

December 2014

## NIEHS Spotlight



### [APHA meeting inspires attendees with calls for a healthy nation](#)

Acting U.S. Surgeon General Boris Lushniak, M.D., helped kick-off and set the tone for the annual meeting of the American Public Health Association in New Orleans.



### [Scientists and grantees enjoy high profile at EHC summit](#) ▶ Video

Scientists supported by NIEHS were prominent on the program for the 7th annual Environmental Health Summit Nov. 4-5 in Research Triangle Park, North Carolina.



### [NIEHS signs agreement with Nanjing Medical University](#)

As a result of joining forces, the two institutions will exchange scientists and collaborate on environmental health research projects.



### [Superfund Research Program grantees gather in San Jose for annual meeting](#)

The annual meeting of the NIEHS Superfund Research Program Nov. 12-14 featured discussions of new research, technology, communication, and community engagement.



### [Big Picture. Small Talk presentation showcases GuLF STUDY](#)

A Nov. 18 presentation by epidemiologist Richard Kwok, Ph.D., described efforts to monitor the potential human health effects of the BP oil spill.

## Clinical Feature



### [Clinical researchers learn about NIH interpretation and translation services](#)

A talk by experts from the NIH Clinical Research Center Nov. 17 is helping NIEHS clinical researchers understand the language needs of a quickly changing demographic.

## Science Notebook



### [Parkinson's disease meeting fosters collaborations for advancing research](#)

NIEHS and the National Institute of Neurological Disorders and Stroke co-sponsored a meeting Nov. 3-4 at NIEHS to develop prioritized recommendations for moving ahead.



### [Falk lecture spotlights biomarkers for cancer](#)

Advances in the field of metabolomics were highlighted at the 29th annual Hans L. Falk Memorial Lecture by Frank Gonzalez, Ph.D., Nov. 18 at NIEHS.



### [Woychik talk at Duke explores epigenetics](#)

NIEHS Deputy Director Richard Woychik, Ph.D., spoke Oct. 31 to an audience of students and faculty members at the Nicholas School of the Environment.

## NIEHS Spotlight



### [NIEHS trainee honored with Wetterhahn Award](#) 🏆

The NIEHS Superfund Research Program selected Bradley Newsome, Ph.D., of the University of Kentucky, as the 17th recipient of the annual Karen Wetterhahn Memorial Award.



### [EMGS honors Barbara Shane and Martyn Smith](#) 🏆 📺 Video

The Environmental Mutagenesis and Genomics Society presented 2014 awards to retired NTP toxicologist Barbara Shane, Ph.D., and NIEHS grantee Martyn Smith, Ph.D.



### [NIEHS gets enthusiastic thumbs up for lab animal care](#)

This November marked a milestone for the laboratory animal program at NIEHS with an exemplary recommendation by reviewers from its accrediting association.



### [NIH program speaker explores mixed African and native identity](#) 📺 Video

Historian Gabrielle Tayac, Ph.D., spoke at a Native American Heritage Month Celebration Nov. 12 at the National Institutes of Health in Bethesda, Maryland.



### [NIH honors RTP staff at Office of Director Awards ceremony](#) 🏆

At a recognition ceremony for support staff Nov. 19, two NIEHS employees and five members of the NIH facilities staff at the RTP campus received awards.

## Science Notebook



### [In 2014, Science Days are bigger than ever](#)

The 12th annual Science Days Nov. 6-7 at NIEHS marked a day-and-a-half devoted to celebrating the depth, breadth, and remarkable quality of the institute's science.



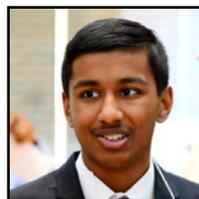
### [PPTOX IV meeting explores early-life exposures and long-term disease](#)

Experts from around the world gathered Oct. 26-29 in Boston to discuss the effects of environmental exposures during early life and later-onset disease.



### [Endocrine researchers explore dimensions of dose response](#)

The Duke University Integrated Toxicology and Environmental Health Program held its annual fall symposium Oct. 24 in the Searle Center Lecture Hall.



### [GEMS meeting focuses on genomics data and risk assessment](#)

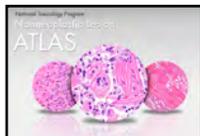
The Genetics and Environmental Mutagenesis Society held its 32nd annual fall meeting Oct. 22 at the North Carolina Biotechnology Center.



### [Seminar tackles inflammatory pathways in obesity-related diseases](#)

Three NIEHS-funded experts explored the connections between inflammation and metabolic disease Oct. 29 during an Inflammation Faculty Seminar and Webcast.

## NIEHS Spotlight



### [NTP expands coverage of Nonneoplastic Lesion Atlas](#)

Several new sections have been added to the National Toxicology Program's Nonneoplastic Lesion Atlas over the last few months.



### [Science Days spotlights mentor and fellow of the year](#) 🏆

This year's 12th annual NIEHS Science Days Nov. 6-7 culminated in a celebration honoring fellow Quaker Harmon, M.D., Ph.D., and mentor Samuel Wilson, M.D.



### [Kunkel signs in at the American Academy of Arts and Sciences ceremony](#) 🏆

After signing the American Academy of Arts and Sciences membership book Oct. 11 NIEHS lead researcher Thomas Kunkel, Ph.D., found himself in good company.

## Inside the Institute



### [Durham researcher discusses caregiver support at NIEHS Veterans Day ceremony](#) ▶ Video

NIEHS welcomed Courtney Van Houtven, Ph.D., to Rodbell Auditorium Nov. 10 as part of the institute's first annual Veterans Day ceremony.

## Science Notebook



### [NIEHS-funded researchers find potential treatment for Parkinson's disease](#)

Blocking the Drp1 protein in mitochondrial fission could be an effective treatment to reverse or slow the progression of Parkinson's, according to a new NIEHS-funded study.



### [Diversity Outbred mice better predict potential human responses to chemical exposures](#)

NIEHS researchers report that Diversity Outbred mice can accurately predict the range of response to chemical exposures that might be observed in human populations.



### [Australian researcher outlines an integrated approach for studying Parkinson's](#)

In his Keystone Science Lecture Nov. 4 at NIEHS, Australian clinical neuroscientist George Mellick, Ph.D., discussed his work with the Queensland Parkinson's Project.



### [NIEHS-funded study shows ADHD-air pollution link](#) ▶ Video

The researchers found that children born to mothers exposed to higher levels of air pollution during pregnancy had an increased number and degree of symptoms.



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

The December issue of Environmental Health Perspectives reports on promising signs of recovery in Detroit and examines the reuse of wastewater for drinking.

## Calendar of Upcoming Events

- **Dec. 2**, in the Executive Conference Room, noon–1:00 p.m. — Receptor Mechanisms Discussion Group, featuring Elizabeth Wilson, Ph.D., discussing “Proto-oncogene Activity of MAGE-A11, a Primate-specific Steroid Receptor Co-regulator”
- **Dec. 2**, in Keystone 2164/2166, 1:00–4:00 p.m. — National Toxicology Program Cellular and Molecular Pathology Branch Seminar Series presentation on “Shaping of Mouse Tumor Genomes by Environmental Exposures,” by Allan Balmain, Ph.D.
- **Dec. 4**, in Rodbell A 11:00 a.m.–12:00 p.m. — NanoString seminar, with Christine Hipsky discussing “Multiplexed Digital Quantification of Nucleic Acids Without Sample Amplification”
- **Dec. 5**, webinar, 12:30–2:00 p.m. — “Reducing Exposure: A Healthy People 2020 Progress Review Webinar Featuring Environmental Health and Tobacco Use,” [register](#)
- **Dec. 8**, in D-350, 11:00 a.m.–noon — Reproductive and Developmental Biology Laboratory special seminar, speaker and topic TBA
- **Dec. 9-10**, in Rodbell Auditorium, 8:00 a.m.–5:00 p.m. — NTP Board of Scientific Counselors meeting
- **Dec. 9**, in F-193, 10:00–11:00 a.m. — Big Picture, Small Talk Series presentation, “How Therapeutic Drugs and Nasty Chemicals Move Around Your Body,” by David Miller, Ph.D.
- **Dec 11**, in Rodbell Auditorium 9:00 a.m.–10:30 a.m. — Inflammation Faculty Seminar and Webcast Series presentation by Andrew Rooney, Ph.D., and Nicole Kleinstreuer, Ph.D., “Analysis and Predictive Toxicology Methods at NTP to Identify Biomarkers of Inflammation”
- **Dec. 12**, in Rodbell Auditorium, 2:00–3:00 p.m. — 2014 NIEHS Awards Ceremony
- **Dec. 15**, webinar, 12:30–2:30 p.m. — “Porewater Concentrations and Bioavailability Webinars, Session IV — Case Studies: Passive Sampling Devices for Organic Contaminants,” with Judy Huang and Rachelle Thompson, [register](#)
- **Dec. 16**, in Rodbell Auditorium, 11:00 a.m.–noon — Distinguished Lecture Series presentation by Kari Nadeau, M.D., Ph.D., on “How Pollution Exposure Leads to Immune Dysfunction: The Role of Epigenetics and Multiplex Immunophenotyping Studies.”
- View More Events: [NIEHS Public Calendar](#)

## Science Notebook



### [Kari Nadeau to present](#) [December distinguished lecture](#)

Stanford University pediatric immunologist Kari Nadeau, M.D., Ph.D., will speak 11:00 a.m. Dec. 16 in the Rodbell Auditorium at NIEHS.

## Extramural Research

### [Extramural papers of the month](#)

- [Health risk assessment examines shrimp consumption after Deepwater Horizon oil spill](#)
- [Meta-analysis tracks progress of contaminants of emerging concern](#)
- [Endocrine-disrupting chemicals interfere with placental thyroid hormone activity](#)
- [Maternal gestational diabetes linked to daughters being overweight later](#)

## Intramural Research

### [Intramural papers of the month](#)

- [A comparison of the effectiveness of RNA-seq and microarrays for clinical toxicological applications](#)
- [NADPH oxidase implicated in Parkinson’s disease associated substance P neurotoxicity](#)
- [Nrf2 polymorphisms correlate with differential susceptibility to acute lung injury](#)
- [MMS exposure is associated with mtDNA mutagenesis](#)
- [Scavenger receptor B-1 plays essential role in immune response to pneumonia](#)

# NIEHS Spotlight

## APHA meeting inspires attendees with calls for a healthy nation

By Robin Mackar

Acting U.S. Surgeon General Boris Lushniak, M.D., helped kick off and set the tone for the American Public Health Association (APHA) 142nd annual meeting Nov. 15-19 in New Orleans.

With energy in his voice and a commanding yet approachable presence, [Lushniak](#) reminded attendees of the progress that has been made in public health, and the journey still ahead.

“You are the heart of public health,” Lushniak told the thousands who gathered Nov. 16 to hear him, and other public health leaders, speak. “The responsibility to ensure that we have a healthy nation, free of tobacco and health disparities, falls on all our shoulders.” This inspirational call to action permeated the sessions that followed.

### NIEHS presence at APHA

NIEHS staff and grantees were prominent among the more than 12,500 public health professionals who attended this year’s conference. Representatives from across the institute presented new findings and initiatives, and led many sessions and discussions.

Christine Ekenga, Ph.D., postdoctoral fellow in the NIEHS Epidemiology Branch, presented two sessions related to the Sister Study, a long-term project looking at environmental and genetic components related to breast cancer. Ekenga focused on new findings related to occupational exposure to solvents.

Attendees representing the NIEHS Division of Extramural Research and Training worked throughout the week to lead numerous sessions, present posters, and moderate round-table discussions highlighting NIEHS efforts, with a special emphasis on Worker Education and Training Program activities and the Partnerships for Environmental Public Health program.



*A poster session at APHA, organized by the Environment section on environmental justice, highlighted efforts by grantees to engage communities to work with their academic partners to better understand vulnerable populations. Pictured, from left, are Amy Schulz, Ph.D.; Yolanda Hill-Ashford; Myra Tetteh; and Donele Wilkins, NIEHS awardees with the Detroit Reproductive Environmental Advocacy Matters Team and the University of Michigan School of Public Health. (Photo courtesy of Sharon Beard)*



*Birnbaum made it a point to stop by the NIEHS exhibit after her presentation on research efforts on the Gulf Coast. Birnbaum congratulated OCPL staff on receiving a third place ribbon for overall appearance of the NIEHS exhibit. (Photo courtesy of Robin Mackar)*

National Toxicology Program (NTP) representative Alex Merrick, Ph.D., participated in a panel led by Kenneth Olden, Ph. D., former NIEHS and NTP director, who is now at the U.S. Environmental Protection Agency. Merrick's session focused on mouse epigenome and gene expression studies that could lead to a better understanding of nutritional status and disease susceptibility in human populations.

Staff from the NIEHS Office of the Director led important sessions about climate change, including a well-attended town hall meeting, where members of the U.S. Global Change Research Program Interagency Crosscutting Group on Climate Change and Human Health presented information and updates on federal activities, including the Third National Climate Assessment, President's Climate Action Plan, and other initiatives.

### Disaster research response

Nicole Lurie, M.D., U.S. Department of Health and Human Services assistant secretary for preparedness and response, joined with Sam Groseclose, D.V.M., of the Centers for Disease Control and Prevention; NIEHS Senior Medical Advisor Aubrey Miller, M.D.; and Joseph (Chip) Hughes, director of the NIEHS Worker Education and Training Program, to talk about a new disaster research response effort to help agencies and communities become better prepared to perform timely health research.

The NIH [Disaster Research Response Project](#), outlined by the NIEHS presenters, includes ready-to-go research data collection tools, research protocols, and a network of trained responders. This year, the NIH Disaster Research Response Project team will be focusing on additional training exercises with various federal, state, academic, and community stakeholders, as well as initiating new efforts to facilitate timely gathering of the environmental and toxicology data needed to compliment the health information collected during a disaster response.

Miller and Hughes discussed some of the lessons learned from such recent disasters as 9/11, Hurricane Katrina and Hurricane Sandy, and the Deepwater Horizon oil spill, and how these responses have led to national recommendations and plans to improve disaster research response.

NIEHS and NTP Director Linda Birnbaum, Ph.D., also discussed NIH disaster research response efforts during her talk, highlighting the NIEHS transdisciplinary research portfolio that is advancing community resilience, and strengthening the public health infrastructure and capacity in Gulf Coast states impacted by the Deepwater Horizon oil spill. She encouraged attendees to use the NIH-supported studies as a platform for future environmental health research, explorations of community and individual resiliency, and advancing understanding of the toxicology of pollutants associated with oil spills, such as polycyclic aromatic hydrocarbons.



*Epidemiologist postdoctoral fellow Ekenga stopped by the NIEHS booth, after giving two presentations on findings from the Sister Study. (Photo courtesy of Robin Mackar)*



*Merrick enjoyed presenting on a panel organized by Olden. (Photo courtesy of Robin Mackar)*



*The acting U.S. surgeon general, left, made the rounds at APHA. He spent some time at the NIEHS exhibit and talked with NIEHS staff, including Miller. (Photo courtesy of Robin Mackar)*



*Liam O'Fallon, NIEHS Partnerships for Environmental Public Health program coordinator, also had an opportunity to talk with Lushniak about environmental health literacy. (Photo courtesy of Aubrey Miller)*

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

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## Scientists and grantees enjoy high profile at EHC summit

*By Eddy Ball*

Scientists supported by NIEHS were prominent on the program for the 7th annual Environmental Health Summit Nov. 4-5 in Research Triangle Park, North Carolina.

Meeting at the North Carolina Biotechnology Center, attendees explored the implications of “[Exposure Science in the 21st Century: Role of Citizens and Communities.](#)”

The summit was organized by the [Research Triangle Environmental Health Collaborative](#) with support from NIEHS, area universities, and other groups concerned with environmental health.



*According to Woychik, NIEHS has supported community-engaged research for more than 20 years and is leading efforts to integrate data collection and databases to make findings more useful in efforts to promote public health. (Photo courtesy of Steve McCaw)*

Although the meeting highlighted three specific areas during its extended workgroup discussions — technology, data integration, and risk communication — the program was united by the theme of community engagement as the driver for study design, data collection and return, and translation of community-based environmental health research. This new approach is quickly effacing the conventional academic top-down focus on researcher interests and priorities, such as publications and tenure, in community-based environmental health research projects.

The plenary speakers and workgroup panelists echoed a telling comment from the first morning by NIEHS grantee [Erin Haynes, Dr.P.H.](#), an associate professor at the University of Cincinnati. “Environmental health research should be conducted with members of the community — not on them,” she explained. “I see myself in collaboration with them [from planning to completion of the research project].”

### Lessons from the report

A major inspiration for the summit was the 2012 report by a special committee of the National Academy of Sciences, [Exposure Science in the 21st Century: A Vision and a Strategy](#). On hand to describe the background and conclusions of the report was the first plenary speaker of the summit, committee member [Paul Gilman, Ph.D.](#), senior vice president and chief sustainability officer for Covanta Energy.

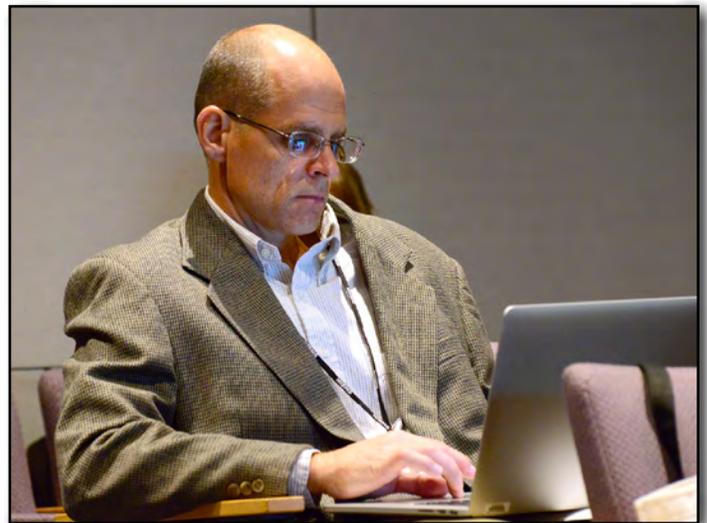
Not surprisingly, Gilman focused his talk on chapter six of the report, “Promoting and Sustaining Public Trust in Exposure Science.” No matter how ambitious the project or how elegantly fit-for-use the technology employed, Gilman said, “We cannot reach the vision [of meaningful exposure science research] without trust.... Communities are not just where we do science, but the key to whether and how we do it.”

### Exposure science at NIEHS

After nearly a full first day of workgroup discussions, the meeting convened for two more plenary talks on day two by NIEHS Deputy Director Richard Woychik, Ph.D., and Duke University Cancer Center Deputy Director Steven Patierno, Ph.D.



*NIEHS program analyst Kimberly Thigpen Tart, J.D., center, talked with collaborative administrator David Brown during a break between presentations. Tart was one of four NIEHS representatives on the summit planning committee. (Photo courtesy of Steve McCaw)*



*NTP Office of Nomination and Selection Director Scott Masten, Ph.D., keeps in touch with his office between sessions. Masten was also a member of the planning committee. (Photo courtesy of Steve McCaw)*

Woychik discussed “NIEHS: Where Exposure and Citizen Science Meet” with an overview of NIEHS programs promoting the development of leading-edge monitoring technology, community-based participatory research, environmental justice, and a better understanding of the concept of the exposome. He tied work underway by the National Toxicology Program (NTP), which is headquartered at NIEHS, the NIEHS Superfund Research Program, and the NIEHS Exposure Biology Program to the institute’s strategic plan.

Throughout his talk, Woychik underscored the NIEHS commitment to advancing community-engaged research for improving public health.

### Risk and translation — the urban epidemic of prostate cancer

In his talk, Patierno discussed “Innovation in Environmental Health Sciences: The Intersection Between Community Engagement and the Human Exposome.” He described how community engagement drives a broad spectrum of laboratory, population level, and health services research conducted by him at Duke and with a cohort of 6,000 African-American males in Washington, D.C. on prostate cancer risk and outcomes.

With interests in epidemiology, gene-environment interactions, health disparities, and global health, Patierno conveyed his enthusiasm for a trans-disciplinary approach and the challenges of uncovering meaningful environmental exposures that threaten health. “There’s an enormous amount of information that we need new technologies to process,” he said.



**Linked video:** (Launches in new window)

[Watch an interview with Patierno about his group's outreach and community-engagement efforts to prevent disease in Washington, which he describes as a cancer disaster area \(15:04\)](#)

Download Media Player: Flash [⌵](#)

As part of its mission as a clearinghouse for environmental health information, the Environmental Health Collaborative has posted presentations and working group recommendations online. Materials are available for each of the seven environmental health summits it has organized since the first one of the series in 2008.



*NIEHS grantee Kim Anderson, Ph.D., contributed information about communication strategies and monitoring technology, based on her field research in Louisiana during the Deepwater Horizon Oil Spill and at fracking sites in Ohio. (Photo courtesy of Steve McCaw)*



*Duke University visiting scholar and collaborative co-chair William Ross introduced Patierno. In his previous career as head of the North Carolina Department of Environment and Natural Resources, Ross worked with NIEHS on the Environmental Stewardship Initiative. (Photo courtesy of Steve McCaw)*



*Patierno studies the social and economic, as well as genomic and epigenomic, aspects of risk for cancer. “Poverty is a carcinogen,” he said of the alarming rates of prostate cancer among African-American men. (Photo courtesy of Steve McCaw)*



*NIEHS program analyst and planning committee member Liam O'Fallon, left, talked with Haynes about her community-engaged study of the health effects of fracking in Appalachian Carroll County, Ohio. (Photo courtesy of Steve McCaw)*



*Head of the NIEHS Exposure, Response, and Technology Branch David Balshaw, Ph.D., left, offered his insights from working with grantees developing increasingly sophisticated and lightweight exposure monitors. He was also part of the planning committee. (Photo courtesy of Steve McCaw)*



*U.S. Environmental Protection Agency scientific administrators Jennifer Orme-Zavaleta, Ph.D., and Hal Zenick, Ph.D., shared efforts at the agency to build infrastructure for community-based research. (Photo courtesy of Steve McCaw)*



*Community-engaged researchers often describe their methodology and technology goals as fit-for-purpose. The same might be said about the summit's venue, where setting encouraged the collaboration, communication, and divergent thinking required for bold initiatives. (Photo courtesy of Steve McCaw)*

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# NIEHS signs agreement with Nanjing Medical University

By Robin Arnette

NIEHS has entered into a partnership with one of the largest universities in China, [Nanjing Medical University](#). As a result of joining forces, the two institutions will exchange scientists and collaborate on environmental health research projects.

NIEHS Scientific Director Darryl Zeldin, M.D., traveled Oct. 27 to Nanjing to sign a Memorandum of Understanding. The agreement will permit up to three early-stage university scientists to do research for two to three years at NIEHS and allow NIEHS senior scientists to lecture at seminars, workshops, school courses, and meetings at the university.

“The goal is to enhance collaborations and interactions with our colleagues in Nanjing, in the hopes it will be a win-win for both of our institutions,” Zeldin said.

Several NIEHS scientists are looking forward to taking part in the trade. So far, Jau-Shyong Hong, Ph.D.; Leping Li, Ph.D.; Honglei Chen, M.D., Ph.D.; Xiaoling Li, Ph.D.; Humphrey Yao, Ph.D.; Perry Blackshear, M.D., D.Phil.; and Kenneth Korach, Ph.D., have signed up.

According to Zeldin, the partnership would not have been formed without Korach. He and Associate Dean of the Nanjing Medical University School of Public Health Yankai Xia, M.D., Ph.D., who are longtime colleagues, were discussing future research plans. When Xia mentioned that the university was interested in doing more environmental health studies and establishing core facilities that were similar to the ones at NIEHS, Korach thought it was an opportunity NIEHS couldn't pass up.

“Air and water pollution are major problems in China, so the School of Public Health is in a unique position to study the impacts on Chinese citizens,” Korach said. “Because they have very large cohorts, working with them will yield a tremendous amount of knowledge that will benefit all humans.”

Established in 1934, the university has 17 schools and one independent school, 23 affiliated hospitals, and more than 50 teaching hospitals. Zeldin added that the school has an excellent record of grant funding, ranking second only to China's largest educational institution, Peking University Health Science Center, previously Beijing Medical University.



University President Hongbing Shen, M.D., Ph.D., seated left, and Zeldin, seated right, signed the MOU in the presence of several university faculty, including, from left, Xia, Ph.D., director of the International Exchange and Cooperation Office; Feng Chen, M.D., Ph.D., dean of the School of Public Health; Zhixu Wang, M.D., Ph.D., director of the Department of Maternal, Child, and Adolescent Health; and Di Wu, Ph.D., deputy director of the Department of Toxicology. (Photo courtesy of Nanjing Medical University)



During his presentation, “A Vision for Environmental Health: Overview of the NIEHS,” Zeldin underscored the significance of environmental health research. (Photo courtesy of Nanjing Medical University)



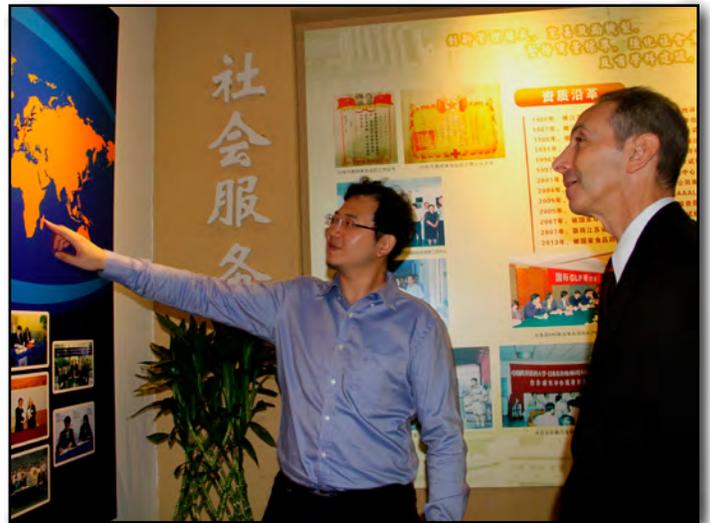
*Zeldin gave university President Shen an autographed photo of NIEHS. (Photo courtesy of Nanjing Medical University)*



*Zeldin, seated front left, and university leadership held several meetings. (Photo courtesy of Nanjing Medical University)*



*Zeldin signed the guest book in a room dedicated to the history of the university. Beautifully decorated with accomplishments and mementos, the room allows visitors to experience the school's contributions to health and biomedical research. The room was completely remodeled in time for the university's 80th anniversary celebration. (Photo courtesy of Nanjing Medical University)*



*Xia served as tour guide through the university's history room. (Photo courtesy of Nanjing Medical University)*

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# Superfund Research Program grantees gather in San Jose for annual meeting

By Sara Mishamandani

The annual meeting of the NIEHS Superfund Research Program (SRP) Nov. 12-14 in San Jose, California, brought together researchers, trainees, and administrators supported by the program, as well as representatives from partner agencies to discuss new research, technology, communication, and community engagement.

Hosted by SRP grantees at the University of California, Berkeley (UCB), the meeting provided a forum for presentations and discussion in areas critical to the program's multidisciplinary research mission, to address human and environmental health challenges related to Superfund and other hazardous waste sites.

## Focusing on practical applications of research findings

SRP Director Bill Suk, Ph.D., and NIEHS Deputy Director Rick Woychik, Ph.D., gave opening remarks. They both emphasized the importance of data sharing and the value of working collaboratively to share and translate research to improve public health.

“This meeting showcased a wide range of problem-based, solution-oriented research that is being performed as part of the SRP,” said Suk. “This outstanding meeting brought together experts from a broad range of environmental health fields in the program to develop new ideas and perspectives to tackle environmental problems and improve public health.”

Researchers presented key results from their work during the meeting. In the environmental sciences and engineering session, diverse topics included modeling pollutant exposure in fish, dust deposition from mine waste, and challenges related to vapor intrusion.

The health sciences session covered research findings from epidemiology, toxicology, and systems biology studies related to adverse effects from early life exposures to chemicals, as well as liver injury from exposure to environmental contaminants.



*The meeting provided opportunities for networking and scientific discussion throughout each day. (Photo courtesy of Carol Kelly)*



*Gwen Collman, Ph.D., NIEHS Director of the Division of Extramural Research, presented trainee Brad Newsome, Ph.D., from the University of Kentucky SRP Center, with the 2014 Karen Wetterhahn Memorial Award (see [story](#)). (Photo courtesy of Christie Oliver)*

The meeting featured keynote speaker Jill Banfield, Ph.D., a Berkeley professor, who discussed the importance of the microbiome to health and environmental research. Banfield is a leader in the field of microbiology with a focus on the fundamental relationship between microorganisms and their chemical environments. David Sedlak, Ph.D., professor at Berkeley and author of the book “Water 4.0,” also gave a keynote address on the need to develop local sources of drinking water, including the cleanup and reuse of contaminated urban groundwater. Sedlak’s talk was followed by a panel discussion on emerging contaminants in water by program grantees, as well as federal and state environmental agency partners.



*In addition to providing welcome remarks, Woychik, center, judged student posters. (Photo courtesy of Martyn Smith)*

### **A spotlight on research translation and community engagement**

The SRP Research Translation and Community Engagement Cores held a daylong separate meeting prior to the opening of the main sessions to showcase successes from the year and identify ways for centers to collaborate and learn from each other.

As part of the main meeting, grantees described how they took basic research findings and moved them from the lab to inform environmental public policy, to start an environmental detection device business, and to create an urban community garden from a brownfield, land previously used for industrial or commercial purposes and contaminated by hazardous waste.

### **Highlighting and rewarding trainee successes**

The meeting, which began and ended with talks by graduate students and postdoctoral researchers, showcased trainee research. During this science presentation session, trainees explained research related to modeling, detecting, and assessing various environmental toxicants. The meeting concluded with talks from six [KC Donnelly Externship Award winners](#), who described their experiences and results from an SRP-funded externship at another center, or federal or state agency.

Continuing the research translation theme, trainees were encouraged to improve how they describe their research through both scientific and lay audience abstracts for their research project posters. Four students received awards in the annual student poster competition. In the environmental sciences and engineering category, the winners were Angela Gutierrez, of the University of Kentucky, and Alden Adrion, of the University of North Carolina at Chapel Hill. In the health sciences category, the winners were Peter William Dornbos, of Michigan State University, and Sarah Carratt, of the University of California, Davis.



*Martyn Smith, Ph.D., the UCB SRP Center Director, moderated sessions and led scientific planning for the meeting. (Photo courtesy of Martyn Smith)*



*The Research Translation Core (RTC) and Community Engagement Core meeting included a variety of sessions from program evaluation to public participation in scientific research. University of Kentucky RTC leader Lindell Ormsbee, Ph.D., reported on his table's discussion related to evaluating the program's research translation. (Photo courtesy of Carol Kelly)*



*Beth Anderson, right, who recently retired from NIEHS, helped plan the meeting. Anderson was presented with a special award for her longtime commitment to the SRP at the meeting. From left are Suk, UCB SRP RTC leader Amy Kyle, Ph.D., and NIEHS Health Scientist Administrator Michelle Heacock, Ph.D. (Photo courtesy of Carol Kelly)*



*Attendees involved in research translation and community engagement are shown with Beth Anderson, first row center, several of whom worked with her many years. (Photo courtesy of Carol Kelly)*



*A career panel was held as part of the trainee session, moderated by Berkeley graduate student Tom Bruton, standing, to provide information on transitioning from graduation to the real world. (Photo courtesy of Danielle Carlin)*

*Adrion, left, received his poster award from Suk during the awards announcements. (Photo courtesy of Carol Kelly)*



*The 2013 KC Donnelly Externship awardees gave 10-minute presentations describing the research and findings that resulted from their externships to another center or a government or state agency. From left: Danielle Carlin, Ph.D., SRP program administrator, joined KC Donnelly winners Erin Madeen, James Rice, Ph.D., Audrey Bone, Shoreh Farzan, Ph.D., Leah Chibwe, and Vanessa De La Rosa. (Photo courtesy of Carol Kelly)*



*The administrative staff for SRP Center grants attended separate sessions to discuss information about grants management, annual updates, and information sharing, and to get to know each other. The administrators from each center are shown here with NIEHS staff. (Photo courtesy of Heather Henry)*

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

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## Big Picture, Small Talk presentation showcases GuLF STUDY

*By Jordan St. Charles*

A Nov. 18 presentation by NIEHS epidemiologist Richard Kwok, Ph.D., described the efforts of the GuLF STUDY (Gulf Long Term Follow-up Study) to monitor the potential human health effects of the BP oil spill.

The talk was part of the Big Picture, Small Talk lecture series, which is an effort organized by National Toxicology Program (NTP) health scientist [Abee Boyles, Ph.D.](#), to present research done at NIEHS in a form that is more accessible for staff who are not scientists or those who are not specialists in that field.

Peggy Mooring of the Administrative Management Branch introduced Kwok and described her own experiences working at the U.S. Environmental Protection Agency (EPA) during the Exxon-Valdez spill in Alaska in 1989.

[Kwok](#), who is a staff scientist in the NIEHS Chronic Disease Epidemiology group, began his talk with the definition and a brief history of epidemiology. The word epidemiology is derived from the Greek root words epi (among), demos (the people), and logos (study of) and is the study of the distribution and determinants of diseases in populations. Epidemiologic studies can involve determining the sources of illnesses and the health impacts of events such as large oil spills.



*Mooring introduced Kwok and described her own experiences with the Exxon-Valdez spill while she worked at an EPA site that was one of the first responders to that disaster. (Photo courtesy of Steve McCaw)*

## Deepwater Horizon oil rig explosion triggers massive undersea oil spill

The Deepwater Horizon exploded on April 20, 2010, leading to the largest maritime oil spill in U.S. history. Crude oil gushed from what Kwok described as a mile long steel drinking straw connecting the Deepwater Horizon to the well head located 5,000 feet under the surface of the ocean. “When the Deepwater Horizon exploded and sank, it bent the straw, rupturing the pipe and causing hundreds of millions of gallons of crude oil to spill out into the Gulf of Mexico,” he said.

The cleanup for the spill started almost immediately with BP hiring thousands of contractors to assist in the effort. The objective of the **GuLF STUDY** is to determine if those cleanup workers have suffered or will suffer any adverse health effects.

“We hypothesize that the cleanup workers have the highest potential for physical contact with the oil and dispersant. These are the folks who are on the beaches and boats picking up the tar balls and pulling up the oiled boom,” Kwok explained.

The GuLF STUDY is a prospective study, meaning that participants are enrolled before they start experiencing any adverse long-term effects. More than 32,000 adults nationwide have enrolled into the study. Exposure ranges from very low-risk individuals, such as those in logistics support, to high-risk individuals who were working directly with the cleanup at the source of the spill. The idea is that the study will consist of a gradient of exposures that can then be correlated with observed health effects.

### Reaching out to cleanup workers

The GuLF STUDY team is following the participants with a combination of telephone interviews, home visits, and clinical screenings in order to document any potential adverse physical or psychological effects. Their preliminary findings show that oil spill workers were more likely to report wheezing and coughing two years after the spill. These same workers are also scoring higher on standardized measures for depression and post-traumatic stress disorder.

The goal is to follow these participants over ten years or more, in order to see what future health complications might arise. Any knowledge gained in these studies may affect organization of cleanup efforts and public health responses to any future spills. More information on the GuLF STUDY can be found at its [website](#).

(Jordan St. Charles, Ph.D., is an Intramural Research and Training Award fellow in the DNA Replication Fidelity Group at NIEHS)

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*Kwok described the science of modern epidemiology beginning with its origin during a cholera epidemic in London during the 1800s and ending with the GuLF STUDY. (Photo courtesy of Steve McCaw)*



*A diverse audience attended the Big Picture, Small Talk lecture, including NTP toxicologist Cynthia Ryder, Ph.D., center, and contract scientific program analyst Yuxia Cui, Ph.D., right, of the NIEHS Division of Extramural Research and Training. (Photo courtesy of Steve McCaw)*

# NIEHS trainee honored with Wetterhahn Award

By Sara Mishamandani

The NIEHS Superfund Research Program (SRP) selected Bradley Newsome, Ph.D., of the University of Kentucky (UK) SRP Center, as the 17th recipient of the annual [Karen Wetterhahn Memorial Award](#).

The award, which recognizes outstanding SRP graduates and postdoctoral researchers, was presented at the 2014 SRP Annual Meeting (see [story](#)) in San Jose, California. The program acknowledged Newsome for his contributions at the interface of basic sciences, environmental engineering, and biomedicine for the larger purpose of impacting public health.

Newsome received his doctoral degree in May 2014 under the guidance of Bernhard Hennig, Ph.D. a professor of nutrition and toxicology at the university and director of its SRP center. During his doctoral work, Newsome investigated how nutrition could modulate the effects of exposure to environmental chemicals and conducted research to develop systems that use nanomaterials for removal of contaminants in water supplies. He is continuing this research at the university as a postdoctoral scholar and will also serve as the graduate and postdoctoral training coordinator for the center.

“Newsome is unique because of his combination of intellect, adept communication ability, and leadership skills, as well as his ability to translate complex knowledge into applied assistance to stakeholders locally and internationally,” said Hennig. “I am convinced that Brad Newsome will continue to display the legacy of Dr. Wetterhahn by continued contribution to research and educational needs related to integrating science, technology, and public health needs with diplomatic and development-related goals.”



*“Although my research interests have evolved over the last decade, the overarching goal has remained steady — to develop strategies and tools that impact public health, with a special focus on the needs of the developing world,” said Newsome. (Photo courtesy of Brad Newsome)*

## Reducing health effects from environmental contaminants — from nutrition to remediation

Newsome’s doctoral work sought to address problems related to chlorinated organic pollutants that pollute waterways, soil, and food sources. Newsome investigated the ways nutrition can decrease inflammation and oxidative stress associated with exposure to these pollutants. His work at the center showed that diet supplementation of polyphenols, which are found in green tea, upregulates a variety of antioxidant enzymes that effectively protect against the toxicities of environmental pollutants, such as polychlorinated biphenyls. This work adds weight to the current center research paradigm that nutrition can positively affect the negative human health effects related to chemical exposures near Superfund sites.

Newsome’s current research combines his work with nutrient polyphenols, which have an affinity for chlorinated organic pollutants, with nanomaterial systems for simple and fast removal of contaminants from contaminated water sources. Newsome and his research team have combined quercetin and curcumin, potent antioxidant polyphenols, with magnetic nanoparticles to form nanocomposite materials that quickly bind water-borne organic pollutants in a polymeric matrix. They can then apply a magnetic field to the system to rapidly remove the material-bound pollutants, leaving the water detoxified.

## Improving global public health outside of the lab

In 2010, Newsome halted his graduate work to spend a year in the African kingdom of Swaziland, where he designed and directed the construction of a large clean water collection system for a local community to battle drought and widespread health issues associated with contaminated drinking water. He also taught math and science to students and teachers, and worked with the local hospital and the University of Cape Town on a public health advocacy research project.

“This experience served to refocus my research efforts upon returning to graduate school toward the development of innovative strategies to address the major global health concerns associated with water pollution,” said Newsome.



*Newsome, second from right, accepts his Wetterhahn Award from Gwen Collman, Ph.D., right, director of the NIEHS Division of Extramural Research and Training, with, from left, NIEHS SRP Director Bill Suk, Ph.D., and Hennig. (Photo courtesy of Carol Kelly)*

As a result of Newsome’s global humanitarian work and scientific research, he hopes to become involved in global health policy to continue to promote public health. Newsome completed an education policy internship with the Council of State Governments, which familiarized him with science and technology research, education policy needs, and translation of research findings for development-related goals. He is also working as part of the center’s Training and Research Translation Cores to more effectively apply multidisciplinary research and training with effective communication and stakeholder engagement.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

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## EMGS honors Barbara Shane and Martyn Smith

*By Eddy Ball*

The Environmental Mutagenesis and Genomics Society (EMGS) presented 2014 awards to retired National Toxicology Program (NTP) toxicologist Barbara Shane, Ph.D., and NIEHS grantee Martyn Smith, Ph.D., during its annual meeting this fall in New Orleans.

The [society](#) honored Shane, who was executive secretary for the NTP Board of Scientific Counselors 2003-2009, with the 2014 EMGS Service Award in recognition of her longstanding dedication and service to the society. Shane has served as treasurer since 2008 and was a councilor in the late 1990s. She is currently a private consultant in toxicology.

Smith was recognized for his outstanding contributions to the field of environmental toxicology with the 2014 EMGS Alexander Hollaender Award. The society pointed to his contributions on the mechanisms of benzene toxicity, applying omic technologies in human population studies, and in promoting the exposome paradigm.

“I’m very proud of the EMGS awards presented to Barbara and Martyn,” said NIEHS and NTP Director Linda Birnbaum, Ph.D. “It reflects well on the winners’ achievements and on the programs that supported their outstanding work.”

## Toxicology in the boardroom and at the bench

Prior to joining NTP, Shane was a professor of toxicology in the Institute for Environmental Studies at Louisiana State University. In 2000 she was elected as a Fellow of the American Association for the Advancement of Science. That same year, she joined Integrated Laboratory Systems in Research Triangle Park, North Carolina, where she directed an NIEHS-funded contract on the evaluation of *in vitro* assays to screen and identify endocrine-disrupting compounds.

During her tenure at NTP, Shane was responsible for managing scientific peer review and developing reports and documents that describe NTP scientific programs and priorities. She also provided information and communication concerning NTP scientific programs to other NTP member agencies and the public. Besides EMGS, she has served on committees in the Society of Toxicology and the Genetic and Environmental Mutagenesis Society.

**Smith** is a professor of toxicology in the University of California, Berkeley School of Public Health and has been director of the NIEHS-funded Superfund Research Program there since 1987. He is a collaborator on numerous other projects examining emerging technologies to develop biomarkers for human studies, improve chemical detection, and facilitate waste remediation.

A leading authority in the field of exposure biology, Smith and colleague Stephen Rappaport, Ph.D., published a high-profile perspective on environmental health study design in *Science*. The article, "[Environment and Disease Risks](#)," presented a compelling argument that a more complete and objective picture is needed in order to help scientists discover the major causes of chronic diseases by better accounting for an individual's total environmental exposure, or exposome.



*A native of South Africa, Shane received her doctorate from the University of the Witwatersrand and, in 1990, received certification as a diplomate of the American Board of Toxicology. (Photo courtesy of Steve McCaw)*



*Smith is a native of the United Kingdom who completed his doctorate at the Medical College of St. Bartholomew's Hospital Charterhouse Square in London and postdoctoral training at the Karolinska Institutet in Sweden. (Photo courtesy of University of California, Berkeley)*

**Linked video:**  
Watch as Smith describes the "Exposome Paradigm" (25:47)

(Launches in new window)

Download Media Player:  Flash [↗](#)

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# NIEHS gets enthusiastic thumbs up for lab animal care

By Eddy Ball

This November marked a milestone for the laboratory animal program at NIEHS with an exemplary recommendation by reviewers from its accrediting association.

Every three years, the NIEHS animal care and use program must undergo a rigorous re-evaluation by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC). The review ensures that the program's use of animals follows all regulations and guidelines, and maintains the highest standards of humane care possible.

"I am pleased to announce that the site visitors will recommend that the AAALAC Council place our institution at the 'exemplary' status, a level of commendation given to only a handful of the more than 900 programs they accredit across the globe," explained NIEHS Scientific Director Darryl Zeldin, M.D., in his Nov. 19 announcement. "In addition, we experienced the very rare event of having the site visitors offer up no suggestions for improvement, a feat that is truly remarkable."

"Quality animal care ensures quality animal-based science," Zeldin said. "We are very fortunate to have a team that provides, and a culture that supports, this mission."

## It takes a village

Preparation for the triennial evaluation requires an extensive amount of time and effort by NIEHS staff, the bulk of which takes place long before the two-day site visit by AAALAC representatives.

Groups involved include the Comparative Medicine Branch (CMB), the Animal Care and Use Committee (ACUC), animal research-related components of the Health and Safety Branch in the Office of Management (OM), and the Office of Research Facilities, as well as support provided by the Operations and Security Branch in OM, and the scientists from the in-house research labs in the Division of Intramural Research and the Division of the National Toxicology Program (see text box).



*According to AAALAC, accreditation benefits an institution and the animals in its care in many ways. Each time a new organization becomes accredited, it helps to raise the global benchmark for animal well-being in science.*

## Special thanks to members of the teams involved

Along with his congratulations to everyone involved, Zeldin recognized key individuals involved in this accomplishment, including the following:

- ACUC chair John Roberts, Ph.D.
- ACUC coordinator Brooke Rogerson
- Animal Resource Services team led by Program Manager Debbie Gaffney and Contract Project Manager Erica Hayes
- Veterinary Medical Services team led by Terry Blankenship-Paris, D.V.M.
- Quality Assurance Laboratory led by David Kurtz, D.V.M., Ph.D.
- Office of Research Facilities team led by Bill Blair
- Health and Safety Branch team led by Scott Merkel
- Operations and Security Branch team led by Mitch Williams

“I would especially like to acknowledge the outstanding leadership of the CMB team led by Kathy Laber, D.V.M., and her deputy, Mary Grant, V.M.D.,” Zeldin said.

The AAALAC will announce its official decision regarding the ongoing accreditation of NIEHS in the spring of 2015.

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## NIH program speaker explores mixed African and native identity

By Eddy Ball

Historian Gabrielle Tayac, Ph.D., spoke at a Native American Heritage Month Celebration Nov. 12 at the National Institutes of Health (NIH) in Bethesda, Maryland.

The talk by [Tayac](#) was part of the “Healing Our Community Through Narrative: The Power of Storytelling” series organized and hosted by the NIH Office of Equity, Diversity, and Inclusion, in partnership with the [Trans-NIH American Indian and Alaska Native \(AI/AN\) Health Communications and Information Workgroup](#) and the AI/AN Research Interest Workgroup.



*“There’s this process of unlearning the stereotypes,” Tayac said of the healing journey toward mixed-heritage identity. “People still have to disentangle all of that.” (Photo courtesy of NIH)*



**Linked video:**  
[Watch a video of Tayac's presentation at NIH \(01:30:00\)](#)

(Launches in new window)

Download Media Player:  Flash [↗](#)

Tayac is a mixed-heritage member of the Piscataway Indian Nation and a historian at the [Smithsonian National Museum of the American Indian](#), who holds a doctorate in sociology from Harvard University.

The co-chair of the Trans-NIH AI/AN Health Communications and Information Workgroup, Mimi Lising, introduced Tayac, who was the third speaker in the latest series sponsored by the initiative, which was established in 2005.

As Tayac constructed a narrative of her personal healing journey as a Native American of mixed heritage interwoven with her work creating exhibits



*In addition to co-chairing the initiative, Lising is a multicultural health educator at the National Institute of Arthritis and Musculoskeletal and Skin Diseases. (Photo courtesy of NIH)*

that reflect emerging cultural concerns in Native American communities, she made use of several visuals and videos created by the museum. As Lising noted in her introduction, “We are bringing the museum to you.”

### **Identity as a source of self-concept and, ultimately, health and well-being**

Tayac opened her talk by telling the audience, “I’ve been very curious about identity... and how to transfer it into a museum setting.”

Tayac highlighted one traveling [exhibit](#), the sometimes controversial “IndiVisible: African-Native American Lives in the Americas,” in a discussion of identity among people of mixed African American and Native American descent. Each of these communities has grappled with the notion of racial purity and been unsure about how to self-identify their people of mixed heritage.

“Native peoples are not only minorities, but [their identities] are also wrapped up in the notion of sovereignty,” she said. Efforts by governments to categorize them racially have tended to discourage acknowledgement of mixed heritage. “[But] we are still here... [and] we have a 60 percent intermarriage rate,” she continued, pointing to the 560 federally recognized and 200 state recognized tribes in the U.S.

One of the several videos that were part of the presentation featured testimonials by people who are now more likely to describe themselves as black Indians. “I can’t deny either side,” one man said of his acceptance of mixed heritage. “I feel like a part of me was being shut off,” a woman added, reflecting on her feelings as she was growing up in a community that looked down on mixed heritage.

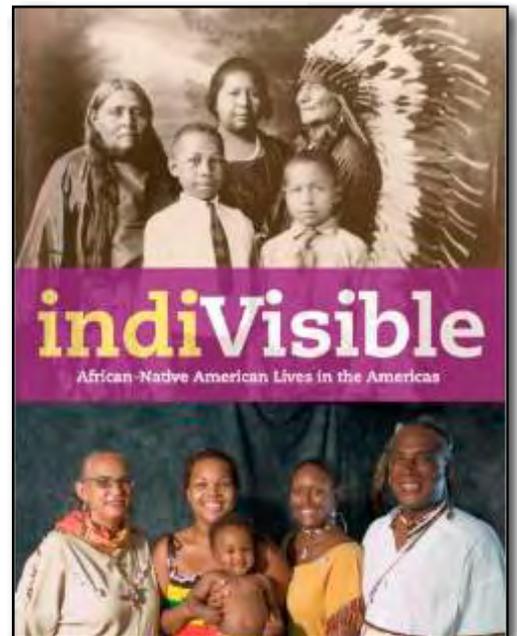
### **Implications for biomedical research**

As Tayac moved from presentation to the questions that followed her talk, she and her audience discussed the impact of identity on health and research. Being a minority is increasingly recognized as a source of socio-psychological stress that can contribute to disease in important ways, and the past experiences of minority communities can influence attitudes about participation in biomedical research.

”People get very nervous about any sort of taking of biological material from the body,” Tayac said in response to a question about genetics research. She pointed to one study that some in the Yucca community called the [Vampire Project](#). “There’s this issue of trust,” she said.



*“We’re coming together to celebrate a priority,” Hill remarked, as he presented Tayac with a plaque. Hill is director of the Office of Special Populations at the National Institute on Aging (Photo courtesy of NIH)*



*Photos used in the exhibit reflect the mixed African and Native heritage of the so-called black Indians all over the Americas. (Photo courtesy of the Smithsonian Institute)*

Wrapping up the program, initiative co-chair Carl Hill, Ph.D., presented Tayac with a plaque as a token of appreciation. He referred to the biomedical implications of identity on diversity training and health disparities initiatives at NIH.

“This presentation of ethnic identity and its impact on diversity in the biomedical workforce and to pathways that sustain health disparities was on target and relevant to many of our ongoing discussions,” he said.

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## NIH honors RTP staff at Office of Director Awards ceremony

*By Eddy Ball*

At its first standalone recognition ceremony for support staff Nov. 19, the National Institutes of Health Office of the Director (NIH OD) honored two NIEHS employees and five members of the NIH Office of Research Facilities staff in Research Triangle Park (RTP), North Carolina.

Representing NIH Director Francis Collins, M.D., Ph.D., NIH Principal Deputy Director Lawrence Tabak, D.D.S., Ph.D., hosted the NIH OD Awards Ceremony in Bethesda, Maryland.

After engaging in some light-hearted banter about the past year, Tabak spoke in earnest about the importance of the people who serve everyday at NIH.

“Team work is at the forefront of what the OD is all about,” Tabak told the audience. “We’re incredibly proud of all of your achievements beyond your job descriptions.”

### Supporting philanthropy, science, and future expansion

NIH Office of the Director recognized members of three teams with NIEHS ties:

- 2013 Feds Feed Families Team, in recognition of exemplary efforts in promoting the Feds Feed Families Campaign at the NIH and throughout the United States — Monya Brace, NIEHS Office of Management
- Administrative Support Group for Stadtman Investigator Searches, for significant, outstanding administrative support of the 2010-2013 Stadtman Investigator searches — Deborah Wilson, NIEHS Office of the Scientific Director
- The Technical Evaluation Team for the RTP Campus for selfless participation and technical excellence in technical evaluations resulting in contract awards that serve as the basis for future construction on the RTP camps — Alison Hawkins, William Hawkins, Donald Jackowski, James Stancil, and Daniel Burk, NIH Office of Research Facilities personnel stationed at NIEHS.



*Brace was co-chair of the 2013 Feds Feed Families at NIEHS. Along with co-chairs, President of the American Federation of Government Employees Local 2923 Bill Jirles and Blacks In Government Research Triangle Park Chapter representative Sheila Withers, Brace oversaw the collection of more than 3,600 pounds of food and personal hygiene items for the needy. (Photo courtesy of Steve McCaw)*

NIEHS Toxicology Liaison Chris Weis, Ph.D., represented NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., at the ceremony. Brace and Wilson were unable to attend in person, but were able to view the ceremony via webcast from Bethesda.

In an upcoming ceremony Dec. 3, NIEHS Scientific Director Darryl Zeldin, M.D., will receive a Partnership Award from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). To be presented by NICHD Director Alan Guttmacher, M.D., the award recognizes Zeldin's consultation during reorganization of the NICHD intramural program and the support he gave to NICHD Scientific Director Constantine Stratakis, M.D., D.Med.Sc.



*Along with her work with the Stadtman Investigator Searches, Wilson coordinates the NIH Summer Intern Program at NIEHS. (Photo courtesy of Steve McCaw)*



*Zeldin's support for reorganization of the in-house research at NICHD included meeting with lead researchers to explain the rationale for restructuring the intramural program at NIEHS and lessons learned during the process. (Photo courtesy of Steve McCaw)*

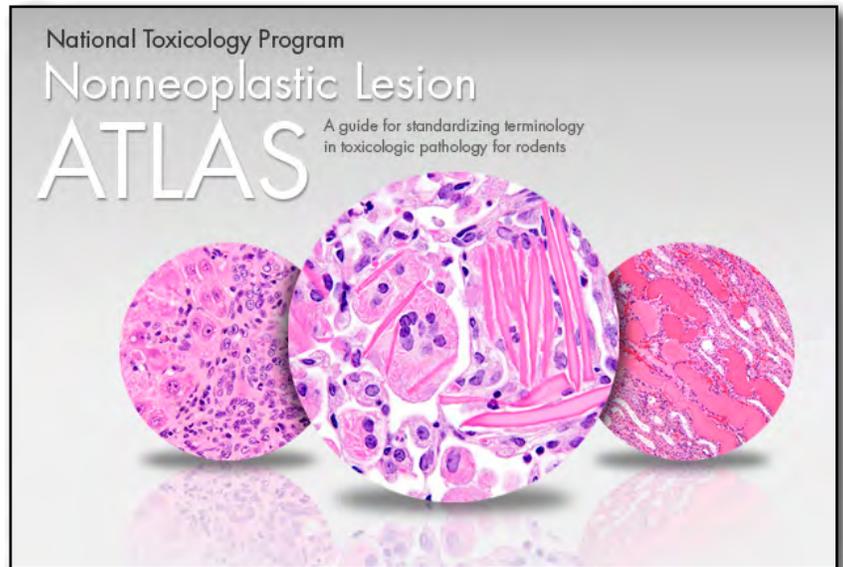
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# NTP expands coverage of Nonneoplastic Lesion Atlas

Several new sections have been added to the National Toxicology Program's Nonneoplastic Lesion [Atlas](#) over the last few months. A whole new section on a very important tissue, the [kidney](#), can now be found under the [Urinary System](#). Three other new systems have been added with hundreds of high quality images and narrative:

- [Endocrine System](#)
- [Male Reproductive System](#)
- [Special Senses System](#) (includes ears and eyes and related glands)

When completed this searchable web-based resource will contain 56 sections covering 13 biological systems.



Look for more detailed information about the Atlas in early 2015, and check the Atlas regularly for updates.

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## Science Days spotlights mentor and fellow of the year

*By Shannon Whirlidge*

This year's 12th annual NIEHS Science Days Nov. 6-7 culminated in a celebration honoring Fellow of the Year, Quaker Harmon, M.D., Ph.D., and Mentor of the Year, Samuel Wilson, M.D.

These prestigious awards, bestowed on recipients nominated and chosen by the scientists at the NIEHS, recognize those who have made especially significant contributions to research and service.

### Fellow of the Year

[Harmon](#), an Intramural Research Training Award fellow in the Epidemiology Branch, is the third annual Fellow of the Year. She was chosen from seven nominees based on her passion and dedication to research, leadership, ability to convey scientific discoveries, collegiality, service, and mentoring. In addition to being recognized for her outstanding achievements, Harmon received a \$1,000 travel grant to attend a future scientific meeting.

Harmon was nominated by her mentor, Donna Baird, Ph.D., a lead researcher in the Epidemiology Branch, who said she was delighted to see Harmon acknowledged with such a well-deserved award. Baird first met and was impressed by Harmon during her graduate studies at the University of North Carolina at Chapel Hill, and said she was thrilled when Harmon decided to pursue her postdoctoral training at the NIEHS.

Baird explained that Harmon demonstrates many qualities that make her deserving of this award. “Quaker is highly regarded by her fellow trainees, does award-winning work, and is a great mentor,” Baird said.

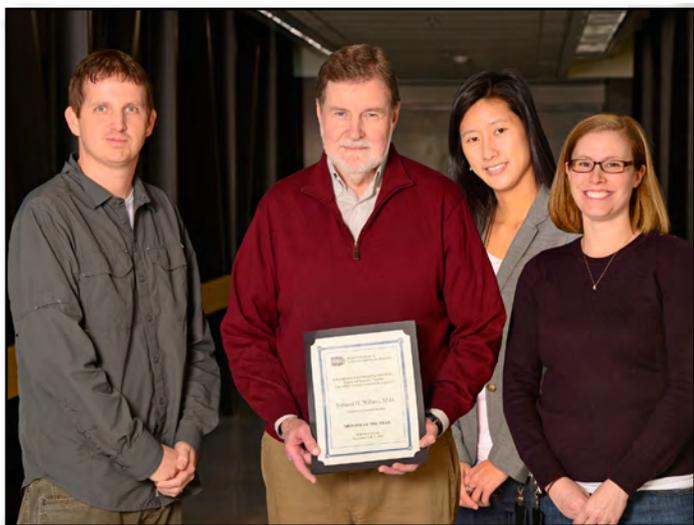
## Mentor of the Year

**Wilson**, a senior lead researcher in the Genome Integrity and Structural Biology Laboratory, was selected as this year’s Mentor of the Year by the NIEHS Trainees Assembly (NTA). Bret Freudenthal, Ph.D., a postdoctoral fellow in Wilson’s lab, spearheaded the nomination and explained how he and the more than 50 other trainees that have been mentored by Wilson have been positively affected by their experience.

Many previous fellows wrote in support of Wilson, stating that his mentorship had such a profound impact on their careers and lives that their current achievements would not have been possible without his individualized guidance and support.

The fact that Wilson received the Mentor of the Year award is no surprise to anyone who has followed the careers of his trainees. “Mentoring and training are the most important roles [for lead researchers] at NIEHS,” he said, “and among their highest priority activities.” Wilson also said of his approach to his trainees, “Mentoring is multifaceted and special to each trainee.”

(Shannon Whirlledge, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction.)



*NIEHS 2014 Mentor of the Year, Wilson, was joined by, from left, Freudenthal, along with NTA representatives Kristin Gabor, Ph.D., and Monica Frazier, Ph.D. “I’m extremely honored to receive the award,” he said. (Photo courtesy of Steve McCaw)*



*NIEHS 2014 Fellow of the Year Harmon, center, accepted her award from her nominator Baird, left, and Tammy Collins, Ph.D., director of the NIEHS Office of Fellows’ Career Development. (Photo courtesy of Steve McCaw)*

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# Kunkel signs in at the American Academy of Arts and Sciences ceremony

*By Eddy Ball*

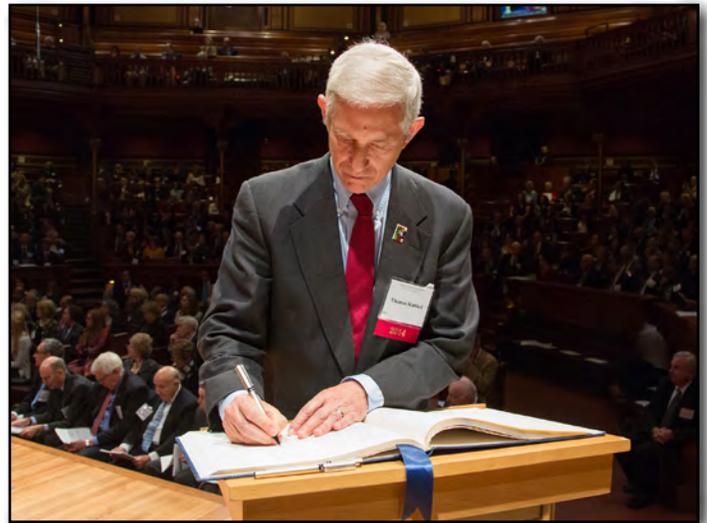
After signing the American Academy of Arts and Sciences membership book Oct. 11 during the academy's induction ceremony in Cambridge, Massachusetts, NIEHS lead researcher Thomas Kunkel, Ph.D., found himself in good company.

Signing the book is a tradition for newly inducted members that dates back to 1780, when the academy was founded by John Adams, James Bowdoin, John Hancock, and other scholar-patriots to recognize the best and brightest men and women at the cutting edge of the arts and sciences.

The current membership includes more than 300 Nobel laureates, some 100 Pulitzer Prize winners, and many of the world's most celebrated artists and performers.

The Environmental Factor ran a feature [story](#) about Kunkel's election to the academy when he was officially notified in May.

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*Kunkel is an NIH distinguished lead researcher, former head of the NIEHS Structural Biology and Molecular Genetics Laboratory, and lead researcher in the NIEHS DNA Replication Fidelity Group. (Photo courtesy of the American Academy of Arts and Sciences)*

# Clinical Feature

## Clinical researchers learn about NIH interpretation and translation services

By Eddy Ball

To be truly inclusive as NIEHS steps up community-engaged clinical research, researchers must understand the language needs of a quickly changing demographic.

That was the take home message of a talk Nov. 17 at NIEHS by two NIH Clinical Center experts — Brenda Robles, coordinator of the Language Interpreter Program, and Adrienne Farrar, Ph.D. head of the Social Work Department. Their talk, “Communicating With Non-English Speaking Study Participants,” was the latest in an NIEHS Clinical Research Seminar Series on “Practical Applications and Regulatory Considerations in Human Research.”

“As we do more outreach into the community, we really need language services,” said Joan Pakenham, Ph.D., director of the NIEHS [Office of Human Research Compliance](#), who hosted the talk. “We have to make a real effort to accommodate other languages and ethnicities.” She also emphasized the importance of cultural competencies as part of interpretation and translation.

### Setting effective communication as the goal in research and treatment

Robles has been on the front lines of communicating with people who have limited English proficiency at NIH since 2006. She began her talk by tracing the legislative background of her program back to the Civil Rights Act of 1964, through the NIH Revitalization Act of 1993 and Executive Order 13166 in 2000, up to the [NIH Language Access Plan](#), which is in its final stages of implementation this year.

“Health care is communication dependent,” Robles told the audience, as she described the ethical and legal requirements for providing patients and research subjects with the best possible interpretation and translation services. Robles made a clear distinction between translation from one language to another and the much more complex process of interpretation. Along with the words themselves, cultural differences, body language, and educational level can be important considerations in effective interpretation.



*“We really need this talk,” Pakenham said in her opening remarks, “because we’re moving toward an asthma clinic with many people who need this service.” (Photo courtesy of Steve McCaw)*



*Robles gave several examples of potential pitfalls when clinicians fail to communicate effectively. Instructions to take one pill daily could be misunderstood by Hispanics, for example, because the word once (on-say) in Spanish means eleven. (Photo courtesy of Steve McCaw)*

For the estimated 55 million Americans who speak a language other than English at home, poor communication can be at worst a life or death matter (see [text box](#)). At best, the outcomes of ineffective communication can lead to inappropriate diagnosis, confusion over how to take medications, and failure to give human patients and subjects meaningful access to treatment and research.

### **Translation and interpretation — the right thing and the required thing to do**

After Robles presented her strong case on the basis of ethics, Farrar spoke directly to the practical needs of the NIEHS Clinical Research team, as it designs projects that will pass muster with Institutional Review Boards (IRBs). She said researchers must preplan the language needs of human participants in clinical studies and provide them with fully translated consent forms, validated research surveys, and questionnaires, presented in ways that are culturally appropriate.

At the Clinical Center, that has meant building a professional bilingual staff of certified health care interpreters. The Language Interpreter Program in Bethesda, she said, has grown from a few volunteers in 1990 to a professional staff. Members include full-time-equivalent certified interpreters, contractors, bilingual linguistics, science or health care student interns from the Hispanic Association of Colleges and Universities (HACU), tested and vetted volunteers, and telephonic interpreter services.

In these ways, the program has served the majority of the 2,200 patients speaking over 60 languages in fiscal year 2014, in person or by telephone. Farrar also noted the importance of hiring bilingual staff and care providers, not to act as interpreters, but to perform their jobs in the language of the patients they serve.

“It’s a constant back and forth,” Farrar said of the process of meeting legal and administrative requirements, beginning with determining an individual’s preferred language for medical communication. She reinforced Robles’ call for comprehensive data collection and documentation, as well as the need for acknowledging and becoming sensitive to cultural differences.

“If acceptable plans are not in place,” she said, “Good luck with getting IRB approval.”

The NIEHS Clinical Research Branch currently has [several studies](#) underway or in enrollment at the Clinical Research Unit in Research Triangle Park, North Carolina. NIEHS clinical researchers also perform studies at the [NIH Clinical Center](#) in Bethesda, Maryland.



*One essential for building an effective language interpretation program, Farrar told the audience, is getting buy-in from leadership. (Photo courtesy of Steve McCaw)*



*Virtually everyone with ties to the NIEHS clinical research program turned out for the talk, including Acting Director Stavros Garantziotis, M.D. Early in Robles’ talk, Garantziotis shared his own experience trying to communicate through a patient’s family member. “It’s hard to tell if you’re being understood,” he said. (Photo courtesy of Steve McCaw)*



*Clinical endocrinologist Janet Hall, M.D., gave an example of why cultural sensitivity can be so important in her research. How can researchers ask important questions in reproductive medicine studies, such as how many sexual partners a subject has had, if they rely on family members for interpreting, she asked. (Photo courtesy of Steve McCaw)*

*The talks were especially relevant for Craig Wladyka, left, and Jane Lambert, who work with NIEHS IRB approvals. As the Clinical Research Division designs more and more community-engaged studies, ensuring that subjects are giving truly informed consent will become increasingly essential to when a study goes forward or not. (Photo courtesy of Steve McCaw)*

## **The case of Willy Ramirez – a treatment fiasco based on a single word**

In 1980, Ramirez suffered an internal brain hemorrhage that was ignored for two days because of failure by staff at a south Florida hospital to understand the difference between the Spanish word *intoxicado* and the English word *intoxicated*.

When emergency room personnel asked Ramirez what was wrong, he told them he was *intoxicado*, which in Cuban Spanish is a kind of an all-encompassing word that means there's something wrong with Ramirez because of something toxic he ate or drank. Thinking instead that he was *intoxicated* by alcohol or drugs, hospital staff failed to order a neurological exam, treated him for drug or alcohol overdose, and let him remain unconscious for more than two days, as his hemorrhage continued to bleed.

By the time doctors had realized their mistake, it was almost too late. The damage left Ramirez paralyzed from the neck down. In an out-of-court settlement of the subsequent malpractice suit, Ramirez received a lump sum payment of \$3.4 million and monthly payments for the rest of his life, according to a [story](#) in the Lakeland (Florida) Ledger.

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# Science Notebook

## Parkinson's disease meeting fosters collaborations for advancing research

By Ernie Hood

NIEHS and the National Institute of Neurological Disorders and Stroke (NINDS) co-sponsored a meeting Nov. 3-4 at NIEHS to develop prioritized recommendations for advancing basic, epidemiological, and clinical research on environmental contributors to Parkinson's disease (PD).

“[Parkinson's Disease: Understanding the Environment and Gene Connection](#)” was designed to bring together experts from across the spectrum of PD science to evaluate the most recent research findings on the impact of environmental factors on PD etiology and to discuss the challenges of translating those findings into public health practice and policy.

NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., speaking in person, and NINDS Acting Director Walter Koroshetz, M.D., speaking via webcast, welcomed participants and underscored the important contributions their institutes are making to PD research and translation.

The conference followed a [January 2014 gathering](#) organized by NINDS that dealt mainly with the genetics of PD. After that meeting, two workgroups were organized to ensure that the November event would incorporate the recommendations that emerged from the first meeting while adding environmental considerations. “It wasn't just a follow-up, we wanted to make sure that we gave the environment the attention it deserves with regard to the development of the disease,” explained Jonathan Hollander, Ph.D., a program administrator in the NIEHS Genes, Environment and Health (GEH) Branch.

### Content-rich proceedings

Day one of the meeting featured presentations and discussions on the themes and recommendations from the clinical and epidemiology workgroup and the basic and mechanistic workgroup.



Meeting co-host Birnbaum welcomed participants, noting that NIEHS and NINDS funding combined comprises 76 percent of PD research supported by the National Institutes of Health. She also described several of the recent advances in PD science by environmental health researchers. (Photo courtesy of Steve McCaw)



Meeting co-host Koroshetz was unable to attend in person, but welcomed participants with a video message from his office in Bethesda, Maryland. (Photo courtesy of Steve McCaw)

The first workgroup focused on opportunities to identify environmental factors that affect prodromal or pre-motor PD, disease progression after diagnosis, biomarkers of exposure, diagnosis and progression, and risk factors. The other workgroup described the impact of environmental chemicals on known genetic abnormalities and pathways in PD, and progress in measuring environmental chemicals in human and animal samples.

Two wide-ranging panel discussions comprised the meeting's second day.

The first panel, moderated by GEH branch chief Cindy Lawler, Ph.D., addressed the challenge of integrating PD environmental research across disciplines, with a concentration on encouraging interdisciplinary collaborations.

The second panel, moderated by Population Health Branch administrator Kimberly Gray, Ph.D., focused on translation of basic and clinical PD findings into practice and policy. The panel included several members of the broader PD advocacy community, who provided their perspectives on the challenges and opportunities related to effective translation.

### **Cross-talk was key**

The meeting was a unique mix of people from both hemispheres of the PD research world — the geneticists and the environmental scientists — as well as representatives of the PD advocacy community. “Bringing together people who don’t normally interact was intentional,” said Hollander. “The most exciting parts of the meeting were the dialogue between the geneticists and the environmental health scientists, and the opportunity to hear very personal stories from a number of people who have PD. The equal representation permeated the entire two days.”

“It was great to be able to pull in people from the larger community, to be able to hear their thoughts and concerns, and look at ways we can all work together going forward to shed new light on this devastating disease,” Lawler observed.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



*Lawler, left, and Hollander spearheaded NIEHS meeting organization efforts. (Photo courtesy of Steve McCaw)*



*Lively discussions were common over the meeting's two days, particularly during panel sessions. (Photo courtesy of Steve McCaw)*



*During the panel discussion on translation, NTP Pathologist David Malarkey, D.V.M., Ph.D., spoke movingly about his own young-onset PD. He said that the progression of his disease seems to be fairly slow, and stressed the importance of exercise in slowing PD progression, although it is unclear why it works. (Photo courtesy of Steve McCaw)*



*Seating arrangements were randomly generated, so that people who would not normally have the opportunity to interact with each other could do so and discover commonalities leading to potential interdisciplinary collaborations. (Photo courtesy of Steve McCaw)*



*Caroline Tanner, M.D., Ph.D., of the University of California, San Francisco co-chaired the clinical and epidemiology workgroup. (Photo courtesy of Steve McCaw)*



*During the translation panel discussion, University of Pennsylvania clinical epidemiologist and Parkinsonologist Allison Willis, M.D., suggested that more research attention should be paid to sexual dimorphism in PD risk. (Photo courtesy of Steve McCaw)*

**Parkinson's Disease:  
Understanding  
the Environment  
and Gene Connection**

Co-sponsored by the National Institute of Environmental Health Sciences  
and the National Institute of Neurological Disorders and Stroke

**November 3-4, 2014**  
Monday, Nov. 3, 8:30 a.m. – 5:00 p.m.  
Tuesday, Nov. 4, 8:30 a.m. – noon

NIEHS Building 101, Rodbell Auditorium  
Research Triangle Park, N.C.

Individuals with disabilities who need accommodation to participate in this event should contact Jon Hollander at 919.541.0467 or hollandj@niehs.nih.gov. TTY users should contact the Federal TTY Relay Service at 800.877.8339. Requests should be made at least 5 business days in advance of the event.

Any individual seeking access to the NIEHS campus will need to be prepared to show a photo ID (e.g., driver's license, or a company, government, or university ID) and provide pertinent information about the seminar (e.g., name of the speaker, host, or title of the seminar).

National Institutes of Health • U.S. Department of Health and Human Services

*More than 60 people attended the meeting in person, with several more logged into the webcast. (Photo courtesy of Steve McCaw)*



*Seated beside neurologist Brad Racetta, M.D., center; members of the NIEHS in-house research team, epidemiologists Freya Kamel, Ph.D., left, and Honglei Chen, M.D., Ph.D., right, contributed to the presentations and panel discussions. (Photo courtesy of Steve McCaw)*

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# Falk lecture spotlights biomarkers for cancer

By Robin Arnette

Advances in the field of metabolomics were highlighted at the 29th annual Hans L. Falk Memorial Lecture Nov. 18 at NIEHS. Metabolomics is the study of all metabolites, or end products of cellular processes, in a biological cell, tissue, organ, or organism.

The seminar, “Search for Cancer Biomarkers Using Metabolomics,” was presented by Frank Gonzalez, Ph.D., head of the Laboratory of Metabolism in the Center for Cancer Research at the National Cancer Institute.

Gonzalez started off by saying that the metabolome, or complete set of small-molecule metabolites found in a biological sample, is derived from a number of sources. Origins include the environment, diet, and products that result from the metabolism of the human body. The number of metabolites may run into the thousands, all of which may be found in the urine. Some of these metabolites may be identified and utilized as a diagnostic tool for diseases.

“Metabolites can be used to define the molecular profile of a drug, and discover biomarkers for organ specific toxicities, or even drug efficacy,” Gonzalez said. “Currently, many research groups search for and validate biomarkers for diseases, such as diabetes and cancer.”

## Tracking down metabolites

Gonzalez said mouse studies are easier to carry out than biomarker discovery studies in humans, because investigators can control all of the testing variables in mice. Biomarkers are key molecular or cellular events that link a specific environmental exposure to a health outcome. Since the human metabolome is influenced by age, sex, diet, health status, and genetic background, it is extremely complex. Hundreds or thousands of volunteers need to be examined to tease out biomarkers for a particular disease.

Metabolomics helped Gonzalez and his colleagues at the National Cancer Institute, notably Curtis Harris, M.D., and others in the Laboratory of Human Carcinogenesis, find four metabolites that were altered in people with early stage lung cancer — N-acetylneuraminic acid, cortisol sulfate, 561+ ion, and creatine riboside. It is likely that one or more of these biomarkers could be a diagnostic for other cancers.



*The research focus of the Gonzalez lab is to understand the mechanisms of chemical carcinogenesis using various mouse bioassays for colon, liver, mammary, and other cancers. (Photo courtesy of Steve McCaw)*



*After the lecture, the Falk family presented the Falk award to Gonzalez. From left, are Negishi; Raymond Falk, Ph.D.; Gonzalez; Donald Falk, M.D.; Gabrielle Falk, the widow of Hans Falk; and Stephen Falk, J.D. (Photo courtesy of Steve McCaw)*

“This work is exciting, because one of the molecules, the creatine riboside, hasn’t been described in the literature before, and the structure of 561+ ion has not been identified,” Gonzalez explained. “We envision that these biomarkers may help identify which people are in the early stages of cancer that could be cured by surgery.”

If an easily accessible urine sample can be used to find biomarkers for early stage cancer, his team could suggest that these patients seek more advanced spectroscopic analysis, said Gonzalez. Cancer biomarkers may also be employed to monitor the effectiveness of chemotherapy and cancer reoccurrence.

Masahiko Negishi, Ph.D., head of the Pharmacogenetics Group at NIEHS, served as host for the lecture. His group examines the effects of metabolites on the liver. Negishi underscored the importance of the work Gonzalez and his group are doing.

“His research on cancer biomarkers will eventually lead to the development of tools that will aid physicians,” Negishi said.

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*NIEHS Falk lecturers receive this exquisite award for making significant contributions to environmental health sciences. (Photo courtesy of Steve McCaw)*

## Woychik talk at Duke explores epigenetics

*By Ernie Hood*

NIEHS Deputy Director Richard Woychik, Ph.D., spoke Oct. 31 to an audience of students and faculty members at the Nicholas School of the Environment at Duke University, as part of the fall 2014 seminar series presented by the Duke University Integrated Toxicology and Environmental Health Program ([ITEHP](#)).

Woychik’s lecture, “Exploring the Epigenetic Landscape of Environmental Exposures,” took his audience of students and faculty members on a journey from the origins of epigenetics to today’s cutting-edge innovations.

### New vistas in epigenetics

As one of the architects of the most recent [NIEHS Strategic Plan](#), Woychik related his talk to the areas of the plan addressing the host, and how the genes and variants of genes inherited from one’s parents affect his or her response to the environment. “How does the environment change the expression of the gene variants you inherit from your parents in a way that contributes to deleterious health effects, or to positive health effects that keep you healthy?” he asked, as he introduced the basic concepts underlying epigenetics.



*Woychik clearly enjoyed the opportunity to address an academic audience. (Photo courtesy of Steve McCaw)*

Woychik described his early work on a mouse agouti gene mutation called viable yellow, in which genetically identical littermates have different coat colors and other varying characteristics, such as obesity or normal weight. He described how a single transposable element (TE) inserted into the agouti gene allowed the TE to hijack the normal expression of the gene. The varying responses in individual animals were caused by epigenetic regulation of the expression of the promoter within the TE.

He cited work from the laboratory of Randy Jirtle, Ph.D., at Duke demonstrating that expression of the viable yellow mutation is influenced by diet, chemicals, and other environmental exposures. Overall, Jirtle's work with the viable yellow allele of *agouti* revealed how a single repetitive element, under epigenetic control, can influence the expression of an adjacent gene in a way that has a powerful influence on the biology of the organism.

### Potential for change across the genome

As Woychik explained, "The genome is chock-full of these elements, and many contain powerful enhancers and promoters. In fact, it has been estimated that up to 60 percent of the mammalian genome is comprised of repetitive elements such as TEs," he said. The question he posed is whether any of the other TE's located across the genome act like the TE in agouti mice. "Are there any of the other repetitive sequences in the genome that can influence the expression of an adjacent gene in a way that affects the biology of the individual?"

Woychik noted that today, next-gen sequencing technology makes it possible to address that question. He described his lab's research, which has been able to demonstrate that repetitive elements can influence the expression of adjacent genes in response to exposure to cocaine in a murine model. He described how that work can serve as a model to study the mechanisms of other environmental exposures that are more closely related to the mission of NIEHS.

"If genetics isn't complicated enough," Woychik concluded, "now tossing in the cell-type specific epigenetic marks on repetitive elements that clearly influence gene expression at different times in development makes the study of environmental exposures even more complicated."

"But, we have to embrace this complexity because that's how biology works."



*The lecture took place in the Field Auditorium in Environment Hall, a room bristling with monitors and other electronics. "I'm a high-tech guy, but this is really over the top!" Woychik quipped. (Photo courtesy of Steve McCaw)*



*Students in the audience paid close attention to Woychik's remarks. (Photo courtesy of Steve McCaw)*



*Annette Kirshner, Ph.D., a program administrator in the Genes, Environment, and Health Branch of the Division of Extramural Research and Training, was one of the NIEHS staff people who made the trip to Durham to hear Woychik speak. (Photo courtesy of Steve McCaw)*



*Edward Levin, Ph.D., a professor of psychiatry and behavioral sciences at Duke and organizer of the ITEHP seminar series, asked Woychik whether the epigenetic mechanisms he described were reversible based on intermittent exposures in adulthood. (Photo courtesy of Steve McCaw)*



*Environment Hall on the Duke University campus, the home of the Nicholas School of the Environment, where Woychik spoke as part of the school's ITEHP seminar series. (Photo courtesy of Steve McCaw)*

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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## **In 2014, Science Days are bigger than ever**

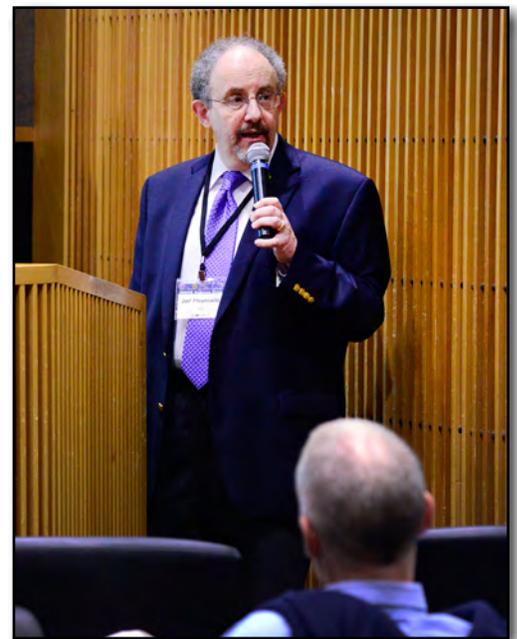
*By Ernie Hood*

The 12th annual Science Days Nov. 6-7 at NIEHS marked a day-and-a-half devoted to celebrating the depth, breadth, and remarkable quality of scientific exploration being carried out across the institute.

“It’s one of the few times in the year when all of the research being conducted at the institute is on display,” said Joel Abramowitz, Ph.D., special assistant to the Deputy Scientific Director, who leads the organizing of the event each year. “It allows everyone to get a feel for what everybody else is doing, so that there is awareness of the types of research and questions being addressed, along with opportunity for potential collaborations between scientists whose interests may overlap.”

### **Growing interest, growing participation**

The scope of the celebration is expanding every year. This year, Science Days attracted 96 posters (see [text box](#) for a list of the nine winners) submitted by fellows, students, and technicians, in addition to 12 oral presentations by trainees selected by their branch and laboratory heads. The best oral presentation award went to Georgia Alexander, Ph.D., of the Neurobiology Laboratory,



*Abramowitz chairs the Science Day Committee, which plans and organizes the Science Days event every year. (Photo courtesy of Steve McCaw)*

for her presentation titled “Manipulating hippocampal network oscillations critical to cognition: implications for schizophrenia.”

Judges for the competitions included 64 NIEHS/ National Toxicology Program (NTP) scientists and nine regional environmental health researchers who donated their time to help recognize the outstanding science being conducted at the Institute. Winners of the Mentor of the Year and Fellow of the Year awards were also honored (see [story](#)).

As NIEHS and NTP Director Linda Birnbaum, Ph.D., noted in her welcoming remarks, it was the third year that Science Days took a One NIEHS approach, actively including participation by representatives of the Division of Intramural Research (DIR), the Division of Extramural Research and Training (DERT), and the Division of the National Toxicology Program (DNTP).

A mini-symposium on neurobiology in environmental health sciences was one of the highlights of the Science Days proceedings, featuring in-depth presentations by speakers from each of the NIEHS divisions. DNTP scientist Mamta Behl, Ph.D., spoke on “Screening compounds with developmental and neurotoxic potential: flame retardants, a case example.” Patricia Jensen, Ph.D., from DIR described “Central noradrenergic neuron subtype development and function,” and DERT scientist Kimberly Gray, Ph.D., presented “Don’t breathe that: air pollution and the brain.”

Attendees also enjoyed a talk by former NIEHS trainee Kirill Lobachev, Ph.D., who is now a faculty member at the Georgia Institute of Technology.

### **Trainees in the spotlight**

Abramowitz stressed that the focus of Science Days is mainly on the trainees whose work is showcased and recognized. “One of the key things that we do during Science Days is to acknowledge their contribution to the science that’s being conducted here,” he said. “Since they are the ones who do most of the bench work in the labs, we really want to highlight the trainees.”

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



*Representing DNTP during the mini-symposium, Mamta Behl, Ph.D., described a novel approach for screening compounds with the potential for development of neurotoxicity, citing the use of flame retardants to evaluate the screen. (Photo courtesy of Steve McCaw)*



*NIEHS Scientific Director Darryl Zeldin, M.D., center right, and DERT Director Gwen Collman, Ph.D., center, enjoyed one of the oral presentations. (Photo courtesy of Steve McCaw)*



*Raja Jothi, Ph.D., of the Systems Biology Group, posed a question following Behl’s presentation. (Photo courtesy of Steve McCaw)*



*In her presentation for the mini-symposium, Kimberly Gray, Ph.D., of the DERT Population Health branch, provided evidence from numerous researchers about the potential role that air pollution may have in general brain health, and the potential role of early exposures leading to life-long changes in normal brain functioning. (Photo courtesy of Steve McCaw)*



*Haruhiro Yamashita, Ph.D., a guest researcher in the Investigative Pathology Branch, makes a point to judges Robert Oakley, Ph.D., left, and Leping Li, Ph.D., about his group's poster on experiments with mice treated with ginkgo biloba leaf extract. (Photo courtesy of Steve McCaw)*



*Senthilkumar Cinghu, Ph.D., a visiting fellow in the Genome Integrity and Structural Biology Laboratory, presents his team's poster on nucleolin and embryonic stem cell homeostasis to judge Douglas Bell, Ph.D. (Photo courtesy of Steve McCaw)*



*The 96 posters occupied a great deal of floor space in the winding corridors at NIEHS and took several hours for the judges to inspect. At least three judges reviewed every poster. (Photo courtesy of Steve McCaw)*



*As part of the neurobiology mini-symposium, DIR scientist Patricia Jensen, Ph.D., spoke about new mouse strains for manipulating genetically defined subpopulations of central noradrenergic neurons. (Photo courtesy of Steve McCaw)*



*Former NIEHS trainee Kirill Lobachev, Ph.D., from the School of Biology and the Institute for Bioengineering and Bioscience at the Georgia Institute of Technology, described his lab's work on chromosomal repeats. (Photo courtesy of Steve McCaw)*



*Lobachev was introduced by Michael Resnick, Ph.D., his training supervisor at NIEHS. "I find this a particularly exciting part of this Science Days series, because we get to see the successes – the successes of our mentorship, and the successes of the people who go out and really do some exciting things," Resnick said. (Photo courtesy of Steve McCaw)*



*Alexander, right, and Abramowitz are all smiles as she accepts her award for best oral presentation. (Photo courtesy of Steve McCaw)*

## Showcasing trainees

Nine winning posters were selected by the panel of judges, with the first five receiving a \$1,000 travel award in addition to the certificates awarded to all.

- Sara Andres, Ph.D., Genome Integrity and Structural Biology Laboratory, “Ctp1 tetramers orchestrate DNA end binding and bridging in DNA double strand break repair”
- Hideki Nakano, Ph.D., Immunity, Inflammation, and Disease Laboratory, “Chemokines coordinate differentiation and trafficking of dendritic cells”
- Katie Burns, Ph.D., Reproductive and Developmental Biology Laboratory, “Chemoattractants and cytokines play key roles in the early initiation of endometriosis-like disease in an immunocompetent mouse model”
- Douglas Ganini da Silva, Ph.D., Immunity, Inflammation, and Disease Laboratory, “Incorporation of iron to MnSODs leads to the formation of a peroxidase: possible implications for iron toxicity”
- Hrisavgi Kondilis-Mangum, Ph.D., Epigenetics and Stem Cell Biology Laboratory, “DNA methyltransferases play non-redundant roles during B cell maturation and activation”
- Jennifer Bradbury, Immunity, Inflammation, and Disease Laboratory, “Soluble epoxide hydrolase regulates macrophage phagocytosis and lung bacterial clearance of streptococcus pneumoniae”
- Sophia Harlid, Ph.D., Epigenetics and Stem Cell Biology Laboratory, “Early life exposure to genistein and downstream effects on DNA methylation and gene expression”
- Matthew Schellenberg, Ph.D., Genome Integrity and Structural Biology Laboratory, “Recognition of poly-ubiquitin by the DNA-damage repair protein Tdp2”
- Natacha Steinckwich-Besancon, Ph.D., Signal Transduction Laboratory, “Role of the calcium sensor protein, STIM1, in neutrophil chemotaxis and infiltration into psoriatic inflamed skin”

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## PPTOX IV meeting explores early-life exposures and long-term disease

*By Thaddeus Schug*

Experts from around the world gathered Oct. 26-29 at the Boston Marriott Long Wharf Hotel, to discuss the effects of environmental exposures during early life and later-onset disease consequences. The meeting, attended by more than 300, showcased 130 posters and 60 presentations.

The conference, “Environmental Stressors in Disease and Implications for Human Health,” was the fourth International Summit of Prenatal Programming and Developmental Toxicity (PPTOX), and was co-sponsored by The Endocrine Society. The PPTOX series of meetings is one of the premier international venues for scientists to evaluate current knowledge in developmental toxicity and guide forward momentum for this burgeoning field.

Philippe Grandjean, M.D., of the Harvard School of Public Health, opened the meeting with a creative cloud-based presentation that summarized the history of research on later-life consequences of early-life exposures, and outlined the history of PPTOX.

### Developmental effects of early-life exposures

Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program, followed with “A Good Start Will Last a Lifetime.” Birnbaum emphasized the need for reducing exposure to environmental agents, during multiple developmental windows, for primary prevention of disease. Birnbaum noted that developmental toxicity is a particularly difficult field to study. “We must focus our concerns on low dose and combined exposures occurring during susceptible time periods, rather than just on acute exposures resulting in diseases such as cancer,” she said.



*From left, Emiko Todaka, Ph.D., of the World Health Organization, shown with Grandjean and Birnbaum, discussed the importance of birth cohort studies in providing evidence of a causal relationship between exposure and disease. (Photo courtesy of Christine Flowers)*

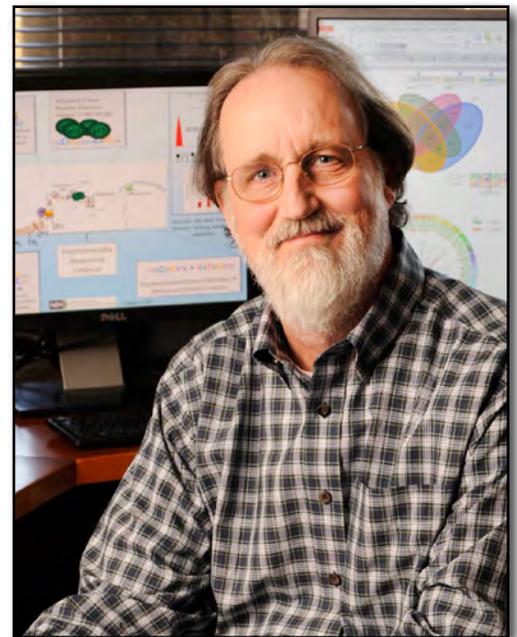
The conference sessions included a wide range of topics, including the developmental origins of endocrine disorders, advances and insights from epigenetics, the role of placenta in prenatal programming, novel strategies for prospective birth cohorts, and strategies for translating scientific research to improve public health.

### The future of PPTOX

NIEHS health scientist administrator Jerrold Heindel, Ph.D., co-chair of the conference organizing committee, summarized the meeting with a word cloud, illustrating the evolution of scientific terms from the first PPTOX meeting held in the Faroe Islands in 2007 to those on the current program.

“While some of the terms from 2007 are still in use, there have been many changes,” Heindel explained. “For instance, we are now focusing on epigenetics, instead of just gene expression, and we are also looking at combined exposures and stressors, instead of just a single chemical.”

Delivering the conference’s closing remarks, Grandjean compared the paradigm-shifting science presented at the PPTOX meetings, to the changes brought about by the famed Boston Tea Party that occurred more than 200 years ago in nearby Boston Harbor. Grandjean, whose research focuses on neural development, said, “It is essential that we toss out the old dogmas and institute this new paradigm of action, to protect the brain development of the next generation.”



*NIEHS senior investigator Douglas Bell, Ph.D., contributed to a large number of presentations demonstrating epigenetic changes resulting from environmental exposures. Bell’s research focuses on the validation of altered epigenetic marks in human blood cells. (Photo courtesy of Steve McCaw)*

The conference statement will be published in the peer-reviewed journal *Endocrinology*. The next PPTOX meeting will be held Nov. 13-16, 2016 in Kitakyushu, Japan.



*From left, NIEHS program analyst Liam O’Fallon and Heindel gathered with NIEHS grantees Frederica Perera, Dr.P.H., Ph.D., of Columbia University, and Philip Landrigan, M.D., of the Icahn School of Medicine at Mount Sinai. (Photo courtesy of Christine Flowers)*



*From left, NIEHS health scientist administrators Lisa Chadwick, Ph.D., and Kimberly Gray, Ph.D., joined Division of Extramural Research and Training Director Gwen Collman, Ph.D., at the NIEHS and EPA Children’s Environmental Health and Disease Prevention Research Centers Annual Meeting just prior to the PPTOX meeting. (Photo courtesy of Christine Flowers)*

(Thaddeus Schug, Ph.D., is a health scientist administrator in the NIEHS Division of Extramural Research and Training.)

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## Endocrine researchers explore dimensions of dose response

*By Eddy Ball*

The Duke University Integrated Toxicology and Environmental Health Program held its annual fall symposium Oct. 24 in the Searle Center Lecture Hall.

Speakers at the symposium shared their latest findings involving a new paradigm of nonmonotonic dose response (NMDR) involved in low-dose exposures to hormones and endocrine-disrupting chemicals. The paradigm, which remains controversial, is counterintuitive for classical toxicologists, who point to the contention by Paracelsus, “The dose makes the poison,” as a guiding principle.

Supporters of the nonmonotonic paradigm argue that exposure to endocrine-disrupting chemicals at low doses can have significant effects that are not seen at higher dose levels. Advocates point to mechanisms unique to the endocrine system, such as receptor saturation and feedback inhibition, that blunt the effects of higher doses.



*Stapleton, whose own research interests include endocrine disruption through exposure to fire-retardant chemicals, introduced each of the speakers and organized the panel discussion that concluded the program. (Photo courtesy of Steve McCaw)*

“Interpretation of these new [low-dose] results is challenging, particularly within regulatory landscapes and risk assessment frameworks that operate under the assumption of a linear relationship between exposure dose and adverse effect,” said symposium chair Heather Stapleton, Ph.D., of Duke University, as she opened the meeting.

Stapleton introduced a program of researchers supported by NIEHS and the U.S. Environmental Protection Agency (EPA), who discussed their findings against a backdrop of two important documents — a [draft state-of-the-science paper](#) written by EPA in June 2013 and the external peer [review](#) of that paper published by the National Research Council (NRC) earlier this year.

### **Chemical-specific dose response — an idea whose time has come**

Although NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., was unable to attend the symposium, several of the speakers, including NIEHS Chief of Staff Mark Miller, Ph.D., referred to Birnbaum’s March 2012 [editorial](#) in *Environmental Health Perspectives*. After a brief review of recent findings on NMDR, her conclusions sounded a note that has resonated throughout the environmental health community (see [side bar](#)).

The first speaker in the program was the acting director of the EPA Office of National Center for Computational Toxicology, David Dix, Ph.D., who presented an “Overview of the U.S. EPA Endocrine Disrupter Screening Program.” Dix traced the development of the screening program for hormone receptors over the past two decades and the program’s relevance for automated high-speed assays for prioritization of chemicals for toxicology testing.

“We’re very happy with the performance of the assays,” Dix said. He emphasized that the EPA paper was a draft that will be revised with NRC recommendations in mind, especially the need to integrate human and animal data.

One of the authors of that paper was Miller, who came to NIEHS from EPA in 2013. Miller’s presentation, “State of the Science for Non-monotonicity: Asking Better Questions,” discussed the framework for the questions posed in the EPA draft review and highlighted the strengths and weaknesses of the report, as identified by the NRC review. He also posed several future questions that should guide upcoming research on NMDR and the EPA’s revision of their document, including the perplexing issue of mixtures.

“I want to give credit to the EPA for taking this [NMDR] on in a meaningful way, and committing to appropriately revise this report based on the best available science,” he said.

## **NMDR — looking at dose response through the endocrine lens**

“The question is no longer whether nonmonotonic dose responses are ‘real’ and occur frequently enough to be a concern — clearly these are common phenomena with well-understood mechanisms,” Birnbaum wrote in her frequently cited editorial. “Instead, the question is which dose–response shapes should be expected for specific environmental chemicals and under what specific circumstances.”



*As Dix described the EPA Endocrine Disruption Screening Program, he made the connection between computational toxicology and the ambitious Tox21 predictive toxicology initiative that includes EPA, NIEHS, National Center for Advancing Translational Sciences, and the U.S. Food and Drug Administration as partners. (Photo courtesy of Steve McCaw)*

## Qualified consensus

With their keynote talks, Dix and Miller established many of the themes that would emerge in the presentations that followed (see [text box](#)). Although this was the kind of scientific meeting in which strong opinions could clash, there was a surprising level of agreement about NMDR and the importance of determining compound-, mixture-, and even tissue-specific dose responses.

However, another of the authors on the EPA paper, Earl Gray, Ph.D., showed more skepticism about the concept in his review of the *in vivo* literature, as suggested by the title he submitted for the agenda, “Non-monotonic Dose Response: Fact or Falderal.” Gray pointed to reproducibility and contamination issues, as well as the practice of exhaustively examining just one animal per litter.

“I think we can improve the testing and protocols,” Gray argued. He concluded that the studies he reviewed did not indicate that robust, reproducible NMDR curves were common events at low levels.



Miller, right, sat with NIEHS grantee Heather Patisaul, Ph.D., left, and NIEHS grant administrator Jerrold Heindel, Ph.D. Responding to Heindel's question later about why the EPA report team rushed publication of its draft, he said, “If you don't get a draft out, you'll never get a final version out.” (Photo courtesy of Steve McCaw)



Vandenberg, left, and Patisaul listened as Dix described EPA Toxcast prioritization assays. Seated behind them are NTP Tox21 lead Raymond Tice, Ph.D., and senior scientist Richard Paules, Ph.D. (Photo courtesy of Steve McCaw)



Gray's review pointed to questions about dose response that need to be addressed in future studies. Confounding factors abound, he argued. “It's doubtful you'll ever find a rack in an animal room without phthalates [a group of endocrine-disrupting chemicals],” he said. (Photo courtesy of Steve McCaw)

## Also on the program

Four other speakers at the symposium also addressed the central thesis of NMDR — that low doses of numerous stressors cause adaptive and maladaptive responses that can profoundly affect health and treatment outcome.

- NIEHS grantee [Laura Vandenberg, Ph.D.](#), of the University of Massachusetts, Amherst — “Non-monotonic Dose Response: Under Which Circumstances?”
- NIEHS grantee [Edward Calabrese, Ph.D.](#), of the University of Massachusetts, Amherst — “Biphasic Dose Responses in Biology, Toxicology, and Medicine.”
- EPA and National Science Foundation grantee [Gerald LeBlanc, Ph.D.](#), North Carolina State University — “Low Dose Effects and Non-monotonic Dose Responses: Secrets Invertebrates Hold.”
- Former NIEHS scientist [Robert Chapin, Ph.D.](#), now of Pfizer, Inc. — “NMDRs: One View From Industry.”



Afternoon speakers LeBlanc, center, and Calabrese, right, took advantage of the break to talk with the many students who attended the symposium. (Photo courtesy of Steve McCaw)



With his market-centered perspective, Chapin was both cautious about NMDR and supportive of challenges to conventional paradigm. “Our predilection for reductionism and accepted dogma seriously hampers real scientific understanding,” he said. (Photo courtesy of Steve McCaw)



NTP fellow Katherine Pelch, Ph.D., was among several NIEHS and NTP scientists who attended the symposium. She is a member of the NTP Office of Health Assessment and Translation, whose systematic review methodology is becoming recognized as a model for evaluating scientific literature. (Photo courtesy of Steve McCaw)

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# GEMS meeting focuses on genomics data and risk assessment

By Ernie Hood

The Genetics and Environmental Mutagenesis Society (GEMS) held its 32nd annual fall meeting Oct. 22 at the North Carolina Biotechnology Center in Research Triangle Park, North Carolina.

The theme for this year's meeting, which was supported in part by grants from NIEHS, was "Innovations and Integration of Genomics Data to Advance Risk Assessment."

Channa Keshava, Ph.D., GEMS president-elect and senior scientist at the U.S. Environmental Protection Agency (EPA), organized the conference and moderated the presentations. "Science is advancing so fast and we have so much more to explore to understand the whole genome. It's really exciting to hear about the latest advances and the latest technology," he said. "With EPA, NIEHS, and all of the industries here in the Triangle, this is a great place to organize a local meeting to share this knowledge and the latest information in the field."

Keshava emphasized that, in addition to serving as a resource for local professionals, the society designs the meeting to provide an opportunity for young, aspiring scientists — graduate students, undergraduates, and high school students — to present to, and interact with, more seasoned scientists.

## Speak locally, think globally

The four talks from senior scientists, featured at the meeting, illustrated the world-class research being conducted in genomics and risk assessment in the Triangle area.

Scott Auerbach, Ph.D., a molecular toxicologist in the National Toxicology Program (NTP) Molecular Toxicology and Informatics Group, led off the day's proceedings with a presentation, "The Application of Toxicogenomic Compendium Data to Forecasting Chemical Effects in Biological Systems." He described the data, resources, and methods being used in omics-based hazard characterization, and provided several examples of applications of the approach.



EPA postdoctoral fellow Natalia VanDuyn, Ph.D., center, won a \$500 cash prize and a \$500 Environmental Mutagenesis and Genomics Society travel award for her oral presentation, "Building Gene Expression Signatures Indicative of Transcription Factor Activation to Predict AOP Modulation." Keshava, left, and current GEMS president William Kaufmann, Ph.D., right, presented the award to VanDuyn. (Photo courtesy of Steve McCaw)



"There are three basic pieces of information that we need to give to the EPA or the FDA [U.S. Food and Drug Administration], in order to do risk assessment," Auerbach told the GEMS attendees. "Number one, what the hazard is. Number two, mode of action, and number three is the dose at which the hazard is nonoccurring." He described how NTP is using genomics and other high-dimensional data to acquire the information. (Photo courtesy of Steve McCaw)

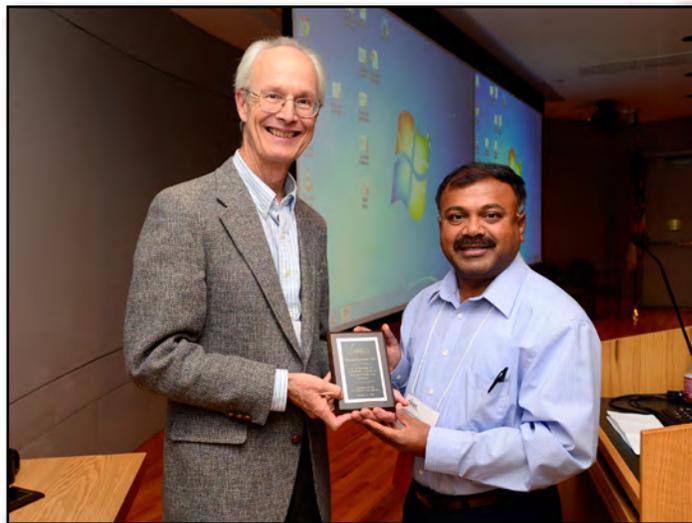
NIEHS grantee Rebecca Fry, Ph.D., associate professor of environmental sciences and engineering at the University of North Carolina at Chapel Hill, presented results of research suggesting that blocking epigenetic modifications, due to environmental contaminant exposures, may be useful in preventing diseases and birth defects. Her lab concentrates on mechanisms of disease associated with toxic metal exposure early in life, particularly arsenic exposure.

Fred Wright, Ph.D., director of the Bioinformatics Research Center at North Carolina State University (NCSU), spoke about [NexGen risk assessment](#) and the prospects for assessing population genetic variation using rapid automated *in vitro* testing, or assays. Using cytotoxicity studies involving hundreds of cell lines and approximately 180 chemicals, these assays are providing important data for chemical prioritization and establishing benchmarks for average risk due to exposure.

U.S. Environmental Protection Agency (EPA) systems biologist Stephen Edwards, Ph.D., discussed how the adverse outcome pathway concept provides an ideal framework for bridging the gap between high-throughput screening toxicity testing, such as [Tox21](#), and the adverse outcomes that are typically used in regulatory decision-making.

Attendees also enjoyed four short talks by graduate students and postdoctoral fellows, and 11 poster presentations. Authors of the best short talk and three best posters received awards.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



*As is customary at the fall GEMS meeting, outgoing president Kaufmann symbolically passed the baton to president-elect Keshava. (Photo courtesy of Steve McCaw)*



*Fry emphasized the need to characterize pathways, in order to get a better sense of how environmental contaminants are associated with disease etiology. “Also, we have to be thinking about the regulators of the pathway in terms of disease prevention,” she told the GEMS audience. (Photo courtesy of Steve McCaw)*



*There was ample time during the meeting to review and discuss the posters that were presented in the lobby at the North Carolina Biotechnology Center. (Photo courtesy of Steve McCaw)*



*The GEMS judges thought so much of the posters that they awarded \$100 cash prizes to three scientists, instead of the intended two — EPA trainees Noffisat Oki, Ph.D., and Jenna Currier, Ph.D., and Kimberly Herman of NCSU. Pictured above, from left, are Keshava, Oki, Kaufmann, and Currier. (Photo courtesy of Steve McCaw)*

*Keshava, right, presented a memento of appreciation to Edwards, after his talk on adverse outcome pathways. (Photo courtesy of Steve McCaw)*



*Kin Chan, Ph.D., an Intramural Research Training Award fellow in the NIEHS Mechanisms of Genome Dynamics Group, spoke about molecular genetic analysis of mutation clusters formed in single-strand DNA. (Photo courtesy of Steve McCaw)*



*Wright, left, offered feedback to poster presenter Arjun Keshava, a student at Wake Early College of Health and Sciences in Raleigh, North Carolina. (Photo courtesy of Steve McCaw)*



*As is always the case at GEMS meetings, NIEHS and NTP were well represented. From left, Gloria Jahnke, D.V.M., of the NTP Office of the Report on Carcinogens, and Kristine Witt, of the NTP Biomolecular Screening Branch, found one of the posters especially interesting. (Photo courtesy of Steve McCaw)*

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# Seminar tackles inflammatory pathways in obesity-related diseases

By Eddy Ball

Three NIH-funded experts explored the connections between inflammation and obesity Oct. 29 during an Inflammation Faculty Seminar and Webcast.

Speakers included Jenny Ting, Ph.D., University of North Carolina at Chapel Hill; Stephanie Shore, Ph.D., Harvard School of Public Health, who spoke by remote connection; and NIEHS lead scientist emeritus Thomas Eling, Ph.D. The webcast was organized by NIEHS Inflammation Faculty members including Jerrold Heindel, Ph.D., Mike Humble, Ph.D., Nina Jaitly, M.D., and Srikanth Nadadur, Ph.D., of the Division of Extramural Research and Training; and Shepherd Schurman, M.D., of the Division of Intramural Research.

The talks began with a list of grim statistics about the worldwide spread of obesity, insulin resistance, and diabetes. Ting and Shore made convincing arguments about the adverse effects of obesity-related inflammation on metabolic and respiratory health and response to interventions.

In the final presentation, Eling reported on experiments with transgenic mice that offer the tantalizing possibility of discovering a novel approach to antiaging medicine that might actually live up to the hype. “There is a profound effect on longevity [from overexpressing this gene],” he said.

## Dire prospects in an ever-fatter world

With one billion people worldwide overweight and 400 million of them clinically obese, a number expected to increase, the outlook for public health is not good, [Ting](#) said as she introduced her subject, “Inflammation and Metabolic Disease.”

In a number of experiments using cell lines and model animals, Ting and colleagues have tested an intriguing hypothesis — that saturated fatty acids in the diet can induce inflammasome activation via the normal fatty acid metabolic pathway. Like a fire burning out of control, inflammation spreads throughout the body, especially through the action of the cytokines interleukin-1 beta (IL-1 beta) and tumor necrosis factor alpha.

“It’s really IL-1 that’s blocking insulin sensitivity,” she said, “[but] both of these cytokines are equally important.”



*Nina Jaitly, M.D., a contractor for the NIEHS Scientific Review Branch, gave opening and concluding remarks. She is the contact person for the Inflammation Faculty Seminar Series. (Photo courtesy of Steve McCaw)*



*Following her talk, Ting took questions from the audience and from Humble, right. (Photo courtesy of Steve McCaw)*

## Obesity-related inflammation in the lung

Ting's reference to inflammation in the lung as related to a high-fat diet segued nicely into Shore's discussion of the synergy of obesity and ozone as a trigger for asthma and airway hyper-resistance, "Responses to Acute Ozone Exposure Are Augmented in Obese Mice: Role of Innate Immune System."

Shore opened with the observation that obesity is a risk factor for asthma, and weight loss improves asthma outcomes.

Pointing to the usual suspects, Shore expanded the IL family list to include more members that contribute differently to ozone in obese versus lean mice. She also reported that obesity changes the baseline for how well animals responded to treatment for lowering the levels of ILs and related metabolites. "What we see is a very different effect of interventions on lean and obese mice," she said.

Shore concluded by underscoring the importance of including obesity as a consideration in respiratory studies.

## Mice that age slowly and with grace

When the subject turned to Eling's lean and mean transgenic mice, the news was almost entirely promising. Eling has spent most of his career studying nonsteroidal anti-inflammatory drug-activated gene (NAG-1), initially for its role in programmed cell death and tumor formation and progression in cancer.

In experiments with transgenic mice overexpressing NAG-1, Eling and colleagues made several important observations about the experimental mice compared to wild-type mice. The transgenic mice had fewer age-associated lesions, less adipose tissue, lower expression of inflammatory cytokines, more efficient energy metabolism, and improved glucose tolerance and utilization. He also reported that caspase-1 activity was lower in lean NAG-1 mice and attenuated in NAG-1 mice on a high fat diet.

Noting this apparent resistance to high-fat diet induced obesity, Eling observed, "The [lean] mice actually eat more, but they're thinning."



*Eling responded to a question, as Schurman, right, looked on. "NAG-1 appears to be a novel protein with potential therapeutic uses in diseases like obesity," Eling said. (Photo courtesy of Steve McCaw)*

## Inflammation Faculty seminar series

The Inflammation Faculty is an interdisciplinary, cross-division initiative that brings together scientists from in-house research labs, scientific grants administration, and the National Toxicology Program to advance understanding of inflammation-related disease processes. As one of its activities, the group is sponsoring leading-edge seminars.

Inflammation is one of the areas identified as a priority in the 2012-2017 NIEHS Strategic Plan.

The next seminar in the series will take place Dec. 11 and highlight "Methods at NTP to Identify Biomarkers of Inflammation."

Individuals interested in the faculty or with needs for accommodation to attend seminars should contact Nina Jaitly, M.D., at (919) 541-7854 or [inflammation@niehs.nih.gov](mailto:inflammation@niehs.nih.gov).

Underscoring NAG-1 as a novel protein with potential therapeutic uses in disease such as obesity, he concluded, “All these are the characteristics of a mouse that’s going to live longer.... There is a profound effect on longevity.”

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## **NIEHS-funded researchers find potential treatment for Parkinson’s disease**

*By Andrew Gould and Joe Balintfy*

Blocking a particular mitochondrial fission protein could be an effective treatment to reverse or slow the progression of Parkinson’s disease, according to a study in mice led by an NIEHS-funded researcher from Plymouth University in the U.K. The study findings were published Nov. 5 in Nature Communications.

“It’s a promising finding that takes advantage of our new understanding of mitochondria as dynamic networks,” said Cindy Lawler, Ph.D., head of the NIEHS Genes, Environment, and Health Branch. “While much further study is needed before the approach can be translated to potential treatments for human patients with Parkinson’s, demonstrating positive results in an animal model is an important step forward.”

This study shows that the processes of mitochondria could be modified to reduce cell death and deficits in dopamine release involved in Parkinson’s.

### **Understanding Parkinson’s and mitochondrial processes**

Mitochondria are small structures within nerve cells that keep the cells healthy and working properly. They undergo frequent changes in shape, size, number, and location, either through mitochondrial fission, which leads to multiple, smaller mitochondria, or through mitochondrial fusion, resulting in larger mitochondria. These processes are controlled mainly by their respective mitochondrial fission and fusion proteins. A balance of mitochondrial fission and fusion is critical to cell function and viability.

Parkinson’s is a complex disorder of the central nervous system, and the second most common progressive neurodegenerative disease in the U.S., after Alzheimer’s disease. Parkinson’s progresses slowly, and motor symptoms emerge as small clusters of a specific type of nerve cell in the midbrain die. The gradual loss of these neurons results in reduction of a critical neurotransmitter called dopamine, a chemical responsible for transmitting messages to parts of the brain that coordinate muscle movement. Understanding why these neurons die or do not work properly could lead to new therapies.



*Tieu said that the next phase of study would be to evaluate this therapeutic strategy further in genetic and toxin-induced rodent models of Parkinson’s. If successfully completed, his team hopes to take the work forward to an animal model that is more closely related to humans. (Photo courtesy of Plymouth University)*

## Blocking the right protein

The research team found that when a particular mitochondrial fission protein, GTPase dynamin-related protein-1, or Drp1, was blocked, using either gene therapy or a chemical approach in experimental models of Parkinson's disease in mice, it reduced both cell death and the deficits in dopamine release, effectively reversing the Parkinson's process. The results suggest that finding a strategy to inhibit Drp1 could be a potential treatment for Parkinson's, also known as PD.

“Our findings show exciting potential for an effective treatment for PD, and pave the way for future in-depth studies in this field,” said [Kim Tieu, Ph.D.](#), team lead at the Plymouth University Peninsula Schools of Medicine and Dentistry. “It's worth noting that other researchers are also targeting this mitochondrial fission/fusion pathway as potential treatments for other neurological diseases, such as Alzheimer's disease, Huntington's disease, and Amyotrophic Lateral Sclerosis.”

Tieu started this research when he was a lead researcher at the University of Rochester School of Medicine and Dentistry in New York, and continued it after his move to Plymouth University.

For more on this story, read the Plymouth University [press release](#).

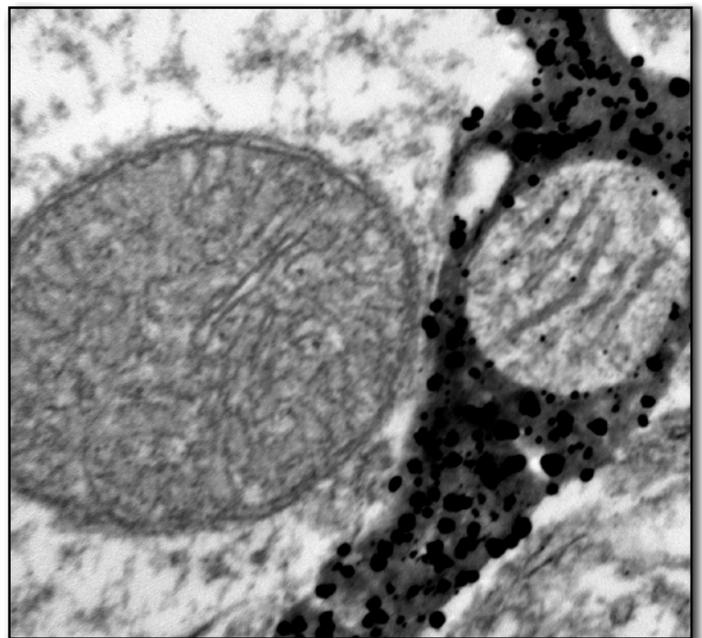
*Citation:* [Rappold PM, Cui M, Grima JC, Fan RZ, de Mesy-Bentley KL, Chen L, Zhuang X, Bowers WJ, Tieu K.](#) 2014. Drp1 inhibition attenuates neurotoxicity and dopamine release deficits in vivo. *Nat Commun*; doi:10.1038/ncomms6244 [Online 5 November 2014].

(Andrew Gould is a public relations specialist for Plymouth University Peninsula Schools of Medicine and Dentistry, and School of Biomedical and Healthcare Sciences. Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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*Lawler is the NIEHS program lead for neurodegenerative diseases, such as Parkinson's disease. NIEHS currently funds 77 research projects that look at how exposure to pesticides, pollution, and other contaminants, alone and in combination with specific genes, affects neurodegeneration. (Photo courtesy of Steve McCaw)*



*Immuno-electron image of mouse striatal mitochondria illustrating a dopaminergic axonal terminal (with black spots) containing a mitochondrion. (Image courtesy of Kim Tieu)*

# Diversity Outbred mice better predict potential human responses to chemical exposures

By Robin Mackar

In a new study, NIEHS researchers report that Diversity Outbred mice can accurately predict the range of response to chemical exposures that might be observed in human populations. The [findings](#) were published online Nov. 6 in the journal *Environmental Health Perspectives*.

Researchers from the [National Toxicology Program \(NTP\)](#), an interagency program headquartered at NIEHS, were able to identify specific genes or chromosomal regions that make some of the Diversity Outbred mice more susceptible, and others more resistant, to the toxic effects of benzene. Benzene is a common air pollutant and human carcinogen found in crude oil, gasoline, and cigarette smoke, and naturally produced by wildfires and volcanoes.

The scientists found that, like humans, each Diversity Outbred mouse developed at The [Jackson Laboratory](#) in Bar Harbor, Maine, responded to the effects of the chemical exposure differently.

## Measuring micronucleated red blood cells

Exposure responses were assessed by measuring the frequency of micronucleated red blood cells, a biological marker of chromosomal damage, which is a hallmark of benzene exposure. The researchers measured the levels of this biomarker in each mouse before and after exposure.

Some mice demonstrated extraordinary sensitivity to the exposure, while others showed no response. The range of response from lowest to highest was approximately 5-fold. Since the researchers knew the genetic makeup of each mouse, they could pinpoint the regions involved in susceptibility or resistance to the chemical exposure, and then look for related genetic regions in human chromosomes.

“This paper points out the significant genetic differences that are found throughout every population that must to be taken into account when extrapolating data from animals to humans,” said Linda Birnbaum, Ph.D., director of NTP and NIEHS.

“The Diversity Outbred mouse is a useful model for predicting the range of response that might be observed in humans following exposure to a chemical.”



*French, who is now retired, devoted several years to studying in vivo animal models to explore individual variability in toxicity response. (Photo courtesy of Steve McCaw)*



*Witt manages the NTP genetic toxicology testing contract, and she provides genetic toxicology test data review and evaluation for inclusion in the NTP Technical Reports. (Photo courtesy of Steve McCaw)*

## Benzene as a case study

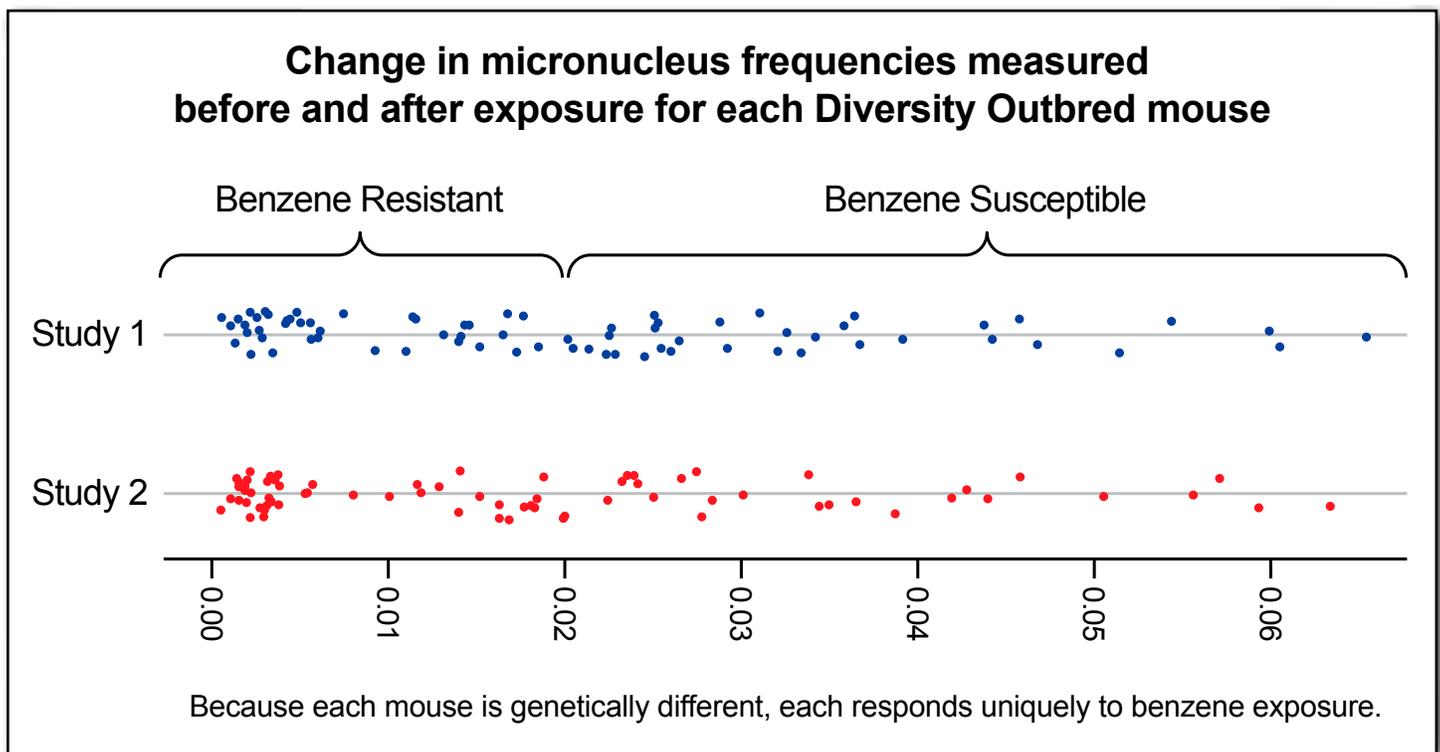
Benzene was selected by NTP as a case study for testing the mouse model, because there is an abundance of animal and human toxicity data for comparison. Benzene can affect people differently, depending on the level and duration of exposure, making it important to accurately estimate the levels at which it may cause harm to the most susceptible individuals.

“These genetically diverse mice provided a reproducible response to benzene exposure across two independently exposed groups, suggesting that each group of genetically unique mice demonstrated the same range of differential susceptibility, much like what you would find in human epidemiology studies,” said Jef French, Ph.D., lead author on the paper.

[Kristine Witt](#), a co-author on the paper, and group leader for the NTP Genetic Toxicology Branch added that the model can provide valuable data for use by regulators and manufacturers conducting chemical risk assessments.

The full text of the paper is available [online](#) in the journal Environmental Health Perspectives.

*Citation:* French JE, Gatti DM, Morgan DL, Kissling GE, Shockley KR, Knudsen GA, Shepard KG, Price HC, King D, Witt KL, Pedersen LC, Munger SC, Svenson KL, Churchill GA. 2014. Diversity Outbred Mice Identify Population-Based Exposure Thresholds and Genetic Factors that Influence Benzene-Induced Genotoxicity. Environ Health Perspect; doi:10.1289/ehp.1408202 [Online 6 November 2014].



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

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# Australian researcher outlines an integrated approach for studying Parkinson's

By Simone Otto

So often in science, researchers are limited by knowing only one piece of a much larger puzzle, such as Parkinson's disease (PD). Even if it is a fascinating piece, it rarely reveals how the whole picture may look.

In his Keystone Science Lecture Nov. 4 at NIEHS, Australian clinical neuroscientist [George Mellick, Ph.D.](#), discussed his work with "The Queensland Parkinson's Project: An Interdisciplinary Approach to Studying Parkinson's From the Population to the Lab," outlining a method for investigating Parkinson's that promises to put the pieces together. "It's very hard to model the entire human picture," he said, pointing to the value of integrating the strengths of human, animal, and cell-line models.

Mellick, an associate professor at Griffith University in Australia, has spent more than 10 years studying PD. Over this time he helped establish Parkinson's Queensland, a non-profit organization that oversees a study with more than 4000 participants, approximately half of whom have been diagnosed with PD, and also funds research, with a vast representative cohort for population studies.

Mellick began his presentation with a little history, referring to descriptions of a shaking palsy disease called *Kampavata* seen in Ayurveda texts dating back to 2000 BCE and earlier, which clearly described Parkinson's disease many hundreds of years ago. Interestingly, ancient plant-based treatments included seeds that contain *leva-dopa*, which is still the mainstay of PD motor symptom management, pointing to the value of understanding nature and valuing the insights of older and different medical systems.

Mellick's talk was hosted by Jonathan Hollander, Ph.D., a program administrator in the NIEHS Genes, Environment, and Health Branch.



*Shunning the podium, Mellick enter the audience space to deliver a more intimate presentation on his work. (Photo courtesy of Steve McCaw)*



*Hollander, center, said he was grateful for the opportunity to hear more about the Queensland Parkinson's Project. He took advantage of Mellick's visit to NIEHS for the large PD meeting Nov. 3-4 to schedule the talk. (Photo courtesy of Steve McCaw)*

## Creating feedback loops to advance research

Eskitis Institute, where Mellick is deputy director, is home to Nature Bank, a repository for thousands of optimized natural product fractions; Compound Australia, which stores some 600,000 compounds from Australian chemists; and Neuro Bank, which maintains human cell lines. These resources afford researchers the opportunity to screen a vast number of compounds with omics testing and understand their relationship to PD.

When this knowledge feeds back into population analysis via the Queensland Parkinson's Project, it creates a positive feedback loop in Mellick's research, with lab experiments informing population studies and data from clinical and population studies refining lab experiments. This bidirectional process supports studies in how genes and the environment interact with the aging process and how this interaction leads to the disease.

Mellick gave listeners many interesting examples of the value of this approach. Population research includes gene-hunting for rare forms of inherited PD, which directs research through unbiased discovery of genes linked to Parkinson's of which there had been no *a priori* knowledge, as well as genetic risk factor analysis for cases with no clear genetic link.

## Building on genome-wide analysis to drive cell-line experiments

Once genetic analysis has connected a gene to the disease, Mellick uses pharmacology to study the protein in human olfactory neurosphere-derived cells (hONS) obtained from people with monogenetic PD in the Queensland Project. Because neurons in PD patients display an aberrant response to stress and toxins unique to these cells, hONS cells provide a human neural-specific way to quickly and effectively study proteins suggested by genomic studies.

This integrated research has led to the discovery of several interesting molecules that are currently being researched, including alpha-synuclein, leucine-rich kinase 2, vacuolar protein sorting-associated protein 35, and nuclear factor (erythroid-derived 2)-like 2, and will likely continue to generate a plethora of clues to how genes and environment interact with small molecules within the cell, ultimately leading to PD.

(Simone Otto, Ph.D., is an Intramural Research and Training Award fellow in the Ion Channel Physiology Group at NIEHS.)

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*A number of Hollander's colleagues in the NIEHS Division of Extramural Research and Training (DERT) turned out for the talk, including Mike Humble, Ph.D., and DERT Deputy Director Pat Mastin, Ph.D. (Photo courtesy of Steve McCaw)*



*Mellick's opening slide was a graphic representation of his integrated approach to studying PD. (Photo courtesy of Steve McCaw)*

# NIEHS-funded study shows ADHD-air pollution link

By Tim Paul and Joe Balintfy

Researchers from the [Columbia Center for Children's Environmental Health](#) at the Mailman School of Public Health, funded by NIEHS and the U.S. Environmental Protection Agency, have found that children born to mothers who were exposed to higher levels of air pollution during pregnancy had an increased number and degree of symptoms related to attention deficit hyperactivity disorder (ADHD). Study [results](#) were published online Nov. 5 in the journal PLOS ONE.

The study is the first to explore the connection between prenatal PAH exposure and ADHD in school-age children over time, according to a university [news release](#).

“This research follows other discoveries by this center linking air pollution to asthma, developmental delay, lower IQ scores, and behavior problems,” explained NIEHS health scientist administrator Kimberly Gray, Ph.D. “This study highlights how increased susceptibility to environmental hazards begins during fetal development.”

## A connection between PAHs and ADHD

The researchers followed 233 nonsmoking pregnant women and their children in New York City from pregnancy into childhood.

The study showed that exposure to toxic air pollutants called polycyclic aromatic hydrocarbons, or PAHs, during the prenatal period was associated with fivefold higher odds of behavior problems associated with ADHD at age 9. PAHs are generated by many sources, such as traffic, residential boilers, and electricity generating plants using fossil fuel.

Levels of maternal PAH exposure were measured using PAH-DNA adducts in maternal blood obtained at delivery. Childhood PAH exposure was measured by PAH metabolites in urine at ages 3 or 5 years. ADHD behavior problems were assessed using the Child Behavior Checklist and the Conners Parent Rating Scale - Revised.

“This study suggests that exposure to PAH encountered in New York City air may play a role in childhood ADHD,” said lead author [Frederica Perera, Dr.P.H., Ph.D.](#), director of the center and professor of Environmental Health Sciences. “The findings are concerning, because attention problems are known to impact school performance, social relationships, and occupational performance.”

The Centers for Disease Control and Prevention estimates that around 10 percent of American children ages 4 to 17 have ADHD. “ADHD is an important indicator of future achievement,” added Gray. “But there are treatments and, most importantly, prevention strategies for ADHD, like reducing environmental exposures.”



*Perera pointed out that ADHD imposes large annual costs to society — an estimated total between \$36 and \$52 billion in the U.S. — and to individuals — estimated at \$12,005 to \$17,458. (Photo courtesy the Columbia University Mailman School of Public Health)*



**Linked video:**  
Watch a webinar that features Perera as the first of four presenters, talking about her studies with the New York City cohort (01:25:00)

(Launches in new window)

Download Media Player:  Flash 

The current findings build on the center's previous studies linking prenatal PAH exposure with behavioral and cognitive issues, including associations with developmental delay at age 3, reduced IQ at age 5, and symptoms of anxiety, depression or attention problems at ages 6 and 7.

Although more research is needed to fully understand the mechanism by which PAH exposure increases the likelihood of ADHD, the researchers say these results are significant, since children with ADHD are at greater risk for risk-taking behaviors and poor academic performance.

*Citation:* Perera FP, Chang HW, Tang D, Roen EL, Herbstman J, Margolis A, Huang TJ, Miller RL, Wang S, Rauh V. 2014. Early-life exposure to polycyclic aromatic hydrocarbons and ADHD behavior problems. PLoS One 9(11):e111670.

(Tim Paul is a science writer at the Columbia University Mailman School of Public Health. Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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Gray noted that the NIEHS Centers for Children's Environmental Health and Disease Prevention Research program conducts [webinars](#) on the second Wednesday of every month. (Photo courtesy of Steve McCaw)

## This month in EHP

The December issue of Environmental Health Perspectives ([EHP](#)) reports on promising signs of recovery in Detroit and examines the reuse of wastewater for drinking.

### Arising from the Ashes: Environmental Health in Detroit

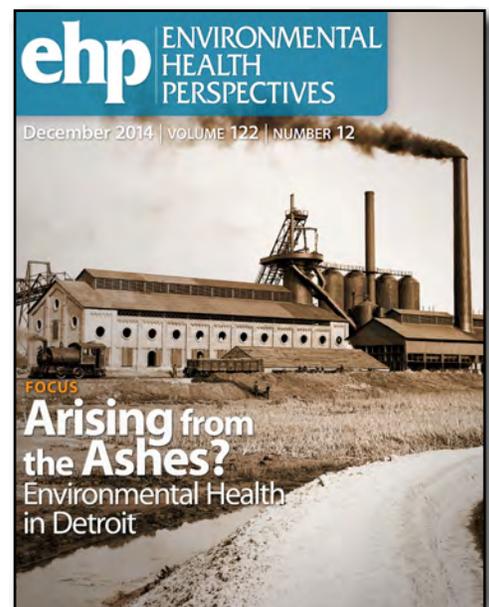
Without visiting Detroit, it is easy to imagine a ruined metropolis, but even the most cursory inspection offers evidence of resilience in the face of repeated economic and environmental injuries. In the words of Detroit's motto, "We hope for better things; it will arise from the ashes."

### Advanced Thinking: Potable Reuse Strategies Gain Traction

An estimated 22 trillions gallons of wastewater are produced annually in North America. The reuse of this wastewater for drinking is not a new idea, but it is getting more attention as the squeeze tightens between drinking-water supply and demand.



<http://twitter.com/ehponline>



## Featured research and related news articles this month include:

- **Ritual Risk: Incense Use and Cardiovascular Mortality** — Scientists find an association between long-term incense use and increased cardiovascular mortality.
- **Assessing the Impact of Aerial Pesticide Spraying: Mancozeb Exposures Among Pregnant Women Living near Banana Plantations** — Researchers report that pregnant women living near banana plantations in Costa Rica have elevated urinary levels of ethylene thiourea, a metabolite of mancozeb, at levels nearly twice the normal limit of pregnant women in California who lived near ground spraying of the pesticide.
- **PFOA [Perfluorooctanoic Acid or C8] and High Cholesterol: Basis for the Finding of a Probable Link** — The C8 Science Panel finds a probable link between exposure to PFOA and high cholesterol.
- **EDCs [Estrogen-disrupting Chemicals] and Estrogen Receptor Activity: A Pathway to Safer Chemical Design?** — Biochemical, structural, biophysical, and cell-based experiments reveal critical information about the interaction of 12 EDCs with estrogen receptors.

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## Kari Nadeau to present December distinguished lecture

*By Kelly Lenox*

The final talk of the 2014 NIEHS Distinguished Lecture Series 11:00 a.m. Dec. 16 will feature Kari Nadeau, M.D., Ph.D., director of the Allergy Center at Stanford University School of Medicine. Hosted by Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, Nadeau will discuss “How Pollution Exposure Leads to Immune Dysfunction: The Role of Epigenetics and Multiplex Immunophenotyping Studies.”

“Dr. Nadeau effectively works to link mechanistic immunology studies with epidemiological outcomes of ambient air pollution exposure,” said Collman. “As a practicing clinician, Kari brings a unique perspective to her work.”

Early life exposure to ambient air pollution is associated with childhood asthma, but the mechanisms are not well understood. Through NIEHS-supported research at two NIEHS/EPA Children’s Environmental Health and Disease Prevention Research Centers — the Dartmouth College center and the University of California, Berkeley/Stanford center — Nadeau focuses on the link between exposure indicators and asthma outcomes by studying immune system changes in children exposed to elevated levels of polycyclic aromatic hydrocarbons.

In addition to her NIEHS-funded research, Nadeau is renowned for her translational research into childhood food allergies. At the [Stanford Allergy Center](#), she oversees therapy and prevention studies, networking with scientists from a broad range of disciplines.



*Nadeau has published more than 70 peer-reviewed papers, many of which focus on T cells and health outcomes. (Photo courtesy of Stanford University)*

Dr. Nadeau has received honors and awards from the American Academy of Allergy, Asthma, and Immunology; the American Lung Association; the Clinical Immunological Society; Food Allergy Research and Education Inc.; and National Institutes of Health. She has also received grant support from the U.S. Environmental Protection Agency [STAR Grant](#) program.



**Linked video:**  
[Watch Dr. Nadeau and two of her patients discuss successful treatment of multiple food allergies in this Food Allergy Research and Education video. \(4:56\)](#)  
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## Extramural papers of the month

By [Nancy Lamontagne](#)

- [Health risk assessment examines shrimp consumption after Deepwater Horizon oil spill](#)
- [Meta-analysis tracks progress of contaminants of emerging concern](#)
- [Endocrine-disrupting chemicals interfere with placental thyroid hormone activity](#)
- [Maternal gestational diabetes linked to daughters being overweight later](#)

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

## Health risk assessment examines shrimp consumption after Deepwater Horizon oil spill

A risk assessment carried out by NIEHS grantees showed that people who frequently consume shrimp from an area affected by the Deep Water Horizon oil spill had no serious health risks or increased cancer risk from eating this seafood. Although it was thought that seafood from the area of the oil spill would contain high levels of polycyclic aromatic hydrocarbons (PAHs), a toxicant found in crude oil, the shrimp actually showed very low levels of PAHs.

After the Deep Water Horizon oil spill of 2010, there was concern about health risks associated with eating seafood contaminated from the spill. To assess these risks, the researchers used a community-based approach to survey and assess shrimp consumption, food preparation methods, and personal bodyweight in a group of Vietnamese-Americans in Southeast Louisiana. Many Vietnamese-Americans in the Gulf-coast region are involved in commercial shrimping and fishing and frequently consume white shrimp. The investigators analyzed levels of 81 PAHs in locally harvested white shrimp and combined this information with survey data they collected from the Vietnamese-Americans. The results showed no excess cancer or non-cancer health risks.

*Citation:* [Wilson MJ, Frickel S, Nguyen D, Bui T, Echsner S, Simon BR, Howard JL, Miller K, Wickliffe JK. 2014. A targeted health risk assessment following the Deep Water Horizon Oil Spill: polycyclic aromatic hydrocarbon exposure in Vietnamese-American shrimp consumers. Environ Health Perspect; <http://dx.doi.org/10.1289/ehp.1408684> \[Online 21 October 2014\].](#)

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# Meta-analysis tracks progress of contaminants of emerging concern

An NIEHS-funded meta-analysis of 143,000 peer-reviewed research papers revealed that the time between when the initial safety concern about a contaminant emerges and when that concern warrants appropriate action is about 14 years. The study's author says that decreasing both the number of contaminants of emerging concern that enter commerce and the time required to take action is necessary to better protect human health and the environment.

The author examined 30 years of publishing activity for the following 12 contaminants of emerging concern: dichlorodiphenyltrichloroethane (DDT), trichloroacetic acid (TCAA), N-nitrosodimethylamine, methyl tert-butyl ether, trichloroethylene, perchlorate, 1,4-dioxane, prions, triclocarban, triclosan, nanomaterials, and microplastics. Harmful environmental agents showed a common pattern of rising to a level of peak concern over 14 years and then declining to a baseline level. The author reports that contaminants of concern emerge, and some re-emerge, because of improved scientific analysis capabilities; scientific paradigm shifts such as the discovery of infectious proteins; and the development, marketing, and mass consumption of new products such as antimicrobial personal care products, microplastics, and nanomaterials.

*Citation:* [Halden RU](#). 2014. Epistemology of contaminants of emerging concern and literature meta-analysis. *J Hazard Mater*; doi: 10.1016/j.jhazmat.2014.08.074. [Online 28 September 2014].

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## Endocrine-disrupting chemicals interfere with placental thyroid hormone activity

An NIEHS grantee and colleagues report strong evidence that endocrine-disrupting chemicals can interfere with thyroid hormone action in pregnant women without changing their blood levels of thyroid hormone. The findings show that truly understanding how endocrine-disrupting chemicals may affect pregnancies will require studying not only hormone levels detected in the blood but also hormone activity at the cellular level.

The researchers chose to analyze placental tissue because it is an important regulator of maternal thyroid hormone for the developing fetus. Using placental tissue samples from 164 pregnant women with no thyroid disease, they analyzed the messenger RNA (mRNA) expression for the enzyme CYP1A1. Prior studies showed that CYP1A1 can change certain endocrine-disrupting chemicals, such as PCBs, into a form that can directly activate the body's thyroid hormone receptors.

The researchers found that levels of CYP1A1 mRNA varied 5-fold across the 132 placental samples in which it was detected. Although the mothers' thyroid hormone blood levels remained the same, pregnancies where the placenta contained higher levels of CYP1A1 mRNA expression tended to exhibit signs of thyroid disruption in the placenta. CYP1A1 mRNA expression also strongly correlated with expression levels of two thyroid-regulated genes. Expression levels of each gene correlated with each other, which suggests that they share a common activator.

The findings are consistent with the hypothesis that CYP1A1 allows some endocrine disrupting chemicals such as PCBs to activate the thyroid hormone receptor. The current study is the first to show this correlation in humans and suggests that CYP1A1 may be an important tissue biomarker of susceptibility to thyroid signaling disruption.

*Citation:* Wadzinski TL, Geromini K, McKinley Brewer J, Bansal R, Abdelouahab N, Langlois MF, Takser L, Zoeller RT. 2014. Endocrine disruption in human placenta: expression of the dioxin-inducible enzyme, Cyp1a1, is correlated with that of thyroid hormone-regulated genes. *J Clin Endocrinol Metab*; <http://dx.doi.org/10.1210/jc.2014-2629> [Online 9 October 2014].

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## Maternal gestational diabetes linked to daughters being overweight later

NIEHS grantees report that women who developed gestational diabetes and were overweight before pregnancy were at a higher risk of having daughters who were obese later in childhood. The findings suggest that helping women reduce weight gain and improve lifestyle before and during pregnancy may also help reduce the risk of obesity in their children.

The researchers studied associations between childhood obesity and gestational diabetes in 421 girls and their mothers who were part of the Cohort study of Young Girls' Nutrition, Environment, and Transitions (CYGNET). Each year from 2005 to 2011, the researchers recorded the girls' height, weight, body fat, abdominal obesity, and other parameters. Kaiser Permanente's comprehensive electronic medical records allowed researchers to link data collected on the girls to information about their mothers.

Twenty-seven mothers in the study had gestational diabetes. If a girl's mother had gestational diabetes, her risk of having a body mass index at or above the 85th percentile was 3.5 times higher than girls whose mothers did not have gestational diabetes. This association was independent of other factors that influence obesity such as race/ethnicity, maternal obesity, and a girl's pubertal stage. If the girl's mother was overweight in addition to having gestational diabetes, the daughter's risk of being overweight was about 5.5 times higher.

*Citation:* Kubo A, Ferrara A, Windham GC, Greenspan LC, Deardorff J, Hiatt RA, Quesenberry CP Jr, Laurent C, Mirabedi AS, Kushi LH. 2014. Maternal hyperglycemia during pregnancy predicts adiposity of the offspring. *Diabetes Care* 37(11):2996-3002.

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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## Intramural papers of the month

*By Tara Ann Cartwright, Monica Frazier, Jacqueline Powell, Jordan St. Charles, and Qing Xu*

- A comparison of the effectiveness of RNA-seq and microarrays for clinical toxicological applications
- NADPH oxidase implicated in Parkinson's disease associated substance P neurotoxicity
- Nrf2 polymorphisms correlate with differential susceptibility to acute lung injury
- MMS exposure is associated with mtDNA mutagenesis
- Scavenger receptor B-I plays essential role in immune response to pneumonia

# A comparison of the effectiveness of RNA-seq and microarrays for clinical toxicological applications

In a recent collaboration with the MicroArray Quality Control (MAQC) consortium, led by the U.S. Food and Drug Administration, National Toxicology Program and NIEHS researchers found that, depending on the treatment effect, RNA-seq and microarrays can similarly detect expression changes in rat livers treated with one of 27 different chemicals with varying mechanisms of action. Microarrays have been a staple to detect differentially expressed genes and to predict toxicity outcomes of new drug treatments. RNA-seq technology is being adopted by researchers for use in a variety of gene expression analyses. This study was part of the sequencing quality control phase of MAQC, which rigorously tests emerging technologies, ensuring they are reliable for these applications.

The researchers determined as long as the agents used induced a large enough transcriptional response, both RNA-seq and microarrays detected a similar set of differentially expressed genes, although RNA-seq was slightly better at detecting changes and agreed more with external validation. However, when the treatment agent did not induce a large effect, there were discrepancies between the two data sets that resulted from genes with below-median expression. In comparison with previous studies that have examined similar questions, this study examined differences in detection between the two methods with a large variety of treatment conditions.

The authors suggest that RNA-seq may be used instead of microarray experiments when comparing samples with similar biological conditions. However, microarrays or RNA-seq may be equally effective when developing genomic biomarker tests. **(JS)**

*Citation:* Wang C, Gong B, Bushel PR, Thierry-Mieg J, Thierry-Mieg D, Xu J, Fang H, Hong H, Shen J, Su Z, Meehan J, Li X, Yang L, Li H, Labaj PP, Kreil DP, Megherbi D, Gaj S, Caiment F, van Delft J, Kleinjans J, Scherer A, Devanarayan V, Wang J, Yang Y, Qian HR, Lancashire LJ, Bessarabova M, Nikolsky Y, Furlanello C, Chierici M, Albanese D, Jurman G, Riccadonna S, Filosi M, Visintainer R, Zhang KK, Li J, Hsieh JH, Svoboda DL, Fuscoe JC, Deng Y, Shi L, Paules RS, Auerbach SS, Tong W. 2014. The concordance between RNA-seq and microarray data depends on chemical treatment and transcript abundance. *Nat Biotechnol* 32(9):926-932.

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## NADPH oxidase implicated in Parkinson's disease associated substance P neurotoxicity

Scientists in the NIEHS Neurobiology Laboratory have discovered the first evidence that the endogenous peptide, substance P, utilizes a neurokinin-1 receptor independent pathway of neurotoxicity at subpicomolar concentrations, mediated by NADPH oxidase. Substance P, produced in neurons, amplifies proinflammatory responses in the central nervous system. This type of response has been implicated in Parkinson's disease pathogenesis, because it leads to loss of dopaminergic neurons and motor behavior control.

The researchers noted that previous studies have suggested substance P toxicity is both dependent and independent of the substance P receptor, neurokinin-1. They hypothesized that different signaling pathways were at work at different substance P concentrations.

To test their hypothesis, the researchers treated mice and primary cell cultures with two toxins that cause dopaminergic neurodegeneration, and found that substance P toxicity is mediated by activation of microglial NADPH oxidase at extremely low concentrations, independent of neurokinin-1. Further, they found that at high substance P concentrations, toxicity is dependent on neurokinin-1. Interestingly, intermediate concentrations showed decreased toxic effects, further pointing to bimodal mechanisms of substance P toxicity. In particular, their novel discovery of NADPH oxidase's role in mediating substance P's effects may lead to new insights in Parkinson's disease pathogenesis. **(MF)**

*Citation:* Wang Q, Chu CH, Qian L, Chen SH, Wilson B, Oyarzabal E, Jiang L, Ali S, Robinson B, Kim HC, Hong JS. 2014. Substance P exacerbates dopaminergic neurodegeneration through neurokinin-1 receptor-independent activation of microglial NADPH oxidase. *J Neurosci* 34(37):12490-12503.

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## **Nrf2 polymorphisms correlate with differential susceptibility to acute lung injury**

NIEHS researchers have identified single nucleotide polymorphisms (SNPs) of Nrf2 in diverse mice strains, and have associated these SNPs with differential susceptibility to acute lung injury. The findings help better understand the role of Nrf2 polymorphisms in oxidative lung disorders.

Nrf2 is a master transcriptional factor that mediates induction of a variety of genes involved in antioxidant defense. Previous studies using mice with simple deletion of Nrf2 have given limited information about its function and regulation.

By compiling information from public databases and resequenced data, the researchers were the first to discover more than a thousand Nrf2 SNPs across multiple inbred mouse strains. After exposing the strains that were grouped into three SNP haplotypes to lung-damaging hyperoxia, or excess oxygen, they observed that haplotype 2 and haplotype 3 strains were more susceptible to hyperoxia-induced injury than haplotype 1 strains. Therefore, Nrf2 haplotypes significantly correlated with hyperoxia susceptibility.

The team also determined the functional effects of Nrf2 SNPs on the expression and activity of Nrf2, which may contribute to the difference in susceptibility. Since many genetic mutations of Nrf2 are found in human oxidative disorders, mouse strains characterized by Nrf2 haplotypes in this work provide useful tools to learn how Nrf2 is involved in these diseases. **(QX)**

*Citation:* Cho HY, Jedlicka AE, Gladwell W, Marzec J, McCaw ZR, Bienstock R, Kleiberger SR. 2014. Association of Nrf2 polymorphism haplotypes with acute lung injury phenotypes in inbred strains of mice. *Antioxid Redox Signal*; doi:10.1089/ars.2014.5942 [Online 12 November 2014].

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## MMS exposure is associated with mtDNA mutagenesis

Researchers from the NIEHS Genome Integrity and Structural Biology Laboratory have identified a novel genetic and environmental interaction which alters mitochondrial DNA (mtDNA) replication efficiency. Maintenance of mtDNA is essential for cellular survival in eukaryotic cells, and the inability to properly replicate results in mitochondrial disease states and toxicity. Scientists investigated mtDNA replication efficiency, by examining yeast strains previously characterized with mutations in the mtDNA polymerase gene, in the presence of the alkylating base damaging agent, methyl methanesulfonate (MMS).

The study, published in PLOS Genetics, demonstrated that MMS exposure increased mtDNA mutagenesis in strains with disease-associated mutations that disrupt polymerase activity. Approximately half of the mutations arising from MMS exposure were cytosine to guanine transversions. Further observations suggested that MMS-induced mutagenesis did not arise by disrupting exonuclease activity.

Mechanistically, the authors have demonstrated that MMS exposure induced mtDNA mutagenesis in single-stranded mtDNA. Furthermore, this study supports a polymerase switching mechanism in mtDNA replication, which exposes single-stranded DNA to mutagenesis that was previously not described. Since the current study was conducted in yeast, it raises the question whether a similar mechanism occurs in mammalian mtDNA, and offers new insights for patients suffering from mitochondrial diseases and their susceptibility to DNA damaging agents. (TAC)

*Citation:* [Stumpf JD](#), [Copeland WC](#). 2014. MMS exposure promotes increased mtDNA mutagenesis in the presence of replication-defective disease-associated DNA polymerase gamma variants. PLoS Genet 10(10):e1004748.

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## Scavenger receptor B-I plays essential role in immune response to pneumonia

NIEHS researchers recently discovered that the scavenger receptor B-I (SR-BI), which has an environmentally regulated level of expression, is critical to survival during bacterial pneumonia.

After the scientists inoculated SR-BI deficient mice with the bacterium *Klebsiella pneumoniae*, the mice suffered markedly increased mortality compared to controls. The SR-BI deficient mice also had significantly elevated levels of bacteria in the lung, blood, and liver following inoculation, suggesting a deficit in both the innate immune response of the lung, as well as the host defense response throughout the body.

Because these increased bacteria levels were accompanied by sustained elevations of neutrophils and neutrophil-recruiting cytokines in the airway, the investigators examined whether SR-BI may mediate clearance of bacterial lipopolysaccharide (LPS) from the airspace. SR-BI deficient macrophages were, in fact, defective in clearing LPS from the lung, and also produced elevated levels of proinflammatory cytokines in response to LPS. The investigators also found that SR-BI deficient mice had defective production of adrenal stress steroid hormones during pneumonia, and this deficit in adrenal steroids also enhanced migration of neutrophils into the lung. Despite the increase in neutrophils, bacterial killing function was defective in SR-BI deficient neutrophils, compromising host defense.

These findings suggest that SR-BI plays an important role in guiding macrophages to clear LPS from the airway, and in regulating neutrophil migration to the lung via dual effects on innate cytokine production and adrenal function. Taken together, the researchers have uncovered an essential new role for SR-BI in the integrated physiologic response to pneumonia and in phagocyte antimicrobial function. **(JP)**

*Citation:* [Gowdy KM, Madenspacher JH, Azzam KM, Gabor KA, Janardhan KS, Aloor JJ, Fessler MB. 2014. Key role for scavenger receptor B-I in the integrative physiology of host defense during bacterial pneumonia. Mucosal Immunol; doi:10.1038/mi.2014.88 \[Online 22 October 2014\].](#)

(Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group. Monica Frazier, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Mechanisms of Mutation Group. Former NIEHS postdoctoral fellow Jacqueline Powell, Ph.D., is a writer and analyst with Education and Training Systems International. Jordan St. Charles, Ph.D., is an IRTA fellow in the NIEHS DNA Replication Fidelity Group. Qing Xu is a biologist in the NIEHS Metabolism, Genes, and Environment Group.)

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# Inside the Institute

## Durham researcher discusses caregiver support at NIEHS Veterans Day ceremony

By Ian Thomas

NIEHS welcomed Courtney Van Houtven, Ph.D., to Rodbell Auditorium Nov. 10 as part of the institute's first annual Veterans Day ceremony. Van Houtven's talk, "Supporting Informal Caregivers of Veterans: A Critical Component of Veteran-Centered Health Care," highlighted the value of informal care to veterans' health.

"At present, there are an estimated 20-65 million informal caregivers in America, and roughly 5.5 million of those are helping veterans," said Van Houtven, a research scientist with the Durham Veterans Affairs Medical Center and associate professor of medicine at the Duke University School of Medicine in North Carolina.

Van Houtven's research interests encompass how family caregiving affects health care utilization and expenditures, as well as health and work outcomes of care recipients and caregivers.



**Linked video:**  
Watch a video interview with Van Houtven about the [economics of informal care](#) (08:45)  
(Launches in new window)

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### A legion of support

An informal caregiver is typically a relative, friend, spouse, or neighbor who provides daily assistance to someone with a disability who couldn't otherwise perform those tasks independently.

"About half of all informal caregivers report having no medical training to provide in-home care," Van Houtven said. "They help with things like paperwork or money management, though in some instances they do aid with tasks like administering meds or bed transference."

Van Houtven also noted that the vast majority of informal caregivers are unpaid.



Austin, left, presented Van Houtven with a framed copy of the day's event poster. (Photo courtesy of Steve McCaw)



During her talk, Van Houtven stated that only three percent of U.S. caregiver services are reached through direct programs. The rest are provided by family and friends. (Photo courtesy of Steve McCaw)

“Studies show that if informal caregivers were paid a competitive wage, their estimated value as a field would be somewhere near \$450 billion per year,” she said. “That’s a figure just shy of our nation’s entire annual Medicare budget.”

### A legacy of service

“Veterans comprise roughly eight percent of our workforce here at NIEHS,” said Joellen Austin, NIEHS associate director of management, host of the talk, and, at one time, an informal caregiver herself. “Every day, they share with us things like leadership, character, or teamwork, and we can’t thank them enough for their service.”

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)



From left, Mark Miller, Ph.D., Leroy Worth, Ph.D., and Michelle Owens discuss the ceremony, during a reception in the building 101 main lobby. (Photo Courtesy of Steve McCaw)



Originally designated as Armistice Day in 1919 by President Woodrow Wilson as a means of honoring those who fought in World War I, it was later renamed Veterans Day in 1954 to honor all American veterans. (Photo courtesy of Steve McCaw)



The Veterans Day National Ceremony is held each year on Nov. 11 at Arlington National Cemetery. (Photo courtesy of Steve McCaw)



Members of NIEHS leadership turned out to show their support for the institute’s many veterans. (Photo courtesy of Steve McCaw)

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