of dietary methylselenocysteine (MSC) can reset and enhance the rhythmic expression of core circadian genes and circadian-controlled genes (CCGs). Dietary MSC significantly also restored the intracellular circadian oscillations in the NAD⁺/NADH ratio, resulting in increased NAD⁺-dependent histone deacetylase activity of Sirt1 in the mammary cells in vivo and in vitro. Sirt1 normally counters the histone acetyl transferase activity of the Clock protein to allow normal epigenetic control of circadian gene expression. Restoring circadian oscillations in Sirt1 activity restored cyclical deacetylation and deacetylation of Bmal1 (AcBmal1) and histone 3 Lys 9 (AcH3K9) at E-box motif of Per2 gene promoter, restoring circadian transcriptional of the Per2 gene. Together, these findings suggest that activation of NAD⁺-dependent Sirt1 deacetylase activity by a chemopreventive regimen of MSC restores epigenetic regulation of circadian gene expression in carcinogen-treated mammary epithelial cells. These findings form the basis for an ongoing an occupationally-based randomized trial investigating the ability methylselenocysteine to mitigate the increased risk of cancer breast associated with disruption of circadian rhythm by shift work.

OUTREACH HIGHLIGHT POSTER

Environmental Justice, Emergency Responses, Research Discussions and Summer Research Experiences

Laura E Liang, Joanna Burger, Erin Caswell, Kimi Nakata, Jorge Gutierrez, Lauren M Aleksunes, Debra L Laskin, Zhi Hua Fan, and Robert Laumbach

ABSTRACT: CEED researchers study asthma exacerbation among children residing near diesel truck routes in the Ironbound, South Ward, Elizabeth and Port Newark Communities of NJ. These communities represent a densely populated urban environment crisscrossed by transportation corridors, and experiencing multiple types of exposure (e.g., air quality, water and soil contaminants, industrial pollutants, noise). COEC is working to align its activities with ongoing environmental research within the communities.

CEED/COEC also became immediately involved in the response to Hurricane Sandy to assess local conditions and needs, developing Webinars on clean-up hazards and protection for volunteers and workers. Investigators participated in and assessed the safety clean-up recovery efforts in affected communities and tested homes for mold growth, bacteria, volatile chemicals, and disinfectant residuals. CEED/COEC is working with the NJ Governor's office and NJDEP on long-term initiatives to minimize residual risks, and improve response planning.

COEC also translates the CEED research information into tools and resources for the Community, which is divided into three segments: Research Attentive, Research Interested, and Future Researchers. COEC's goals are to develop partnerships with community stakeholders, translate and disseminate Center research information, enhance dialogue between community stakeholders and Center researchers regarding environmental health issues, and increase awareness and understanding of environmental health research.

SUPPLEMENT PROJECT POSTER

Mechanisms of Response to Diesel Exhaust in Subjects with Asthma

UMDNJ-CEED: Howard Kipen, Robert Laumbach, Andrew Gow: PENN-CEET: Reynold Panettieri

ABSTRACT: Epidemiologic and human experimental studies associate asthma morbidity with exposure to traffic-related air pollution, of which diesel exhaust (DE) is a major component. DE causes respiratory tract inflammation in animals and healthy humans, but surprisingly little evidence of airway inflammation in asthmatics despite reduced lung function. Therefore, current data presents the paradox that DE appears to impair pulmonary function in asthmatics without increasing inflammation. These findings lead us to hypothesize that DE promotes airway inflammatory dysregulation and obstruction in asthmatics dependent on epithelial damage manifested by increases in 20-HETE and 15-HETE as well as proteasome dysregulation. Further, these airway changes will be associated with compromised Surfactant Protein-D (SP-D) function, reducing its normal cytoprotective function in response to oxidative injury. We aim to harmonize human DE exposures between Penn-CEET and EOHSI-CEED, defining the kinetics and response of DE-induced pro-inflammatory airway changes and obstruction in asthmatics. Each center will expose ten asthmatics to DE and clean air using identical protocols; pulmonary function will be measured and airway inflammation will be characterized using EBC and induced sputum. Eicosanoids, prostaglandins, and nitrite/nitrate will be quantified in EBC. Differential cell counts, SP-D modification state, proteasome function, and chemokine/cytokine profiles will be measured in sputa.

CENTER **Research in Environmental Health Sciences (NYU)**
LOCATION New York University, NY, NY
PI Max Costa
COEC DIRECTOR Judy Zelikoff
ADMINISTRATOR Alex Buslovich
WEB SITE <http://environmental-medicine.med.nyu.edu/niehs-center>

THEME: The theme of our NIEHS Center is to understand the environmental causes of diseases by investigating which pollutants, genes, epigenetic programs, and cell signaling pathways influence the processes of disease development. Center members this year have published 226 publications, many of which address the theme and focus of our center. Our Center focuses on several important research areas including early detection and prevention, health effects of metals and particulate matter, and susceptibility to environmental disease. Our Center strives to build upon our mounting strength in epigenetics to focus further on this aspect of our theme. We have recruited new Center members in the area of epigenetics and this field continues to grow in our center. In fact we have added a new Epigenetic core as part of our Molecular core. Despite being new and a spin off from the directors fund for this year the Epigenetics core has seen substantial usage.

RECENT SCIENCE HIGHLIGHTS

Using data from the Health Effects of Arsenic Longitudinal Study (HEALS), an ongoing population-based, prospective cohort study in Bangladesh, Yu Chen and colleagues conducted analyses on the association of arsenic exposure from drinking water and arsenic methylation capacity with preclinical and clinical endpoints of cardiovascular disease (CVD), including risk of fatal and non-fatal heart disease and stroke, carotid intima-media thickness (cIMT), and electrocardiographic abnormality of QT (QTc) prolongation. They found a positive association between baseline drinking well arsenic and risk of fatal and nonfatal CVD, especially heart disease; a positive association between baseline urinary arsenic and cIMT; as well as a dose-response relationship between drinking well arsenic concentration and QTc prolongation.

Drs. Costa and Qu conducted a study funded by NIEHS in a Chinese population to determine whether occupational exposure to Ni was associated with differential gene expression profiles in peripheral blood mononuclear cells (PBMCs) of Ni-refinery workers. There were a total of 2756 differentially expressed genes (DEG) in the Ni-refinery workers relative to the control subjects (FDR adjusted $p < 0.05$) with 770 up-regulated and 1986 down-regulated genes. DNA repair and epigenetic genes were significantly overrepresented ($p < 0.0002$) among the DEG. Of 31 DNA repair genes, 29 were repressed in the high exposure group and two were overexpressed. Of the 16 epigenetic genes, 12 were repressed in the high exposure group and 4 overexpressed.

Drs. Gordon and Chen's NIEHS-supported research project has focused on the role of physical-chemical characteristics of nanoparticles in their interactions with cells and organs after in vivo exposure of mice via inhalation. They have assessed the acute toxicity of cerium, nickel, and silver nanoparticles under 3 different physical-chemical states. Significant dose-dependent increases in PMNs were observed in the lavage fluid of mice exposed to silver and nickel nanoparticles at concentrations of 250, 500, and 1000 $\mu\text{g}/\text{m}^3$. No lung inflammation, however, was observed in mice exposed to cerium nanoparticles, thus suggesting that particle size alone is not responsible for the acute pulmonary effects of inhaled nanoparticles. Importantly, these studies also demonstrated that fresh silver and nickel nanoparticles were more toxic than aged nanoparticles.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

We have undertaken several new initiatives in 2012 while continuing our ongoing Environmental Health Website efforts, high school and undergraduate student research mentoring, and participation as a specialized site for the Center for Talented Youth program that identifies and develops the talents of advanced K-12 learners. In addition, we have continued our participation in environmental health effects education for the Lang Youth Medical Program at NY-Presbyterian Hospital that prepares young adults from underserved NYC communities for careers in biomedical science/medicine.

The NYU COEC has recently established (Nov. 2012) a partnership agreement with the town of Garfield (http://www.garfieldnj.org/filestorage/2548/3131/Partnership_Agreemnent.pdf), to assist community members who may have been exposed to Cr from groundwater contamination resulting from a three-ton discharge in 1983 (from a partially-below ground storage tank) of chromium plating solution containing ~5,400 pounds of chromium from the E.C. Electroplating company. The site (declared a Superfund site by the EPA in 2011) is located in a mixed residential and commercial area with ~700 homes located on the plume area.

The COEC, along with the NYU Center Director Dr. Costa, have begun engaging in community-based participatory environmental research and education activities with the impacted communities. We are providing educational tools to the community. Working closely with Dr. Gany, we have developed/participated in many events with NYC South Asian communities. On October 14, 2012, the NYU COEC and CHI participated in a SAHI-organized Health Fair at the Memorial Sloan Kettering Annual Dewali Mela Festival of Lights in Jackson Heights, NYC. Over 10,000 community members attended the event. The NYU COEC Program Coordinator and CIH staff members took “street side surveys” to gather information from the communities about their awareness of arsenic (As) and its effects on the health of Bangladeshi populations in NYC and the surrounding boroughs. A 4-hr workshop focused on As was held December 1, 2012 at the Memorial Sloan Kettering Rockefeller building where NYU Center members Drs. Costa, Klein, and Zelikoff discussed health impacts, chemoprotection, and As impacts on daily living skills with BAYA-affiliated undergraduates.

HIGHLIGHTED PUBLICATIONS

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Sun H, Shamy M, Kluz T, Munoz AB, Zhong M, Laulicht F, Alghamdi MA, Khoder MI, Chen LC, Costa M. Gene expression profiling and pathway analysis of human bronchial epithelial cells exposed to airborne particulate matter collected from Saudi Arabia. *Toxicology and applied pharmacology*. 2012;265(2):147-57. Epub 2012/10/23. doi: 10.1016/j.taap.2012.10.008. PubMed PMID: 23085030.

Trasande L, Attina TM, Blustein J. Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents. *JAMA - Journal of the American Medical Association*. 2012;308(11):1113-21.

Chen Y, McClintock TR, Segers S, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman M, Hasan R, Sarwar G, Ahsan H. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *International journal of cardiology*. 2012. Epub 2012/05/09. doi: 10.1016/j.ijcard.2012.04.041. PubMed PMID: 22560940

RESEARCH HIGHLIGHT POSTER

Research Highlights - NYU NIEHS Center of Excellence

Costa, M and Gordon, T

ABSTRACT: The broad goals of the NYU NIEHS Center are the identification, evaluation, prevention, and control of the adverse impacts of environmental factors on human health, with strong focuses in the areas of ambient air pollution effects, environmental and occupational exposures to heavy metals, and the roles of dietary factors in the causation and prevention of human cancer and disease. Further, the Center reaches out to the community (local and regional) providing assistance, information, and education on environmental issues, and training graduate and medical students for productive careers in research, teaching, and other professional services. The Center also guides its members into new research areas of interest to the NIEHS involving modern technology or research areas that are timely and may have significant environmental impact (e.g., our rapid response to the WTC disaster; currently, we have recruited cohorts from those exposed to WTC dust for long term disease follow up). The Center supports investigator-initiated pilot projects, as well as encourages initiatives via RFPs in new areas that the Center and NIEHS deem important for future studies of the impacts of the environment on human health and disease. The NYU NIEHS Center is a highly interdisciplinary research organization that has successfully applied a wide range of research talents and perspectives to the studies of environmental health issues. Because of its scope, the Center has created opportunities for collaborative and multidisciplinary research across diverse program areas, such as epidemiology with molecular biology, and human exposure assessment with basic toxicology, as well as integrating molecular biology into all aspects of toxicology.

OUTREACH HIGHLIGHT POSTER

New York University environmental health community-university partnership: Translation and Dissemination of EHS Center Science on metal and air particulate pollution.

Judith T. Zelikoff, Francesca Gany, Pavan Gill, Shannon Doherty NYU School of Medicine, Department of Environmental Medicine, Tuxedo, NY 10987, Immigrant Health and Cancer Disparities Service, Memorial Sloan-Kettering Cancer Center, 300 E. 66th Street, NY, NY 10065

ABSTRACT: NYU COEC continues addressing public knowledge gaps about Environmental Health science to communities and policy makers, educational programs to underserved minorities, Web-based Environmental Health education, and assistance to communities facing environmental adversities. A primary community-based initiative targets Garfield, NJ which is concerned with exposure to hexavalent chromium Cr(VI) resulting from an underground electroplating tank discharge of 3 tons of chromic acid in 1983 into the groundwater. In 1993, Cr(VI) levels up to 2,640,000 μ g/m² were measured in dust wipe samples in basements near the Garfield plant. The plume, placing more than 3,500 people at potential risk for Cr exposure, impacts over 600 homes. As the site has only partially been remediated, residents remain concerned 30 years later about health implications from possible Cr(VI) exposure from this recently-declared Superfund site. This COEC partners with Garfield leaders to carry out Focus Groups/Town Hall meetings on this issue. Toenail clippings/blood samples from adult volunteers living on/near the contaminated plume will be tested to assess Cr burdens. Another community-based COEC initiative (with Memorial Sloan Kettering Immigrant Health Service) is to measure in-vehicle levels of ambient particulate matter (PM) to which South Asian taxi drivers are exposed and provide PM Center-generated science in Town Hall meetings.

CENTER	Southwest Environmental Health Sciences Center (UA)
LOCATION	University of Arizona, Tucson, AZ
PI	Serrine S Lau
COEC DIRECTOR	Marti Lindsey
ADMINISTRATOR	Susanna Herndon
WEB SITE	https://swehsc.pharmacy.arizona.edu/
THEME	The mission of SWEHSC is to understand the mechanisms behind the modulation of human disease risk by environmental exposures.

RECENT SCIENCE HIGHLIGHTS

The mission of SWEHSC is to understand the mechanisms behind the modulation of human disease risk by environmental exposures. Our long-term goal is to bring an improvement to the lives of the people of the Southwest by developing rational approaches to mitigating their risks of hazardous environmental exposures and by maximizing their protective environmental exposures. Leaders have been charged with developing interdisciplinary groups aimed at integrating investigators with diverse expertise to produce environmental health deliverables through the incorporation of key elements of our philosophy for environmental health science, including (i) a human/translational focus, (ii) defining protective as well as harmful environmental exposures, (iii) viewing environmental problems through an international perspective, and (iv) utilizing cutting edge technology to enable systems-level biological analysis. Research Focus Group (RFG) 1 emphasizes studies on hazardous environmental exposures pertinent to populations/communities of the arid southwestern United States, with significant representation of Caucasian, Hispanic and Native American ancestries (e.g. indigenous American populations that include a spectrum of genetic and cultural admixture with non-indigenous peoples). RFG1 Members focus on the molecular mechanisms by which chemicals initiate cell/tissue injury and disease. Cutting edge technology is being employed to query the role of epigenetics in the response to chemical exposure. RFG1 members are also engaging in population-based studies that incorporate exposure assessment as an important component of study design. A second theme is environmental lung diseases. RFG2 members are interested in determining the adverse effects of inhaled dusts and dusts components that would be encountered in the desert Southwest. Investigators are determining levels of exposure and correlating the exposures with adverse pulmonary outcomes, such as asthma or chronic obstructive pulmonary disease. The third theme focuses on the specific role of reactive oxygen species (ROS) in disease initiation and progression, and how this knowledge can be used to prevent disease. RFG3 members promote research into the mechanisms by which various environmental factors (UV light, ROS-generating chemicals, etc.) interact with combinations of genes to produce adverse health effects. An emphasis on UV exposure is particularly relevant to the desert southwest, with Arizona suffering from the highest incidence of skin cancer in the USA.

RECENT OUTREACH & PUBLIC ENGAGEMENT HIGHLIGHTS

The Southwest Environmental Health Sciences Center (SWEHSC) Community Outreach and Education Core (COEC) chose Youth and American Indian communities as foci, with the goal of improving environmental health literacy among all participants of COEC activities.

August 2012 the SWEHSC COEC was awarded a supplement, Inter Center Pilot Project: "Defining Environmental Health Literacy" to conduct a grounded theory investigation to produce a consensus definition of environmental health literacy. Interviews are underway

and coding is an ongoing process.

The COEC Director presented professional development sessions to the Inter Tribal Council of Arizona (ITCA) American Indian Environmental Managers:

- Spring 2012: “Pharmaceutical and Hazardous Waste – What is Risk?”, “Haboob (Severe Dust Storms) & Health, and “Risk Communication”
- Fall 2012: “Important EH Topics in Tribal Communities in Arizona”
The COEC was invited to partner with the Institute for Tribal Environmental Professionals on issues of Asthma and Indoor Air Quality.

Paramount among SWEHSC COEC activities is the KEYS Summer High School Student Research Internship. In 2012 thirty-six interns successfully presented research posters. Forty-eight interns are accepted for summer 2013. They learn about asthma and toxicology from readings, lectures and experiments. Most SWEHSC members host interns each summer.

The COEC conducted three summer youth programs for tribal communities in 2012: “Toxicology Testing with California Blackworms” and “UV light protection experiment” at the request of environmental managers from Tohono O’odham Nation (TON) and the Arizona Area Health Education Center (AHEC) Program coordinator for the Pascua Yaqui Nation. In addition fifteen White River Indian Community children came to Tucson to participate in the UV light protection experiment and take a tour of a SWEHSC lab.

ITCA, TON and the COEC director are submitting an RO1 in response to PAR-11-346-Interventions for Health Promotion and Disease Prevention in Native American Populations for submission in May 2013. The collaboration submitted a UA Community Connections grant to support training for SWEHSC investigators on community research projects in American Indian communities, a conference for tribal leaders and members concerning arsenic contamination, UV exposure, and the health effects of environmental dust / pollution exposure, and follow up outreach activities.

HIGHLIGHTED PUBLICATIONS

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Severson, P.; Tokar, E.; Vrba, L.; Waalkes, M.; and Futscher, B.W., Agglomerates of aberrant DNA methylation are associated with toxicant induced malignant transformation. *Epigenetics*, 2012. 7: 1238-1248. PMID: 22976526; PMCID: PMC3499325

RESEARCH HIGHLIGHT POSTER

XBP1, SYVN1 and NRF2: At the crossroads of ER stress and oxidative stress

Tongde Wu and Donna D. Zhang.

ABSTRACT: The transcription factor Nrf2 is well known as the master regulator of intracellular redox homeostasis. As an adaptive response to oxidative stress, Nrf2 activates

the transcription of a battery of genes encoding antioxidant proteins, detoxification enzymes and xenobiotic transporters by binding to the cis-antioxidant response elements in the promoter region of these genes. Previous studies done by our lab and others have demonstrated that Nrf2 is subject to poly-ubiquitin-mediated proteasomal degradation by Keap1 in a redox-sensitive manner through modifications of cysteine residues in Keap1. In this study, we report that the active form of XBP1, XBP1s suppresses Nrf2 and its downstream signals under ER stress conditions, through transcriptional activation of synovial apoptosis inhibitor 1 (SYVN1). We have determined that SYVN1 directly interacts with the Neh4 and Neh5 domain within Nrf2. SYVN1 functions as an E3 ubiquitin ligase that accelerates the clearance of Nrf2 protein by promoting ubiquitination of Nrf2. Overexpression of SYVN1 attenuates Nrf2 signaling, whereas knockdown of SYVN1 enhances expression of Nrf2 and its downstream genes. Furthermore, in patient samples with end stage alcoholic liver cirrhosis, where XBP1s and SYVN1 are upregulated, Nrf2 is significantly reduced, demonstrating the pathological relevance of the negative regulation of Nrf2 by XBP1s/SYVN1 in liver damage.

OUTREACH HIGHLIGHT POSTER

Responding to Community Needs: Outreach Programs and Activities to Engage Specific Audiences and Address Community Questions

Marti Lindsey, PhD

ABSTRACT: According to the Arizona State & County QuickFacts, 5% of the US population is American Indian and 30% Hispanic. These populations are mostly of lower socio-economic status and experience disproportionate hazardous environmental exposures. These populations represent at-risk targeted groups typical of the southwestern United States. Moreover, their exposure to ultraviolet light, dust-borne airborne contaminants, contaminated water, and poor nutrition all represent areas of active research of Southwest Environmental Health Sciences Center (SWEHSC) members. The Community Outreach and Education Core (COEC) has worked with these Arizona Tribal communities for ten years, progressively gaining acceptance for the SWEHSC and developing a reputation as a trusted resource and partner for environmental health information and issues, presenting bi-annually at the environmental managers meetings and doing public presentations at community requests.

According to the Nation's Report Card, Arizona students have significantly lower scores on Science assessments and did not make significant improvements between 2009 and 2011. Since 1997, School administrators and secondary science teachers have depended upon SWEHSC investigators and the COEC for teacher education and the KEYS high school student summer research internships. The Health Literacy – Service Learning course Lindsey teaches provides avenues of science education to elementary students, using the ToxRAP curricula.

SUPPLEMENT PROJECT POSTER

Defining Environmental Health Literacy – Arizona1 & Rochester2

Chen, S.2, Lindsey, M.1, Valdez, MV1, Velez, MD2

ABSTRACT: The focus on the consequences of poor health literacy has spawned interest in specific content areas of health. The content knowledge required to navigate cancer versus diabetes is likely to be very different, and the skills associated with managing a chronic disease versus a single treatment are likely to be different as well. As providers of environmental health information and services who have first-hand experience with the difficulties of risk communication and interpretation, we are interested in the unique content and skills associated with processing environmental health hazards. What makes someone “environmentally health literate?” We seek to answer this question by actively seeking the input of diverse groups and identifying areas of consensus and negotiating differences. We

will use areas of agreement to develop a definition of EHL and compare it to how different at-risk groups process environmental information. This will set the stage for further research that includes developing comprehensive measures, identifying the consequences of low versus high EHL, and implementing methods of improving EHL.

OTHER POSTERS

Partnerships for Environmental Health Resource Center: Connect & Share

Liam O'Fallon and Justin Crane

ABSTRACT: Through the Partnerships for Environmental Public Health (PEPH) program, the NIEHS has supported the PEPH Resource Center (<https://connect.niehs.nih.gov/peph/index.cfm>) to foster sharing and exchange of materials created by NIEHS grantees and community partners that are part of the PEPH network. A goal of the Resource Center has been to reduce the duplication of efforts, promote interactions, and stimulate the advancement of new communication strategies. As a tool for grantees and their partners, the PEPH Resource Center facilitates entry, management, viewing, and publishing of educational and outreach materials.

This poster highlights the “Connect” and “Share” aspects of the Resource Center and emphasizes user benefits. Over the past year, we have made exciting changes to the Resource Center based on user feedback. These enhancements include:

- Grantee user profiles
- “Trending Topics/Materials” on the Resource Center homepage
- Comment functions that allow users to give and receive peer-feedback on published materials
- A Resource Center users listserv

These social media-like enhancements should increase the ability of PEPH grantees and community partners to share, connect, and collaborate, so that the PEPH network can increase the impact of environmental public health research.

Center for Child Environmental Health Risks Research

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ABSTRACT: The Center for Child Environmental Health Risks Research (CHC) was formed to learn more about children's susceptibility to pesticides and the way pesticides affect normal development and learning. The CHC brings together a multi-disciplinary team of experts from within the University of Washington and the Fred Hutchinson Cancer Research Institute whose goals is to protect children's health, with specific objectives to: (1) identify cellular, biochemical and molecular mechanisms for the adverse developmental neurotoxicity of pesticides; (2) identify susceptibility factors for developmental neurotoxicity of pesticides; (3) improve our understanding of critical pathways of pesticide exposure for children; (4) intervene to reduce children's exposure to pesticides; and (5) provide core support for the development and application of risk assessment methods. This will enable basic research on pesticide toxicity and exposure to inform risk decisions to protect children's health from pesticides; and (6) foster partnerships between academic researchers and the community in which information requested by the community and basic research questions are translated into studies that address the needs of both.

Pacific Northwest Center for the National Children's Study

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ABSTRACT: The National Children's Study is a multi-year research study that examines the effects of environmental influences on the health and development of more than 100,000 children across the United States, following them from before birth until age 21, with the goal of improving the health and well-being of children. The Pacific Northwest Center for the National Children's Study (PNWNCS) is a regional collaborative response to this call to push our understanding of children's health into the 21st century. The NCS serves as a Vanguard for recruitment of a mother-child cohort in Grant County and has established infrastructure for recruitment in King County. The Grant County NCS is a diverse, rural density region that employs an Enhanced Household-Based Recruitment (EHBR) strategy to enroll participants. The National Children's Study has initiated several formative research projects that are limited in scope and duration and are intended to augment and inform the main Study to address specific technical questions and provide information about scalability, acceptability, and feasibility. The PNWNCS has developed a large team working on genomic research development of biomarker and exposure measurements, iPad-based information programs and neurobehavioral endpoints for longitudinal studies.

Pacific Northwest Center for Human Health and Ocean Studies

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ABSTRACT: The University of Washington's Pacific Northwest Center for Human Health and Ocean Studies (the Center) was created in response to the critical need to understand links between ocean processes and human health. It is jointly funded by the National Science Foundation (NSF) and the National Institutes of Environmental Health Sciences. The focus of the Center is on mechanisms that underlie development of toxic blooms of the diatom *Pseudo-nitzschia* and the public health consequences of toxic events. Domoic acid (DA) is produced by *Pseudo-nitzschia*. Consuming fish (finfish or shellfish) contaminated with DA can cause amnesic shellfish poisoning. The Center brings together researchers from 5 different departments within the University of Washington with expertise in fisheries and biological, chemical and physical oceanography to work with researchers with expertise in molecular and cellular mechanisms of toxicity, neurodevelopmental biology, behavior and risk assessment. Research is coordinated across this multi-disciplinary group through the concept of a "risk chain" illustrating the ways that ocean processes influence toxic algal blooms and how these blooms cause public health impacts and risks. Center researchers

foster the development of a next-generation of oceans and human health researchers by supervising early-career scientists consisting of post-doctoral researchers, graduate students, undergraduates, and research scientists.

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