



# Environmental Factor

Your Online Source for NIEHS News

March 2010

## NIEHS Spotlight



### [On the Road with Director Linda Birnbaum](#)

NIEHS/NTP Director Linda Birnbaum, Ph.D., showed no sign of slowing down as she traveled the country recently, building and strengthening partnerships.



### [Collins' Priorities Frame Council Discussion](#)

The new NIH research agenda articulated by Director Francis Collins, M.D., Ph.D., played an important role in the winter meeting of the National

Advisory Environmental Health Sciences Council.



### [Mason Receives 2010 Bruker Award](#)

The Electron Spin Resonance (ESR) Spectroscopy Group of the Royal Society of Chemistry (RSC) has honored NIEHS Principal Investigator

Ron Mason, Ph.D., with the 25th Annual Bruker Prize.



### [Superfund Researcher Elected to National Academies](#)

On Feb. 17, the National Academy of Engineering (NAE) announced the election of NIEHS SRP grantee Lisa Alvarez-Cohen, Ph.D., as one of 68 new members.



### [Birnbaum Revisits TSCA in Senate Testimony](#)

When Senator Frank Lautenberg (D-NJ) convened hearings on chemical safety Feb. 4, NIEHS/NTP Director Linda Birnbaum, Ph.D.,

was one of the expert witnesses testifying.

## Science Notebook



### [Ancient Fires – Modern Dilemma](#)

Long-time NIEHS grantee Kirk Smith, Ph.D., presented his findings on household fuel use and its connection to indoor and

outdoor air pollution and health in a talk at Duke University Feb. 17.



### [Epidemiology Shines at Advisory Council Meeting](#)

A distinctive feature of the February 18-19 meeting of the NIEHS Council was a three-part series of scientific presentations on a wide-range of

Institute-funded epidemiological studies.



### [NIEHS Welcomes Four New Principal Investigators](#)

NIEHS began its new fiscal year with four new tenure track principal investigators — Guang Hu, Ph.D., Patricia Jensen, Ph.D., Raja Jothi,

Ph.D., and R. Scott Williams, Ph.D.



### [Researcher Underscores Importance of Intracellular Communication](#)

Yale University Professor of Pathology and Genetics Gerald Shadel, Ph.D., spoke Feb. 2 on

“Mitochondrial Signaling in Disease and Aging,” hosted by NIEHS Postdoctoral Fellow Jeffery Stumpf, Ph.D.

## NIEHS Spotlight



### [Hearing Sparks Call for Environmental Justice in Alaska](#)

In a press release timed to coincide with a hearings on chemical safety Feb. 4, spokespersons for an NIEHS grantee called for action on circumpolar atmospheric pollution in Alaska.



### [Jung Joins NIEHS as Chief of Staff](#)

In a February statement to employees, NIEHS/NTP Director Linda Birnbaum announced the appointment of Commander Paul Jung, M.D., of the U.S. Public Health Service as NIEHS chief of staff.



### [Fellows Participate in Biotech Career Workshop](#)

NIEHS fellows joined their counterparts in the region Feb. 9 for the first session of the North Carolina Biotechnology Center's (NCBC) three-part Ph.D. Workshop Series.



### [Shepard Edits EJ Issue on Climate Change](#)

A special issue of the journal Environmental Justice edited by NIEHS grantee Peggy Shepard highlights the disproportionate effects of global warming and pollution on disadvantaged communities worldwide.



### [Superfund Video Offers Plain Talk on Arsenic](#)

NIEHS-funded researchers at the Dartmouth Toxic Metals Research Program premiered their new short film for the general public, "In Small; Doses: Arsenic," Feb. 11 in Concord, N.H.



### [NIEHS and NTP Gear Up for a Productive Year at SOT](#)

Staff from NIEHS and NTP will speak at more than 30 different sessions and present more than 60 posters at the Society of Toxicology meeting in Salt Lake City March 7-11.

## Science Notebook



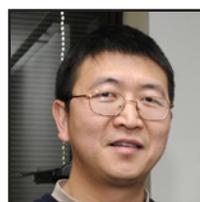
### [Estrogen Receptors and Tumor Development](#)

On Feb. 4, NIEHS Principal Investigator Kenneth Korach, Ph.D., presented a talk on "Estrogen Receptors: Are They Involved in Tumorigenesis and Toxicity?" to a capacity audience.



### [Researchers Confirm Link Between Maternal Age and Autism](#)

In a new NIEHS-funded study, researchers have confirmed a link between advanced maternal age and an elevated risk of having a child with autism.



### [Mining the Genome with Deep Sequencing](#)

On Jan. 27, guest lecturer and computational biologist Yuan Gao, Ph.D., delivered a seminar to a standing-room-only audience of NIEHS researchers.



### [Superfund Research Prompts Review of Antimicrobials](#)

A call for more stringent regulations for antimicrobial compounds by Rep. Edward Markey (D-MA) could mean that the days of antibacterial trash bags are numbered.



### [Linking Disease Incidence with Environmental Exposure Data Over Time](#)

Elena N. Naumova, Ph.D. and her research team describe a dynamic mapping strategy for visualizing complex spatio-temporal data, in a new study funded by NIEHS and NIAD.

## Inside the Institute



### [NIEHS Celebrates Culture During Black History Month](#)

The NIEHS Diversity Council called on the considerable talent of Institute employees and contractors to celebrate the wealth of African American culture on Feb. 23.



### [EPA Leadership Development Participants Visit NIEHS](#)

A delegation of EPA leaders-in-training joined NIEHS/NTP Director Linda Birnbaum, Ph.D., and members of her senior staff on Jan. 12 in Rodbell Auditorium for a presentation about NIEHS.

Auditorium for a presentation about NIEHS.



### [Future PIs Wow NIEHS Judges](#)

NIEHS Program Administrator Mike Humble and Program Analyst Jerry Phelps participated in the Annual Science Fair at St. Timothy's School in Raleigh on January 28.



### [Lecture Series Announces Upcoming Speakers](#)

The editorial staff of the American Scientist magazine invites NIEHS scientists and staff to talks by the next two speakers in its Pizza Lunch Lecture Series held each month in Research Triangle Park.

Series held each month in Research Triangle Park.



### [Environmental Enthusiast Colleen Anna Retires](#)

After 34 years of government service, 29 here at NIEHS, Eicosanoid Biochemistry Group Biologist Colleen Anna spent her last day at work on Feb. 26.

## Science Notebook



### [NIEHS Clinical Researchers Present Grand Rounds Lecture](#)

NIEHS Environmental Autoimmunity Group Principal Investigator Frederick Miller, M.D., Ph.D., and Deputy Chief Lisa Rider, M.D., presented a Clinical

Rounds lecture Feb. 24 at Masur Auditorium on the NIH Campus.



### [This Month in EHP](#)

The eye-catching cover of the March issue of EHP provides a backdrop for a news feature on "Better Burning, Better Breathing: Improving Health with Cleaner Cook Stoves."



### [Eskenazi is Upcoming Distinguished Lecturer](#)

Epidemiology takes center stage March 16 with the next talk in the NIEHS Distinguished Lecture Series by veteran NIEHS grantee Brenda Eskenazi, Ph.D.

## Extramural Research

### [Extramural Papers of the Month](#)

- [Obesity is a Tumor Promoter](#)
- [Phthalate Exposure Alters Children's Behavior and Cognitive Function](#)
- [Asthma Symptoms in Children Associated with Acetaminophen Use During Pregnancy](#)
- [PCBs Found in Indiana Harbor](#)

## Intramural Research

### [Intramural Papers of the Month](#)

- [Reciprocal Epigenetic Modifications of Histone H2B in Apoptosis](#)
- [Obese Male Mice Have Reduced Fertility and Increased Sensitivity to Environmental Chemicals](#)
- [Acetaminophen-Induced Transcriptional Changes Predict Liver Injury](#)
- [Estrogen Receptor Enhances p53 Transcriptional Activity](#)

## Calendar of Upcoming Events

- **March 4**, in Rall D450, 10:00–11:00 — Laboratory of Molecular Carcinogenesis Seminar Series presentation by Angela Ting, Ph.D., on “Utilizing MBD-isolated Genome Sequencing to Study Genome-wide DNA Methylation Pattern”
- **March 16**, in Rodbell Auditorium, 11:00–12:00 — NIEHS Distinguished Lecture Series with Brenda Eskenazi, Ph.D., speaking on “Organophosphate Pesticide Exposure and the Development of Children Living in an Agricultural Community: Results of the CHAMACOS Study”
- **March 23**, in Rodbell Auditorium, 8:00–4:30 — Environmental Stewardship Initiative Annual Meeting
- **March 23 (Offsite Event)**, at the University of North Carolina at Chapel Hill Sonja Haynes Stone Center Theater, 6:30 p.m. — UNC Institute for the Environment Environmental Speaker Series, featuring Linda Birnbaum, Ph.D.
- **March 25**, in Rodbell Auditorium, 9:00–10:00 — Keystone Science Lecture Seminar Series presentation on “Environmental Risk Factors for Copy Number Variation in Human Chromosomes,” by Thomas Glover, Ph.D.
- **March 26**, in Rodbell Auditorium, 2:00–3:00 — NIEHS Spirit Lecture with Linda Birnbaum, Ph.D. Reception follows.
- **March 27 (Offsite Event)**, at Meredith College — NC Science and Engineering Fair 2010
- **March 30 (Offsite Event)**, at the North Carolina Biotechnology Center, 12:00–1:00 — American Scientist Lecture Series featuring Geoffrey Ginsburg, M.D., Ph.D., topic TBA. [RSVP](#) for pizza
- **March 30**, in Rodbell Auditorium, 2:00–3:00 — Rescheduled: Distinguished Lecture Series Annual Rodbell Lecture featuring Jennifer Lippincott-Schwartz, Ph.D., speaking on “Advances in Super-Resolution Imaging”
- **March 30 (Offsite Event)** at North Carolina State University (NCSU) Toxicology Building on the NCSU Centennial Campus, 4:00 — Seminar on “The Glucocorticoid Receptor in Health and Disease” with John Cidlowski, Ph.D.
- **March 31**, in Rodbell Auditorium, 8:30–2:30 — Harmonization of Human Chamber Air Pollution Exposure Studies
- View More Events: [NIEHS Public Calendar](#)

# NIEHS Spotlight

---

## On the Road with Director Linda Birnbaum

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., showed no sign of slowing down as she traveled the country recently, building and strengthening partnerships. In final days of January alone, Birbaum spoke to grantees and stakeholders in Detroit and Washington. She also took advantage of her time at the Capitol and nearby Bethesda to meet with members of Congress and colleagues at NIEHS grantees and partners.

### Building bridges through collaborations

Birnbaum delivered the keynote address Jan. 20 at the University Research Corridor conference at Wayne State University (WSU) in Detroit. Researchers from WSU joined their counterparts from the University of Michigan (UM) and Michigan State University in an effort to develop collaborative approaches to solve problems and create opportunities in environmental health sciences.

Emphasizing the importance of “big science” involving cross-disciplinary teams of experts to better understand complex disease risk from complex environmental factors, Birnbaum focused on cancer, autism, climate change, and the potential health risks from exposure to nanomaterials. Each of these problems, she noted, can best be addressed through the kind of divergent thinking that cross-disciplinary team science fosters.

“We need a lot of people with a lot of knowledge from different areas,” she said, “[and] it’s easier if we all pull together.”

Along with Birnbaum, a cross-disciplinary group of leaders in environmental health science research participated in a panel discussion at the conference. They included Howard Hu, M.D., Sc.D., National Science Foundation International chair and UM professor; Norbert Kaminski, Ph.D., Center for Integrative Toxicology director and MSU professor; Christine Cole-Johnson, Ph.D., biostatistics and research epidemiology chair at Henry Ford Health Systems; and Melissa Runge-Morris, M.D., acting director of WSU’s Institute for Environmental Health Sciences.

### Reaching out to public health educators

On Jan. 29 Birnbaum and NIEHS Senior Advisor for Public Health John Balbus, M.D., attended a meeting of 14 deans and other



*Birnbaum, above, sees her busy schedule as a way of building relationships in the effort to improve the state of environmental public health worldwide. (Photo courtesy of Steve McCaw)*



*Balbus, above, is working to increase our engagement with the public health academic and advocacy communities, such as ASPH. (Photo courtesy of Steve McCaw)*

representatives of public health schools from the Association of Schools of Public Health (ASPH) in Washington. An additional 20 public health education leaders joined the meeting by phone.

Birnbaum's remarks were part of a dialogue between NIEHS leaders and public health educators on ways to integrate environmental health initiatives into training for the next generation of public health professionals and ways NIEHS grants can be utilized to support training. "We are committed to developing, translating, and sharing critical public health knowledge for the protection of communities and reduction of health disparities," she told the audience.

Meeting participants pledged to follow up on their discussion and work more closely in the future to help educators stay abreast of new developments in environmental public health, such as global health initiatives, the National Children's Study, and cutting-edge research in the area of exposure biology. For their part, ASPH members welcomed help from NIEHS leadership to raise the profile of public health on the national level with decision-makers at NIH, the U.S. Department of Health and Human Services, and Congress.



*Shown during the September 2009 advisory council meeting, NIEHS Legislative Liaison Mary Gant is the longest serving member of the Institute's Bethesda staff. Gant set up meetings for Birnbaum with members of Congress. (Photo courtesy of Steve McCaw)*

### **A very busy two weeks on the road**

In addition to these two stops, Birnbaum managed to squeeze in several additional meetings in Washington — including a Gene-Environment Integration (GEI) Workshop and 3rd Annual GEI Exposure Biology Grantees Meeting as well as meetings with the ad hoc Congressional Biomedical Caucus, Representative Ben Chandler (D-Ky.), and U.S. Department of Health and Human Services Assistant Secretary for Health Howard Koh, M.D.

[Return to Table of Contents](#)

## **Collins' Priorities Frame Council Discussion**

*By Eddy Ball*

The new NIH research agenda articulated by Director Francis Collins, M.D., Ph.D., played an important role in the winter meeting of the National Advisory Environmental Health Sciences Council. NIEHS/ NTP Director Linda Birnbaum, Ph.D., scientists, and administrators joined Council members Feb. 17 for a retreat organized around Collins' [priorities](#). Collins' five "areas of particular promise" also emerged in presentations and discussions during the Council's public sessions Feb. 18 and 19 (see [text box](#)).

During the first report of the public meeting Feb, 18, Birnbaum referred to Collins' research agenda and its



*Kleeberger, shown during a lighter moment in his presentation, said organizers "decided that this would be the best format we could follow for this retreat to actually provide not only for our own interests but also for Dr. Collins' interests." (Photo courtesy of Steve McCaw)*

bearing on the future direction of NIEHS and NTP research as part of her review of the Institute's activities and accomplishments since the last Council meeting in September.

### **Retreat tackles how to best position environmental health**

Birnbaum left it to NIEHS Acting Deputy Director Steve Kleeberger, Ph.D., to explore in greater depth the implications of the challenge to Institutes and Centers to “identify what we are currently doing that is consistent” with Collins’ research agenda. As Kleeberger explained, the process will be an opportunity for NIEHS to “think creatively about new directions for environmental health in the priority areas” as well as “examine and expand the priority areas themselves in ways that Francis and maybe others in Building 1 may not have considered.”

Kleeberger opened his report by acknowledging the major contributions of NIEHS Division of Extramural Research and Training Interim Director Gwen Collman, Ph.D., and Director of the NIEHS Office of Policy, Planning, and Evaluation Sheila Newton, Ph.D., who was responsible for creating most of the presentation. As he went through the five priorities, Kleeberger offered a few examples of related NIEHS/NTP activities and opportunities for the Institute to help shape the research agenda discourse:

- **Genomics and other high-throughput technologies** — the NTP High Throughput Screening Initiative, Tox 21, and efforts to expand bioinformatics resources at NIEHS to support new technologies and systems biology approaches
- **Translating basic science into new and better treatments** — opportunities for establishing prevention as an NIH goal and increasing awareness of the importance of primary prevention through environmental interventions to complement traditional secondary prevention measures, such as screening
- **Using science to enable health care reform** — taking comparative effectiveness research beyond the level of treatment to evaluate prevention strategies, expanding health disparities research, and better understanding gene-environment interactions for prevention
- **Focusing on global health** — merging global health with environmental health and primary prevention at home and abroad, expanding partnerships, and balancing ongoing and emerging issues into a unified initiative
- **Reinvigorating the biomedical research enterprise** — advocating for early career opportunities focused toward environmental health science research, recruiting and retaining minority scientists, promoting innovative high-risk research, and fostering cross-disciplinary collaborations



*During her report, Birnbaum noted that she was marking her thirteenth month as NIEHS/NTP director and said, “It’s been a wonderful and exciting ride so far.” (Photo courtesy of Steve McCaw)*



*NIEHS Chief of Staff Paul Jung, M.D., above, was on hand for his first Council meeting, as Birnbaum described her progress in building her leadership group here and in Bethesda. (Photo courtesy of Steve McCaw)*



*As part his discussion of the NTP Board of Scientific Counselors’ role as advisors, Portier, above, emphasized, “The board doesn’t just rubber stamp NTP recommendations.” (Photo courtesy of Steve McCaw)*

Kleeberger closed his report by emphasizing that the priorities are related concepts. “High throughput approaches are going to be required to meet the challenges of translational research and the problems raised under the rubric of health care reform,” he said. “Translational research will be a component of a robust global health research program. And all these areas will contribute to reinvigorating the biomedical research enterprise.”



*Drew, left, and Reinlib fielded questions and suggestions from members — some of them with current or past experience in the Core Centers. (Photo courtesy of Steve McCaw)*



*A comment from member George Leikauf, Ph.D., above, that “maybe we’re under-funding the centers” may foreshadow a more extensive reexamination of the extramural program. Birnbaum described the topic as one offering the Council “a very rich area” for future discussion. (Photo courtesy of Steve McCaw)*

## Council Agenda

Along with its animated discussion of future directions and program priorities, Council was treated to science talks by three epidemiologists from the intramural and extramural programs (see related [story](#)). Members also dealt with the business of considering grant awards and heard reports on program areas and activities (agenda and reports available [online](#)):

- Legislative activities — Director of the NIEHS Office of Policy, Planning, and Evaluation Sheila Newton, Ph.D., discussed her office’s legislative activities, such as preparing legislative reports, gathering information and clearances for congressional testimony, and tracking legislation that bears on the Institute’s activities.
- NTP Board of Scientific Counselors (BSC) — BSC Chair Ken Portier, Ph.D., outlined the board’s make-up, range of involvement in NTP study design and draft reports, and the importance of NTP research for regulatory agencies.
- Division of Extramural Research and Training (DERT) — DERT Interim Director Gwen Collman, Ph.D., updated members on “the fruits of the labors of Council,” including staff activities, grant approval success rates, funding opportunities in Collins’ thematic areas, and the possibility of additional funding from the American Recovery and Reinvestment Act.
- Program evaluation of Environmental Health Science (EHS) Core Centers (P30) — Health Science Administrator Les Reinlib, Ph.D., reviewed proposed strategies for evaluating the effects of three years of effort to streamline the [EHS Core Centers](#) program and reduce funding, as he and Program Analysis Chief Christie Drew, Ph.D., received comments and suggestions from members.

[Return to Table of Contents](#)

# Mason Receives 2010 Bruker Award

By Laura Hall

The Electron Spin Resonance (ESR) Spectroscopy Group of the Royal Society of Chemistry (RSC) has honored NIEHS Principal Investigator Ron Mason, Ph.D., with the [25th Annual Bruker Prize](#) for his “major contribution to the field of ESR spectroscopy.”

Mason has the honor of an invitation to give the Bruker Prize Lecture at the [43rd Annual International Meeting of the ESR Spectroscopy Group of the RSC](#) at Cardiff University, Cardiff, Wales, on March 23, although NIH ethics policy prevents him from receiving the cash prize.

Mason, head of the Free Radical Group, was recognized as “a world leader in the development and application of the spin-trapping technique (see text box) for use in chemical, biological, and medical systems, as well as in the application of ESR to the study of oxidative stress molecular mechanisms,” said ESR Spectroscopy Group Chairman David Collison, Ph.D., professor at The University of Manchester, Manchester, United Kingdom. Mason’s work on the characterization of tryptophan and tyrosine free radicals in proteins was also cited as important research.

“Dr. Mason is a pioneer and a visionary in free radical research,” said Dario Ramirez, Ph.D., principal investigator at the Oklahoma Medical Research Foundation and former Mason laboratory research fellow. “I am not the first to recognize Dr. Mason as a great advisor, friend, and a brilliant scientist.” Ramirez continued, “This honor is greatly deserved.”

[Past Bruker Lecturers](#), RSC ESR Spectroscopy Group Committee members, and the presidents or chairs of other National and International Electron Paramagnetic Resonance Societies nominate candidates for the Bruker award.



*Ron Mason, Ph.D., this year’s Bruker Award recipient, based the immuno-spin trapping technique on his novel idea of using spin-traps as tags. Spin-traps bind to the atoms in a macromolecule where a free radical is located. (Photo courtesy of Steve McCaw)*

## Immuno-Spin Trapping

Oxidative radicals are generated during normal cellular metabolic processes. By their very nature, these free radicals are highly reactive and can cause oxidative stress — damaging cells and tissues and causing injury, inflammation, and disease. As a result, the generation and modification of free radicals needs to be carefully controlled by special enzymes in cells. Previously, the role of free radicals in cellular and disease processes was not appreciated because free radicals have ultra short lives and were difficult to detect.

Mason’s laboratory developed the pioneering immuno-spin trapping technique that allows oxidative radicals induced by reactive oxygen species to be immuno-chemically quantified directly by virtually any scientist. This technique gives researchers the ability to track the appearance and disappearance and the location of free radicals in cells — allowing a much better understanding of free radical involvement in cellular processes and disease development.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)

[Return to Table of Contents](#)

# Superfund Researcher Elected to National Academies

*By Rebecca Wilson*

On Feb. 17, the National Academy of Engineering (NAE) announced the election of [NIEHS grantee](#) Lisa Alvarez-Cohen, Ph.D., a researcher in the Superfund Research Program (SRP) at the University of California, Berkeley (UCB), as one of 68 new members. [NAE](#) is one of the prestigious National Academies, and membership is one of the highest professional distinctions accorded to an engineer.

[Alvarez-Cohen](#) is the Fred and Claire Sauer Professor and chair of the Civil and Environmental Engineering Department at UCB. She was elected as an NAE member in recognition of her “discovery and application of novel microorganisms and biochemical pathways for microbial degradation of environmental contaminants.” Alvarez-Cohen’s work in the UC-Berkeley SRP involves genome-enabled approaches to environmental microbiology, such as application of expression microarrays and meta-omics analyses in order to improve bioremediation of Superfund contaminants.

With the new members, NAE membership now includes nearly 2,500 distinguished U.S. and foreign scientists. Academy membership honors individuals who have made outstanding contributions to engineering research, practice, or education or have made major advancements in the field.

(Rebecca Wilson is an environmental health information specialist with MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

[Return to Table of Contents](#)

## Birnbaum Revisits TSCA in Senate Testimony

*By Eddy Ball*

When Senator Frank Lautenberg (D-NJ) convened hearings on chemical safety Feb. 4, NIEHS/NTP Director Linda Birnbaum, Ph.D., was one of the expert witnesses testifying (watch archived [webcast](#)). Birnbaum spoke on the use of next-generation personal exposure monitoring, answered several questions about chemical exposures and vulnerable populations, and submitted more detailed [written testimony](#) into the record.

Birnbaum spoke before a U.S. Senate Subcommittee on Superfund, Toxics and Environmental Health hearing on “Current Science on Public Exposures to Toxic Chemicals,” as part of a panel of government experts (see [text box](#)) testifying on the need to update the Toxic Substances Control Act (TSCA). Subcommittee Chairman [Lautenberg](#) is the Senate sponsor of the [Kid Safe Chemical Act](#), which “would ensure for the first time that all the chemicals used in baby bottles, children’s toys and other products are proven to be safe before they are put on the market,” according to a press release from his office.



*In her 2008 Spirit Lecture at NIEHS, Alvarez-Cohen spoke of her NIEHS/SRP-funded work on “Application of Omics-Based Tools and Microarrays to Optimize Bioremediation.” At the beginning of her talk (see [story](#)), she said, “I’m incredibly grateful to the Institute for supporting this work.” (Photo courtesy of Steve McCaw)*

## Cutting-edge personal monitoring

Describing recent advances in biomonitoring technology, Birnbaum pointed to several examples of the way this “critical information” can lead to groundbreaking studies of carcinogens, such as the NTP studies on tungsten. She noted that positive health outcomes resulted when exposures to pesticides were reduced because of biomonitoring data, demonstrating the effectiveness of regulatory controls.

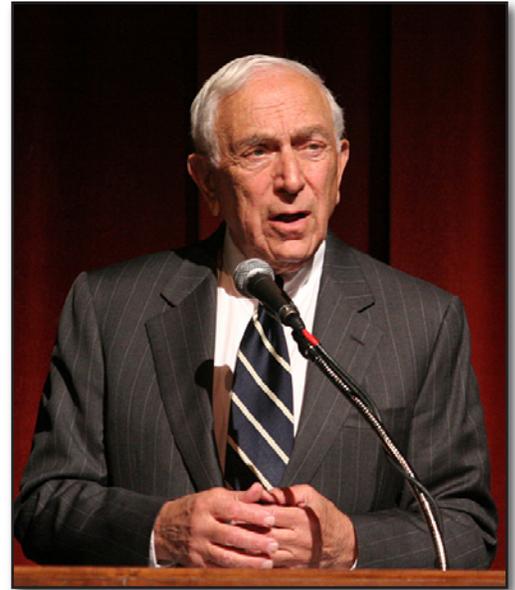
Birnbaum noted that NIEHS is the lead on the trans-NIH Genes and the Environment Initiative to support the development of increasingly smaller and more powerful personal monitoring micro- and nano-biosensors. These devices, she said, are capable of more accurately evaluating the biological effects of chemical exposures, diet, and psychosocial stress.

## Looking at complex exposures

“While our technical capacity for measuring exposure continues to grow, we still have a way to go in our general understanding of exposure in the United States,” she explained. More research is needed so scientists can better understand the effects of mixtures, cumulative low-level exposures, and the synergistic effects of exposure to different chemicals that act in the same way, such as those that target thyroid hormone homeostasis.

“In summary, we are committed to advancing the science of exposure assessment to meet emerging public health challenges,” Birnbaum said. “We look forward to the increased contributions of exposure scientists, as we work to understand the role of the environment in the etiology of disease.”

Joining Birnbaum at the hearing were NIEHS Bethesda staff members Senior Advisor for Public Health John Balbus, M.D., and Program Analyst Mary Gant. Along with Lautenberg, Senators Barbara Boxer (D-Calif.), Mark Udall (D-Colo), Amy Klobuchar (D-Minn.), and Sheldon Whitehouse (D-RI) made majority statements during the hearing, while Senators James Inhofe (R-Okla.) and David Vitter (R-La.) offered statements reflecting the minority perspective.



*Lautenberg, shown above at an earlier speech, set the tone for the hearing with his opening remarks. “Our children should not be used as guinea pigs,” he said. (Photo courtesy of the State of New Jersey Department of State)*



*Birnbaum emphasized the importance of biomonitoring for protecting “our most vulnerable populations, such as the unborn, infants, young children, and those living in poverty and disadvantaged communities.” (Photo courtesy of Steve McCaw)*

## Witnesses Tackle TSCA

Three other government experts joined Birnbaum on the hearing's first panel:

- Steve Owens, assistant administrator of the Office of Prevention, Pesticides and Toxic Substances, at the U.S. Environmental Protection Agency (EPA)
- Henry Falk M.D., acting director of the National Center for Environmental Health/Agency for Toxic Substances and Disease Registry at the Centers for Disease Control and Prevention (CDC)
- John Stephenson, director of Natural Resources and Environment at the U.S. Government Accountability Office (GAO)

A second panel of witnesses from the private sector included a patient, a practitioner, a researcher, and a representative of an environmental advocacy group:

- Molly Jones Gray, a mother and a participant in a biomonitoring study
- Charles McKay, M.D., of the Division of Toxicology, Department of Emergency Medicine, Hartford Hospital
- Tracey Woodruff, Ph.D., associate professor and director of the Program on Reproductive Health and the Environment in the Department of Obstetrics, Gynecology, and Reproductive Sciences at the University of California, San Francisco
- Ken Cook, president of the Environmental Working Group

[Return to Table of Contents](#)

## Hearing Sparks Call for Environmental Justice in Alaska

*By Eddy Ball*

In a press release timed to coincide with a hearing on chemical safety Feb. 4 (see related [story](#)), spokespersons for an NIEHS [grantee](#) called for action on circumpolar atmospheric pollution in Alaska.

Native leaders working with [Alaska Community Action on Toxics \(ACAT\)](#) pointed to the effects of persistent toxic chemicals that drift northward on wind and water currents from where they are used in the lower

48 states. They urged chemical management reform of the Toxic Substances Control Act (TSCA) by the Senate Environment and Public Works Subcommittee on Superfund, Toxics, and Environmental Health.



“Indigenous Arctic communities are suffering the most from chemicals emitted in the lower 48 states,” said Vi Waghiyi, a St. Lawrence Island Yupik and ACAT Environmental Health and Justice Program director. “Because many industrial and commercial chemicals are long lasting and persistent in the atmosphere, they are in our traditional foods and affecting our health and the health of our children. We are calling on Congress and the Obama Administration to affect policy to regulate chemicals to end the ‘contamination without consent’ on our people from distant sources.”

According to ACAT spokespersons, the Yupik people of St. Lawrence Island, and rural communities across the state of Alaska, are concerned about health problems associated with persistent organic pollutants present in their air, water, and food. This past fall, a delegation of local leaders and elders from the island communities of Savoonga and Gambell traveled to Washington, D.C. to raise awareness of the dire health effects in their communities.

St. Lawrence Island residents have experienced alarming rates of disease including cancers, diabetes, reproductive health problems, thyroid disease, nervous and immune system disorders, and learning disabilities. These toxins are particularly prevalent among those who have used the Northeast Cape area for traditional hunting, fishing, and food gathering, according to the spokespersons.

A 2005 NIEHS-funded community-based participatory research [study](#) published by ACAT demonstrated that the people of St. Lawrence Island have elevated polychlorinated biphenyls (PCBs) in their blood, at six to nine times the U.S. average. As part of its grant activities, ACAT also prepared two reports for delegates to the [Stockholm Convention on Persistent Organic Pollutants \(POPs\)](#) in 2009: [Lindane: Pharmaceutical and Agricultural Alternatives](#) and [Persistent Organic Pollutants in the Arctic](#).

“While we are not physically near the action in Washington, D.C., Congress has a responsibility to address the needs of tribal governments throughout the United States, especially remote Alaska,” Jane Kava said in the press release. Kava is a St. Lawrence Island community health Researcher and mayor of Savoonga, Alaska.

[Return to Table of Contents](#)

## Jung Joins NIEHS as Chief of Staff

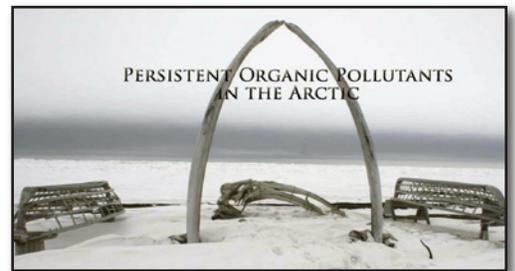
*By Eddy Ball*

In a February statement to employees, NIEHS/NTP Director Linda Birnbaum announced the appointment of Commander Paul Jung, M.D., of the U.S. Public Health Service as NIEHS chief of staff. Jung officially assumed the duties of his new position overseeing operational and staffing activities for the NIEHS Office of the Director on March 1.

In welcoming Jung to NIEHS, Birnbaum pointed to his potential for pursuing strategic improvements to the Institute’s overall performance. “Paul’s extensive background in broad public health matters and his government leadership experience will be valuable assets in identifying and implementing NIEHS key initiatives,” she said.



*ACAT spokesperson Vi Waghiyi, above, was one of a group of ACAT members who met with NIEHS/NTP Director Linda Birnbaum, Ph.D., in 2009. (Photo courtesy of ACAT and Vi Waghiyi)*



*The cover photo for the report for delegates to the [Stockholm Convention on Persistent Organic Pollutants \(POPs\)](#) underscores ACAT concerns about the hidden effects on Arctic populations of pollutants from the lower 48 states. (Photo courtesy of ACAT)*

Jung is a licensed physician board-certified in preventive medicine, who received an M.D. from the University of Maryland with residencies in internal medicine at Case Western Reserve University and in preventive medicine at Emory University. He also holds advanced degrees in public health from Johns Hopkins University, political management from George Washington University, and business administration from the University of Baltimore. He has experience in epidemiology, public health, and policy (see text box).

Prior to joining NIEHS, he was an investigator for the U.S. House Energy and Commerce Committee's Oversight and Investigations Subcommittee. In December 2009, he gave a guest lecture at NIEHS on his evaluations of the use of bisphenol A in infant formula packaging, scientific integrity in clinical trials, and other health issues and industry practices (see [story](#)).

When asked about his decision to accept the position at NIEHS, Jung said, "To me, environmental health is the future of medicine." Jung sees NIEHS as the point of convergence of his interests in public health and the environmental factors that interact with genetics to cause disease. "It just makes sense that we should apply public health principles to chemicals and other environmental agents as we move beyond the traditional public health focus on bacteria and viruses."

"NIEHS seems to me to be the agency that is best positioned to address those issues," Jung concluded. "This is the place where the primary research is being done and being supported on the toxins and chemicals we should be addressing."



*Jung, above, noted that as scientists and public health professionals better understand the range of complex disease, there is bound to be a growing recognition of the key role that the environment plays in public health. (Photo courtesy of Steve McCaw)*

## A Career in Public Service

- **Robert Wood Johnson Clinical Scholar** at Johns Hopkins University, conducting research into state medical boards' disciplinary actions against physicians and medical residents' quality of life and errors related to call schedules
- **Montgomery County (Maryland) Health Commission Member**, advising the County Council on the health needs and programs for Maryland's largest county
- **Senior Faculty Lecturer** at the University of Maryland, teaching "Introduction to Health Policy: Things They Don't Teach in Medical School"
- **Medical Officer, Food Safety Adverse Events Reporting System** at the U.S. Food and Drug Administration, managing the review, evaluation, and resolution of adverse events from regulated food products
- **Chief of Epidemiology** for the U.S. Peace Corps, supervising, monitoring, and evaluating the Peace Corps' worldwide health and disease surveillance system — receiving the 2009 "Best Original Paper" award from the International Society of Travel Medicine
- **Investigator** for the U.S. House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, examining the use of bisphenol A in infant formula packaging, questionable conduct of pharmaceutical trials, deceptive direct-to-consumer advertising for prescription drugs, and the federal human subjects protection system

# Fellows Participate in Biotech Career Workshop

By Eddy Ball

NIEHS fellows joined their counterparts Feb. 9 for the first session of the [North Carolina Biotechnology Center's \(NCBC\)](#) three-part Ph.D. Workshop Series. Held at the organization's Research Triangle Park headquarters, the first session focused on "Life Science Industry Careers: Bench to Boardroom."

The estimated 175 participants hailed from region universities and scientific organizations, with students and fellows traveling from as far east as Greenville's East Carolina University and as far west as Winston-Salem's Wake Forest University.

The capacity audience filled the NCBC auditorium to hear panel presentations that ranged from career alternatives for science Ph.D.s in the biotech industry to developing interviewing, negotiating, networking, and resume-building skills appropriate in the industrial setting. Panelists talked informally as they responded to prompts from session moderators and questions from the audience — speaking candidly about their own transition from the academic sphere to the world of biotech and offering advice for young scientists interested in pursuing alternative careers (see [text box](#)).

During their free time at breakfast, on coffee breaks, and at lunch, young scientists mingled and networked with panelists and other industry representatives. The final session of the day was devoted to meeting with people from the biotech companies exhibiting at the workshop.

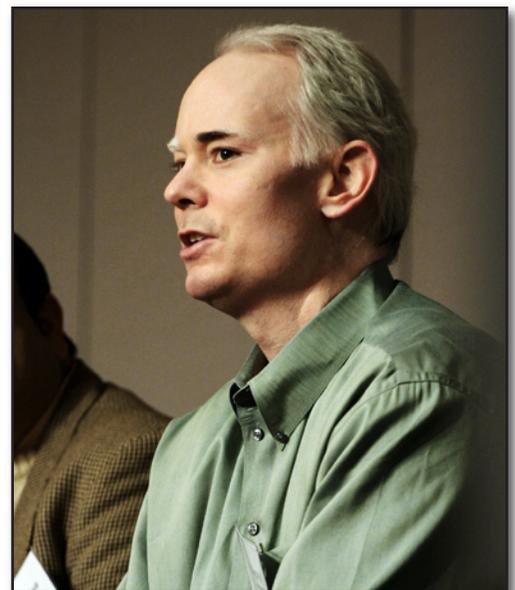
One of the NIEHS postdoctoral fellows at the event was Dana Hancock, Ph.D., who has served as a panel moderator at the [NIEHS Biomedical Career Fair](#), scheduled this year on April 30 at the U.S. Environmental Protection Agency (EPA). Asked about her experience at the NCBC workshop, Hancock said she appreciated the opportunity to attend. "It was very informative and valuable," she explained. "We can use every opportunity we can get to hear this kind of inside information about scientific careers away from the bench."

Workshop organizer [Shobha Parthasarathi, Ph.D.](#), is the technology development director of the Center's Business and Technology Development Program and head of the Center's [Industrial Fellowship Program \(IFP\)](#). IFP fellows served as moderators for two of the four panel discussions and shared their experiences in industry with students and trainees.

The second session of the workshop series, "Agencies and Research Institutes," will take place on March 24 at NCBC and feature panel discussions by representatives from non-profit organizations, such as RTI, and government agencies, including NIEHS and EPA.

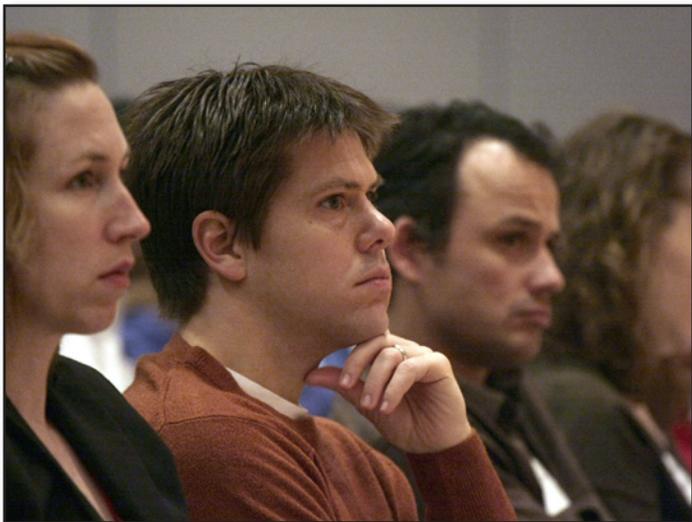


*IFP Fellow Joann O'Connor, Ph.D., above, moderated the session on "R&D Roles in Industry." She works at the clinical-stage biopharmaceutical company Targacept in Winston-Salem. (Photo courtesy of Steve McCaw)*



*Panelist Ted Murphy said of his own transition, "The most difficult step is that first step." He urged the audience to "be bold in trying to seek out new experiences." (Photo courtesy of Steve McCaw)*

The final session on April 29 at NCBC, “Discovery to Product Development,” will focus on scientific careers in discovery, pre-clinical, and clinical phases of product development in pharmaceuticals, medical devices, and biotechnology in agriculture, known in biotech circles as “agbio.”



*NIEHS Postdoctoral Fellow Jeff Stumpf, Ph.D., center left, has worked to develop communication and leadership skills with his involvement in the [NIEHS Trainees Assembly](#) and the [Laboratory of Molecular Genetics Trainee Action Committee](#). (Photo courtesy of Steve McCaw)*



*NIEHS Postdoctoral Fellow Zack Zalinger, Ph.D., above, enjoyed a few laughs during the coffee break networking time as he mingled with attendees and speakers in the crowded lobby at NCBC. (Photo courtesy of Steve McCaw)*

## Comments from Workshop Panelists

- “Leadership, presentation, writing, tackling the unfamiliar, communication” —Biogen Idec Principal Scientist Vijay Jethwa, listing the non-scientific skills trainees should make an effort to develop
- “In the end, everything is about money.” — Armindo Gaspar, Research and Development (R&D) scientist at Novozymes, summing up the important difference between science in academia and science in industry
- “You have to move beyond the resumes and cover letters.... Never underestimate the importance of communicating and networking.” — Doreen Grech, director of Business Development at UCB Pharmaceuticals, talking about landing that first job
- “We see cover letters that are all over the map. Write it well.” — Ted Murphy, vice president of R&D for BioMarck Pharmaceuticals, pointing out the importance of developing writing skills and paying attention to details
- “It’s important to be able to talk science at all different levels.” — Inspire Pharmaceuticals Ophthalmic Medical Scientist Zina Johnson
- “I’ve never worked for a company that didn’t value creativity.” — Lee Trevino, director of Drug Discovery at Cirrus Pharmaceuticals
- “Never limit yourself to bench science. Show an interest in things beyond the lab.” — Anil Goyal, vice president of Business Development at Ophtherion, who also recommended that postdocs develop skills in “managing people who don’t report to you”
- “I was so afraid of leaving the bench, ... [but] I soon came to love doing science vicariously.” — Lakshmi Goyal, editor of the Elsevier journal *Cell Host and Microbe*

# Shepard Edits EJ Issue on Climate Change

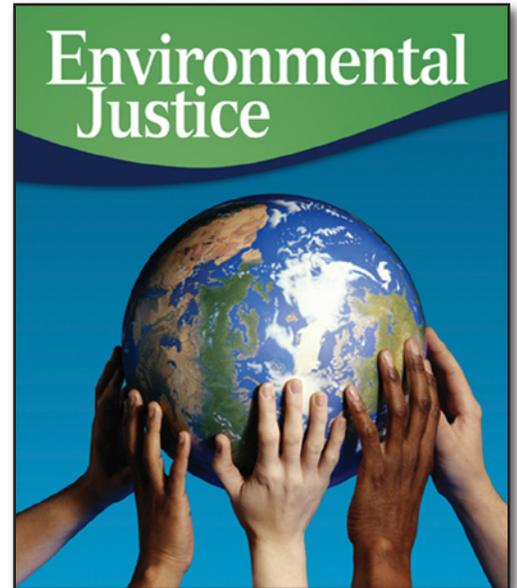
By Eddy Ball

A [special issue](#) of the journal Environmental Justice edited by NIEHS grantee Peggy Shepard highlights the disproportionate effects of global warming and pollution on disadvantaged communities worldwide. Shepard, who is executive director New York-based [WE ACT for Environmental Justice](#), also co-authored a guest editorial on “Climate Justice.”

Announcing the special issue, the WE ACT Newsletter said, “Global warming, pollution, and the environmental consequences of energy production impose a greater burden on low-income, disadvantaged communities, and strategies to prevent these inequities are urgently needed.” According to an editorial by Environmental Justice Editor-in-Chief Sylvia Hood Washington, Ph.D., the seven original articles — several of them authored or co-authored by NIEHS grantees — are an outgrowth of a 2009 [Advancing Climate Justice conference](#) hosted by WE ACT and co-sponsored by NIEHS (watch [videos](#)).

The special issue reflects the growing awareness among global health researchers and environmental justice advocates that climate change will be most keenly felt in developing nations and in disadvantaged communities everywhere. In her comments on global health, NIEHS/NTP Director Linda Birnbaum, Ph.D., has reinforced the Institute’s awareness of the environmental justice implications of climate change and commitment to support efforts to reduce its impact on public health — most recently by supporting high-profile research on the co-benefits of intervening to mitigate or reverse the effects of climate change (watch [video](#)) and by reaffirming support to EJ grantees (see [text box](#)).

Shepard’s selection as the guest editor is the latest in a long list of honors she has received for her work. Shepard received a Heinz award in 2004 (watch [video](#)) and won the prestigious 2008 Jane Jacobs Medal for Lifetime Leadership (see [story](#)). She has held positions on major environmental health and justice advisory bodies, including the NIEHS National Advisory Environmental Health Sciences Council and currently serves on the Institute of Medicine’s committee on Ethics of Housing-Related Health Hazard Research Involving Children, Youth, and Families.



*The cover of the inaugural issue of the journal Environmental Justice. (Photo courtesy of Karen Ballen and Mary Ann Liebert, Inc.)*



*Guest editor Peggy Shepard (Heinz Awards photo courtesy of photographer Jim Harrison)*

## Affirming Support for Environmental Justice

Birnbaum underscored NIEHS support for Institute-funded programs in the area of environmental justice (EJ), with a statement released at the 2010 Conference on Environmental Justice, Air Quality, Goods Movement, and Green Jobs: Evolution and Innovation; and the Worker Education and Training Program Awardee Meeting in New Orleans Jan. 25–27. NIEHS was a co-sponsor of the meeting in conjunction with the U.S. Environmental Protection Agency (EPA) and Dillard University.

“We will continue to fulfill our mission as a federal agency by partnering with EPA and EJ communities, championing environmental health research and public health interventions, and pursuing the goal of a safe, healthy, and just environment for all people,” she told delegates at the meeting.

Birnbaum emphasized the ongoing commitment of NIEHS to EJ in several areas — the NIEHS Partnerships for Environmental Public Health (PEPH) program — the newest tool in the Institute’s environmental justice portfolio; safe green jobs training through the Worker Education and Training Program (WETP); and the EJ component of the NIEHS climate change research agenda.

[Return to Table of Contents](#)

## Superfund Video Offers Plain Talk on Arsenic

*By Eddy Ball*

NIEHS-funded researchers at [Dartmouth Toxic Metals Research Program](#) premiered their new short film, “In Small Doses: Arsenic,” Feb. 11 in Concord, N.H., before an audience of legislators, representatives of regulatory agencies, and members of the regional media (watch [video](#)).

Created for the general public, the ten-minute video brings home findings of research on arsenic in well water by identifying high-concentration areas in New England and offering pointers for residents relying on wells for their drinking water. The film is part of a research translation and outreach program funded by the NIEHS Superfund Research Program (SRP) to raise public awareness of the need to test well water on a regular basis.

### Many residents with wells could be exposed

According to scientists appearing in the film, up to one-quarter of the 2.3 million people who routinely consume water from wells in New England may be exposed to potentially harmful levels of arsenic. Although public water sources undergo regular testing, it is not a requirement for most private water systems.

Arsenic is a naturally occurring element found in bedrock and moves through groundwater. Because the geography of the exposures doesn’t necessarily follow a set pattern, “there’s no predictive power, and the bottom line is that everybody needs to test their well water,” said Joshua Hamilton, Ph.D., former director of the Center for Environmental Health Sciences at Dartmouth.



*The [video](#) speaks to the general public with tips for homeowners using water from wells and recommendations for getting water tested regularly.*

## Compelling reasons to test well water

In the film, Hamilton and Dartmouth toxicology graduate student Courtney Kozul, Ph.D., discuss their recent research on low-dose arsenic exposure in laboratory animals at and below the U.S. Environmental Protection Agency (EPA) threshold of 10 parts per billion (10 ppb). “We’ve certainly seen effects at 10 ppb and even lower,” and researchers have yet to determine a no-effects or “safe” level of exposure, Kozul explained. Hamilton said his experiments have shown endocrine-disrupting effects at levels below 1ppb.

In an effort to educate residents about the problem and what they can do to protect themselves, Dartmouth provides [links](#) to further information from the EPA and U.S. Geological Survey as well as to state agencies that offer well-water testing for as little as \$10. According to a homeowner who appears in the video, commercially available point-of-use filtration systems are “pretty affordable” and easily installed under the sink by a plumber or handy homeowner.



*Kozul, shown above in her lab at Dartmouth, received four awards at last year’s Society of Toxicology meeting (see [story](#)) for her work with arsenic. (Photo courtesy of Dartmouth SRP)*



*Hamilton, shown above in his office at Dartmouth (see [story](#)) when he was Kozul’s advisor, is now chief academic and scientific officer at the Marine Biological Laboratory in Woods Hole, Mass. (Photo courtesy of Joseph Mehling, Dartmouth College)*

[Return to Table of Contents](#)

## NIEHS and NTP Gear Up for a Productive Year at SOT

*By Robin Mackar*

Staff from NIEHS and NTP will speak at more than 30 different sessions and present more than 60 posters on topics ranging from improving toxicity testing to translational research at this year’s [Society of Toxicology Meeting](#) in Salt Lake City, Utah, March 7–11. Many NIEHS grantees will also showcase their research.

A highlight of the meeting will be an opportunity for SOT attendees to hear from and talk to NIEHS/NTP Director Linda Birnbaum, Ph.D. “A Conversation with the NIEHS Director” will be held Wednesday, March 10, 2009 from 2:30 p.m. to 3:30 p.m. Birnbaum will provide an overview of NIEHS/NTP accomplishments since she became director in January 2009 and will set aside time to answer questions and to hear suggestions for future research. For a full listing of NIEHS and NTP activities at SOT, please visit the NIEHS SOT Meeting [Web page](#).



For the first time this year, live updates will be provided by conference participants on the NIEHS and NTP [Web site](#) and on [Twitter@LiveatSOT](#).

“If you are interested in knowing what researchers and toxicologists in government, academia and industry are doing to advance the pace of biomedical research and safeguard the public’s health, the SOT meeting is the place to be,” said NIEHS/NTP Director Linda Birnbaum, Ph.D. “For toxicologists, this is our Olympics” (see [video](#)).

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

[Return to Table of Contents](#)



NIEHS/NTP PROVIDING  
**LIVE UPDATES**  
AT THE SOCIETY OF TOXICOLOGY  
CONFERENCE IN SALT LAKE CITY  
(March 7-11)

JOIN US AT: [www.niehs.nih.gov/liveatsot](http://www.niehs.nih.gov/liveatsot)

OR FOLLOW ALONG ON TWITTER:  
[www.twitter.com/liveatsot](http://www.twitter.com/liveatsot)

# Science Notebook

## Ancient Fires – Modern Dilemma

By Ed Kang

For the modern world, cooking is safe and convenient. A quick turn of the dial on any stove, and within seconds, there's clean, efficient heat. But for millions of families in developing nations, meals are cooked over an open fire, with serious implications for health and the environment. Long-time [NIEHS grantee](#) Kirk Smith, Ph.D., presented his findings on household fuel use and its connection to indoor and outdoor air pollution and health in a talk at Duke University Feb. 17.

Sponsored by Duke University's Global Health Institute, [Smith](#) spoke on "Incomplete Combustion—the Unfinished Global Agenda for Health, Environment and Climate Protection," a subject on which he is a preeminent authority. Smith's talk focused on the health effects of air pollution in developing countries and the urgent need for new and accessible technologies in mitigating exposure.



*A member of the U.S. National Academy of Sciences and Heinz Award recipient, Smith measures the benefit that can be gained by applying new technologies to the world's oldest task. (Photo by Ed Kang)*

### Cooking up toxic soup

Smith began by mentioning CO<sub>2</sub>, the by-product of complete combustion. "While CO<sub>2</sub> is most important to global warming because of its persistence and quantity, products of incomplete combustion (PICs), such as black carbon emitted from traditional biomass use in the home, are far worse from health, climate, and ecological standpoints."

"Wood smoke is not benign," pointed out Smith. When it burns, 6 to 20 percent is converted into PICs, not heat. "Essentially, it's a toxic soup of classic air pollutants — small particles, carbon monoxide, NO<sub>2</sub>, and a vast range of other organic materials, including benzopyrene, benzene, formaldehyde, styrene, even dioxin."

Examining the circumstances of exposure reveals the ubiquity of the problem: using solid fuels for cooking is a highly polluting activity. Half the world's households cook several times a day — just when people are present — and the most vulnerable populations, poor women and children, are affected. Smith calls the combination of risk factors "a perfect storm" for health effects.

### A panorama of health implications

"We've done the work in Guatemala for what we think is the first randomized trial in air pollution history," explains Smith. That study is now looking at chronic effects of the ancient task of traditional cooking. "There's quite a panorama of things that we're looking at — cognitive effects for children exposed *in utero* or in early childhood, birth defects, including cleft, and on the adult side, lung cancer and maybe other cancers, tuberculosis, and heart disease."

Smith is quick to note one of the lessons from his research, “The chimney doesn’t get rid of the smoke, just moves it.” The smoke comes back in the kitchen or the bedroom, or it lingers in the community. He is adamant about the need to replace stoves now in use with devices that don’t produce pollution in the first place. “There are such devices now... even stoves that bring levels down to where a chimney would not be needed.”

### Immediate returns for health and climate

Products of incomplete combustion present an ancient but large risk to climate and health. Smith estimates 14 percent of global deaths and 10 percent of the burden of disease are attributable to “combustion mismanagement.” He also explains the immediate benefit of reducing the cumulative effect of these micro-emissions for the climate. “Unlike CO<sub>2</sub>, with a lifespan of 100 years or more, if you eliminated all the black carbon today, there would be no black carbon in the atmosphere next week. You can get short-term returns both for health and for climate.”

Smith was one of the scientists involved in the NIEHS-sponsored climate change series published in *Lancet* prior to COP15, and he was a participant in a simulcast [workshop and press conference](#) with partners from the United Kingdom. His University of California, Berkeley programs and publications [Web site](#) has links to an impressive number of his publications.

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

[Return to Table of Contents](#)

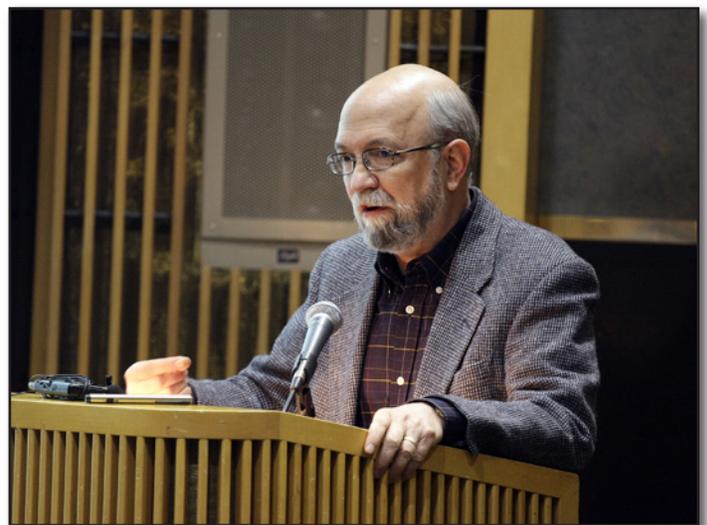
## Epidemiology Shines at Advisory Council Meeting

*By Thaddeus Schug*

A distinctive feature of the February 18-19 meeting of the National Advisory Environmental Health Sciences Council (NAEHSC) was a three-part series of scientific presentations on a wide-range of epidemiological studies supported by NIEHS. Presenting talks were NIEHS Senior Investigator [Allen Wilcox, M.D., Ph.D.](#), Principal Investigator [Stephanie London, M.D., Dr.P.H.](#), and grantee Julie Herbstman, Ph.D.



*NIEHS Senior Research Assistant Windy Boyd, Ph.D., center, and others contemplate the impact of ancient cooking traditions on health and climate. (Photo by Steve McCaw)*



*Wilcox explored the difficulty in “determining whether genetic susceptibilities are causal or whether they are occurring by chance or confounding factors.” (Photo courtesy of Steve McCaw)*

### Testing genetic susceptibility as a cause of disease

Wilcox led off the trio of talks describing his attempt at using genetic susceptibility to discover environmental causes of disease. As Wilcox explained, “People vary genetically in their susceptibility to particular exposures, and if we can identify genetically susceptible subgroups we can find stronger associations between exposure and disease. So the ultimate goal is to use this information so that we can gain insights into biological mechanisms of action.”

Wilcox’s group examined epidemiology data obtained from a population-based study conducted in Norway, which has one of the highest rates of oral clefts in Europe. The study aimed to determine the roles of prenatal exposures — smoking, alcohol use, and folic acid supplementation — and genetic susceptibility in facial cleft birth defects.

Although his group was not able to link prenatal smoke or folic acid exposure to genetic susceptibility, they found that maternal “binge” alcohol consumption was associated with a two to three times greater likelihood that their babies will be born with oral clefts (see [story](#)).

### Taking advantage of GWAS to link genes to complex diseases

Next up was Stephanie London, who uses newly developed genome-wide association studies (GWAS) to couple genetic variation with disease state. London, whose primary focus is pulmonary diseases, stated, “We know that asthma is a chronic childhood disease that is influenced by both genetic and environmental factors, but so far, no genes have been definitively shown to influence asthma development. By using new approaches that have emerged in the past two years, such as GWAS, we’re able to home in on specific regions that might be involved in the disease process.”

Using data from a Mexican population study, London’s group has discovered that chromosome 9q21.31 may underlie some of the differences observed in cases of childhood asthma. The variants were located near the TLE4 gene, which codes for a protein involved in cell fate determination and differentiation. London noted that these variations may be due to ethnic backgrounds, and that it will be important to compare different groups to determine disease susceptibility.

### Using sibling pairs to study the epigenetic effects of prenatal exposure

Recent NIEHS K99-R00 grantee Julie Herbstman rounded out the series of talks with a discussion of how prenatal exposure to polycyclic aromatic hydrocarbon (PAH) leads to epigenetic gene



*London looked at more than 500,000 variants across the genome in 492 Mexican children with asthma and their parents to identify genes that may influence asthma (see [story](#)). (Photo courtesy of Steve McCaw)*



*Acting NIEHS DERT Director Gwen Collman, Ph.D., looked on approvingly as Herbstman compared completing phases of her newly issued K99-R00 grant to learning three new languages at the same time. (Photo courtesy of Steve McCaw)*

modifications that likely result in increased susceptibility to disease. She discussed sources of inter-individual epigenetic variation and how this variation limits the ability to detect significant associations in conventional epidemiologic studies of unrelated individuals.

Working at the [Columbia Center for Children's Environmental Health \(CCCEH\)](#) at Columbia University, Herbstman is planning to use a sibling-pair study to control some of this variation to better study the relationship between prenatal PAH exposure and DNA methylation (see [story](#)). She is now looking at global DNA methylation and plans to narrow her focus to determine what specific genes undergo epigenetic modifications and how those modifications result in changes in disease susceptibility related to growth and development.

Herbstman concluded her talk by detailing a well mapped-out study design that she hopes will eventually lead to development of strategies designed to help prevent disease among urban infants.



*"My goal is not to become fluent in bioinformatics, laboratory biology and biostatistics, but to get to the point where I am conversant, so that I can use these skills to collaborate and foster new research projects," said Herbstman. (Photo courtesy of Steve McCaw)*



*Council member Stephen Baylin, M.D., offered Herbstman technical advice regarding methods to quantify DNA methylation. His own research interest is the role of epigenetics in cancer (see [story](#)). (Photo courtesy of Steve McCaw)*

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction.)

[Return to Table of Contents](#)

## NIEHS Welcomes Four New Principal Investigators

*By Laura Hall*

NIEHS recently welcomed four new tenure track principal investigators in the Division of Intramural Research (DIR) — Guang Hu, Ph.D., Patricia Jensen, Ph.D., Raja Jothi, Ph.D., and R. Scott Williams, Ph.D. These outstanding young researchers have impressive expertise in stem cell research, bioinformatics, neuronal development, and structural biology.

Acting Scientific Director, John Pritchard, Ph.D., said NIEHS recruited these scientists to help the DIR program move into new areas of research. In conjunction with the DIR laboratory chiefs, Pritchard also put two

other new positions on the division's priority list —environmental epidemiologist and developmental biologist —but said filling these two positions is unlikely this fiscal year.

### **Guang Hu — Stem Cell Biologist**

**Hu**, a principal investigator of the Stem Cell Biology Group in the [Laboratory of Molecular Carcinogenesis \(LMC\)](#), studies stem cells. Unlike other cells, stem cells can renew themselves indefinitely and differentiate — change into numerous cell types. Hu studies the molecular basis of stem cell differentiation and self-renewal, screening for the genes involved and their effects on development.

“We were delighted to be able to recruit Dr. Guang Hu from Harvard to establish the stem cell biology group in the LMC last fall,” said Trevor Archer, Ph.D., chief of the LMC. “Guang is a terrific young scientist who will bring exciting new expertise in genome-wide RNAi screens to the LMC and NIEHS. His studies will improve our knowledge about mammalian embryogenesis and may facilitate the development of stem cell therapies.”

### **Patricia Jensen — Neurobiologist**

**Jensen** is the principal investigator of the Developmental Neurobiology Group in the [Laboratory of Neurobiology \(LN\)](#). She studies how genes and environmental factors affect neuronal development to help understand cognitive diseases like autism and Alzheimer's disease. Jensen uses genetic fate-mapping techniques in mice to visually track a specific brain neuronal subtype and define the molecular requirements for each step in its development.

“Environmental disruption of brain development produces lifelong costs in human cognitive potential and quality of life,” explained Dave Armstrong, Ph.D., chief of the LN. “Dr. Jensen will use genetic techniques to identify functional subsets of neurons in the brain and then selectively disrupt their function. The resulting behavioral phenotypes should complement human imaging studies and provide new model systems for testing new pharmacological treatments for some of these disorders.”

### **Raja Jothi — Biostatistician**

Systems Biology Principal Investigator Jothi ([See Story on page 14](#)) is the newest member of the [Biostatistics Branch \(BB\)](#). Jothi uses computational and experimental methods to characterize gene regulatory elements — segments of DNA to which [regulatory proteins](#) bind preferentially to control gene expression — to understand the inherent patterns of gene expression and silencing as cells develop and differentiate.



*At Harvard, Guang Hu developed new tools and methods for gene silencing and large-scale high-throughput functional RNAi screens in mammalian cells. (Photo courtesy of Steve McCaw)*



*Patricia Jensen is currently investigating how genetic and environmental perturbations during development alter the fates and functions of noradrenergic neurons. (Photo courtesy of Steve McCaw)*



*Raja Jothi comes to NIEHS from another NIH Institute, the National Heart, Lung, and Blood Institute, where he was a research fellow. Jothi had an earlier postdoctoral fellowship at the National Center for Biotechnology Information, part of the National Library of Medicine, NIH. (Photo courtesy of Steve McCaw)*

“We are extremely pleased with the addition of Dr. Raja Jothi to our branch,” said Clarice Weinberg, Ph.D., chief of the Biostatistics Branch. “Raja is an accomplished computational biologist, bringing to NIEHS a unique array of skills in biomathematics and wide-ranging interests in the dynamics and mechanisms of gene regulation.” Weinberg noted that Jothi received the NIEHS Early Career Award in November 2009, less than a year after his arrival.

### **R. Scott Williams — Structural Biologist**

**Williams** is the principal investigator of the Genome Stability Structural Biology Group in the [Laboratory of Structural Biology \(LSB\)](#). He uses techniques such as x-ray crystallography, small angle x-ray scattering, and biochemical analyses to examine protein complexes that sense, signal, and repair chromosomal double strand breaks (DSBs). Without repair, DSBs can lead to chromosomal rearrangements, genome instability, and cancer.

“Scott is an expert in the structural biology of proteins involved in the repair of DNA damage resulting from environmental stress,” said Tom Kunkel, Ph.D., chief of the LSB. “His expertise nicely complements the research being performed by a number of other local and NIH Bethesda scientific groups,” Kunkel explained. “Scott’s presence provides the opportunity to develop the type of synergistic interactions among investigators that DIR values so much.”



*One of R. Scott Williams’ research interests is the mechanisms of DNA repair factor inactivation in heritable diseases. (Photo courtesy of Steve McCaw)*

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)

[Return to Table of Contents](#)

## **Researcher Underscores Importance of Intracellular Communication**

*By Brian Chorley*

Yale University Professor of Pathology and Genetics [Gerald Shadel, Ph.D.](#), spoke Feb. 2 on “Mitochondrial Signaling in Disease and Aging.” Shadel’s research is on the leading edge of efforts to unravel the pathology of dysfunctional mitochondria implicated in normal aging tissues, certain tumors, and late-onset diseases such as Alzheimer’s, Parkinson’s, and diabetes.

### **Nuclear-derived factors mediate mitochondrial disease**

Commonly referred to as the “powerhouse of the cell,” the mitochondria supply cells with chemical energy used by many cellular processes including motility, biosynthesis, and signaling. In his talk,



*Shadel said he was especially honored to be invited to speak by the LMG fellows and congratulated them and their colleagues on “the real gem of a lab here.” (Photo courtesy of Steve McCaw)*

Shadel explained that coordinated interaction exists between nuclear-derived factors and the mitochondria. Mutations in the nuclear and mitochondrial genomes can disrupt this molecular coordination, which can lead to mitochondrial-mediated disease.

As an example, Shadel described how inner ear hair cell loss can result from gene mutation of mitochondrial-derived ribosomal RNA (rRNA). The loss of these hair cells can lead to severe deafness in some individuals. The mutation alters methylation of the rRNA by the nuclear-derived enzyme methyltransferase, h-mtTFB1, which is important for mitochondrial protein translation and ribosome biogenesis.

Through a series of sophisticated experiments, Shadel's lab demonstrated that h-mtTFB1 overexpression resulted in altered global gene expression patterns similar to patterns found in cells that harbored a deafness-associated mtDNA mutation. Analysis of the gene expression pattern pinpointed dysregulation of multiple downstream processes that could be involved in hair cell loss, including expression of genes that coordinate cell cycle and cell death.

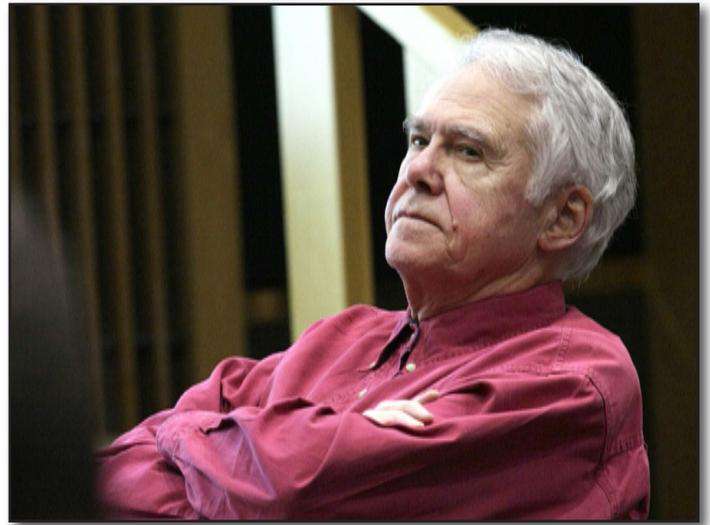
### **Ataxia-telangiectasia, a mitochondrial disease?**

Patients with the rare inherited disorder ataxia-telangiectasia (A-T) can exhibit an array of symptoms, including neurodegeneration, sensitivity to DNA damage, and immune system defects. These symptoms stem from specific mutations in the nuclear-derived gene Ataxia Telangiectasia Mutated (ATM). While the exact mechanisms that lead to clinical signs of the disease are not fully understood, Shadel presented compelling evidence that the mitochondria may be involved.

Shadel demonstrated that reduced amounts of functional ATM protein inhibited mitochondrial repair and maintenance. Importantly, mitochondrial disrepair was linked to memory T cell loss in preliminary studies. These findings may point to the mitochondrial-mediated suppression of immune response seen in A-T patients.

### **Efficient mitochondrial oxygen consumption may slow aging**

In addition to its role in disease etiology, nuclear and mitochondrial communication appears to be important in aging. Reactive oxygen species (ROS), produced endogenously by the mitochondria as a byproduct of chemical energy synthesis, can have damaging effects on cellular macromolecules and DNA. Shadel said that many scientists believe that damage from more than average ROS exposure and resulting oxidative stress can shorten cellular lifespan.



*LMG Chief Jan Drake, Ph.D., was one of several LMG principal investigators in the audience. (Photo courtesy of Steve McCaw)*



*Scientists from other NIEHS labs, such as Laboratory of Molecular carcinogenesis Principal Investigator Paul Wade, Ph.D., above, shared Shadel's research interests in interactions between nuclear-derived factors and the mitochondria. (Photo courtesy of Steve McCaw)*

This theory holds true in yeast, worms, and mouse cells, where reduced activity of the nuclear protein, mammalian target of rapamycin (mTOR), increases lifespan. Shadel explained that this effect is due to increased mitochondrial respiration and protein translation, which his lab demonstrated to be mediated by mTOR. As a result of reducing mTOR, the mitochondria consumed oxygen more efficiently, with less ROS production, while still creating chemical energy.

Shadel did warn that balance is key, however, and that ROS also benefits mitochondrial homeostasis. “ROS are not only damaging agents, but are also important signaling molecules that are sensed and controlled by conserved signal transduction pathways,” he said. “Thus a new paradigm for mitochondrial pathogenesis is emerging in which signaling defects, as opposed to oxidative stress and disruption of energy metabolism, are the culprits.”

Hosted by NIEHS Postdoctoral Fellow Jeffery Stumpf, Ph.D., of the Mitochondrial DNA Replication Group, Shadel’s talk was the most recent presentation in the Laboratory of Molecular Genetics (LMG) Fellows Guest Lecturer series.

(Brian Chorley, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

[Return to Table of Contents](#)

## Estrogen Receptors and Tumor Development

By *Omari J. Bandele*

On Feb. 4, NIEHS Principal Investigator [Kenneth Korach, Ph.D.](#), presented a talk on “Estrogen Receptors: Are They Involved in Tumorigenesis and Toxicity?” to a capacity audience of trainees and fellow principal investigators. The lecture was part of the Laboratory of Molecular Carcinogenesis Seminar Series.

Korach’s research involves using mouse models to assess the contribution of estrogen receptor (ER) alpha and beta in tumorigenesis and hormone-induced toxicity. According to him, a better understanding the role of ERs could help researchers develop targeted therapies for a range of ER-linked diseases.

During his talk, Korach, who is chief of the Laboratory of Reproductive and Developmental Toxicology within the NIEHS



*LMG Fellow Omari Bandele, Ph.D., above, stayed on the edge of his seat during most of the talk. Omari and Stumpf are members of the [LMG Trainee Action Committee](#) that sponsors the lecture series. (Photo courtesy of Steve McCaw)*



*Korach said that he’s made several exciting discoveries in the course of his research on ERs, which are active in nearly every system of the body. “Estrogen doesn’t do the same thing in every tissue,” he explained. (Photo courtesy of Steve McCaw)*

Environmental Disease and Medicine Program, emphasized that most female and male organ systems — including the reproductive, immune, and cardiovascular — express ERs and have estrogenic activity. He also explained that many environmental chemicals have estrogenic and other hormonal activity that can induce toxic effects.

### **Mice lacking estrogen receptors recapitulate clinical conditions**

To evaluate the contribution of the ERs to tumorigenesis and hormone toxicity, Korach and colleagues generated estrogen receptor knockout (ERKO) mice that lack ER alpha (alpha ERKO) or beta (beta ERKO). These animals demonstrated for the first time that loss of ER activity is not lethal.

According to Korach, the ERKO mice are infertile, insulin resistant, and obese, and they experience bone loss — conditions also described in a patient lacking ER activity. “These results demonstrate that ERKO mice are good experimental systems to explore clinical conditions due to loss of ER activity,” he contends. “This system allows one to appreciate how alterations in hormone signaling can modify the function of several organ systems.”

### **WNT-ERKO mice clarify ER involvement in tumor progression**

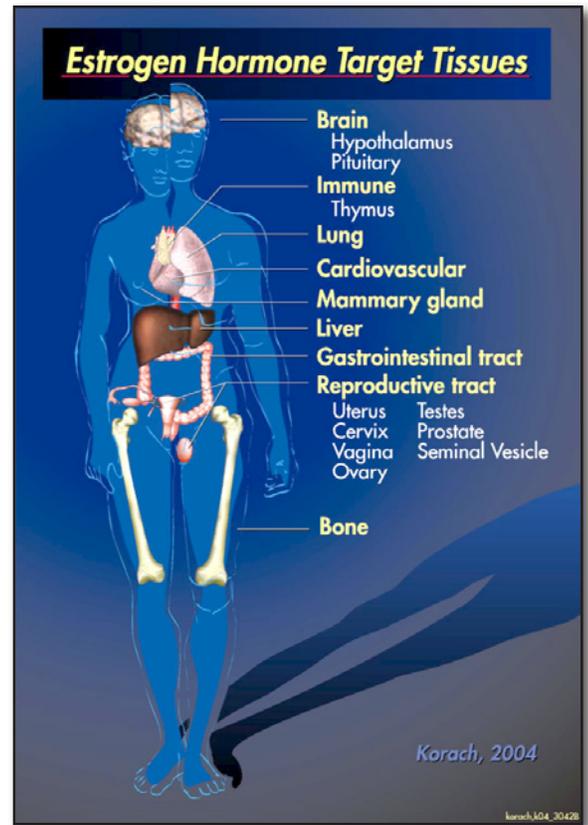
Breast cancer affects individuals throughout the world, and Korach believes ERKO mice will help to further understand the role estrogen receptors play in mammary tumorigenesis.

Some mammary tumors develop in the absence of receptor activity — a type known as hormone resistant — and are unresponsive to anti-hormone therapy such as tamoxifen. This mouse model provides a unique opportunity to study the biology of hormone-resistant tumorigenesis and progression.

To define the role of estrogen receptors in mammary tumorigenesis, Korach led a collaborative study with Harold Varmus, M.D., former NIH director. In this study, ERKO mice were crossed with transgenic mice that develop mammary tumors due to expression of the Wnt-1 oncogene. While WNT-ERKO mice developed Wnt-1-induced tumors in the absence of the ER, they experienced a delay in tumorigenesis. Although this study suggests that the receptor does not contribute to the initiation of mammary tumors, Korach highlighted that it indicates a role for the ER in tumor progression.

### **ER alpha and beta contribute to hormone-induced toxicity**

After years on the market, the prescription drug Diethylstilbestrol (DES) was found to be a toxic synthetic estrogenic compound. Korach and colleagues sought to determine whether estrogen receptors mediate the toxicity of DES. They evaluated the effect of DES exposure in female ERKO mice and observed that wild-type animals exhibited a high incidence of uterine lesions, whereas alpha ERKO mice had no abnormal growths. This finding led Korach to believe ER alpha-mediated regulation of HOX gene expression — involved in reproductive tract development — may contribute to the toxic effects of DES.



*Korach uses this slide of a merged male and female figure to underscore discoveries that estrogen targets tissues throughout the body in both genders. (Slide courtesy of Ken Korach)*

Korach concluded by illustrating that male mice are also susceptible to the toxic effects of DES. Exposure to DES suppressed seminal vesicle development and gene reprogramming in wild-type and beta ERKO mice — while alpha ERKO mice were protected. These results suggest ER alpha mediates DES-induced toxicity in female and male mice.

Korach said he hopes these mice will provide a unique opportunity to determine whether estrogen can act as a carcinogen in the absence of the estrogen receptor — an important question for cancer biologists in the field of hormonal carcinogenesis as they search for ways to control tumor proliferation.

(Omari J. Bandele, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

[Return to Table of Contents](#)

## Researchers Confirm Link Between Maternal Age and Autism

*By Thaddeus Schug*

In a new NIEHS-funded study, researchers at the University of California, Davis (UCD) confirmed a link between advanced maternal age and an elevated risk of having a child with autism, regardless of the father's age.

According to the [study](#), which analyzed nearly five million births in California during the 1990s, the risk of having a child with autism increased by 18 percent — nearly one fifth — for every five-year increase in the mother's age over the age of 30. The study appears online in the journal *Autism Research*.

### Revising current theory through the power of numbers

“This study challenges a current theory in autism epidemiology that identifies the father's age as a key factor in increasing the risk of having a child with autism,” said Janie Shelton, the study's lead author and a doctoral student in the UCD Department of Public Health Sciences. “It shows that while maternal age consistently increases the risk of autism, the father's age only contributes an increased risk when the father is older than 30 and the mother is under 30 years old. Among mothers over 30, increases in the father's age do not appear to further increase the risk of autism.”

Autism is a pervasive developmental disorder of deficits in social skills and communication, as well as repetitive and restricted behaviors, with onset occurring prior to age 3. Abnormal brain development, most likely beginning in the womb, is known to be fundamental to the behaviors that characterize autism.

Because of the large study size, researchers were able to show how risk for autism was affected by each parent's age by holding one parent's age constant and then examining the risk associated with five-year increases in the other parent's age. The subtle interaction of how each parent's age increases the risk of autism allowed the researchers to identify different effects from maternal and paternal age. This methodology is effective at teasing out effects of highly correlated variables (mother's and father's age) and was only possible with an extremely large dataset, according to the researchers.



*Shelton, above, was corresponding author on the paper (Photo courtesy of Janie Shelton)*

The researchers also used the power of their large study to revise another assumption — that the dramatic rise in incidence of autism during the 1990s could be explained by the 300 percent increase in the number of California women over 40 giving birth. As Shelton explained, “We found only about five percent of the increase could be attributed to trends toward older mothers,” suggesting other factors, such as environmental exposures, are more significant.

### **Increased parental age may foster changes in fetal gene expression**

The researchers note that understanding the relationship between increased parental age and autism risk is critical to understanding its biological causes. Earlier studies cited by the authors observed that advanced maternal age is a risk factor for a variety of other birth-related conditions, including infertility, early fetal loss, low birth-weight, chromosomal aberrations, and congenital anomalies.

Senior author [Irva Hertz-Picciotto, Ph.D.](#), a UCD professor of epidemiology and preventive medicine, said the reason that having an older parent places a child at risk for autism is not known. “We still need to figure out what it is about older parents that puts their children at greater risk for autism and other adverse outcomes, so that we can begin to design interventions.”

The authors suggest that epigenetic changes over time may enable an older parent to transfer a multitude of molecular functional alterations to a child. Environmental exposures independent of one’s genetic makeup can lead to histone modifications and alter methylation patterns, which can ultimately affect gene expression patterns in subsequent generations. Thus, they conclude, “Epigenetics may be involved in the risks contributed by advancing parental age as a result of changes induced by stresses from environmental chemicals, co-morbidity, or assistive reproductive therapy.”

*Citation:* [Shelton JF, Tancredi DJ, Hertz-Picciotto I](#). 2010. Independent and Dependent Contributions of Advanced Maternal and Paternal Ages to Autism Risk. *Autism Res* (3). Epub ahead of print. DOI: 10.1002/aur.116

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction.)

[Return to Table of Contents](#)

## **Mining the Genome with Deep Sequencing**

*By Tara Ann Cartwright and Negin Martin*

On Jan. 27, guest lecturer and computational biologist Yuan Gao, Ph.D., delivered a seminar to a standing-room-only audience of NIEHS researchers. His lecture on “Illuminating the Epigenome Landscape by Deep Sequencing” was hosted by the NIEHS Laboratory of Neurobiology.

In his talk, Gao described his group’s efforts to revolutionize genome sequencing by making it affordable, efficient, and accessible. “High throughput genomics,” he explained, “opens the door for advanced gene expression analysis and epigenetic study of the entire organism.” Ultimately, advanced genome analysis can be used to customize drug development and treatments to offer personalized medicine for each individual.

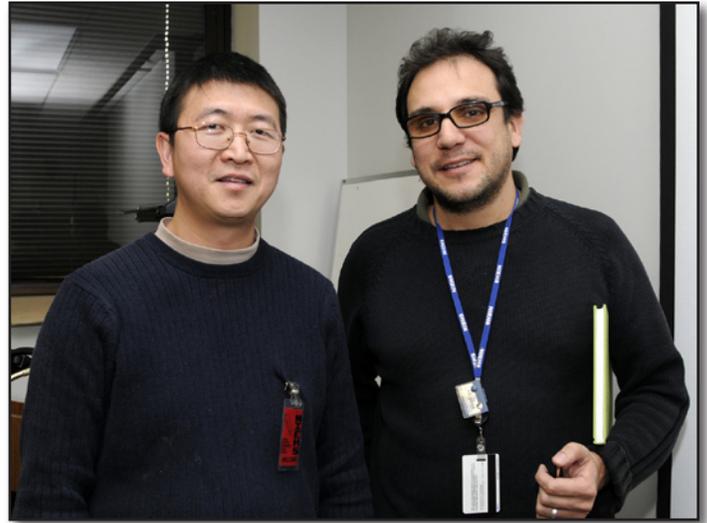


*Principal Investigator Hertz-Picciotto has called for more research into the environmental causes of autism. She and colleagues at UCD are participating in the Early Autism Risk Longitudinal Investigation (EARLI) launched in June 2009. (Photo courtesy of UCD Office of Communications)*

Gao is an assistant professor in the Department of Computer Science and the Center for the Study of Biological Complexity at Virginia Commonwealth University. His primary research interests involve developing and applying new inexpensive, consistent, and simple-to-use sequence technologies to identify sequence variations within a genome and new technologies to study epigenetics.

### Advanced research through team science

The enormous amount of data generated by high throughput systems has rapidly overwhelmed current acquisition and storage strategies and made data analyses inefficient and costly. New research increasingly relies on collaborations among experts from different disciplines such as bioinformaticians, computer programmers, biologists and medical scientists to solve this problem — an example of what Linda Birnbaum, Ph.D., director of NIEHS/NTP, describes as “big science.”



*Gao, left, posed with NIEHS scientist Alejandro Colaneri, Ph.D., a senior visiting fellow in Birnbaumer's group. There was an enthusiastic show of interest in Gao's research by a range of NIEHS investigators from various disciplines intrigued by Gao's development of comprehensive systems to analyze large volumes of data generated by his collaborators. (Photo courtesy of Steve McCaw)*

Although Gao recognizes the uncertainty of genome sequencing and is modest about his accomplishments, he has overcome a number of challenges in sequencing strategies to produce some fascinating scientific findings. A recent collaboration on a [study](#) with [Karen Adelman, Ph.D.](#), principal investigator of the Transcriptional Responses to the Environment Group in the Laboratory of Molecular Carcinogenesis, led to the discovery that promoter-proximal stalling of RNA polymerase II is a general feature of early elongation in *Drosophila* cells. Their study was selected as both a February 2010 [Intramural Paper of the Month](#) and a [2009 Paper of the Year](#).

In another study, Gao and his colleagues observed gene-body methylation in the highly expressed genes of human B-lymphocytes by developing two next-generation sequencing technologies — bisulfite padlock (molecular inversion) probes (BSPP) and methyl-sensitive cut counting (MSCC). The first sequencing technology can recognize selected locations for cytosine methylation. The second utilizes the methylation-sensitive enzyme HpaII to profile methylation across the entire genome.

Gao further explained that padlock probe bisulfite sequencing also has clinical applications for identifying abnormalities of chromosomes. He and his group demonstrated that no significant global changes in methylation patterns were detected on genes of chromosome 21 after electroshock therapy.

### Potential clinical applications for deep sequencing data

Gao stressed that the ability to sequence genomes faster and more cheaply via these new sequencing technologies promises to accelerate knowledge of the molecular basis of disease states such as cancer, Alzheimer's, and autism. Additionally, such technologies could transform our understanding of epigenetic modifications, such as DNA methylation.

In addition to his work with Adelman and NIEHS Bioinformatics Information Specialist David Fargo, Ph.D., Gao collaborates with NIEHS researcher [Lutz Birnbaumer, Ph.D.](#), head of the Transmembrane Signaling Group in the Laboratory of Neurobiology. Gao encouraged scientists to use his powerful sequencing technology in their studies and said he looks forward to future collaboration with NIEHS scientists.

(Tara Ann Cartwright, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Neurobiology Membrane Signaling Group. Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences.)

[Return to Table of Contents](#)

## Superfund Research Prompts Review of Antimicrobials

By Jessica Barnwell

A call for more stringent regulations for antimicrobial compounds by Rep. Edward Markey (D-Mass) could mean that the days of antibacterial trash bags are numbered. Markey's [petition](#) to the U.S. Environmental Protection Agency (EPA) in January was based in part on Superfund Research Program (SRP) findings by [grantee](#) Rolf Halden, Ph.D. Halden's research on the synthetic biocides triclosan (TCS) and triclocarban (TCC), demonstrated the chemicals' environmental persistence and bioaccumulation in aquatic species.



In response to a request from Rep. Markey, who is chairman of the Energy and Environment Subcommittee of the Energy and Commerce Committee, Halden provided a synopsis of the state of the science as background information. [Halden](#) is an associate professor in the School of Sustainable Engineering and the Built Environment at Arizona State University (ASU) and author of several studies on the compounds, including a 2005 [analysis](#) cited by Markey in his letter and a 2009 [review](#).

### Confronting health concerns about biocide exposures

Triclosan is found in soaps, deodorants, toothpastes, shaving creams, mouth washes and cleaning supplies, and it is infused into an increasing number of consumer products, such as kitchen utensils, toys, bedding, socks, and trash bags. Triclocarban is used most widely in soaps and detergents. However, the safety of both antimicrobials has been questioned in regard to environmental and human health. While the companies that manufacture products containing these chemicals claim them to be safe, according to its [fact sheet on triclosan](#), the EPA is taking a closer look at the two chemicals, which are registered as pesticides with the agency.

Concerns are driven in part by the molecular structures of both compounds, which resemble other persistent toxic chemicals, such as dioxins and PCBs. Indeed, technical grade triclosan contains trace amounts of toxic dioxins as manufacturing impurities and can be converted by heat and irradiation to form additional dioxins.

In his [letter](#) to EPA Administrator Lisa Jackson on Jan. 5, Markey indicated there may be a "strong basis" for triclosan chemicals to be tested in EPA's endocrine disruptor screening program and regulated under the Safe Drinking Water Act (SDWA).



*Halden's lab is housed in the ASU Biodesign Institute, which brings together hundreds of researchers striving to solve some of the world's most urgent problems affecting human health and the health of the planet. (Photo courtesy of Rolf Halden and ASU)*

The EPA recognizes the growing body of data regarding triclosan and other persistent antimicrobial agents. In its fact sheet on triclosan, the agency said it intends to begin its next review of triclosan's registration in 2013, ten years earlier than originally planned.

### **SRP support for additional research**

In addition to Halden's work at ASUxtensive environmental monitoring and endocrine disruption work on triclosan and triclocarban has also been conducted with [SRP support](#) in the laboratory of [Bruce Hammock, Ph.D.](#), at the University of California – Davis (UCD). The UC Davis team provided evidence for endocrine disrupting effects of TCC and TCS. In addition to their respective parent project involvement with TCC and TCS, the ASU and UCD groups are collaborating on an SRP American Recovery and Reinvestment Act-funded supplement to study TCC toxicity in animals and humans, as well as to determine the TCC body burden in the general US population.

(Jessica Barnwell is a communication specialist with MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

[Return to Table of Contents](#)

## **Linking Disease Incidence with Environmental Exposure Data Over Time**

*By Erin D. Hopper*

Epidemiological studies are often hindered by the challenges associated with visualizing environmental exposures and disease incidence as they evolve over time. To address this challenge, Elena N. Naumova, Ph.D., and her research team describe a dynamic mapping strategy for visualizing complex spatio-temporal data, in a new [study](#) funded by NIEHS and the National Institute of Allergy and Infectious Disease (NIAID).

Using dynamic maps, researchers can examine the timing and geographic locations of disease incidence, the duration of time that the disease persists, and the dynamics of disease transmission (see sample [video](#)) — all important elements for understanding an outbreak of infectious disease and for planning an effective public health intervention. In a description of her research, Naumova commented that “dynamic mapping creates a visual representation of data over time, allowing us to detect relationships between disease and environmental factors that cannot be observed in static maps.”



*Principal Investigator Elena Naumova is a professor of biostatistics at Tufts University. (Photo courtesy of Elena Naumova)*

### **Applying dynamic mapping to a food-borne pathogen**

In the study, Naumova and her team sought to determine if dynamic mapping could be used to investigate complex data sets and develop new hypotheses. To this end, the researchers applied the technique to a data set from 2002 relating environmental exposures to *Salmonella* infections. They compared infection rates from season to season, across geographic locations in the U.S. and among locations with varying rates of broiler chicken sales.

This analysis led them to conclude that *Salmonella* infection rates are generally higher during the summer months, are often particularly concentrated in the South, and are frequently correlated with levels of broiler chicken sales. Levels of these sales are an indicator for the amount of livestock production in a particular geographic location.

### **Principles of user-friendly dynamic mapping**

Creating a successful dynamic map requires careful consideration of several parameters, and as part of their study, Naumova and her team defined a set of principles to aid researchers in constructing these maps. For example, researchers must choose an effective color scheme that is well-labeled and that allows for easy differentiation between colors. Another critical factor is the selection of an effective aggregation scheme for the organization of data. Researchers must carefully choose a frame speed that allows viewers to absorb the data in a particular image before moving on to the next image, and the map should incorporate a control interface to allow viewers to move through the images at their own pace.

### **A tool with potential for epidemiological studies**

Dana Hancock, Ph.D., a postdoctoral IRTA fellow at NIEHS, agrees, saying “There is a complex array of environmental factors, time, and geography to consider when investigating patterns of disease occurrence. Dynamic maps provide a simplified way to explore these data and to generate new hypotheses, and perhaps future development of dynamic maps will provide a mechanism to test such hypotheses,” said Hancock.

A professor of public health and community medicine at Tufts University School of Medicine, Naumova also serves as the director of the Tufts University Initiative for the Forecasting and Modeling of Infectious Diseases (Tufts InForMID). She plans to present the results of this study in November at the American Society of Tropical Medicine and Hygiene (ASTMH) 59th Annual Meeting.

*Citation:* [Castronovo DA](#), [Chui KK](#), [Naumova EN](#). 2009. Dynamic maps: a visual-analytic methodology for exploring spatio-temporal disease patterns. *Environ Health* 8:61.

(Erin D. Hopper, Ph.D. is a postdoctoral fellow in the NIEHS Laboratory of Structural Biology Mass Spectrometry Group.)

[Return to Table of Contents](#)

# NIEHS Clinical Researchers Present Grand Rounds Lecture

*By Eddy Ball*

NIEHS [Environmental Autoimmunity Group](#) Chief [Frederick Miller, M.D., Ph.D.](#), and Deputy Chief Lisa Rider, M.D., presented a Clinical Grant Rounds lecture on Feb. 24 at the Masur Auditorium on the NIH Campus in Bethesda. The presentation, “Phenotypes as Clues to Deciphering the Pathogenesis and Treatment of Myositis,” was [webcast](#) and is available for view at the [NIH VideoCasting and Podcasting site](#).

[Myositis](#) causes inflammation of the skeletal muscles resulting in chronic muscle weakness, immune activation, and, in some types of myositis, skin rashes, functional disability, and cardiovascular involvement. The various types of myositis are among the approximately 80 conditions grouped as autoimmune diseases that occur when the body’s immune system attacks healthy cells in the body.

Autoimmune diseases are especially challenging for physicians because the conditions are difficult to diagnose and treat. According to the presentation, there are no FDA-approved therapies for myositis, and there is a need for further research to refine diagnostic criteria for the various forms of the disease and better understand environmental and genetic factors involved in disease etiology and progression.

Miller and Rider are part of the NIEHS Clinical Research program. They lead a research team that is investigating autoimmune diseases at the [NIH Clinical Research Center](#) in Bethesda. Their current research interests include idiopathic inflammatory myopathies in adults and juveniles — dermatomyositis, inclusion body myositis, and polymyositis; rheumatoid arthritis and juvenile rheumatoid arthritis; systemic lupus erythematosus (lupus); and systemic sclerosis (scleroderma).

[Continuing Medical Education \(CME\)](#) activities offered by NIH as part of the [Clinical Rounds series](#) are jointly sponsored in partnership with The Johns Hopkins University School of Medicine.

[Return to Table of Contents](#)



*NIEHS Principal Investigator Fred Miller highlighted the role of ultraviolet exposures and photosensitivity in myositis. (Photo courtesy of Steve McCaw)*



*Rider, above, delivered the first half of the presentation with a discussion of the various types of myositis and attendant manifestations throughout the body. (Photo courtesy of Cure JM [Juvenile Myositis] Foundation)*

# This Month in EHP

By Eddy Ball

The eye-catching cover of the March issue of [Environmental Health Perspectives \(EHP\)](#) provides a backdrop for a news feature on “Better Burning, Better Breathing: Improving Health with Cleaner Cook Stoves.” The article describes new initiatives by governments and nongovernmental organizations aimed at mass producing and distributing affordable, cleaner-burning stoves to improve public health.

A second new article, “Synthetic Biology: Environmental Health Implications of a New Field,” explores the concepts behind the emerging field of synthetic biology and discusses some of the risks and limitations experts say need to be considered as this discipline advances in efforts to “rewire” cells and put them to work as sensors and miniature factories.

The March issue also highlights new studies, including ones on the health effects of exposure to formaldehyde and flame retardants:

- Formaldehyde Exposure and Asthma in Children
- Organophosphate (OP) Flame Retardants and Endocrine Markers in Men
- PBDEs and HBCD from Flame Retardants in U.S. Food Samples

[Return to Table of Contents](#)

## Eskenazi is Upcoming Distinguished Lecturer

By Eddy Ball

Epidemiology takes center stage March 16 at 11:00 in Rodbell Auditorium with the next talk in the NIEHS Distinguished Lecture Series by veteran [NIEHS grantee](#) Brenda Eskenazi, Ph.D. Hosted by NIEHS Principal Investigator [Matthew Longnecker, M.D., Sc.D.](#), Eskenazi’s talk will explore her research findings in the seminar, “Organophosphate Pesticide Exposure and the Development of Children Living in an Agricultural Community: Results of the CHAMACOS Study.”

[Eskenazi](#) is the Jennifer and Brian Maxwell Professor of Maternal and Child Health and Epidemiology at the University of California, Berkeley (UCB). As both a neuropsychologist and epidemiologist, she has investigated the relation of environmental exposure and child development and reproductive health for the last 30 years. She is the principal investigator (PI) and director of an NIH/EPA Center for Excellence in Children’s Environmental Health Research (the “CHAMACOS” Project), which investigates pesticide, flame retardant, bisphenol A, and other environmental exposure in farm workers and their children.



<http://twitter.com/ehponline>



Eskenazi is also the PI on other NIEHS-funded projects on endocrine disruption — one based in Seveso, Italy investigating the reproductive health and dioxin, and another examining the effects of persistent and non-persistent endocrine-disruptors on neurodevelopment. Additionally, Eskenazi is the PI on a grant from EPA examining whether children with certain PON1 genotypes are at higher risk from exposure to pesticides and on an NIEHS grant examining benzene exposure in China and effects on genetic and non-genetic markers in human sperm.

Eskenazi is a fellow of the American College of Epidemiology and serves on the editorial boards of the American Journal of Epidemiology and Environmental Health Perspectives. She has served on the State of California’s Scientific Advisory Board for the Toxics Initiative (Proposition 65), the Scientific Advisory Board of the Children’s Health Environmental Coalition and for Health Children Healthy World, and on the Study Design Working Group of the National Children’s Study. She was a member of the National Academy of Sciences Board on Children, Youth, and Families and is currently a member of the Expert Committee for the Stockholm Convention.



*Distinguished Lecturer Brenda Eskenazi in her office at UCB (Photo courtesy of Brenda Eskenazi)*

Along with Phil Landrigan, M.D., Eskenazi was instrumental in establishing a Children’s Health Section in Environmental Health Perspectives, and they served as the first co-editors.

[Return to Table of Contents](#)

## Extramural Papers of the Month

*By Jerry Phelps*

- [Obesity is a Tumor Promoter](#)
- [Phthalate Exposure Alters Children’s Behavior and Cognitive Function](#)
- [Asthma Symptoms in Children Associated with Acetaminophen Use During Pregnancy](#)
- [PCBs Found in Indiana Harbor](#)



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

## Obesity is a Tumor Promoter

Scientists at the University of California, San Diego confirm that obesity acts as tumor promoter in a recent publication in the prestigious journal *Cell*. Jointly funded by NIEHS and the Superfund Research Program, their study suggests that anti-inflammatory drugs taken routinely by millions of people may also reduce the risk of cancer in those at high risk due to obesity and other factors.

The research team found that liver cancer is promoted by a chronic inflammatory state that coincides with obesity. Liver cancer development was dependent on two well known inflammatory factors, IL-6 and tumor necrosis factor. These inflammatory cytokines caused liver inflammation and activation of an oncogenic transcription factor known as STAT3.

Mice prone to develop hepatocellular carcinoma were given a dose of a chemical carcinogen at two weeks of age and then divided into two groups — one on a regular, relatively low-fat diet and another on a high-fat diet. The mice on the high-fat diet developed more cancer. Additional studies using a strain of mice prone to obesity but fed a normal diet and given the same carcinogen, at the same age produced similar results.

Surprising results came in an experiment in which mice given the carcinogen at three months of age and fed a high fat diet developed cancers. Obese mice lacking receptors for either of the two cytokines did not show the same rise in liver cancer.

*Citation:* [Park EJ](#), [Lee JH](#), [Yu GY](#), [He G](#), [Ali SR](#), [Holzer RG](#), et al. 2010. Dietary and genetic obesity promote liver inflammation and tumorigenesis by enhancing IL-6 and TNF expression. *Cell* 140(2):197-208.

[Return to Table of Contents](#)

## Phthalate Exposure Alters Children's Behavior and Cognitive Function

NIEHS-funded research from the Mount Sinai School of Medicine indicates that women with higher exposures to phthalates during pregnancy report more disruptive behaviors in their children. This study included 188 children whose mothers enrolled in the New York Children's Environmental Health Study. It is the first study evaluating the neurobehavioral development of older children in relation to their *in utero* phthalate exposure.

Phthalates are chemicals used to make plastics and are found in wide variety of consumer items including bottles, cosmetics, shampoo, lotions, and vinyl flooring. Ten phthalate metabolites were measured in the mothers' urine samples during the third trimester of pregnancy. When their children were 4 to 9 years old, the mothers were interviewed up to three times and completed a standard questionnaire to assess their children's behavior and cognitive abilities.

The results demonstrate that prenatal exposure to a group of phthalates commonly found in personal care products was significantly associated with poorer scores for aggression, conduct, and emotional control. There were no differences between boys and girls in the study and the associations were stronger as the level of phthalate exposure rose; however, few children's scores fell in the range of clinical significance. The results suggest the need for further research on the possible relationships between phthalate exposures and neurodevelopment and behavior.

*Citation:* [Engel SM](#), [Miodovnik A](#), [Canfield RL](#), [Zhu C](#), [Silva MJ](#), [Calafat AM](#), [Wolff MS](#). 2010. Prenatal Phthalate Exposure is Associated with Childhood Behavior and Executive Functioning. *Environ Health Perspect*. Jan. 8 [Epub ahead of print]

[Return to Table of Contents](#)

# Asthma Symptoms in Children Associated with Acetaminophen Use During Pregnancy

Children whose mothers took acetaminophen while pregnant are more likely to have persistent symptoms of asthma at age five according to a new NIEHS-funded study by researchers at the Columbia Center for Children's Environmental Health involving 300 African-American and Dominican Republic children living in New York City.

The study found that the relationship was stronger in a subset of children with a variant gene for glutathione S transferase, an enzyme involved in the detoxification of foreign substances in the body. This result suggests that less efficient detoxification may be the link between acetaminophen and asthma.

The researchers found that children of mothers reporting acetaminophen use during pregnancy were more likely to wheeze, visit an emergency room for respiratory problems, and develop allergic symptoms than children whose mothers did not take the common analgesic, with effects diminishing as the children aged.

Acetaminophen use among children in the U.S. has increased dramatically since the early 1980's, possibly due in part to the discovery of the association between aspirin use and Reye's syndrome in children. This rise coincides with the increase of asthma diagnoses. The findings in the current study provide a possible explanation for the rise in asthma, especially in minority populations, and suggest caution for the use of acetaminophen during pregnancy.

*Citation:* Perzanowski MS, Miller RL, Tang D, Ali D, Garfinkel RS, Chew GL, et al. 2010. Prenatal acetaminophen exposure and risk of wheeze at age 5 years in an urban low-income cohort. *Thorax* (2):118-23.

[Return to Table of Contents](#)

## PCBs Found in Indiana Harbor

University of Iowa researchers supported by the Superfund Research Program report finding polychlorinated biphenyls (PCBs) in sediments of the Indiana Harbor and Ship Canal in East Chicago, Ind., which is scheduled to be dredged in the near future.

The canal is part of the Calumet River that flows out of Lake Michigan. Scientists and policy makers aren't sure whether dredging will help the estuary by removing the PCBs from past industrial discharge or hurt the environment by stirring them up.

PCBs are a class of organic compounds that were used for decades in many applications including electrical transformers, capacitors, and coolants. The U.S. Congress banned all uses of PCBs in 1979, but because of their stable chemical structure and persistence, their presence in water and sediments continues to be a source of contamination for fish, wildlife, and humans. PCBs are known to cause a wide variety of adverse health effects including cancer, immune dysfunction, neurodevelopmental disorders in children, and other effects associated with endocrine disruption.

The dredging project will remove the sediment from the canal and dispose of it nearby in a confined disposal facility. The project provides a unique opportunity to study the effectiveness of the project and will provide insights for the cleanup of other contaminated sites.

*Citation:* [Martinez A, Wang K, Hornbuckle KC](#). 2010. Fate of PCB Congeners in an Industrial Harbor of Lake Michigan (dagger). *Environ Sci Technol*. Feb 4 [Epub ahead of print].

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training. Each month, he contributes summaries of extramural papers to the Environmental Factor.)

[Return to Table of Contents](#)

## Intramural Papers of the Month

*By Laura Hall and Omari Bande*

- [Reciprocal Epigenetic Modifications of Histone H2B in Apoptosis](#)
- [Obese Male Mice Have Reduced Fertility and Increased Sensitivity to Environmental Chemicals](#)
- [Acetaminophen-Induced Transcriptional Changes Predict Liver Injury](#)
- [Estrogen Receptor Enhances p53 Transcriptional Activity](#)

## Reciprocal Epigenetic Modifications of Histone H2B in Apoptosis

NIEHS scientists have discovered that histone H2B in chromatin has two adjacent amino acids — serine at position 14 (S14) and lysine at position 15 (K15) — that are epigenetically modified during apoptosis. In normal non-apoptotic cells, K15 is acetylated and there is little S14 phosphorylation. In apoptotic cells, however, there is a switch to deacetylation of K15 and phosphorylation of S14.

The researchers found that deacetylation of K15 is necessary to allow S14 phosphorylation and inhibiting K15 deacetylation inhibits internucleosomal DNA degradation — the second of two major steps of DNA degradation during apoptosis.

Apoptosis plays a critical role in eliminating unhealthy cells from the body. Improperly controlled apoptosis can lead to diseases such as cancer if cells that should be eliminated remain, or neurodegenerative disorders if too many healthy cells are killed. During apoptosis, a programmed series of biochemical events in the cell leads to cell death — with accompanying changes in cell structure. These changes include fragmentation of chromosomal DNA in the form of internucleosomal DNA degradation.

The authors had previously shown that H2B was phosphorylated at S14 during the induction of apoptosis. This study showed that the acetylation state of K15 regulates apoptosis-specific S14 phosphorylation.

*Citation:* [Ajiro K, Scoltock AB, Smith LK, Ashasima M, Cidlowski JA](#). 2010. Reciprocal epigenetic modification of histone H2B occurs in chromatin during apoptosis in vitro and in vivo. *Cell Death Differ* doi:10.1038/cdd2009.199 [Epub ahead of print].

[Return to Table of Contents](#)

## Obese Male Mice Have Reduced Fertility and Increased Sensitivity to Environmental Chemicals

Male mice, obese from eating a high-fat diet, have significantly reduced fertility and greater sensitivity to acrylamide (AA), a reproductive toxin, compared to their lean littermates. AA is a known carcinogen, mutagen, and neurotoxin, which is found in baked and fried carbohydrate-rich foods like potato chips, French fries, and bread.

Obesity is a global epidemic. Obese adults have an increased risk of heart disease, diabetes, cancer, and stroke. Studies have also suggested a relationship between obesity and human infertility.

NIEHS researchers compared fertility of male mice by mating males with control females. Female mice partnered with obese males showed lowered numbers of vaginal semen plugs indicating mating and pregnancies, one fifth as many as lean mice. Obese mice had sperm with decreased motility and reduced hyperactivated progression, an indicator of sperm viability and fertilization potential.

Both obese and lean mice treated with AA showed decreased fertility, but the deleterious effects of AA were greater in obese mice. This work suggested that obese men may be more susceptible to reproductive toxins and possibly other environmental chemicals.

NIEHS scientists also found that the obese mice had five-fold greater leptin and insulin levels and significant differences in the mRNA of several genes in their testes compared to lean mice — changes clearly indicative of diabetes in diet-induced obese mice.

*Citation:* [Ghanayem BI, Bai R, Kissling GE, Travlos G, Hoffler U. 2010. Diet-induced obesity in male mice is associated with reduced fertility and potentiation of acrylamide-induced reproductive toxicity. Biol Reprod 82\(1\):96-104.](#)

[Return to Table of Contents](#)

## Acetaminophen-Induced Transcriptional Changes Predict Liver Injury

A collaborative research effort led by NIEHS scientists demonstrated that non-toxic doses of acetaminophen induce transcriptional changes in humans similar to those observed in overdose patients and rats exposed to toxic doses of the drug. These findings reveal potential biomarkers that may indicate early signs of drug-induced liver injury (DILI).

Acetaminophen is the most common cause of acute liver failure in the U.S. However, limitations in traditional clinical approaches have hampered the diagnosis of DILI. Paules and colleagues previously demonstrated in rats exposed to high doses of liver-damaging chemicals that transcriptional signatures in peripheral blood (PB) outperform traditional clinical markers in detecting the presence and severity of DILI.

The authors in the current study examined changes in human PB gene expression in response to a dose of acetaminophen that did not induce detectable levels of liver injury. They observed a distinct transcriptional signature — including downregulation of genes associated with oxidative phosphorylation — and metabolic changes that led to increased serum lactate levels.

The identification of acetaminophen-induced transcriptional and metabolic signatures in human PB may address the need for better biomarkers of DILI. These expression profiles may assist clinicians and provide more meaningful liver safety data in clinical trials of new drugs.

*Citation:* [Fannin RD](#), [Russo M](#), [O'Connell TM](#), [Gerrish K](#), [Winnike JH](#), [Macdonald J](#), et al. 2010.

Acetaminophen dosing of humans results in blood transcriptome and metabolome changes consistent with impaired oxidative phosphorylation. *Hepatology* 51(1):227-236.

[Return to Table of Contents](#)

## Estrogen Receptor Enhances p53 Transcriptional Activity

Researchers from NIEHS have demonstrated that estrogen receptors (ER) can enhance the transcriptional activity of the p53 tumor suppressor by binding ER-specific sequences near p53-target sites. This study also reveals the ability of p53 to function at noncanonical sites — significantly expanding the p53 regulatory network.

p53 and ER are prominent sequence-specific transcription factors that directly regulate the expression of a variety of genes. p53-mediated transactivation involves binding to a well-defined consensus sequence composed of two decamers. Resnick and colleagues recently observed that within the promoter of the *FLT* gene, p53 could function at a noncanonical binding site in about 5 percent of the population, which contains only half the consensus sequence. In addition, transcriptional activity increased upon ER binding at a nearby site.

The authors further examined the generality of this p53/ER transactivation synergy by replacing the p53 site in the *FLT* promoter with a variety of canonical and noncanonical p53-target sequences. Luciferase reporter assays in human cancer cells revealed that p53 and ER could, indeed, cooperate to drive transactivation of p53-responsive sequences. The researchers also observed that ER displays a similar relationship with cancer-associated p53 mutants and other p53 family members, p63 and p73.

The identification of sequence-specific transcription factors that enhance p53 transactivation activity encourages further studies to identify additional transcription factors that modulate p53-mediated gene expression and suggests new roles for estrogen in p53-mediated human stress responses.

*Citation:* [Menendez D](#), [Inga A](#), [Resnick MA](#). 2010. Estrogen receptor acting *in cis* enhances WT and mutant p53 transactivation at canonical and noncanonical p53 target sequences. *Proc Natl Acad Sci USA* 107(4):1500-1505.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor. Omari J. Bandele, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

[Return to Table of Contents](#)

# Inside the Institute

## NIEHS Celebrates Culture During Black History Month

By Eddy Ball

The NIEHS Diversity Council called on the considerable talent of Institute employees and contractors to celebrate the wealth of African-American culture during a Black History Month (BHM) event Feb. 23. The RTP Chapter of [Blacks In Government \(BIG\)](#) co-sponsored the celebration, which was moderated by Diversity Council Vice-Chair and BHM Program Co-Chair Eli Ney.

Following a welcome by BHM Co-Chair Wanda Holliday, the celebration began with the audience singing “Lift Every Voice and Sing.” With words from the 1900 poem by James Weldon Johnson set to music in 1905 by his brother John, the hymn is widely recognized as the African-American national anthem.

The program of spoken word, dance, theatre, and literature reflected the themes introduced by “Lift Every Voice and Sing.” Like the hymn, the presentations celebrated African-American faith, perseverance, creativity, and triumph over adversity and suffering.

NIEHS Biologist Annette Rice led the audience in reciting the BIG Covenant of mutual respect and love. Biologist Joyce Snipe then read her poem “Imagine,” tracing the African-American experience from the initial bondage on the shores of Africa of the first American-bound slaves, through the struggles for freedom and civil rights, to the election of an African-American President in 2008. Closing out the first half of the program, the Millennium Revival Center Mime Group took the stage for a dance performance.

The final half of the program featured a dramatization in five scenes of the novel “The Color Purple” by Alice Walker, the first African-American woman awarded a Pulitzer Prize in Literature. The ensemble cast (see text box) made creative use of minimalist sets and static lighting on the stage in Rodbell Auditorium to keep the audience entertained, amused, and moved by the story of the brutalization and ultimate triumph of the main character, Miss Celie.

At the end of scene five, “Liberation,” with her children and self-respect restored, Miss Celie faces the audience and exclaims, “I’m poor and black. I might even be ugly. But, dear God, I’m here!”



Poet Joyce Snipe asked the audience members to imagine themselves reliving the collective five-hundred-year history of African Americans living in the Western Hemisphere. (Photo courtesy of Steve McCaw)



From left to right, ensemble members Engram, Holliday, and Mosley share a final dinner as discoveries about Mister’s treachery propel the action toward Celie’s climactic speech. (Photo courtesy of Steve McCaw)

Moved by the dramatic resolution, the audience, which spent much of the performance laughing at the antics of the cast, stood to give the players a round of enthusiastic applause.

Following the performances, people flocked to the NIEHS cafeteria to sample an impressive array of African-American and Caribbean cuisine. Also on tap at the reception were performances by the vocal ensemble “Ohennema” and Omega Psi Phi Fraternity stompers.



*The reception following the performances offered the audience and others a chance to enjoy food and fellowship in the NIEHS cafeteria. (Photo courtesy of Steve McCaw)*



*The players posed for a group photo during the reception and food sampling. Shown left to right on the back row are Davis, Wilder, Mosley, and Braithwaite, with Register, right, and Holliday in the foreground. (Photo courtesy of Steve McCaw)*

## “The Color Purple” Players in Order of Appearance

- Miss Celie, the physically and sexually abused daughter, wife, and mother of two, speaking *soto voce* through most of the performance — played affectingly both in the character’s utter humiliation and in her ultimate empowerment by NIEHS Occupational Health Nurse Lindia Ingram
- Sophia, the loving, but uncompromising wife of Harpo — portrayed with feminine strength and boisterousness by NIEHS contract employee Lakesia Register
- Harpo, the would-be abuser whose tables are turned, hen-pecked husband of Sophia, Jut Joint lover of Squeak, and son of Mister — rendered by Tyrone Davis with the same slap stick flair and hilarity he brought to the role of the son in last year’s “A Raisin in the Sun” (see [story](#))
- Albert, a.k.a. Mister, the brutal husband of Celie and frustrated lover of Shug Avery — acted with gusto by NIEHS Administrative Tech Edward Mosley, the banker in last year’s “A Raisin in the Sun”
- Shug Avery, the seductive performer and entrepreneur who steals the hearts of Mister and Celie, paving the way for Celie’s triumph — engagingly and humorously portrayed by “Raisin in the Sun” mother and NIEHS Contract Specialist Wanda Holliday
- Squeak, the sensuous and sultry Jut Joint beauty who fires Harpo’s passion as she tries to wreck his marriage — captured endearingly on stage by NIEHS Staff Scientist Elena Braithwaite, Ph.D.
- Narrator, the voice offstage contextualizing the five scenes with background from Walker’s novel — an essential role filled capably by NIEHS Administrative Specialist Pinkney Wilder

[Return to Table of Contents](#)

# EPA Leadership Development Participants Visit NIEHS

*By Dona McNeill*

A delegation of U.S. Environmental Protection Agency (EPA) leaders-in-training joined NIEHS/NTP Director Linda Birnbaum, Ph.D., and members of her senior staff on Jan. 12 in Rodbell Auditorium for a presentation about NIEHS — its mission, current projects, and plans for the future. The guests included eleven inaugural members of the EPA Senior Leadership Development Program (SLDP) and three members of the program’s staff.



In her opening remarks (see [video](#)), Birnbaum emphasized opportunities for expanding collaborations between NIEHS and EPA locally and nationwide. She also told the visitors that she and her staff were eager to learn more about SLDP because of plans to develop a leadership program at NIEHS.

The SLDP trainees work for the agency’s [Office of Research and Development \(ORD\)](#) and represent branches throughout the United States. They are engaged in a very personalized series of developmental activities based on the results of competency assessments scored to the U.S. Office of Personnel Management’s [Executive Core Qualifications \(ECQs\)](#) for senior level executives.

Participants spend time on Capitol Hill learning from those who deal with the EPA appropriation. As part of their training, they take on rotational assignments and receive mentoring from retired senior executive service staff.

On hand to greet the visitors and explain their respective roles at NIEHS were Deputy Ethics Counselor Bruce Androphy, NTP Associate Director John Bucher, Extramural Division Interim Director Gwen Collman, Communications Director Christine Flowers, Executive Officer Marc Hollander, Policy Director Shelia Newton, Acting Scientific Director John Pritchard, and Acting Clinical Director Darryl Zeldin.

Making up the EPA visitors’ group were SLDP participants Amy Battaglia, Kevin Crofton, Alva Daniels, Hiba Ernst, Lynn Flowers, Jeff Frithsen, Tim Gleason, Roy Haught, Alan Lindquist, Robert Puls, and Tim Watkins. Accompanying the trainees were program advisors Tom Voltagio and Dave O’Connor and program coordinator Chris Zarba.

(Dona McNeill is manager of NIEHS Employee Services.)

[Return to Table of Contents](#)

## Future Pls Wow NIEHS Judges

*By Jerry Phelps*

NIEHS Program Administrator Mike Humble and I participated in the [Annual Science Fair](#) at [St. Timothy’s School](#) in Raleigh on Jan. 28. As part of the Institute’s support for science education, we volunteered to serve as judges for the poster competition at the invitation of Perry Suk — a science teacher at St. Timothy’s and wife of Bill Suk, director of the NIEHS Center for Risk and Integrated Sciences.

Perry asked us to take a few hours to have fun and offer positive feedback to the children as we evaluated presentations on their experiments. The Fair is open to the entire school of first through eighth graders, but it’s mandatory for students in the fourth and seventh grades. Mike, a former science teacher himself and a veteran

of NIEHS outreach efforts in science education (see [story](#)), has been a judge for three years running, but this was my first time.

### The future may be brighter than it sometimes seems

The popular and scientific press paints a pretty bleak picture these days of the scientific and math literacy of U.S. middle and high school students. Many articles say we are falling behind in terms of training the future workforce for jobs in technology and science.

But the kids Mike and I interacted with at St. Timothy's are certainly bucking that trend, and they, and their teachers, should be congratulated. Collectively, their grasp of the scientific method at such a young age is quite impressive and offers naysayers a refreshing ray of hope about the future of scientific research.

### Getting a good start in science, early on

We were highly impressed by the creativity and breadth of the projects — everything from testing the optimal shape for airplane wings and determining the best commercially available germ-killing mouth wash to experiments targeted to establish whether cats are predominantly left- or right-“handed” (the data suggest a slight but probably not statistically significant preference for the left paw).

The title of the winning poster by a fourth grader at the school (see [text box](#)) was “Keepin’ it Fresh.” The future principal investigator tested a variety of agents and preparations to determine the best method for inhibiting the oxidation reaction that browns sliced bananas, apples, and avocados. She tested agents individually and in a variety of combinations, and she scored for browning during a 24-hour period.

According to the visual evidence and data, the combination of vacuum sealing, lemon juice, and refrigeration inhibited the oxidation reaction better than the other treatments. The young scientist's future plans include a placebo-controlled, double-blinded taste test.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training.)



*Phelps, left, talks with a participant during the Annual Science Fair at St. Timothy's. While the school permitted photographs, it asked that students not be identified by name. (Photo courtesy of Jerry Phelps)*



*Humble, shown above working his way through the aisle of posters, talked about experiments with two young scientists. (Photo courtesy of Jerry Phelps)*



*This first-prize poster display may launch the career of a young scientific investigator. (Photo courtesy of Jerry Phelps)*



*Proud science teacher Perry Suk, left, presented the future PI with a blue ribbon for her project, "Keepin' It Fresh." (Photo courtesy of Perry Suk)*

[Return to Table of Contents](#)

## Phelp's First Impressions of an All-Around Winner

When Phelps first approached the earnest young woman presenting her poster at the annual scientific meeting, he said he was immediately impressed by her firm handshake, her poise, and the complexity of her poster. As she launched into a lively description of her hypothesis, methods, and findings, her excitement and commitment to her work were immediately evident. Moreover, she was already thinking about follow-up experiments to explore questions that arose from her current line of investigation, and her answers to the judge's questions were at once well composed and extemporaneous.

This may sound like a description of talented students and junior investigators at many scientific meetings, but the eager "young scientist" in this case was only 9 years old.

## Getting Ready for 2011 — An Open Call for Judges

During Phelps and Humble's visit, K-4 Science Lab Instructor Perry Suk extended an invitation to NIEHS scientists and grantees in the area to serve as judges next year. The judges serve two important functions — they encourage scientific curiosity in young minds, and they offer young people role models from the "real world" of science. They also get a chance to see poster competitions from the other side and discover first-hand the qualities that can help them perform better as presenters.

People who want to spend an enjoyable few hours with some interesting people and do their part to turn kids on to science should contact Perry Suk for further details:

Perry Suk  
Email: [psuk@sttimothys.org](mailto:psuk@sttimothys.org)  
Phone: (919) 787-3011  
"St. Timothy's School  
4523 Six Forks Road  
Raleigh, NC 27609

# Lecture Series Announces Upcoming Speakers

By Eddy Ball

The editorial staff of the [American Scientist](#) magazine (watch [video](#)) invites NIEHS scientists and staff to talks by the next two speakers in its Pizza Lunch Lecture Series held each month in Research Triangle Park.

On March 30 from 12:00 to 1:00 p.m., Duke University Professor [Geoffrey Ginsburg, M.D., Ph.D.](#), will discuss his work at the Duke University Center for Genomic Medicine. Ginsburg will speak at the [North Carolina Biotechnology Center](#) at 15 T.W. Alexander Drive in Research Triangle Park ([map](#); access [videos](#)).

Director of the University of North Carolina at Chapel Hill Bryson Program in Human Genetics [Jim Evans, M.D., Ph.D.](#), will explore new developments in “Genetics, Health and Society” beginning at noon on April 20. Evans’ talk will be held at the series’ regular venue at [Sigma Xi](#) headquarters at 3106 East N.C. Highway 54 in Research Triangle Park ([directions](#); watch [video](#)).

Guest lecturers in the series address a broad range of scientific topics. Speakers have included such prominent area scientists as Duke University Lemur Center Director Ann Yoder, Ph.D., North Carolina State University (NCSU) Professor of Ecology Rob Dunn, Ph.D., and NCSU Professor of Biology Heather Patisaul, Ph.D. — an NIEHS grantee and Outstanding New Environmental Scientist awardee.

American Scientist has posted several podcasts of past talks [online](#).

The staff of the American Scientist welcomes area scientists and science communicators to the free lunchtime lectures. Anyone planning to attend, however, should RSVP to Associate Editor [Catherine Clabby](#) to help with planning for complimentary pizza and drinks.

[Return to Table of Contents](#)



*Described in a cover story in the March-April issue of American Scientist, the accordion-like blubber on the underside of the blue whale or rorqual, shown above, extends from mouth to bellybutton. This unique structure can stretch to more than twice its original length and hold many tens of tons of water and krill for feeding this enormous creature. (Cover courtesy of Nick Pyenson)*

# Environmental Enthusiast Colleen Anna Retires

*By Laura Hall*

After 34 years of government service, 29 here at NIEHS, Eicosanoid Biochemistry Group Biologist Colleen Anna spent her last day at work on Feb. 26. “I will miss all the interesting people here at NIEHS,” said Anna. “It has been a privilege to work in such a friendly, exciting atmosphere as I have experienced at NIEHS. I will have to work hard to find that in the retirement crowd.”

Nevertheless, Anna will be busy in retirement. She plans to visit her grandchildren more often and take them on trips. She’ll continue to volunteer at the Durham Urban Ministries and her church and spend more time on her hobbies — stained glass, quilting, and gourd crafts and gardening.

Like any good gardener, Anna knows how to cultivate plants — when to sow seeds, when to tend the growing plants, and when to step aside and watch them bloom. Her careful nurturing spills over into other areas of her life as well — in her personal relationships, her scientific endeavors, and in the causes that are important to her. Indeed, like the plants in her garden, all those around her reap the benefit.

## Caring about the environment

One of those causes is environmental responsibility in everyday life, so it is not surprising that she became a charter member of the NIEHS Environmental Awareness Advisory Committee (EAAC). The EAAC is a committee of administrative staff and volunteers that advises NIEHS management on environmental matters and promotes employee awareness of the environmental impact of everyday activities and ways to mitigate those impacts.

“As one of the 1991 EAAC charter members, Colleen helped to develop the mission, direction, and practical implementation of environmental activities at NIEHS,” said National Toxicology Program Biologist Rachel Frawley, a former coworker of Anna and member of the EAAC. Anna became co-chair of the EAAC in 2001 and served for over six years. According to Employee Services Support Specialist Dick Sloane, who was her EAAC co-chair, “She was always one of the principal driving forces for the plant exchanges which took place in the Spring and a prime mover for Earth Day events.”

Anna expanded Earth Day activities at NIEHS with new presenters and educational activities. She also participated in Bring Your Child To Work Day programs where she explained organic farming techniques and vermicomposting. Anna was active on the steering committee that advocated for and worked at getting on-site daycare. She was and continues to be an advocate for institutional recycling.



*Trish Castranio, Jeanelle Martinez, and Colleen Anna (left to right) at a table displaying gardening information during an NIEHS Earth Day event. (Photo courtesy of Steve McCaw)*

## Taking an interest in others

“One thing I’ve observed about Colleen is that almost everyone in her circle becomes ‘family,’” said Institutional Review Board Administrator Jane Lambert, a former coworker and longtime friend. “She takes great interest in the lives of others and is always asking how things are going. She brought wide varieties of people together during her time at NIEHS.”

“Colleen is a very nice person. Everyone in my lab will miss her,” said her supervisor, Tom Eling, Ph.D. “She has helped out every postdoc who came into the lab — helping them get established in a new lab and frequently a new country, as well as teaching them scientific protocols. She is our ‘Go To’ person.”

Anna has passed the EAAC chair to others, but she is still sowing seeds for environmental awareness and sustainability. In her last weeks here, she spent time in the cafeteria demonstrating to fellow employees how to properly sort leftover food and used serving items for the new post-consumer composting program.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)

[Return to Table of Contents](#)



*Colleen Anna in her laboratory. Despite all her activities, Anna still maintained a full work load in research. She was first author or co-author on more than 20 scientific papers. (Photo courtesy of Steve McCaw)*



**NIEHS**  
National Institute of  
Environmental Health Sciences

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
National Institutes of Health

*The e-Factor, which is produced by the Office of Communications and Public Liaison, is the staff newsletter at the National Institute of Environmental Health Sciences. It is published as a communication service to NIEHS employees. We welcome your comments and suggestions. The content is not copyrighted. It can be downloaded and reprinted without permission. If you are an editor who wishes to use our material in your publication, we ask that you send us a copy for our records.*

- Director of Communications: [Christine Bruske](#)
- Writer-Editor: [Eddy Ball](#)
- Science Editor: [Robin Arnette](#)