

FEATURED ACTIVITIES of DERT
February 2010

MEETINGS

Asbestos: A Science-Based Examination of the Mode of Action of Asbestos and Related Mineral Fibers

December 16-17, 2009
Chapel Hill, North Carolina

Key questions still remain to be answered in understanding asbestos-induced health effects, particularly related to the mode of action of asbestos. The mode of action encompasses processes of fiber dosimetry and target tissue responses as key events leading to disease. There is a critical need to better define the fiber characteristics that dictate dosimetry and lead to toxicity and potential adverse human health outcomes and to understand the modes/mechanism of actions of these asbestos-like fibers in order to make better informed risk assessment and regulatory decisions. The workshop held in Chapel Hill brought together NIEHS scientists, federal partners, representatives from industry, and members of the academic community to discuss the state of the science on asbestos and develop recommendations for future work.

Prior to the workshop six teams of experts developed background documents focused on several aspects of asbestos toxicity including pulmonary toxicology, pleural toxicology, non-pulmonary toxicology, role of mutagenicity in fiber-induced carcinogenicity, factors that impact susceptibility and extrapolation of environmental exposure levels. The charge to the six working groups was to develop consensus statements based on the strength of the published data on asbestos and related mineral fibers as to levels of confidence. The statements are:

- Based on existing evidence we are confident of the following....
- We consider the following to be likely but require confirmation....
- Research on asbestos and related mineral fibers suggests several broad themes which we believe should be pursued on future investigations and include...

Following plenary presentation of key findings, workshop participants met in four interdisciplinary groups to address confidence areas, data gaps, and research needs for five over-arching questions that included:

1. What are the physico-chemical attributes (mineralogy, morphology, dimension) contributing to target organ deposition/clearance/response (durability, biopersistence and bioreactivity)?
2. Do mode of action/mechanisms findings from *in vitro* studies operate *in vivo* in laboratory animals?
3. What is known about the direct and indirect mutagenicity of the various asbestos fiber types?
4. What mechanistic studies *in vivo* or *in vitro* best bridge to current clinical outcome measures?
5. There is limited information on exposures in potentially susceptible populations (children, women, elderly, sick, etc). Would you expect there to be a dosimetry difference or susceptibility issue in any of these groups?

There was a considerable amount of discussion and debate during this meeting. Over the two days the working teams identified many data gaps and needs as well that may be useful in formulating future research directions. A few examples of research recommendations and needs that were identified during the workshop include:

- A unanimous call for graduate students to be trained in interdisciplinary research methods to interact with scientists from a wide range of disciplines.
- A need for studies to be conducted at ever-lower doses.

- Investigate health endpoints beyond heart and lung effects.
- Develop standardized well characterized fibers (types and sizes) for research studies and when possible should be representative of past and current occupational and environmental exposures where there is epidemiological information.
- Develop short-term testing strategies to assess potential carcinogenicity of well-characterized mineral fiber preparations and engineered nanomaterials.
- Determine how mineral fibers interact with target cells in the pleura at multiple stages during the development of mineral fiber-induced malignant mesothelioma (MM).
- Explore the mechanistic links between chronic inflammation and development of mineral fiber-induced MM.
- Create multi-center collaborations, with databank and bioinformatic support, to identify genetic risk factors connected with familial and sporadic MM and other asbestos-related diseases.
- Genetic murine models of susceptibility are needed to better understand risk of asbestos-induced lung cancer and MM.
- More precise descriptions of the effect of different types of asbestos on fiber loading in the lung as related to the development of lung cancer and fibrosis need to be based on comprehensive dose-response inhalation studies including low-level exposures and an appropriate index of fiber dose (surface area, numbers).
- Validate individual in vitro tests with results in inhalation assays in order to develop assays to test the potential health hazards of new fibers in the environment or fibers/fragments of certain dimensions.

Following the conclusion of the two day meeting, six documents that provide the state of the science in the six topic areas will be finalized for publication. In addition, the results of the breakout sessions will be compiled and drafted into a consensus statement that reflects the views of the entire workshop. This document is in preparation and will be submitted for publication.

Priorities for NIH Research on Climate Change and Health Workshop

December 9-10, 2009

Bethesda, Maryland

The National Institute of Environmental Health Sciences (NIEHS) and Fogarty International Center (FIC), with input from several other NIH Institutes and Centers, recently co-sponsored a workshop to help develop Priorities for NIH Research on Climate Change and Health. The meeting was held on the NIH main campus at the Lawton Chiles International House. Approximately 60 individuals attended the meeting, including several invited speakers from the NIH extramural research portfolio, members of the trans-NIH Climate and Health working group, and representatives from sister federal agencies.

The workshop brought together leading investigators in the field of climate and health and elicit their ideas on specific scientific opportunities and public health needs in this area. The first day of the workshop consisted of several presentations by invited speakers that were focused on three topics of scientific opportunity: exposure response studies, projecting future disease burden, and research and training toward public health and medical intervention. The second day of the workshop was open only to NIH staff to discuss the ideas and opportunities presented during the previous day and how these could be addressed in our future research and training programs.

A number of themes were identified based upon speaker presentations, including the need for:

- Research on potential co-benefits of climate change mitigation and adaptation strategies.
- Additional empirical research on mechanisms by which climate parameters may impact human health.
- Downscaled climate models for use in health impact studies to better understand health responses. and identify/prioritize potential climate-health risks at a local level.
- Improved data and methods for vulnerability mapping and health impacts surveillance.

- Improved understanding of how climate change and health will impact fundamental public health and healthcare systems.
- Development of risk communication methods for all relevant audiences (policymakers, community members, etc.).

Specific action items for the trans-NIH Climate and Health working group moving forward include:

1. Raise visibility both within NIH and the extramural community. A one-page meeting summary of workshop findings will be drafted for distribution within NIH. The group will also look for opportunities to publish workshop findings in a scientific journal and possibly host a larger public meeting on climate change and health in summer 2010.
2. Facilitate funding opportunities. Working group members will identify existing NIH initiatives to which additional language could be added to encourage more climate change relevant research within these programs and consolidate such opportunities on a webpage. The group will also create a list of potential reviewers with expertise in climate and health for the NIH Center for Scientific Review to help facilitate peer-review of unsolicited grant applications.

Roundtable: Risk Communication and Environmental Public Health

December 8, 2009

Society for Risk Analysis

Baltimore, Maryland

Purpose: The goal of the roundtable was to identify current risk communication issues of importance to NIEHS and to ascertain the best opportunities to engage in advancing theory, methods and practice of risk communication. NIEHS has a long history of promoting partnerships among diverse groups, using myriad communication strategies, to increase awareness of environmental health concepts and to engage community participation in research. Within the Partnerships for Environmental Public Health (PEPH) program, NIEHS is interested in examining the process and impact of risk communication as it relates to environmental health concepts. Approximately 15 people participated in the roundtable which was hosted by *Mr. Liam O'Fallon, SPHB, and Ms. Beth Anderson, CRIS/SRP.*

Key Recommendations:

1. Learning from the past.
 - a. Host a meeting with leaders in the field. Participants agreed that there has been a failure to learn from the past. The best way for NIEHS to engage in the risk communication discussion, would be to partner with SRA and other professional organizations in risk analysis or evaluation.
 - b. Support a meta-synthesis of previous work. Participants stated that a compilation of case studies would be a valuable contribution to the field.
2. Advance research on risk communication in the face of uncertainty.
3. Support evaluation of risk communication. Participants agreed that evaluation is a big gap in risk communication and cannot be added on to the end of a project.

Key Themes:

General Concepts

1. Behavior change/informed decision making – do we really want behavior change or is informed decision making sufficient?
2. Precaution – context of uncertainty
3. Commonality of metrics
4. Definition of 'Risk Communication' – more of a way of thinking. The group discussed this issue briefly acknowledging that there are so many components to Risk Communication that it may be very difficult to actually come up with one definition that all could agree to.

Practice

5. Know your audience – different communication approaches with different impacts
6. Systems approaches to risk communication. Food safety as an example.
7. Ethics of communication
8. Risk communication to vulnerable populations
9. Analysis of where people go for information

Audience

10. Digital message – track what people are talking about. Use visualization. Dynamics of messages. Participants noted that now with the dissemination of health messages via the web and other electronic media, that once the message is out, it is difficult to control the message and know how it is exactly being used.
11. Attenuation threshold – understanding how much information people can handle on a given topic before your message is weakened.
12. Vocabulary and scientific understanding. Need to examine understanding of what was said/communicated. Need to consider the culture of the community and its understanding of the issues.

Potential Partners: Industry (do a lot to minimize risk), USDA, non-profits, other societies

Next Steps

There was considerable excitement by roundtable participants about the fact that NIEHS had organized this session at the Society for Risk Assessment annual meeting. This roundtable session provided us with good information in terms of how best to engage in risk communication research. The recommendations and key themes fit nicely within the model and vision of the PEPH program. Based on the outcomes of this roundtable, we anticipate hosting a longer, more in-depth discussion with leaders in risk communication research to identify the best opportunities for NIEHS to become involved in risk communication research.

Prenatal Programming and Toxicology II (ppTOX-II)

Role of Environmental Stressors in the Developmental Origins of Disease

December 7-10, 2009

Miami, Florida

Background: An international conference on “Prenatal Programming and Toxicology II (PPTOX II): Role of Environmental Stressors in the Developmental Origins of Disease” was held December 7-10. This conference was a follow up to PPTOX I which was held in Torshavn, Faroe Islands in 2007. Over 280 scientists, including more than 75 students and postdocs, from around the world gathered in Miami South Beach to present both animal and human data supporting the hypothesis that environmental exposures during development lead to altered programming which results in increased susceptibility to disease/dysfunction later in life. The conference had broad national/international support from a number of agencies including the World Health Organization, NIEHS, Food and Drug Administration/National Center for Toxicological Research, Centers for Disease Control, Agency for Toxic Substances and Disease Registry (ATSDR), National Institute of Child Health and Human Development, U.S. Environmental Protection Agency (EPA), National Cancer Institute, Superfund Research Program, National Center for Environmental Studies, European Environment Agency and the International Union of Toxicology. NIEHS was the major contributor to the meeting both in terms of funds and program development.

The meeting started with overviews of the developmental origins of disease hypothesis focusing on altered nutrition and exposures to environmental chemicals in humans and animal models followed by an examination of this hypothesis in the ecological developmental biology field. Overviews of animal models and epigenetics as the underlying mechanism of the altered programming concluded the first night activities. The hypothesis was then examined in more detail in sessions that focused on both the human and animal data linking developmental exposures to environmental chemicals to various cancers, reproductive diseases, immune dysfunction and diseases, metabolic syndrome, neurobehavioral deficits

and abnormalities and transgenerational effects. In addition, there were discussions on National Children's Studies, Clinical and Industry Perspectives, and Regulatory Challenges and Approaches. The session on regulatory challenges focused on the fact that current regulatory protocols and risk assessment methods are poorly equipped to consider latent health impacts of early exposures especially if they cross generations. Two poster sessions highlighted over 120 abstracts including those of the 38 student travel awardees.

Outcomes: The conference identified numerous data gaps, obstacles and challenges including the need for more collaboration between animal researchers, epidemiologists and clinicians, the need for more mechanistic studies showing not just correlations but actual causation, improved exposure measurements in human studies and animal models, the development of banked biospecimens to link developmental exposures to diseases later in life and the study of mixtures and multiple exposures across the lifespan. The presentations will be published in Toxicological Sciences, Reproductive Toxicology and the Journal of Developmental Origins of Disease.

Dr. Jerrold Heindel, COSPB, was the originator and the chair of the organizing committee for PPTOX II: Role of Environmental Stressors in the Developmental Origins of Disease. Dr. Gwen Collman, Interim Director, DERT/OD gave a keynote address, "Developmental basis of disease: environmental impacts." Drs. Les Reinlib and Kimberly Gray, SPHB, Cindy Lawler, Lisa Chadwick, Michael Humble, Annette Kirshner, COSPB, and J. Patrick Mastin, OD, also attended the meeting.

Sixth Annual Early Environmental Exposures Meeting

November 19-20, 2009
Sausalito, California

Background: The Breast Cancer and the Environment Research Centers (BCERC) Network originated in September 2003 in response to a congressional mandate with support from both the breast cancer advocacy and research communities. This seven-year program aims to advance the understanding of environmental factors that influence mammary gland architecture and the entry and progression through female puberty. The studies are conducted by four collaborating centers at Fox Chase Cancer Center (Dr. Jose Russo); University of California, San Francisco (Dr. Robert Hiatt), University of Cincinnati (Robert Bornschein), and Michigan State University (Dr. Sandra Haslam).

Objectives: The BCERC Network is pursuing epidemiological and biological studies investigating the influence of Early Environmental Exposures on pubertal maturation, mammary gland development, and the potential of these exposures to alter the risk of breast cancer later in life. The latest scientific findings from the BCERC were presented along with results from investigations in other studies in the field. The content of the meeting included basic biology of breast development, environmental exposures that influence puberty, breast development and future breast cancer risks, and public health communication of the risks associated with these exposures.

Highlights and Recommendations: This year's annual scientific meeting focused on the integration of laboratory-based biology and epidemiology studies in research programs while continuing to assimilate community participation and advocacy concerns through panel discussions, a Mentoring Session, a poster session, and "Lunch with the Experts", an opportunity for attendees to share their thoughts over lunch with speakers and investigators. Research updates from the members of the BCERC Network, as well as platform presentations from invited speakers provided thoughtful perspectives to the participants on studies related to mammary gland biology, puberty, and breast cancer as well as the action of environmental chemicals and diet on the developing breast. In addition to the well received scientific sessions, this year's meeting included sessions on Translation and Dissemination and Public Health and Policy Implications. Speakers included Jared Huffman, Assembly Member from California's 6th State Assembly District, speaking on California's Green Chemistry Initiative, and Dr. Kenneth Olden, former

Director, NIEHS, speaking on the topic of the Health Care Delivery System in the United States: Failure in Translation.

Opening remarks were provided by *Dr. Gwen Collman, Interim Director, DERT*, followed by the keynote address “Halogenated Flame Retardants: Does the Benefit Justify the Risk?” by Dr. Linda Birnbaum, Director, NIEHS. Dr. Collman hosted one of the “Lunch with the Expert” tables with Dale Eastman, former NAEHS Council member, to discuss the Breast Cancer and the Environment Research Act.

The NIEHS, NCI, and Avon Foundation were able to provide partial travel support for a number of advocates and young scholars. The symposium was videotaped and will be made available to the public through the BCERC web-site in the near future. *Drs. Caroline Dilworth, Elizabeth Maull, and Les Reinlib, SPHB*, oversaw the organization of the meeting and contributed to planning the scientific sessions.

Roadmap Epigenomics Program Investigators’ Meeting

November 5–6, 2009

Bethesda, Maryland

Introduction/Background: Epigenetics is an emerging frontier of science that involves the study of changes in gene regulation and expression that are not dependent on gene sequence. For purposes of this program, epigenetics refers to both heritable changes in gene activity and expression (in the progeny of cells or of individuals) and also stable, long-term alterations in the transcriptional potential of a cell that are not necessarily heritable. While epigenetics refers to the study of single genes or sets of genes, epigenomics refers to more global analyses of epigenetic changes across the entire genome. The NIH Roadmap Epigenomics Program established five interactive programs in 2008: the Reference Epigenome Mapping Centers (REMCs); the Epigenomics Data Analysis and Coordinating Center (EDACC); the Technology Development in Epigenomics Initiative; the Discovery of Novel Epigenetic Marks in Mammalian Cells Program; and the Epigenomics of Human Health and Disease Initiative. This grantee meeting was the first of five annual meetings scheduled to accomplish the following goals: 1) exchange information about all of the individual projects across the five programs; 2) to encourage and foster collaboration; and 3) to develop plans to maximize utility of the consortium component to the human health and disease component.

Meeting Highlights: The mapping centers discussed the progress made by the individual components of the REMCs, including the first complete mapping of two human methylomes. The EDACC provided a presentation that outlined how data will be verified before submission to the National Center for Biotechnology Information (NCBI). NCBI serves as the public interface for the REMC data and NCBI staff demonstrated how data can be accessed by the public as well as informing what data had been publicly released from the REMCs. Four presentations from the Novel Marks Program highlighted the following: the epigenetics of human centromere formation; identification, validation, and initial characterization of lysine propionylation and lysine butyrylation in histones; discovery of epigenetic marks in human cells by high throughput siRNA screening; and the identification and characterization of novel epigenetic marks of non-histone proteins. Four presentations highlighted the following aspects of the Technology Development program: kinetics of nucleosome turnover in the drosophila genome revealed through metabolic labeling of histones; role of protein lysine methylation signaling in health and disease; targeted bisulphite sequencing of CpG islands; and epigenomic analysis on a nanoscale device. The fourth session of the meeting featured brief introductions by the 22 PIs of the newly awarded Epigenomics of Human Health and Disease grants. Input from the REMCs External Science Panel (ESP) members helped focus the rest of the meeting on how to develop greater utility from the resources developed by the REMC component. The meeting consisted of 20 speakers, 22 informal introductions and approximately 30 poster presentations. The meeting was attended by 170.

Outcomes/Recommendations: Several collaborative relationships were initiated between members of the 5 NIH Roadmap Epigenomics programs. Additionally, the need for an interactive web-based tool to facilitate interactions between the groups was identified, with the REMCs taking the lead on its development. Additionally, a need was identified to develop a protocol for prioritizing cells/tissues to be mapped by the REMCs that would allow for better integration of the REMCs with the Epigenomics of Human Health and Disease grantees.

Dr. Tyson, COSPB, chaired the planning committee that organized the meeting. *Dr. Tyson* moderated the opening session of the meeting devoted to providing research highlights and objectives of the REMCs, the function and accomplishments of the EDACC and the role of the NCBI in making the data generated by the centers available to the community. *Dr. Lisa Chadwick, COSPB*, moderated a session and was on the planning committee; *Dr. Kim McAllister, SPHB*, was a co-moderator for steering committee meeting; *Ms. Astrid Haugen, COSPB*, served on the planning committee, worked on the developing the agenda and worked as the primary contact for the meeting contractor; *Dr. Pat Mastin, OD*, served on planning committee and gave an overview of evaluation program and led panel discussion; and *Dr. Christie Drew, PAB*, was involved in detailed evaluation process of the program.

Superfund Research Program Annual Meeting

November 2 – 5, 2009

New York City, New York

Over 300 Superfund partners, grantees, researchers, post-doctoral fellows, and graduate students gathered for the NIEHS Superfund Research and Training Program annual meeting, at Columbia University in New York, New York. The theme of this meeting was "Emerging Issues, Emerging Progress".

The overall goals of the meeting were to discuss the emerging environmental health issues and to identify emerging technologies and their applications to understanding and mitigating the risks of hazardous waste sites. Together, these advances will facilitate more accurate assessments of exposure and human health risks to Superfund chemicals. A key aspect of the meeting was the application of these research developments to the evaluation of real-world issues, sites, and situations. Four plenary sessions highlighted student and researcher/post-doc advances in environmental health. Presentations focused on research advances in fate, transport and remediation; emerging research methodologies; toxic effects of Superfund chemicals; and exposure, risk, and epidemiology.

Two keynote speakers were featured at the meeting. On Tuesday, *Dr. Stephen Safe*, Texas A&M University, shared the late *Dr. K.C. Donnelly's* scientific career and achievements with meeting attendees. *Dr. Donnelly's* involvement in the SRP and his interest and concern for people and public health issues will have a lasting impact on his colleagues, friends, and family. On Wednesday, *George Pavlou*, Acting Regional Administrator of Region 2 of the U.S. Environmental Protection Agency (EPA), gave a summary of the recent work and advances in the Hudson River Superfund site. *Mr. Pavlou's* presentation, "Update on the Hudson River Remediation," included photos of the cleanup effort and outlined several remediation tactics under consideration by the EPA.

A workshop on Research Translation was conducted on Thursday. The theme centered on forming partnerships and sharing innovative approaches for outreach. In the workshop, attendees noted that we should expand our partnerships with other organizations that have inroads with our intended audience to reinforce credibility. SRP should also identify the needs of stakeholders like EPA and ATSDR, and then identify points of contact for those things. Another recommendation was that SRP form "translation clusters" or forums specifically focused on ecological risk, biomarkers, and human risk exposure models.

The clusters would serve to start collaborative efforts among grantees, partners, and stakeholders. Finally, it was recommended that SRP establish a K.C. Donnelly team award for collaboration.

Concurrent to the Research Translation workshop was an R01 workshop focusing on Remediation Effectiveness: Green & Sustainable Remediation, Bioavailability, and Risk Reduction. The workshop brought together SRP R01 Researchers, who specialize in remediation approaches, as well as SRP's federal research partners from numerous offices of the U.S. EPA and the Army Corps of Engineers. In addition, a number of graduate students participated in the workshop. By convening these two groups, the workshop promoted dialogue between SRP researchers and federal partners in an effort to gain a better understanding of each perspective.

Drs. William Suk, Heather Henry and Janet Cakir, CRIS, and Sally Eckert-Tilotta, SRB, and Ms. Beth Anderson, CRIS, and Ms. Michelle Victalino, GMB, participated in the meeting.

Remediation Effectiveness: Green & Sustainable Remediation, Bioavailability, and Risk Reduction

November 5, 2009

New York City, New York

Introduction: The NIEHS Superfund Research Program (SRP) held this workshop titled "Remediation Effectiveness: Green & Sustainable Remediation, Bioavailability, and Risk Reduction" to identify critical research directions for the SRP pertaining to remediation effectiveness. Green and sustainable remediation (GSR) approaches take into account the full life cycle of a remediation process seeking to maximize efficiency in the use of resources and to minimize the impact to human health and ecosystems.

In a global sense, GSR relates to remediation effectiveness because it achieves a net reduction in the overall detrimental consequences of hazardous substances – rather than creating an environmental problem in another location or media. Bioavailability refers to the individual physical, chemical, and biological interactions that determine the exposure of plants and animals to chemicals associated with soils and sediments. Hence, reduction in contaminant bioavailability can be a critical achievement for remediation approaches to effectively protect health. Risk reduction is the ultimate goal of remediation activities; however, once a clean-up goal has been met, it is difficult to determine whether or not the remediation activity was successful in reducing exposures to hazardous substances.

Meeting Highlights: The workshop was held on Thursday, November 5th at the Marriott Marquis in New York City and was a satellite meeting of the SRP Annual Meeting, held November 3-4 at Columbia University. The workshop brought together SRP R01 Researchers, who specialize in remediation approaches, as well as partners from U.S. EPA and the Army Corps of Engineers (ACE) and graduate students. By convening these two groups, the workshop promoted dialogue between SRP researchers and federal partners in an effort to gain a better understanding of each perspective. The workshop began with an overview of the state of the practice for green and sustainable remediation, bioavailability, and risk reduction provided by U.S. EPA and ACE. Following the overviews, breakout groups were formed to identify critical research needs, opportunities and roadblocks for the three focus areas using questions developed by the workshop planning committee.

Recommendations/Outcomes: With regard to bioavailability, the overriding sentiment was that not much has changed since the NRC report (2003) indicating there have been few advances in this field since then (except maybe pore-water measurements and use). This could be a research niche for SRP. Attendees also identified the need for continued mechanistic research, as this is essential to explain the phenomena occurring at field-scale. Connecting with the right regional staff or site program managers would bring about additional translational opportunities for SRP researchers. Webinars on these subjects may allow greater participation by stakeholders with limited travel budget. In terms of green/sustainable remediation, SRP staff will provide an overview of SRP's Green research at an upcoming OSRTI Green Remediation meeting in Amherst, MA Summer 2010. There was interest in forming an SRP GSR working group. In

addition, there was interest in drafting a bioavailability white paper (working group) possibly followed by webinars. SRP will also be holding sessions at NARPM and SETAC to connect researchers with practitioners on these subject areas.

Dr. Heather Henry, CRIS/SRP, was an organizer and member of the Scientific Planning Committee. The meeting was also attended by Drs. William Suk, CRIS/SRP and Claudia Thompson, SRP/SPHB.

Health and Environmental Science Institute (HESI) Epigenetics Meeting

October 28-30, 2009

Research Triangle Park, North Carolina

An HESI workshop on the state of the science of epigenetics was held at NIEHS on Oct 28-30. While the NIEHS hosted the workshop and had representation on the planning committee, the meeting was funded by HESI, which is a global branch of the International Life Science Institute (ILSI). HESI brings together academia, government, industry and regulatory agencies to address and reach consensus on issues of mutual interest. The goal of this meeting was to provide an international forum to advance the understanding of scientific issues related to human health, toxicology and risk assessment.

The focus of the meeting was to define the data needed prior to the addition of epigenetic endpoints to guideline risk assessment studies. The meeting sessions focused on state of the science of epigenetics: epigenetics in development, how to measure epigenetic changes, what constitutes an epigenetic change, an overview of basic research in epigenetics, role of epigenetic changes in carcinogenesis and an overview of epigenetics at NIEHS. The sessions were meant to set the stage for the breakout group meetings on the last morning. Their focus was to discuss the following questions (four breakout groups assessed the same set of questions):

- What model systems might be employed to evaluate the ability of a chemical to produce an epigenetic change (affecting the F1 and/or F3 generation)?
- What endpoints/targets might be evaluated?
- What techniques might be employed?
- Regulatory Perspective: When is it appropriate to incorporate “new” science, in this case epigenetics, into the regulatory process? What does one need to know, what are the pitfalls and how might these be overcome/avoided?

The four breakout groups then reported back their answers to the questions and there was general discussion to try to reach consensus on how to move forward.

The results of the meeting are being prepared for publication.

Drs. Frederick Tyson and Jerrold Heindel co-organized the meeting. Dr. Tyson gave a brief overview of NIEHS supported programs in epigenetics, including the Fetal Basis of Disease Program, the Environmental Influences on Epigenetic Regulation, the NIEHS led Roadmap Epigenome Program, as well as an overview of two NIEHS intramural research programs on chromatin remodeling complexes. This presentation was designed to introduce the workshop participants to the breadth of investments the NIEHS has committed to examining the role of the environment in perturbing epigenetic processes that contribute to the pathogenesis of multiple of disease outcomes.

WETP Workshop: Global Safety and Health Issues and Their Impact on Worker Training

October 21-22, 2009

Chapel Hill, North Carolina

The NIEHS Worker Education and Training Program's workshop "Global Safety and Health Issues and Their Impact on Worker Training" provided a forum on emerging developments in global health and safety that promise to have a major impact on worker training. New developments in nanomaterials manufacturing, hazard communication and regulation of chemicals in the European Union could fundamentally influence workplace safety and health in the U.S. and abroad.

WETP Director *Chip Hughes* described the agenda as an engagement of "back-burner issues that are now becoming front-burner issues" in worker safety and health. *Dr. Gwen Collman, Interim Director, DERT*, provided an overview of NIEHS global environmental health initiatives, saying that she hoped to help the grantees better understand "how your work does dovetail with other programs" funded by NIEHS in an increasingly interconnected world. Representing the National Institute for Occupational Safety and Health (NIOSH), Drs. Margaret Kitt and Paul Schulte described what Schulte called "NIOSH's global view" as the Institute explores the future of worker safety.

The conference consisted of several topic oriented panels: implications of the United Nations Globally Harmonized System of Classification and Labeling of Chemicals; increase of engineered nanomaterials in the workplace and potential hazards both in manufacturing and waste disposal; European Union mandate on the Registration, Evaluation, Authorisation and Restriction of Chemical substances (REACH); and an overview of the experience of WETP awardees in occupational safety and health in Latin America. Powerpoint presentations from the conference can be found on the NIEHS website at <http://tools.niehs.nih.gov/wetp/events.cfm?id=2481>.

NIEHS Engineered Nanomaterials (ENMs) Grand Opportunity (GO) Grantee Meeting

October 20, 2009

Research Triangle Park, North Carolina

Background: *Dr. Sri Nadadur, COSPB*, organized a one-day meeting of all grantees funded through GO (RC2) and Challenge (RC1) grant mechanisms under the American Recovery and Reinvestment Act (ARRA) on October 20 at NIEHS. The major goal of this meeting was to initiate collaborative research efforts to address the basic research questions on developing reliable and reproducible research methods to predict safety and health effects of engineered nanomaterials. This meeting was attended by ten GO grantees, three RC1 grantees and their collaborators totaling 36 participants. The meeting started with welcome by *DERT Interim Director, Dr. Gwen Collman* and Acting Deputy Director, NIEHS, *Dr. Steve Kleeberger*.

Highlights: In the opening session *Dr. Nadadur*, provided an overview of the program including the critical need to establish a consortium to carry out round robin testing on selected ENMs using a select set of assay systems. This was followed by three scientific presentations. *Dr. Marty Fritts*, Nano Characterization Lab, National Cancer Institute, gave two talks, one on the importance of comprehensive characterization of ENMs in safety studies and one on the need for nanotoxicology informatics. *Dr. Nigel Walker*, NTP, NIEHS, in his presentation highlighted current efforts at NTP on ENMs health and safety.

The rest of the day's activities involved three panel discussion sessions to identify collaborative opportunities to establish "consortium efforts" to conduct round-robin testing among grantees. The first session was moderated by Drs. *Nadadur* and *Fritts* to identify a set of ENMs available within the group to be used in round robin testing and the minimal physical and chemical characterization data needed for the ENMs. The second session moderated by Drs. *Nadadur* and *David Balshaw, SPHB*, focused on identifying *in vitro* cell culture systems that can be utilized by grantees within the consortium and biological endpoints to be assayed. The third session similarly focused on identifying *in vivo* approaches to be used by the consortium.

Outcomes: This meeting led to successful establishment of a collaborative consortium guided by three working groups: ENM characterization, *in vitro* screening and *in vivo* studies. Four ENMs (TiO₂, ZnO,

carbon nanotubes, Titanium nanowires) available within the consortium has been selected to be investigated by members of the consortium following both in vitro and in vivo approaches to develop reliable and reproducible methods for ENM health and safety. The consortium agreed to follow up with quarterly conference calls by the working groups to finalize details of the studies and discussions by the consortium. The consortium set milestones to complete one set of *in vitro* studies before the next face-to-face meeting to discuss the data and outcomes of these efforts.

Centers for Neurodegeneration Science (CNS) Annual Grantee Meeting

October 7-8, 2009

Research Triangle Park, North Carolina

Background: The NIEHS Centers for Neurodegeneration Science (CNS) held its first annual meeting on October 8-9 at the main NIEHS campus in Research Triangle Park. The CNS program addresses the need for integrated research efforts involving basic and clinical scientists to discover the causes of and possible treatments for neurodegenerative diseases. In 2008, NIEHS awarded five-year CNS grants totaling 4.25 million dollars each year to Emory University, University of California at Los Angeles (UCLA) and the Burnham Institute. Each Center supports an administrative core, service/facility cores and a research development core for pilot studies. The interdisciplinary research approaches underway at these Centers enable scientists to incorporate risk and protective factor clues emerging from epidemiologic investigations with results from human genetic and clinic-based studies; disease models in animals and alternative organisms; and basic cellular and molecular neurobiologic studies of vulnerable neuronal populations. Such integration is essential for rapidly identifying the initiating and/or sustaining environmental stressors and primary biologic events that participate in the injury to the neuronal populations targeted by specific neurodegenerative diseases. This knowledge is expected to provide novel therapeutic targets for intervention of existing disease and prevention strategies for reducing exposure in vulnerable individuals.

Goals: The goals of the first meeting of CNS investigators were to foster interaction among the centers that could lead to collaborative research; highlight findings emerging from each of the centers, enable trainees to become more integrated within the program; and introduce Center investigators to NIEHS intramural and NTP investigators involved in research or research development efforts related to neurodegenerative disease.

Meeting Highlights: NIEHS Acting Deputy Director, Dr. Steven Kleeberger welcomed more than 30 scientists and trainees from the three Centers who attended the meeting. His opening remarks noted the growth of the NIEHS neurodegenerative disease portfolio over the past ten years in response to increasing evidence of environmental contributors to Parkinson's Disease (PD) and stressed the importance of interactions between multiple disciplines in understanding disease pathogenesis.

Presentations on the first day of the meeting began with an overview by Emory Center Director Gary Miller, Ph.D. The overall goals of this Center are to determine how environmental and genetic disruption of dopamine (DA) storage leads to oxidative damage; to identify novel mechanisms by which DA neurons respond to oxidative stress; to determine how environmental toxicants disrupt redox balance; and to identify novel biomarkers of environmental toxicant exposure associated with PD.

The overall goals of the Burnham investigators were outlined by Center Director Stuart Lipton, M.D., Ph.D. His group focuses on the ability of S-nitrosylation and oxidation of proteins to mimic genetic mutations seen in PD. These mutations cause protein mis-folding, abnormal signaling and eventual cell injury and death. Lipton's group proposes to generate "novel hits" from chemical library screens that could possibly be used as targets for therapeutic intervention.

Marie-Françoise Chesselet, M.D., Ph.D., Principal Investigator of the UCLA Center described the efforts of her group to identify novel mechanisms that contribute to the pathogenesis of sporadic PD.

Researchers at this Center are investigating primary cellular pathways affected by agricultural pesticide use, particularly in the well-characterized patient cohort in the agricultural region of the California Central Valley. Initial evidence suggests that pesticide exposures are linked to aberrant folding of proteins and the involvement of the ubiquitin-proteasome system (UPS), adverse effects on microtubule assembly and inhibition of aldehyde dehydrogenase.

A poster session featuring the work from the different laboratories within each Center was held after the first day of talks. A trainee meeting organized by *Dr. Mike Humble, COSPB*, provided useful information on training and career development.

The second day of the meeting featured presentations by several intramural and NTP scientists whose work was relevant to the CNS program. Presenters included investigators from the Epidemiology Branch, Drs. Honglei Chen and Freya Kamel, the National Toxicology Program, Raymond Tice, and the Laboratory of Molecular Toxicology, Jean Harry.

The final session of the meeting focused on a discussion of collaborative opportunities among Centers, including publication of joint papers, sessions at scientific meetings, possible trainee exchanges and pilot projects involving investigators at two or three Centers.

The CNS Program is managed collaboratively by *Drs. Cindy Lawler, COSPB, Kimberly Gray, SPHB, and Annette Kirshner, COSPB*. The NIEHS extramural division provided partial support for travel of trainees at CNS institutions to this meeting.

Bisphenol A Grantee Meeting

October 6, 2009

Research Triangle Park, North Carolina

Dr. Jerrold Heindel, COSPB, organized a day-long meeting of all grantees studying bisphenol A (BPA) including the 12 new grantees funded under the ARRA program. The meeting was held at NIEHS with the goal of improving interactions and collaborations among the grantees in order to provide the best possible data for use by the FDA regulators. The meeting started with discussions of how to work with BPA in the lab to avoid contamination, measurement of BPA and the importance of measuring blood and urine total and free the importance of diet in BPA studies and discussions on the doses, routes of exposures and the development of additional overlapping endpoints that would provide more useful data for the FDA. The meeting consisted primarily of discussion groups of grantees working in the same areas to stimulate the development of tissue sharing and the addition of endpoints that were common among the endpoints: first with animal researchers and epidemiologists working separately and then collectively. The meeting ended with a discussion of the NTP/FDA BPA research program and how the grantees could share tissues and thereby contribute to the data set for these studies. The grantees were very enthusiastic about the meeting and all were interested to add additional overlapping endpoints and to share endpoints and tissues with each other. Attendees developed a listing of needs including assessment of phytoestrogen content of the diets, access to glucuronidated and sulfated BPA, the development of a list ser to keep in touch, improved bioinformatics and sharing of data for collective examination and samples of BPA for use by all from the same batch.

There have been grantee meetings before at NIEHS but this was the first one with the focus specifically on a chemical with the goal to develop coordination of protocols, sharing of tissues and endpoints and the development of additional overlapping endpoints to provide high quality data for use by regulatory agencies, in this case the FDA.

“Next Generation Superfund Contaminants”

August 10th - 12, 2009
Tucson, Arizona

Introduction: As of January 2006, there were more than 239,000 substances on the Chemical Abstracts Service list of regulated chemicals. The production of more than 4,800 of these chemicals exceeded 1,000 metric tons/year. Add to that massive quantities of “naturally occurring” contaminants from commercial production, such as mining, groundwater pumping, and agricultural practices. In order to be proactive about avoiding new superfund sites, how is it possible to identify those contaminants of most environmental concern, and then winnow the list down to those contaminants most likely to be the foci of attention in future mega-contamination sites? This was the question tackled by the 24 experts assembled at the SRP-sponsored Workshop entitled “Superfund Contaminants: The Next Generation.”

Meeting Highlights: The workshop participants were selected to ensure expertise in such areas as toxicology, pharmacokinetics, pharmacology, contaminant fate and transport, chemical bioaccumulation, bioavailability and persistence, chemical parameter estimation and modeling, hazardous substance production and disposal, and monitoring and assessment technology. The meeting itself was structured to maximize the amount of interaction between and discussion from all participants. The workshop agenda was composed primarily of breakout sessions which were followed by full assembly synthesis sessions in which the full body of participants discussed the outcomes of the preceding breakout sessions.

Recommendations/Outcomes: The initial question tackled by the participants was what attributes delimit emerging Superfund contaminants as distinct from the broader universe of emerging contaminants in general. Persistence, volume of production, likelihood of toxicity, and tendency to accumulate rather than disperse were some of the attributes commonly identified as defining emerging Superfund contaminants. The next task was to develop a Top 10 List of chemicals or groups of chemicals recommended for consideration by SRP, e.g.: phthalates, brominated flame retardants, polyfluorinated organic compounds, and siloxanes. Some breakout groups felt that it was more appropriate and instructive to identify top processes rather than chemicals that are likely to create the next generation of Superfund sites. For example, electronics recycling, land application of wastewater biosolids, disposal of landfill leachate, and photovoltaic solar panel manufacturing were identified as industrial processes likely to generate heavily contaminated sites with contaminants of future concern. Next, workshop participants identified and prioritized the research and information gaps needs to address issues regarding the chemical (and/or process) candidate lists. This was followed by a second round of discussion sessions that was convened with the objective being to draft specific research approaches and outcomes.

The participants of the workshop will author a paper describing the outcomes of the workshop discussions. The workshop organizers and executive committee are currently preparing the first draft consensus document which will be submitted to Environmental Health Perspectives (EHP). Submission to EHP is targeted in early 2010. *Dr. Henry, SRP*, was a member of the Scientific Planning Committee and attended the meeting.

DETR PAPERS OF NOTE

Secrets of Drought Resistance Revealed

Julian L. Schroeder, Ph.D.
University of California San Diego
P42ES010337

The three-dimensional structure of abscisic acid, a plant hormone critical for drought survival, has been discovered by a team of scientists including Superfund Research Program-funded grantees at the University of California San Diego. The elucidation of the molecular structure helps to explain the mechanism behind drought tolerance in plants.

Drought resistant plants synthesize abscisic acid when they detect dry conditions. Increased levels of the hormone cause changes in all parts of the plants. Seeds lie dormant in the soil, leaf pores are closed conserving water, and growth is slowed. Plants reprogram themselves for the sole purpose of surviving.

The research team made crystals of abscisic acid bound to its protein receptor called PYR1. Using x-ray crystallography they determined the three-dimensional structure of the complex and found that PYR1 has an open space, akin to the inside of a tin can, where abscisic acid binds. As the binding occurs, a part of the protein called “the lid” is induced to close. Other structural changes to other parts of PYR1 initiate binding with other proteins triggering processes for drought resistance.

The authors suggest that chemicals mimicking the action of abscisic acid could be developed and sprayed on crops to protect them from droughts. It may also be possible to alter crops through selective breeding or genetic manipulation to produce more abscisic acid. According to NOAA, major droughts in the US in the last three years alone have caused more than \$10 billion in crop losses.

Citation: Nishimura N, Hitomi K, Arvai AS, Rambo RP, Hitomi C, Cutler SR, Schroeder JI, Getzoff ED. Structural mechanism of abscisic acid binding and signaling by dimeric PYR1. *Science*. 2009 Dec 4;326(5958):1373-9.

Crystal Structure of Variant P450 Determined

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R01ES003619

The crystal structure of a genetic variant of cytochrome P450 2B6 in complex with its inhibitor has been determined by an NIEHS grantee at the University of California San Diego. Structural insights like this are critical to understanding how the enzymes bind to substrates and metabolize compounds, and how different genetic variations affect the enzyme’s ability to initiate metabolism.

The multiple forms of cytochromes P450 metabolize a wide variety of endogenous and exogenous chemicals including prostaglandins, steroids, drugs, and environmental chemicals. P450s interact with a variety of substrates, inhibitors, membrane lipids and proteins that modulate their activity. P450s are heme-containing monooxygenase enzymes.

Genetic differences in the expression levels or activities of P450s are major determinants of individual responses to medications and environmental toxicants. This finding provides the first view of an important human enzyme that has been gaining in significance as the list of compounds it interacts with has grown.

Citation: Gay SC, Shah MB, Talakad JC, Maekawa K, Roberts AG, Wilderman PR, Sun L, Yang JY, Huelga SC, Hong WX, Zhang Q, Stout CD, Halpert JR. Crystal Structure of a Cytochrome P450 2B6 Genetic Variant in Complex with the Inhibitor 4-(4-Chlorophenyl)imidazole at 2.0 Å Resolution. *Mol Pharmacol*. 2010 Jan 8.

Lead Exposure Linked to Depression and Panic Disorders

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K01ES012653

Young adults with elevated blood lead levels are more likely to have major depression and panic disorders according to research supported by NIEHS.

Lead is a well known neurotoxicant causing behavioral and learning problems in children and young adults. It has also been associated with cognitive difficulties in older adults. It is ubiquitous and is found in air, soil, dust, and water. The elimination of lead from gasoline in the late 1970s has produced dramatic decreases in the average blood lead levels of children in the U.S.

Data were analyzed from participants in the National Health and Nutrition Examination Survey aged 20-29. Of the almost 2000 participants, 134 met diagnostic criteria for major depressive disorder, 44 had panic disorder, and 47 had generalized anxiety disorders. The one-fifth of the participants with the highest blood lead levels (2.11 micrograms per deciliter) were 2.3 times more likely to have major depressive disorder and nearly five times more likely to have panic disorder than the one-fifth with the lowest blood lead levels (< 0.7 micrograms per deciliter). These blood lead levels are considerably lower than the national average in the 1960s-70s and provide further evidence that there is no safe level of lead exposure.

Although this study was not designed to determine a causal link between lead and depression or panic disorder, the authors point out that low-level lead exposure disrupts brain processes involving the neurotransmitters catecholamine and serotonin. Disruptions of these processes are known to be involved in depression and panic disorders. Its plausible that exposure to lead in individuals predisposed to these conditions could trigger their development, make them more severe, or reduce their response to standard treatments.

Citation: Bouchard MF, Bellinger DC, Weuve J, Matthews-Bellinger J, Gilman SE, Wright RO, Schwartz J, Weisskopf MG. Blood lead levels and major depressive disorder, panic disorder, and generalized anxiety disorder in US young adults. Arch Gen Psychiatry. 2009 Dec;66(12):1313-9.

Can a Genetic Risk Score Predict Multiple Sclerosis?

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T32ES016645

A large, multinational team of epidemiologists has developed a promising mathematical algorithm for predicting the likelihood of developing multiple sclerosis (MS). With additional refinement, it could become a useful tool in identifying people for early intervention or prevention efforts.

MS is a complex neurological disease with an unknown origin characterized by demyelination of the central nervous system. Disease onset usually occurs in young adults, and it is more common in females. It has a prevalence that ranges between 2 and 150 per 100,000 people. Genetic epidemiology studies indicate that first degree relatives of people with MS are 15-35 times more likely to develop MS themselves. Recent genome-wide association studies have identified a number of genetic loci; however, despite the number of genes confirmed as being involved in MS there is still no clear understanding of the genetic contribution to disease susceptibility. Environmental factors with convincing evidence of involvement with MS include sunshine, vitamin-D, Epstein-Barr viral exposure, and smoking.

The current study attempts to answer the question, can we predict who will develop MS? The team employed a factor called the C statistic, which defines how well a model can differentiate between patients and controls. A model with C statistic equal to 0.5 predicts no better than simply tossing a coin while a perfect model has a C statistic of one. For clinical prediction, a C statistic of 0.8 or higher is considered useful.

In the current study which examines 16 genetic loci associated with MS, the researchers used three different cohorts. The C statistics obtained ranged from 0.64 to 0.72 depending on whether gender, smoking history, and Epstein-Barr virus titers were incorporated. Although below the standard of 0.8, by incorporating other data and environmental factors, this study could lead to the development of a model

with strong predictive power, which could identify individuals that would benefit from early intervention efforts.

One member of the research team, K. Claire Simon of the Harvard School of Public Health is supported by an NIEHS training grant.

Citation: De Jager PL, Chibnik LB, Cui J, Reischl J, Lehr S, Simon KC, Aubin C, Bauer D, Heubach JF, Sandbrink R, Tyblova M, Lelkova P; Steering committee of the BENEFIT study; Steering committee of the BEYOND study; Steering committee of the LTF study; Steering committee of the CCR1 study, Havrdova E, Pohl C, Horakova D, Ascherio A, Hafler DA, Karlson EW. Integration of genetic risk factors into a clinical algorithm for multiple sclerosis susceptibility: a weighted genetic risk score. *Lancet Neurol.* 2009 Dec;8(12):1111-9.

Chronic Glucocorticoid Use Raises Risk of Bladder Cancer

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P42ES007373

The most recent study by NIEHS grantee Margaret Karagas at Dartmouth University reports that chronic use of glucocorticoid drugs is a risk factor for bladder cancer. The findings appear in the *British Journal of Cancer*.

Glucocorticoids are often prescribed for immunosuppressive therapy for organ transplant patients, asthma sufferers, or people with an autoimmune disorder such as rheumatoid arthritis. The study matched 786 bladder-cancer patients to 1,083 control subjects. The risk of bladder cancer was three-fold higher for people who had taken glucocorticoids for more than five years.

These results raise the possibility of an increased risk of bladder cancer from long-term use of glucocorticoids and a potential role of immunological effects in bladder cancer etiology.

Citation: Glucocorticoid therapy and risk of bladder cancer. Dietrich K, Schned A, Fortuny J, Heaney J, Marsit C, Kelsey KT, Karagas MR. *Br J Cancer.* 2009 Oct 20;101(8):1316-20.

Discovery in Aflatoxin Formation

Craig A. Townsend, Johns Hopkins University
R01ES001670

A *Nature* article by NIEHS grantee Craig Townsend reports advances in the understanding of how the fungal toxin aflatoxin is synthesized opening new avenues that might lead to possible methods to prevent the formation of the toxin and its harmful effects.

Aflatoxin is produced by molds in the aspergillus family. They are ubiquitous and are found in many crops such as corn, rice, wheat, and peanuts. The toxin is consumed directly by eating contaminated crops or by drinking milk from cows fed contaminated food stuffs. The toxin is a known human carcinogen causing liver cancer.

Using xray crystallography, the research team determined the three-dimensional structure of an enzyme in the polyketide synthase family, which is a component of the multi-step process of toxin synthesis. They discovered a region known as the product template domain responsible for producing a precursor of the toxin. The researchers hope to further their discoveries and possibly develop a method to prevent the formation of aflatoxin.

Citation: Crawford JM, Korman TP, Labonte JW, Vagstad AL, Hill EA, Kamari-Bidkorpheh O, Tsai SC, Townsend CA. Structural basis for biosynthetic programming of fungal aromatic polyketide cyclization. *Nature*. 2009 Oct 22;461(7267):1139-43.

Bacterial Toxin Linked to Parkinson's

Guy A. Caldwell, Ph.D., University of Alabama
R21ES014426

NIEHS funded researchers in Alabama discovered that a common soil bacterium produces a metabolite that disrupts a protein degradation pathway associated with Parkinson's disease. This finding suggests that exposures to metabolites from common bacteria may contribute to the development of Parkinson's disease.

Parkinson's disease is a progressive neurodegenerative disorder involving the loss of dopamine producing neurons from the substantia nigra region of the brain. For the past several years, scientists have speculated that environmental causes of the disease are more important than genetics because studies in twins suggest that genetic predisposition is only possibly responsible for the disease occurrence. A clinical hallmark of the disease is misfolding and accumulation of proteins, such as α -synuclein, in inclusions called Lewy Bodies.

In the current study, funded through an exploratory R21 grant, Alabama scientists discovered that a common streptomyces bacterium found in soil produces a natural proteasome inhibitor that blocks protein degradation and caused gradual degeneration of all neuronal cells examined. Dopamine neurons were particularly vulnerable to the metabolites effects. The studies were carried out in a Parkinson's disease model using the nematode.

Citation: Caldwell KA, Tucci ML, Armagost J, Hodges TW, Chen J, Memon SB, Blalock JE, DeLeon SM, Findlay RH, Ruan Q, Webber PJ, Standaert DG, Olson JB, Caldwell GA. Investigating bacterial sources of toxicity as an environmental contributor to dopaminergic neurodegeneration. *PLoS One*. 2009 Oct 6;4(10):e7227.

Social Isolation Speeds Breast Tumor Growth

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P50ES012382

A socially isolated and stressful environment may speed up the growth of breast tumors according to NIEHS-supported researchers at the University of Chicago. The effects are believed to be caused by changes in gene expression in mammary glands.

Previous human epidemiologic studies have shown a link between cancer and stress. The current study was conducted in a strain of laboratory mice genetically susceptible to breast cancer. Mice are generally very social animals and social isolation is recognized as a severe stressor for them. Mice were randomly assigned to be isolated at a very early age. The isolated mice developed larger and more breast cancers than the group-housed mice.

Gene expression changes in mammary tissue were also measured in the mice. Genes involved in metabolism were turned on and off in the isolated mice in a very reproducible manner. Certain metabolic pathways and changes are known to contribute to the increased growth of breast cancer. The isolated mice also had much higher stress hormone levels than their group-housed counterparts.

These findings are preliminary, but suggest that reducing stress and increasing social activity may be important factors in the prevention and treatment of breast cancer in women.

Citation: Williams JB, Pang D, Delgado B, Kocherginsky M, Tretiakova M, Krausz T, Pan D, He J, McClintock MK, Conzen SD. A model of gene-environment interaction reveals altered mammary gland gene expression and increased tumor growth following social isolation. *Cancer Prev Res (Phila Pa)*. 2009 Oct;2(10):850-61.

Carbon Nanotubes Can Affect the Lining of the Lungs

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R21ES015801

Carbon nanotubes are being used in many products including sports equipment, clothing, and cosmetics and are being considered for additional uses such as targeted drug delivery devices. The toxicity of these materials is to a great extent unknown; however, a new collaborative study shows that inhalation of these particles can affect the outer lining of the lung. Long-term effects of the exposure are yet to be determined.

Laboratory mice were exposed, through inhalation, to nanotubules for a single six-hour window. Within one day, the research team noticed immune cells clustering on the surface of the pleura, the tissue that covers the outside of the lungs. Scarring or fibrosis began on the pleura about two weeks after exposure. These same effects at the same location are seen after exposure to asbestos, a known carcinogen.

The study showed that the scarring and immune responses disappeared about three months after the exposure. It is unknown if the effects would continue with chronic exposure to the nanotubes as is generally the case in asbestosis. Additional research with longer exposures is needed to determine the long-term effects of nanotube exposure.

Citation: Ryman-Rasmussen JP, Cesta MF, Brody AR, Shipley-Phillips JK, Everitt JI, Tewksbury EW, Moss OR, Wong BA, Dodd DE, Andersen ME, Bonner JC. Inhaled carbon nanotubes reach the subpleural tissue in mice. *Nat Nanotechnol*. 2009 Nov;4(11):747-51.

Electronic “Nose” Smells Toxins

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University of Illinois
U01ES016011

A modern-day sophisticated version of the canary in the coal mine has been developed by NIEHS grantees at the University of Illinois. As part of the NIH Genes, Environment and Health Initiative, the university researchers teamed up with a small biotechnology firm and developed a postage-sized sensor that detects poisonous gases and changes color to demonstrate the detection.

When the sensor is fully developed, it will be useful for detecting exposures to toxic materials in industrial and laboratory settings. While nuclear power workers, medical personnel, and other people working with radiation wear badges to monitor their exposure, such technology does not exist as yet for chemicals. The investigators hope to be able to market the device with two years. And since the device monitors a variety of toxins, it can be customized for specific industrial settings. The sensor is engineered such that the level of exposure can also be determined.

The developmental sensor detects 19 representative toxic industrial chemicals, including ammonia, chlorine, nitric acid, and sulfur dioxide. In testing, the sensors were exposed to the chemicals for two

minutes. Most of the chemicals were identified by the array color change in a matter of seconds and almost all were detected within two minutes.

Citation: Lim SH, Feng L, Kemling JW, Musto CH, Suslick KS. An optoelectronic nose for the detection of toxic gases. *Nature Chemistry*. 2009 Sep 13; 1:562-7.

Arsenic and Heart Arrhythmia

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P30ES000002, R01ES014663 and R01ES015172

The consumption of arsenic-contaminated drinking water is a known risk-factor for skin and bladder cancer and is associated with other diseases including diabetes and cardiovascular diseases. Now, researchers at the University of North Carolina at Chapel Hill report that low-level exposure to arsenic is associated with a prolongation of the Q-T portion of the heart rhythm.

Long Q-T syndrome (LQTS) is a disorder of the heart's conduction system. The disorder affects the recharging of the heart after each heartbeat. Congenital LQTS is a rare disorder that is usually inherited. In other cases, LQTS can be caused by certain medicines, including arsenic trioxide, which is a highly effective treatment for promyelocytic leukemia. LQTS can lead to an abnormal heart rhythm, fainting, or even sudden death.

The researchers performed a cross-sectional analysis of elderly men from the Normative Aging Study. The study included 226 participants and analyzed toe nail clippings for arsenic content, which is a recognized biomarker for arsenic ingestion. Electrocardiograms were conducted on all study participants. Most of the participants lived in the Boston region and obtained their water from the Massachusetts Water Resources Authority. The arsenic concentration of this water resource is generally less than 1 microgram per liter, far below the current EPA standard of 10 micrograms per liter.

The study participants' use of calcium channel blockers was also determined. Previous research suggested that the use of these drugs could ameliorate arsenic trioxide-induced Q-T prolongation seen during treatment of acute promyelocytic leukemia. In the current study, there was no evidence of an effect of medication use on Q-T interval. The results of this study provide new information to guide efforts to reduce the arrhythmic effects of arsenic exposure.

Citation: Mordukhovich I, Wright RO, Amarasiriwardena C, Baja E, Baccarelli A, Suh H, Sparrow D, Bokonas P, Schwartz J. Association between low-level environmental arsenic exposure and QT interval duration in a general population study. *Am J Epidemiol*. 2009 Sep 15;170(6):739-46.

Prostate Gene Polymorphism Linked to Bladder Cancer

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P42ES007373

A fifty-member, international and interdisciplinary team of researchers report the discovery of a single nucleotide polymorphism in the prostate stem cell antigen gene (PSCA) as a urinary bladder cancer gene. The research team includes NIEHS grantees from the M.D. Anderson Cancer Center and Dartmouth University.

The group conducted a genome-wide association study on 969 bladder cancer cases from Texas. This study was combined with ongoing efforts in three other US populations and nine European groups. A consistent association of a missense variant in the PSCA gene dubbed rs2294008 was found with

bladder cancer in all populations. In combining all study subjects, the number of participants included 6,667 cases of bladder cancer and 35,590 controls and produced a highly statistically significant result.

The missense variant alters the start codon, is thought to shorten the protein by nine amino acids, and reduces promoter activity. Resequencing the PSCA genomic region identified rs2294008 as the only common missense polymorphism in the gene. Recent studies demonstrated that the same alteration is associated with gastric cancer in an Asian population. It remains to be seen whether this is true for people of European descent. Additional studies are planned to determine the physiological significance and functional consequences of the variant gene.

Citation: Wu X, Ye Y, Kiemeny LA, Sulem P, Rafnar T, Matullo G, Seminara D, Yoshida T, Saeki N, Andrew AS, Dinney CP, Czerniak B, Zhang ZF, Kiltie AE, Bishop DT, Vineis P, Porru S, Buntinx F, Kellen E, Zeegers MP, Kumar R, Rudnai P, Gurdau E, Koppova K, Mayordomo JI, Sanchez M, Saez B, Lindblom A, de Verdier P, Steineck G, Mills GB, Schned A, Guarrera S, Polidoro S, Chang SC, Lin J, Chang DW, Hale KS, Majewski T, Grossman HB, Thorlacius S, Thorsteinsdottir U, Aben KK, Witjes JA, Stefansson K, Amos CI, Karagas MR, Gu J. Genetic variation in the prostate stem cell antigen gene PSCA confers susceptibility to urinary bladder cancer. *Nat Genet.* 2009 Sep;41(9):991-5.

Maternal Exposure to Air Pollution Lowers Children's IQ

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Mailman School of Public Health, Columbia University

P01ES009600, R01ES008977, R01ES11158, R01ES012468, and P30ES009069

Public health experts at Columbia University report that a mother's exposure to polycyclic aromatic hydrocarbons (PAHs) can lower her child's IQ. PAHs are widely found in urban air and result from the combustion of coal and automotive fuel. They are also found in tobacco smoke.

Non-smoking pregnant women of African-American or Dominican-American descent living in the South Bronx or Harlem were enrolled in the study. They wore personal air monitors during pregnancy and provided additional information about their work and home environments. The women were split into high- and low-exposure groups based on whether their PAH exposure was above or below the median of 2.26 nanograms per cubic meter of air. Their children were monitored from the perinatal period until age five when they were given a standard intelligence exam. On average, the IQ scores of children in the high exposure group were about four points lower than children in the low exposure group.

IQ deficits in the range of four points are believed to affect how well children perform in school and how well they score on standardized tests. These deficits are similar to those seen in children with significant lead exposure.

Citation: Perera FP, Li Z, Whyatt R, Hoepner L, Wang S, Camann D, Rauh V. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. *Pediatrics.* 2009 Aug;124(2):e195-202.

Diesel Exhaust Linked to Cancer Development Through Blood Vessel Growth

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New York University School of Medicine and Ohio State University

P30ES000260, R01ES015495, and K01ES016588

NIEHS-supported scientists have determined a way that exposure to diesel exhaust stimulates the growth of cancerous tumors. Using a laboratory mouse research model, the research team from New York University and Ohio State University determined that exposure to diesel exhaust particles stimulates the growth and formation of new blood vessels necessary for solid tumors to grow. The studies were carried

out at exposure levels similar to those found in urban areas with heavy commuting traffic and were lower than levels typically encountered by workers using diesel-powered equipment.

Inhaled diesel exhaust particles are mostly less than 0.1 micrometers in diameter, which enables them to penetrate the circulatory system and other organs, and allows them to cause damage in just about any tissue in the body.

The researchers employed a two-prong research approach. First they implanted small platforms embedded with normal endothelial cells, the cells that line blood vessels, under the skin of healthy mice. In another set of mice, the researchers surgically created an ischemic condition in the hind limbs. Ischemia causes hypoxia, which is a severe lack of oxygen, and a condition seen in certain diseases. Mice from both groups were assigned to breathe either filtered outdoor air or air contaminated with diesel exhaust particles for 6 hours per day. The rest of time the animals breathed filtered air.

Effects were seen beginning after just two-weeks of exposure, but the longer the experiment was continued the more severe the effect. Exposure to diesel exhaust caused a six-fold increase in new blood vessel formation in the ischemic limbs at eight weeks and a four-fold increase in the non-ischemic limbs compared to the mice breathing normal air. Similar effects were seen in the mice with the implanted cells. The researchers found three types of blood vessel development; the development of new capillaries, re-started growth of existing blood vessels, and the formation of new vessels. All of these processes are needed for solid tumor growth.

The team conducted additional studies to try to determine the mechanism behind the vascular changes. They found that exposure to diesel particles activates vascular endothelial growth factor, a chemical signal associated with new blood vessel development. They also found that a blood vessel growth factor is activated by diesel exposure and lowered activity for an enzyme involved in tumor suppression. The researchers are now conducting experiments to determine whether exposure to diesel exhaust influences metastasis of tumors as well.

Citation: Xu X, Kherada N, Hong X, Quan C, Zheng L, Wang A, Wold L, Lippmann M, Chen LC, Rajagopalan S, Sun Q. Diesel exhaust exposure induces angiogenesis. *Toxicol Lett.* 2009 Aug 14.

“Sloppier Copier” Mysteries Solved

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R01ES012259

New discoveries by University of Southern California biologists solved a vexing question about the role of the protein RecA in DNA repair. These researchers also discovered the exact composition of the active form of the DNA repair enzyme polymerase V.

RecA is a nucleoprotein filament which is a long line of proteins bound to a single-stranded DNA. Experiments demonstrated that RecA transfers two molecules to polymerase V resulting in the enzymes activation. The molecules transferred are ATP for fuel, and a single RecA protein, one of many that make up the filament. RecA does not actively participate in the repair process; its role is merely to activate polymerase V. As soon as the molecules attach, polymerase V begins walking down the damaged DNA segment copying a new strand. As soon as it reaches the end of the damaged section, it drops off the DNA and immediately deactivates. It must be reactivated by RecA to copy more DNA, which is different than all other DNA polymerases.

Polymerase V was discovered in this laboratory in 1999 as was nicknamed the “sloppier copier” because it makes frequent copying mistakes which show up as mutations in the cell’s DNA. The researchers postulate that polymerase V may be more important for the long-term success of a species than its more

accurate counterparts. Some of the mutations are likely to be helpful, enabling organisms to better adapt to their environments. These helpful mutations then spread through the species by natural selection.

Citation: Jiang Q, Karata K, Woodgate R, Cox MM, Goodman MF. The active form of DNA polymerase V is UmuD'2C-RecA-ATP. *Nature*. 2009 July 16; 460(7253): 359-63.

Bisphenol A reduces the effectiveness of chemotherapeutics

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University of Cincinnati

T32ES007250 and R01ES012212

Recent research results suggest that the environmental estrogen, bisphenol A (BPA), in addition to its potential carcinogenic and reproductive health effects, reduces the effectiveness of three common chemotherapeutic agents used to treat breast cancer.

BPA is structurally similar to diethylstilbesterol (DES) and its carcinogenic potential is of strong concern to scientists and regulators. Similar to DES, BPA has estrogenic activity, and exposure in young rodents leads to increased rates of hormonally related cancers as the animals age. Since estrogen has been shown to antagonize some anticancer drugs, the research team wanted to test BPA for its potential to reduce the effectiveness of these anticancer agents.

The findings were clear. At nanomolar concentrations of BPA, levels routinely found in humans, estrogen receptor-positive and –negative breast cancer cells lines were protected from the chemotherapeutic effects of doxorubicin, cisplatin, and vinblastine. The researchers speculate that the protective effect could be the result of increased expression of antiapoptotic proteins caused by BPA. This study highlights a previously unrecognized effect of BPA in carcinogenicity and therefore adds strong support to the growing knowledge of the adverse effects of BPA on human health. It also suggests that BPA exposure may be a factor in choosing therapeutic regimens in patients undergoing treatment for hormonally-related cancers.

Citation: Lapensee EW, Tuttle TR, Fox SR, Ben-Jonathan N. Bisphenol A at low nanomolar doses confers chemoresistance in estrogen receptor-alpha-positive and –negative breast cancer cells. *Environ Health Perspect*. 2009 Feb; 117(2):175-80.

Progesterone Triggers Breast Inflammation

Sandra Z. Haslam, Ph.D., Jian-Wei Xie, Ph.D., Richard J. Miksicek, Ph.D., Susan E. Conrad, Ph.D., and Richard C. Schwartz, Ph.D.

Michigan State University

U01ES012800

NIEHS-funded researchers at Michigan State University report that exposure to the hormone progesterone activates genes that trigger inflammation in the mammary gland. This inflammation may be a key factor in increasing the risk of breast cancer.

Paradoxically, progesterone promotes normal development of the breast, but it has been previously identified as a risk factor for breast cancer. Exposure to progesterone in normal amounts causes breast inflammation which leads to development. Exposure to progesterone in post-menopausal hormone therapy is a known risk factor for breast cancer.

In a laboratory mouse study, the researchers examined genes activated by progesterone and the effects of their activation. They found that progesterone regulates 162 genes in pubertal cells, 104 genes in

adult cells and 68 genes in cells during both developmental stages. Some of these genes code for small proteins called chemokines active in the process of inflammation.

The study identified the targets of progesterone receptor A in mammary cell development. These links provide avenues of research and potential therapies in reducing the influence progesterone has on developing breast cancer.

Citation: Santos SJ, Aupperlee MD, Xie J, Durairaj S, Miksicek R, Conrad SE, Leipprandt JR, Tan YS, Schwartz RC, Haslam SZ. Progesterone receptor A-regulated gene expression in mammary organoid cultures. *J Steroid Biochem Mol Biol.* 2009 Jul;115(3-5):161-72.

Potential Discovery of New Asthma Therapy.

Istvan Boldogh, Ph.D. and Satish Srivastava, Ph.D.
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P30ES006676

Clinical investigators at the NIEHS-funded Center at the University of Texas Medical Branch in Galveston discovered that a single enzyme is critical in most allergen-induced asthma attacks. The activity of the enzyme, aldose reductase, can be significantly reduced by drugs which have already undergone clinical trials for diabetes complications. These discoveries open a pathway for human clinical investigations to determine their effectiveness in treating asthma.

In a wide variety of diseases including cancer, atherosclerosis, asthma, diabetes, etc. exposure to high levels of reactive species leads to the release of a barrage of inflammatory signaling proteins. These proteins stimulate more immune system cells to enter the affected tissue causing the release of even more reactive oxygen species, producing a cycle of ever-increasing inflammation.

Aldose reductase plays a pivotal role in the activation of inflammatory processes. In previous studies, the research team found that when aldose reductase is blocked, the inflammation does not develop. Knowing that asthma is a chronic disease of inflammation, they postulated that aldose reductase inhibition would have beneficial effects in preventing asthma exacerbations.

Experiments were carried out in cultures of human airway epithelial cells. Some cells were treated with an aldose reductase inhibitor. After exposure to ragweed pollen, the untreated cells responded in the same way airway cells respond during an asthma attack, with increased rates of apoptosis, activation of key inflammatory transcription factors, and the generation of a host of molecules associated with inflammation. Cells treated with the enzyme inhibitor had a much milder inflammatory response to the ragweed pollen. Similar studies were also carried out in live mice with similar results. Mice given an aldose reductase inhibitor had a dramatically reduced inflammatory response after exposure to ragweed pollen.

The research team plans to conduct clinical trials to determine whether aldose reductase inhibitors will be beneficial in treating human asthma.

Citation: Yadav UC, Ramana KV, Aguilera-Aguirre L, Boldogh I, Boulares HA, Srivastava SK. Inhibition of aldose reductase prevents experimental allergic airway inflammation in mice. *PLoS One.* 2009 Aug 6;4(8):e6535.

Natural Food Products Can Treat Cancer

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P30ES000210

Combinations of natural food compounds and chemotherapy drugs provide promise as powerful and potentially less toxic chemotherapeutic treatments strategies according to researchers at the Linus Pauling Institute. A recent study supported by NIEHS, found that chlorophyllin, a derivative of chlorophyll, was 10 times more potent in killing colon cancer cells than the commonly used chemotherapeutic agent hydroxyurea.

The study, carried out in human colon cancer cell lines, found that chlorophyllin kills cancer cells by causing a disruption in cell division. The cells tend to be stalled in the S-phase of cell division when DNA replication occurs. The compound then induces apoptosis in a cytochrome c-independent manner resulting in cell death.

Chlorophyllin is inexpensive and has been proven in other NIEHS-funded research to be an effective treatment for aflatoxin-induced liver cancer. It can be ingested at relatively high levels without causing toxicity; however, it is poorly absorbed in the gut. Levels needed for therapeutic purposes as well as delivery systems are currently under study.

The researchers point out that other dietary cancer fighters show promise. Organic forms of selenium have shown promise in targeting colon and prostate cancers.

Citation: Chimpoy K, Díaz GD, Li Q, Carter O, Dashwood WM, Mathews CK, Williams DE, Bailey GS, Dashwood RH. E2F4 and ribonucleotide reductase mediate S-phase arrest in colon cancer cells treated with chlorophyllin. *Int J Cancer*. 2009 May 11;125(9):2086-2094.

Carbon Monoxide and Cardiovascular Disease in the Elderly

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Yale University

R01ES015028

Low-dose exposure to the acutely poisonous gas carbon monoxide, even at levels far below national exposure limits, is associated with increased risk of adverse cardiovascular outcomes in elderly persons requiring hospitalization. This report comes from NIEHS grantee, Michelle Bell of Yale University and her colleagues Jonathan Samet of the University of Southern California and Francesca Dominici of John's Hopkins University. Bell is the recipient of an Outstanding New Environmental Scientist award from NIEHS.

The research team conducted an epidemiologic investigation of 126 urban communities across the U.S. The study results show that with each one part per million increase in the maximum daily one-hour exposure to carbon monoxide, the risk of hospitalization due to cardiovascular disease increases about one percent in people over age 65.

This evidence suggests that the currently accepted regulatory level of carbon monoxide may still be posing a health risk at least for this vulnerable population. The study indicates that as carbon monoxide levels rose, the risk of hospitalization increased. The findings were based on the analysis of hospital records for more than 9 million Medicare recipients matched to data on air pollution levels and weather from 1999 through 2005.

The research team points out that additional research is necessary to determine if the observed effect is due to exposure to carbon monoxide alone or in combination with other traffic-related pollutants. However, this study points toward a "positive and statistically significant association" between same-day carbon monoxide levels and increased risk for hospitalization for multiple cardiovascular diseases such as ischemic heart disease, heart rhythm irregularities, heart failure, and stroke.

Citation: Bell ML, Peng RD, Dominici F, Samet JM. Emergency Hospital Admissions for Cardiovascular Diseases and Ambient Levels of Carbon Monoxide. Results for 126 United States Urban Counties, 1999-2005. *Circulation*. 2009 Aug 31.

STAFF PUBLICATIONS

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Astrid C. Haugen, Nicholas A. Di Prospero, Joel S. Parker, Rick D. Fannin, Jeff Chou, Joel N. Meyer, Christopher Halweg, Jennifer B. Collins, Alexandra Durr, Kenneth Fischbeck, Bennett Van Houten. 2010. Altered Gene Expression and DNA Damage in Peripheral Blood Cells from Friedreich's Ataxia Patients: Cellular Model of Pathology. *PLoS Genet* 6(1): e1000812. doi:10.1371/journal.pgen.1000812.

Ashwell MS, Ceddia RP, House RL, Cassady JP, Eisen EJ, Eling TE, *Collins JB*, Grissom SF, Odle J. 2010. Trans-10, cis-12-conjugated linoleic acid alters hepatic gene expression in a polygenic obese line of mice displaying hepatic lipidosis. *J Nutr Biochem*. 2009 Oct 2. [Epub ahead of print]

Sherry Baron, Raymond Sinclair, Devon Payne-Sturges, Jerry Phelps, Harold Zenick, Gwen W. Collman, and Liam R. O'Fallon. 2009. Partnerships for Environmental and Occupational Justice: Contributions to Research, Capacity and Public Health. *Am J Public Health*. 99: S517-S525.

GRANTEE HONORS and AWARDS

The Human Genome Decoded was named number two on the top ten scientific discoveries of 2009 by TIME Magazine. The Reference Epigenome Mapping Center sequenced the first two complete human methylomes: an embryonic stem cell line (H1) and a differentiated fibroblast line (IMR90). This work was supported by a cooperative agreement managed by NIEHS and funded with NIH RoadMap dollars. Dr. Bing Ren, Ludwig Institute Cancer Research Center, is the principal investigator of the Mapping Center. Other leaders include Drs. Joseph R Ecker, The Salk Institute, James A Thomson, University of Wisconsin, Wei Wang, University of California at San Diego and Michael Q Zhang, Cold Spring Harbor Laboratory. To read the article please see: http://www.time.com/time/specials/packages/article/0,28804,1945379_1944416_1944420,00.html

Three NIEHS grantee have been elevated to the rank of Fellow by the American Association for the Advancement of Science (AAAS):

Dr. Kathleen S. Rein, Florida International University (FIU), received the honor: "For distinguished contributions in the field of algal toxins, establishing a center for environmental health sciences at a minority serving institution, and for mentoring minorities." Dr. Rein is the principal investigator on the Advanced Research Cooperation in Environmental Health Research grant at FIU.

Dr. Barry Dellinger, Patrick F. Taylor Chair for the Environmental Impact of Hazardous Waste at Louisiana State University (LSU) was honored, "For seminal contributions to the origin of toxic combustion by-products, concentrating most recently on dioxins, combustion-generated nanoparticles and environmentally persistent free radicals." Dr. Dellinger is the director of the Superfund Research Program at LSU.

Dr. Carol Folt, Dartmouth University, was honored for her groundbreaking limnological work on salmon restoration and conservation, and on metal toxicity in aquatic ecosystems and implications for human health. She was also recognized for advancing scientific education and literacy as dean of the faculty at Dartmouth. Dr. Folt is a grantee in the Superfund Research Program at Dartmouth.

Dr. James Halpert, Professor and Associate Dean for Student Affairs at the University of California San Diego (USCD), has been selected to receive the Bernard B. Brodie Award in Drug Metabolism for 2010.

The Bernard B. Brodie Award was established in 1977 by the ASPET (American Society for Pharmacology and Experimental Therapeutics) Drug Metabolism Division to honor Dr. Brodie's fundamental contributions to the field of drug metabolism and disposition. The Award, consisting of an honorarium and a commemorative medal, is presented every other year to recognize outstanding original research contributions that follow in Dr. Brodie's footsteps, particularly those having a major impact on future research in the field. Dr. Halpert went to USCD from the University of Texas Medical Branch where he served as Chairman of the Department of Pharmacology and Toxicology and Director of the EHS Core Center. Dr. Halpert's research for the past 30 years has involved the structure and function of cytochrome P450, drug-metabolizing enzymes central to individual response to medications and environmental toxicants and his latest publication to resolve the structure of a P450 variant is the result of over five years of efforts, with NIEHS support, to produce the solid crystals that serve as the basis for examination. The formal presentation of the Award and medal is made at the annual ASPET meeting in Anaheim, California, April 24-28.

STAFF HONORS and AWARDS

Ms. Martha Barnes, PAB, received an NIH Merit Award as part of the Division of Program Coordination Planning and Strategic Initiatives NIH Tracking and Inclusion Committee, "In recognition of exceptional contributions to monitoring compliance with the NIH Policy on the inclusion of women and minorities as subjects in clinical research" at the Office of the Director Honor Awards Ceremony held in Bethesda, Maryland, on January 8.

Dr. Elizabeth Maull, SPHB, received a 2009 NIAID Merit Award on December 16 in Bethesda, Maryland, "For leadership, teamwork, and notable contributions from a three-year Institute wide working group charged with the preparation of NIAID for NIH RCDC system deployment."

The following Extramural staff received NIH Merit Awards at the NIEHS ceremony on December 17.

Dr. Jerrold Heindel, COSPB, received an individual award, "For extraordinary efforts in building and bringing visibility to the extramural reproductive toxicology, endocrine disruptor, and fetal basis of adult disease programs."

Ms. Beth Anderson, and Drs. David M. Balshaw and Heather Henry, CRIS; Ms. Martha I. Barnes, Ms. Helena Davis, and Mr. Jerry Phelps, PAB; Ms. Jennifer Collins, Mr. Liam R. O'Fallon and Drs. Caroline Dilworth, Kimberly Gray, Elizabeth Maull, Kimberly McAllister, Leslie Reinlib and Daniel Shaughnessy, SPHB; Ms. Astrid Haugen and Drs. Lisa Helbling Chadwick, Jerrold Heindel, Michael C. Humble, Annette Kirshner, Cindy Lawler, Srikanth Nadadur, Carol Shreffler and Frederick L. Tyson, COSPB; and Ms. Kathy Ahlmark, Mr. Theodore Outwater, Mr. James Remington and Ms. Sharon D. Beard, WETP, received a group award, "For exemplary efforts in identifying and facilitating the funding of the most meritorious research applications submitted under the American Recovery and Reinvestment [Act]."

Drs. Linda K. Bass, Sally Eckert Tilotta, Leroy Worth, and Ms. Rose Anne McGee and Ms. Michelle Victalino, SRB, received a group award, "For superior efforts in completing numerous successful reviews for the American Recovery and Reinvestment program during a period of greatly increased workload and decreased staff."

Drs. Linda K. Bass, Gwen Collman, Kimberly Gray, Annette Kirshner, Cindy Lawler, and Mr. Aaron Nicholas received a group award for, "In recognition of exemplary leadership in creating the vision for and the coordination, implementation and management of the Children's Environmental Health/disease Prevention Centers Program."

Drs. Linda K. Bass, GMB, Gwen Collman and J. Patrick Mastin, OD, Christina Drew, PAB, William A. Suk, CRIS, Claudia Thompson, SPHB, and Ms. Dorothy Duke, GMB, Mr. Joseph Hughes, WETP, and Ms. Margarita Roque, OM, received a group award for, "For exceptional leadership/administration of the

American Reinvestment/Recovery Act Stimulus Program leading to the enhanced funding for NIEHS extramural investigators at universities/institutions across the USA.

Ms. Wanda Boggs, Ms. Pamela Clark, Mr. Dwight B. Dolby, Ms. Lisa A. Edwards, Mr. Donald Ellis, Ms. Barbara Gittleman, Ms. Natasha Hurwitz, Ms. Carolyn Mason, Mr. Aaron Nicholas, Mr. Jerry Phelps, Ms. Donna Roach, Ms. Michelle Victalino, Mr. James Williams, and Ms. Carolyn Winters, GMB, received a group award, "For extraordinary effort in completing an unprecedented number of grant awards for the American Recovery and Reinvestment Act within an exceptionally short timeframe."

Ms. Kathy Ahlmark, Ms. Sharon Beard, Mr. Joseph Hughes, Mr. Theodore Outwater and Mr. James Remington, WETP, received a group award, "For creation of green job training initiative by bringing from the emerging fields of green chemistry, green engineering, green remediation, and for building new partnerships."

Ms. Margarita Roque, OM, Drs. Gwen Collman and J. Patrick Mastin and Ms. Rachel Gross, DERT/OD, and Ms. Dorothy Duke, GMB, in conjunction with other NIEHS staff, received a group award, "For extraordinary effort in the coordination of the financial management in the awarding of funds from the American Recovery and Reinvestment Act."

Ms. Margarita Roque, OM, was part of an NIEHS group who received an award, "For successfully consolidating more than 300 NIEHS staff from two separate facilities to the new Keystone Building."

Ms. Lisa Edwards, GMB, was one of three NIEHS employees who received a Peer award. The NIEHS Peer Recognition Awards were established in 1999 and provide a unique mechanism by which NIEHS employees can recognize fellow employees who have consistently provided extraordinary assistance to their fellow workers.

Ms. Rose Anne McGee, SRB, was one of six NIEHS employees who received the Unsung Heroes Award. The NIEHS Unsung Hero Award provides Branch and lab Chiefs with a mechanism to recognize employees who make valuable contributions that have a huge impact on the programs of the Institute. These are often people who work hard behind the scenes whose contributions might otherwise go unrecognized.

STAFF ACTIVITIES

Mr. Phelps, PAB, and Dr. Humble, COSPB, were judges at St Timothy's K-8 School Science Fair in Raleigh on January 28. 130 science projects were entered in the contest. Each judge was responsible for reviewing and rating 8-9 projects and then selecting the overall grade/class winners. Perry Suk, wife of Bill Suk, CRIS, is a Science Instructor at the school.

THE NIEHS WETP, the U.S. EPA, Office of Air Quality Planning and Standards (OAQPS) and the Deep South Center for Environmental Justice at Dillard University co-sponsored the 2010 Conference on Environmental Justice, Air Quality, Goods Movement, and Green Jobs: Evolution and Innovation on January 25-27 in New Orleans, Louisiana. This conference brought together over 450 individuals to showcase grass roots leaders and other experts from across the country who are experienced with best practices for communities that are facing environmental justice challenges. The NIEHS WETP also held their Awardee Meeting on the afternoon of January 27. *Dr. Collman, Interim Director, DERT/OD,* spoke at the meeting.

Drs. Allen, SRB and Heindel, COSPB, were invited lecturers at the NCSU Toxicology Curriculum Seminar Series January 12. They presented an overview of the new NIH application and review guideline changes as well as discussed aspects of grant writing and communication skills.

Dr. Thompson, SPHB/CRIS, organized a workshop with Drs. Scott Masten, NTP, and Dr. Maureen Gwinn, U.S. EPA, entitled “Asbestos: A Science-Based Examination of the Mode of Action of Asbestos and Related Mineral Fibers,” that was held at the Sheraton in Chapel Hill, North Carolina, December 16-17. This workshop was sponsored by NIEHS, the NIEHS Superfund Research Program, US EPA and ATSDR.

Mr. Hughes, WETP, presented on a panel addressing emerging health and safety issues related to the development of new green industries at the NIOSH Making Green Jobs Safe Workshop held at the Mandarin Oriental Hotel, December 14–16, in Washington, DC.

Drs. William Suk, Claudia Thompson, Heather Henry and Ms. Beth Anderson, Superfund Research Program (SRP), met with Mr. Mathy Stanislaus, the Assistant Administrator for the EPA Office of Solid Waste and Emergency Response and other senior EPA officials to introduce Mr. Stanislaus to the program, describe the SRP Strategic Planning process and to advance future collaborations. The meeting had many positive outcomes, including the recommendation of establishing a Memorandum of Understanding between the SRP and the EPA Superfund Office.

Dr. Heindel, COSPB, organized and led the discussion at a brainstorming meeting held in Miami Beach, Florida, on December 11. It was attended by over 40 scientists interested in understanding the role of environmental exposures in obesity, diabetes and metabolic syndrome.

Mr. Hughes, WETP, and WETP staff organized and led the DOE/NIEHS WETP Collaborative Safety Training Self Assessment Workshop at the DOE Savannah River Site Office (SRS) In Aiken, South Carolina on December 8-9. Key emerging safety and health training issues were addressed by a broad cross-section of stakeholders in the DOE cleanup process.

Mr. O’Fallon, SPHB, and Ms. Beth Anderson, CRIS/SRP, convened a roundtable session on Risk Communication and Environmental health. *Dr. Drew, PAB*, assisted with the development of questions and facilitated interactions with the Risk Communication Specialty Group at Society for Risk Analysis, in Baltimore, Maryland, December 6-8. A full roundtable summary with recommendations and key topics can be found under Meetings.

Dr. Heindel, COSPB, was the invited Keynote speaker at the 8th Annual Pediatric Scholars Meeting in Reston, Virginia, December 4-5. His presentation was titled, “The Developmental Origins of Disease/ Dysfunction: Implications for Pediatricians. He also presented a grantsmanship talk focusing on the new NIH review criteria.

Dr. Maull, SPHB, attended the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Stakeholders Workshop 2009 held at the Marriott Wardman Park Hotel, Washington, D.C., December 2-3.

Dr. Henry, CRIS/SRP, chaired the “Total Petroleum Hydrocarbons / Polycyclic Aromatic Hydrocarbons” session at the Phytotechnologies 6th International Conference, December 1-4, St. Louis, Missouri. The session brought together researchers

Mr. Hughes and Mr. Remington, WETP, presented an overview on the current state of hazmat training issues at the IAFF Instructor Development Conference (IDC) and National Advisory Board on December 1-3, in San Antonio, Texas.

Dr. Heindel, COSPB, was on the planning committee for the Health and Environmental Sciences Institute Workshop on the State of the Science of Epigenetics, which was held at NIEHS in Research Triangle Park, North Carolina, November 28-30. The meeting was looking at what data are needed before epigenetics can be incorporated into risk assessment.

Dr. Suk, CRIS/SRP, was a keynote speaker, and presented in a technical session, at the 13th International Conference for the Pacific Basin Consortium for Environment and Health Sciences, held in Perth, Australia, November 20-22, 2009. The theme of the conference was Environmental Exposures in the Era of Climate Change. The Pacific Basin Consortium has promoted information exchange and cooperative research on issues related to environmental pollutants and human health for more than two decades through twelve international conferences and numerous training programs held throughout the Pacific Basin region. The conference had about 350 participants from over 30 countries and disseminated scientific information and analysis supporting the management of regional environmental problems, including exposure to metals such as mercury, arsenic, fluoride and lead, organic compounds such as persistent pesticides, PCBs and dioxins, and emerging toxic threats. Related conference sessions involved participants with primary interests in toxicology, ecology, engineering and management of hazardous wastes. Dr. Suk's plenary address was entitled "Coordinated Global Environmental Health Network to Address Environmental Exposures and Reduce the Burden of Disease." In addition, he chaired a session on lead, and presented in a session on Arsenic a talk entitled "Multidisciplinary Strategies for Reducing Arsenic Exposures." The thirteenth in a series, this international conference is designed to identify solutions to human environmental health problems and to facilitate the establishment of sustainable collaborative programs around the world.

Dr. Henry, CRIS/SRP, organized a session at the Society of Environmental Toxicology and Chemistry (SETAC) in New Orleans, Louisiana held November 19-23. The session, titled "Engineered Nanomaterials: Regulation, Life Cycle Perspectives, and Environmental Applications," considered the challenges and possible implications of the use of engineered nanomaterials directly applied to the environment for soil and groundwater remediation.

Drs., Gwen Collman, Interim Director, DERT, and Dilworth, Maull, Reinlib, and Thompson, SPHB, attended the annual business meetings of Breast Cancer and Environment Research Centers held at Cavallo Point, Sausalito, California, on November 18.

Dr. Heindel, COSPB, developed a session and presented a talk at the 6th Annual Developmental Origins of Health and Disease International Meeting held November 17-24, in Santiago, Chile.

Drs. Maull, Reinlib, and Thompson, SPHB, attended the Mammary Gland Evaluation and Risk Assessment Workshop held at the Waterfront Hotel, in Oakland, California, November 16-17. This workshop was supported by the Environmental Protection Agency, NIEHS, and the California Breast Cancer Research Program.

Ms. Beard, WETP, continued her involvement in the Brownfields Federal Working Group as the NIEHS Lead in the Technical Program Review Committee for the "Brownfields 2009: Sustainable Communities Start Here" as well as in the planning and organizing of the several sessions/meetings including the Environmental Justice Caucus, the NIEHS Minority Worker Training Awardee Meeting (which was co-moderated by Mr. Outwater, WETP) and the eight NIEHS Sessions of Interest for the 2009 Brownfields Conference that was held in New Orleans, Louisiana on November 15-18. This was the first year that NIEHS organized and sponsored a mobile tour for Brownfields 2009 entitled "Green Job Training in the Bayou: NIEHS Job Training Programs at Work". She also presented on WETP health and safety programs, the integration of green jobs training, and NIEHS ARRA specific green job funding on a panel entitled "Brownfields Revitalization and Green Jobs." Mr. Outwater, WETP co-moderated the WETP MWTP session at the EPA national Brownfields conference in New Orleans, Louisiana, on November 15-18. More on the tour and the full conference activities of NIEHS can be found at <http://www.brownfieldsconference.org/en/Page.MobileWorkshops.aspx> and at <http://tools.niehs.nih.gov/wetp/events.cfm?id=2487>.

Mr. Hughes, WETP, gave an overview of existing hazmat training programs at the CDC-ATSDR Chemical Emergencies Work Group Meeting of the National Chemical Conversation on Friday, November 13, at the BWI (Baltimore, Maryland) Airport Marriott. The presentation given in conjunction with OSHA reviewed

the current state of NIEHS programs with regard to preventing, preparing for, responding to, and recovering from acute chemical incidents.

Mr. Hughes, WETP, and Daniel Youhas from the MDB Clearinghouse gave a national webinar to the Interstate Chemical Threats Workgroup on Thursday, November 12. The webinar focused on the use of Social Media in Emergency Response. This presentation provided a basic overview of social media, in particular the technologies Twitter and Facebook, and their potential use to the emergency response community in response operations.

Dr. Drew, Mr. Phelps, and Ms. Davis, PAB, attended the American Evaluation Association's Annual Conference titled "Evaluation 2009" in Orlando Florida on Nov 11-14 where Dr. Drew chaired a session. The session, titled "Out of Control? Selecting Comparison Groups for Analyzing National Institute of Health Grants and Grant Portfolios," examined the different ways NIH Institutes/Centers select comparison groups for analyses. Dr. Drew also presented a paper titled "Establishing a Comparison Set for Evaluating Unsolicited P01s at the National Institute of Environmental Health Sciences" during the session.

Dr. Heindel, COSPB, was an invited presenter at the November 10-13 meeting, "Substances with Endocrine Disrupting Properties under the New European Union Plant Protection Product Regulation - Establishment of Assessment and Decision Criteria." The meeting, held in Berlin, Germany, was sponsored by the German Federal Institute for Risk Assessment. His talk was titled, "Importance of Dose and Timing in Studies of Endocrine Disrupting Chemicals." He also led a break-out session on low dose effects of endocrine disrupting chemicals.

Mr. O'Fallon, SPHB, organized, moderated and presented in a session at the American Public Health Association meeting in Philadelphia, Pennsylvania, November 7-11 that highlighted the key areas of the PEPH program. Dr. Collman, DEDT/OD, was one of the session presenters and spoke on the importance of federal coordination. Mr. O'Fallon highlighted the need for capacity building for all research partners.

Mr. Hughes, WETP, presented on safety and health issues with green jobs development as part of an Occupational Health Section Panel on Energy Policy, Green Chemistry, and Occupational Health at the American Public Health Association Annual Meeting in Philadelphia, Pennsylvania, November 4-10. *Ms. Beard, WETP*, moderated the session on safety and health issues with green jobs development. She also presented on safety and health issues entitled "Expanding green jobs and sustainability initiatives within the NIEHS Worker Training Program as a part of a Joint Occupational Health and Safety and Environment Section Session on Blue/Green Issues - Green Schools, Safe Jobs, and Better Chemicals.

On November 6, the American Journal of Public Health released a special on-line issue the development of which was funded by NIEHS, NIOSH, EPA and the University of Massachusetts at Lowell. *Mr. O'Fallon, SPHB*, conceived of this special issue, obtained support from NIEHS leaders, coordinated with the other federal partners, and worked with AJPH staff to make the special issue a reality. Mr. O'Fallon co-authored an article that examines the outcomes and accomplishments of the NIEHS-led Environmental Justice program. See: <http://www.ajph.org/content/vol99/issueS3/>.

Dr. Dilworth, SPHB, chaired a symposium session entitled "Community Engagement to Facilitate Exposure Assessment and Environmental Health Research" at the International Society for Exposure Science annual meeting in Minneapolis, Minnesota on November 5. The purpose of the presentation was to explore opportunities for and benefits of community participation in environmental health research by highlighting success stories from several NIEHS-sponsored research programs within the Partnerships for Environmental Public Health (PEPH) umbrella program. The symposium included presentations from three NIEHS extramural grantees (Drs. Susan Pinney, Thomas Arcury, Victoria Persky) and Dr. Collman, Acting Director of the Division of Extramural Research and Training at NIEHS.

Dr. Maull, SPHB, attended the Global Health Security Initiative Workshop on Public Health Emergency Medical Countermeasures held at the Fairfax at Embassy Row, Washington, D.C., November 4-5.

Drs. Shaughnessy and Dilworth, SPHB, co-presented a talk entitled “the NIH Grant Funding Process” at a student workshop at the International Society for Exposure Science annual meeting in Minneapolis, Minnesota on November 3. The purpose of the workshop, which also included representatives from EPA and the Mickey Leland Center, was to help students and new researchers understand the grant-writing process, learn how to write successful grant applications, and learn about different types of grants awarded by the agencies/programs represented.

Dr. Tyson, COSPB, organized and chaired two sessions on Environmental Influences on Epigenetic Regulation of Gene Expression at the International Society for Exposure Science (ISES) in Minneapolis, Minnesota, on November 2. Epigenetics was identified by the organizers of the ISES annual meeting as a high priority area and these sessions provided an overview of some of the mechanisms associated with various exposures and associated disease outcome studies supported by the NIEHS. Dr. Tyson also gave a presentation describing the NIH Roadmap Epigenomics Program during the second session.

Dr. Heindel, COSPB, was an invited lecturer at the University of Cincinnati, Department of Environmental Health, October 29-30 in Cincinnati, Ohio. He presented a seminar, “The Developmental Origins of Disease: Environmental Exposures and Epigenetic Mechanisms” as well as a grantsmanship seminar to students.

Mr. O’Fallon, SPHB, helped organize a roundtable discussion session on Federal coordination in the context of environmental public health programs at the National Environmental Public Health Conference held in Atlanta, Georgia, October 28-29. Mr. O’Fallon worked with his colleagues at the CDC/NCEH, EPA and CDC/ATSDR to organize the session.

Dr. Humble, COSPB, participated in the Rx for Science Literacy teacher workshop held at Duke University, Durham, North Carolina, on October 28. The workshop was sponsored by the North Carolina Association for Biomedical Research (NCABR) and was attended by approximately 24 North Carolina middle and high school science teachers. Dr. Humble was the moderator for the morning training sessions, introducing the teachers to the science curriculum and activities developed by NCABR and NIH.

Mr. O’Fallon, SPHB, contributed to the planning, moderated a breakout session on communication strategies, reported back on the discussion, and convened a brief meeting of the NIEHS grantees at the Partners in Research (PIR) grantee meeting in Bethesda, Maryland, October 26-27. The PIR program is a trans-NIH program that brings together University researchers with community-based organizations and residents.

Mr. Remington, WETP, participated on the 2009 National Environmental Public Health Conference, October 26-27, in Atlanta, Georgia.

Dr. McAllister, SPHB, helped to organize, with other members of the IGES educational committee, and chair a joint International Genetic Epidemiology Society (IGES) and American Society of Human Genetics (ASHG) meeting session in Honolulu, Hawaii on October 22. The session, entitled “The Next Frontier: Advancing from Genetic Risk to Functionality and Testing” explored the potential next steps beyond GWAS studies for testing the functional aspects of genetic variants and the potential use of direct-to-consumer genetic tests.

Dr. Shreffler, COSPB, participated in an interactive forum on environmental health sciences education at the Arizona Center for Integrative Medicine on October 22. The purpose of the meeting was to identify key elements of an environmental health curriculum for use with medical, nursing and pharmacy students; identify the content, length, focus, and resources to deliver a 5-6 hour on-line module focused on environmental health; and identify key strategies that will lead to the implementation of environmental

curriculums across the country, the use of learning tools such as the module, and engage practitioners. Participants included those with expertise in curriculum development and on-line modules, practicing health care professionals, and leaders in academic medicine.

NIEHS/WETB hosted its Awardee Technical Conference, “Global Safety and Health Issues and Their Impact on Worker Training” October 21- 22, in Chapel Hill, North Carolina.

Dr. Heindel, COSPB, was an invited speaker at the US-China Relations Meeting working group on environmental exposures, which was held in Beijing, China, Oct 21. He presented a talk that overviewed NIEHS and our research opportunities and opportunities for collaborations. He also presented a variation on that talk at Peking University in Beijing and at Fudan University School of Public Health in Shanghai.

Dr. Heindel, COSPB, was an invited speaker at the Mid Atlantic SOT annual meeting in Piscataway NJ Oct 14-15th where he gave his talk titled, “ Chemicals in the Environment: What Doesn’t Make Us Sick...Makes Us Fatter”.

Mr. Remington, WETP, participated on the InterAgency Board October 13-15 in Kansas City, Missouri.

Dr. Heindel, COSPB, was an invited speaker at the NIH workshop on alternative hypotheses for obesity sponsored by the trans-NIH Obesity Task Force Sept 25 in Bethesda, Maryland. His talk was titled, “Chemicals in the Environment: What Doesn’t Make Us Sick...Makes Us Fatter.”

Mr. Outwater, WETP, presented on program goals at the ICWU ARRA train the trainer in September 2009 in Cincinnati, Ohio.

Dr. Shreffler, COSPB, participated in the Environmental Health Sciences Regional Showcase of Fellows in Cincinnati, Ohio, on September 18, 2009, and chaired a panel discussion: Taking Charge of Your Career. The panel explored the perceived future of the environmental health sciences researcher, from the perspective of a senior faculty member and training director, a junior researcher with an Outstanding New Environmental Health Scientist Award, a career development awardee, and an administrator who has observed career outcomes of many trainees. The showcase represented seven T32 Training Programs, two Superfund Centers, two Environmental Health Sciences Centers and several research grants.

Dr. Maull, SPHB, participated in the CounterACT-sponsored Sulfur Mustard Symposium in Albuquerque, New Mexico, September 16-18.

Dr. Henry, SRP, organized a four-part webinar series on “Computational Toxicology: New Approaches for the 21st Century” aired on EPA’s Clu-IN.org on the following dates: May 28, June 24, July 7, and September 9. The seminars featured SRP, NIEHS, and EPA/NCCT researchers and provided an introduction to the key concepts of computational toxicology along with case studies demonstrating the utility of these approaches (e.g. high throughput screening, computer modeling, informatics) to risk assessment.

Mr. O’Fallon, SPHB, in conjunction with staff from the U.S. Environmental Protection Agency, National Institute of Occupational Safety and Health and the University of Massachusetts Lowell, conceptualized and brought to fruition a new resource for those working in public health. A free online supplement to the American Journal of Public Health (AJPH), comprised of 30 research-based articles, editorial and commentaries from community, government and academic leaders, demonstrates the advancement and evolving sophistication of environmental and occupational justice work and the use of community-based participatory research approaches over the past decade. See: <http://www.ajph.org/content/vol99/issueS3//>.

The ATSDR National Conversation planning committee selected *Mr. O'Fallon, SPHB*, to be a member of the 'Serving Communities' working group, which is one of several working groups. Other DERT members who are a part of National Conversation working groups are *Mr. Chip Hughes, WETP*, (Chemical Emergency Response) and *Ms. Anderson, CRIS*, (Policy).

UPCOMING MEETINGS and WORKSHOPS

The National Academy of Science (NAS) meeting entitled "The Exposome: A Powerful Approach for Evaluating Environmental Exposures and Their Influences on Human Disease" will be held at the NAS in Washington, D.C., February 25-26. *Drs. Shaughnessy, SPHB, and Balshaw, CRIS*, are on the organizing committee.

STAFF CHANGES

Arrivals:

Dr. Janet Cakir, joined CRIS, on October 26. Dr. Cakir comes to NIEHS from the Environmental Protection Agency and Natural Resources Conservation Service. At the EPA she worked in the economics group leading teams to perform cost/benefit analyses of new air pollution regulations. From there she went to the Natural Resources Conservation Service (NRCS) and spent a year as a team lead to provide Geographic Information Systems expertise to the Agency. Dr. Cakir has a Ph.D. in Parks, Recreation, and Tourism management from North Carolina State University, an M.S. in Geography from Virginia Polytechnic Institute and State University, and a B.S. in Geography from Radford University.

Ms. Elizabeth Ruben joined PAB on November 23. Ms. Ruben comes to NIEHS from SAS by way of the Department of Agriculture. As Product Manager at SAS, she guided the development of two Web-based and one desktop-based OLAP (multidimensional) viewers from inception to second release. They were part of a larger software bundle that generated approximately \$20 million in revenue in its second year. She was also Product Manager for Data Visualization, which included the approximately \$70 million SAS/GRAPH revenue stream. Prior to SAS, Ms. Ruben was an International Development Consultant at Research Triangle Institute and worked with country governments in Latin American, the Caribbean, and Asia to improve their social and economic policies. She has an M.S. in Appropriate Technology from the University of Pennsylvania and is also a PMP-certified Project Manager.

Ms. Barbara Gittleman, GMB, converted to a permanent staff member as a Grants Management Specialist on November 22. She came to NIEHS as a temporary ARRA employee in GMB.

Departures:

Ms. Donna Roach, GMB, left DERT on November 20, to take a position with the NIEHS/NTP. Ms. Stacy Torian, DEAS, Ms. Natasha Hurwitz, Mr. Dwight Dolby, and Ms. Carolyn Winters GMB, contracted to help with ARRA, have completed their contracts with NIEHS.