

December 2015

## NIEHS Spotlight



### [Children's health highlighted at D.C. events](#)

Children's environmental health research was the focus of the annual meeting of children's centers and a congressional staff briefing.



### [Rogan receives prestigious children's environmental health award](#)

Walter Rogan, M.D., recently retired from NIEHS, received the 2015 Child Advocate award from the Children's Environmental Health Network.



### [Three NIEHS Scholars Connect students win travel awards](#)

Three Scholars Connect participants won travel funding to attend the Annual Biomedical Research Conference for Minority Students in Seattle.



### [Generation Public Health takes over Chicago meeting](#)

Creating the healthiest nation in one generation was a key theme of the American Public Health Association meeting in Chicago.



### [NIEHS Science Days celebrate excellent trainees and mentors](#)

The NIEHS Science Days event Nov. 5-6 recognized the trainee and mentor of the year, as well as best trainee poster and talk.

## Clinical Feature



### [LabTV focuses on NIEHS clinical researcher](#)

A National Institutes of Health video series, aimed at attracting future biomedical researchers, features NIEHS clinical researcher Lisa Rider, M.D.

## Science Notebook



### [Distinguished lecturer advances nuclear receptor field](#)

Bert O'Malley, M.D., a pioneer of nuclear receptor biology, discussed recent advances in his Distinguished Lecture Seminar Series talk.



### [Asian Pacific autism conference includes focus on the environment](#)

At the International Society for Autism Research regional meeting, a keynote talk and panel addressed environmental exposures and autism.



### [NIEHS Science Days offers insights on inflammation](#)

Attendees at the 2015 NIEHS Science Days were treated to a minisymposium on connections between inflammation and disease.

## NIEHS Spotlight



### [Summit addresses safe drinking water from private wells](#)

NIEHS staff and grantees joined the Research Triangle Environmental Health Collaborative summit on North Carolina private well water quality.



### [NIH honors nine NIEHS scientists at Director's Awards ceremony](#) 🏆

The National Institutes of Health conferred its highest honors on nine outstanding NIEHS employees at its annual Director's Awards ceremony.



### [Innovative research and collaboration at SRP Annual Meeting](#)

Participants, guided by the theme, Collaboration for Innovation, pursued collaborations across disciplines and with new SRP partners.



### [Duke symposium addresses toxicity of energy production](#) ▶ Video

NIEHS scientists and grantees took part in the Integrated Toxicology and Environmental Health Program symposium, "The Toxicity of Power."



### [NTP highlights new technologies to protect health and environment](#)

At the FutureToxIII meeting, National Toxicology Program scientists and others assessed the latest technologies for chemical safety testing.

## Science Notebook



### [Simmons speaks on the origins of obesity](#)

The tendency toward obesity may originate prior to conception, according to research presented by Rebecca Simmons, M.D.



### [3-D print fest inspires innovation at NIEHS](#) ▶ Video

Scientists and staff from across NIEHS enjoyed a showcase of NIH and local area innovators who use 3-D print technology to advance research.



### [Genetics society celebrates history and prepares scientists for the future](#)

The 33rd fall meeting of the Genetics and Environmental Mutagenesis Society featured awards for two founders and prizes for student researchers.



### [Toxicologists explore mouse versus man, award postdoc researchers](#)

The North Carolina Society of Toxicology fall meeting, Mouse vs. Man, examined species differences and similarities in toxicological research.



### [Quist wins young investigator award](#) 🏆

The poster by research fellow Erin Quist, already an award-winning scientist, won a blue ribbon at the Society of Toxicological Pathology meeting.

## Inside the Institute



### [NIEHS staff cleans up local highway](#)

NIEHS employees celebrated American Recycles Day Nov. 4 by picking up trash from Hopson Road where it borders institute campus.

## Science Notebook



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

The December issue of Environmental Health Perspectives highlights declines in African fruit trees and racial imbalances in health studies.

## Extramural Research

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

- [Green office environments linked with higher cognitive function](#)
- [Lead exposure can cause multigenerational epigenetic changes](#)
- [Maternal and fetal exposure to parabens](#)
- [Prenatal exposure to PBDEs associated with later attention problems](#)

## Intramural Research

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

- [NTP finds toxicity associated with organophosphorus flame retardants](#)
- [High resolution structure of the APE1-DNA complex](#)
- [Role of a T-type Ca<sup>2+</sup> channel in fertility](#)
- [Mechanism of nuclear uptake of a DNA repair scaffold protein revealed](#)
- [Refined mining of GWAS data reveals new insights into airway disease](#)

## Calendar of Upcoming Events

- **Dec. 2**, Rodbell Auditorium, 8:30 a.m. – 5:00 p.m. — National Toxicology Program Board of Scientific Counselors meeting, register to attend [in person](#) or via [webcast](#)
- **Dec. 2**, Building 101, Room D250, 9:00 – 10:00 a.m. — Amanda MacLeod, M.D., from Duke University School of Medicine, speaking on “Mechanisms of UV-induced Immunosuppression in the Skin,” hosted by Jennifer Martinez, Ph.D.
- **Dec. 2-4 (off-site event)**, Bethesda, Maryland — [Tribal Ecological Knowledge Workshop](#) and training sessions.
- **Dec. 3 (webinar)**, 11:00 a.m. – noon — In Vitro to In Vivo Extrapolation for High Throughput Prioritization and Decision Making, [register to attend](#)
- **Dec. 4**, Rodbell Auditorium, 9:30 – 10:30 a.m. — Joaquin Espinosa, Ph.D., from the University of Colorado Denver School of Medicine, speaking on “Taming the p53 Network for Effective Cancer Therapies,” hosted by Thuy-Ai Nguyen, Ph.D., and Mike Resnick, Ph.D.
- **Dec. 7**, Rodbell C, 1:00 – 2:00 p.m. — Data Science Seminar Series presents Praveen Sethupathy, from University of North Carolina School of Medicine, discussing “Discoveries From Functional Genomics: Non-coding RNAs as Mechanistic Links Between Environment and Human Physiology”
- **Dec. 9 (webinar)**, 1:00 – 2:30 p.m. — NIEHS-EPA Children’s Environmental Health Research Centers Webinar on Food and Children’s Health, featuring Asa Bradman, Ph.D., from the University of California, Berkeley; Anne Hoen, Ph.D., from Dartmouth College; Karen Peterson, D.Sc., from the University of Michigan; and discussion leader Laura Anderko, Ph.D., R.N., from Georgetown University, [register](#)
- **Dec. 14 (webinar)**, 1:00 – 2:30 p.m. — NIEHS Partnerships for Environmental Public Health presents “Meet the Editors,” featuring editors in chief Sally Darney, Ph.D., of Environmental Health Perspectives; Craig Slatin, Sc.D., of New Solutions: A Journal of Environmental and Occupational Health Policy; and John Allegante, Ph.D., of Health Education and Behavior, [registration is required](#)
- **Dec. 17**, Rodbell Auditorium, 8:30 a.m. – 5:00 p.m. — National Toxicology Program Peer Review of the Draft RoC Monograph on Selected Viruses, register to attend [in person](#) or via [webcast](#)
- View More Events: [NIEHS Public Calendar](#)

# NIEHS Spotlight

## Children's health highlighted at D.C. events

By Virginia Guidry

Children's environmental health research was the focus of the Oct. 29-30 annual meeting of the NIEHS-U.S. Environmental Protection Agency (EPA) Children's Environmental Health and Disease Prevention Research Centers. NIEHS and EPA staff and center grantees discussed ongoing research at the Washington, D.C., event.

"The children's centers were established to increase our understanding of children's unique vulnerability to harmful environmental exposures," said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program, in her opening talk. "This research has helped to guide the development of protective measures for children in the United States and around the world."

NIEHS and EPA have jointly funded [23 children's centers](#) across the country since 1998. The centers examine the effects of air pollution, metals, pesticides, and other environmental contaminants on children's health and developmental outcomes. They also provide outreach and education to those concerned about children's environmental health.

### Environmental health across the life span

A common theme among attendees was the need to consider the entire life span when protecting children's health. They stressed that exposures in early life can set a course for health outcomes later in life — a concept called early programming.

[Bradley Peterson, M.D.](#), of Children's Hospital Los Angeles, explained that much of the brain's structure is established during the prenatal period and early childhood. Exposure to common air pollutants, such as polycyclic aromatic hydrocarbons, during this time can result in permanent changes to brain structure.

[Michael Lu, M.D.](#), from the U.S. Department of Health and Human Services Health Resources and Services Administration, addressed the cumulative effects of environmental exposures across a lifetime. "If we want to improve children's health, starting in childhood is not



*"NIEHS spends approximately \$115 million annually on children's health research and we cherish our long-term partnership with EPA on the children's environmental health centers," said Birnbaum, right, while Ruth Etzel, M.D., Ph.D., director of the EPA Office of Children's Health Protection, looked on. (Photo courtesy of Keeli Howard)*



*"The most important thing that we can do to protect children's health is to improve the implementation of our science," said EPA Deputy Assistant Administrator Thomas Burke, Ph.D. (Photo courtesy of Keeli Howard)*

early enough. Even prenatal care is too late to reverse the accumulation of dioxins in maternal body fat, or epigenetic changes that get passed down from parents as a result of early exposures to nutrition, toxic stress, and environmental factors,” Lu said. “So we really need to take a life course approach to children’s health.”

### Research that informs health policy

Children’s centers grantees presented new research on topics ranging from obesity, reproductive health, and neurodevelopmental disorders, to air pollution, nutrition, stress, and poverty. Grantees also discussed how to make their research findings useful for the development of health policies.

A suggestion heard frequently from attendees was the need to include environmental health topics in required training for obstetricians, pediatricians, and family practice providers. “Obstetricians aren’t thinking about how exposures in pregnant mothers now are going to affect their children when they’re 10, 30, 40 years old,” said [Rosalind Wright, M.D.](#), from Mount Sinai Hospital. “If we’re going to focus on pregnant women, we have to educate obstetricians that environmental factors are important.”

[Gregory Diette, M.D.](#), of Johns Hopkins University, encouraged scientists to align their research with the information regulators need to protect public health. “Linking studies so they can be implemented at the policy level is crucial,” he said. “It is not enough to show that ozone is bad — we have to show that ozone at a certain threshold is bad, so regulators can use that information.”

(Virginia Guidry, Ph.D., is a technical writer and public information specialist in the NIEHS Office of Communications and Public Liaison.)

## NIEHS support for children’s environmental health

Birnbaum highlighted ways that NIEHS supports children’s environmental health research, in addition to the children’s centers.

- [Children’s Health Exposure Analysis Resource \(CHEAR\)](#) — Provides access to laboratory and data analyses, to add or expand inclusion of environmental exposures in children’s health research.
- [Pediatric Research Using Integrated Sensor Monitoring Systems \(PRISMS\)](#) — Development of sensor-based, integrated health monitoring systems to measure environmental, physiological, and behavioral factors in pediatric studies of asthma, and eventually other chronic diseases.
- [Patient Reported Outcomes Measurement Information System \(PROMIS\)](#) — A system of highly reliable, precise measures of patient-reported health status for physical, mental, and social well-being, to provide clinicians and researchers with information that not found in traditional clinical measures.
- [Tox21](#) — Development of more efficient and less time-consuming approaches to predicting how chemicals may affect human health.
- [Human Placenta Project](#) — A collaborative research effort, launched by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, to understand the placenta’s role in health and disease.



*“We translate the science from the children’s centers into interventions that local and state health departments can use to make the environment safer for children,” said Patrick Breysse, Ph.D., director of the National Center for Environmental Health and the Agency for Toxic Substances and Disease Registry at the Centers for Disease Control and Prevention. (Photo courtesy of Keeli Howard)*



*Gail Christopher, D.N., vice president for policy and senior advisor at the W.K. Kellogg Foundation, spoke about programmatic interventions designed to help minimize toxic exposures during early life stages during her keynote address. (Photo courtesy of Keeli Howard)*



*Jennifer Lowry, M.D., medical director of the Center of Environmental Health at Children’s Mercy Hospital, explained the role of Pediatric Environmental Health Specialty Units in translating children’s environmental health research to clinical and public health practitioners. (Photo courtesy of Keeli Howard)*



*Virginia Rauh, Sc.D., deputy director of the Columbia Center for Children’s Environmental Health, conducts research on the effects of air pollution on early brain development. (Photo courtesy of Keeli Howard)*



*“Often the people that could benefit the most from environmental health research are the ones with the least access to information — the ones living next to the toxic waste dump or being exposed to endocrine disruptors or pesticides at work,” said Lu, during his keynote address. “So we have to continually ask how we can extend access to those who could benefit the most from the work that we do.” (Photo courtesy of Keeli Howard)*



*Sally Darney, Ph.D., editor of the journal Environmental Health Perspectives (EHP), emphasized that EHP can help play an active role in research translation for children's environmental health. (Photo courtesy of Keeli Howard)*



*Bruce Lanphear, M.D., gave a keynote address about how small health effects for individual children can accumulate into large population level impacts. "Little shifts in children's IQ scores from exposures to chemicals such as lead or flame retardants can result in substantially more children who are intellectually challenged, and fewer who are intellectually gifted. These effects increase when children are exposed to multiple toxins," he said. (Photo courtesy of Keeli Howard)*

## NIEHS and EPA brief congressional staff

A packed crowd attended a congressional briefing about children's environmental health Oct. 28 in Washington, D.C. The offices of North Carolina Reps. Renee Ellmers (R-N.C.) and G.K. Butterfield (D-N.C.) hosted the event.

Birnbaum opened the briefing by explaining that NIEHS makes children's health research a priority, because of the lifelong impacts it can have. She described current initiatives, including the Children's Health Exposure Analysis Resource (CHEAR). Thomas Burke, Ph.D., Deputy Assistant Administrator of the EPA Office of Research and Development, provided a personal look at the importance of children's health, based on his prior work as a state health director and his current position as the EPA science advisor.

Three directors from NIEHS-EPA Children's Environmental Health and Disease Prevention Research Centers shared the impacts of their research:

- Peterson used magnetic resonance imaging (MRI) pictures to show how pesticides and air pollution can alter brain development in children.
- **Rob McConnell, M.D.**, from the University of Southern California, shared growing evidence that air pollution not only worsens, but also causes, asthma.
- **Catherine Metayer, M.D., Ph.D.**, from the University of California, Berkeley, discussed how exposures to chemical mixtures, such as those used when painting, can increase the risk of developing childhood acute lymphocytic leukemia.

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# Rogan receives prestigious children's environmental health award

By Kelly Lenox

Walter Rogan, M.D., who continues work at NIEHS as a special volunteer after retiring in July, received the 10th annual Child Advocate Science Award from the [Children's Environmental Health Network](#) (CEHN) during a Nov. 12 ceremony at the George Washington University Milken Institute School of Public Health.

As an NIEHS epidemiologist, Rogan studied the effects of environmental chemicals on the health of children. He is credited with helping found the field of children's environmental health in the 1970s, along with Philip Landrigan, M.D., and Herbert Needleman, M.D.

"We believe your leadership, passion, and research efforts to reduce environmental threats to children make you a fantastic child health advocate champion," said Nsedu Witherspoon, executive director of CEHN.

## Representing the interests of children

In his comments at the ceremony, Rogan noted that when he came to NIEHS in the 1970s, there was little data on how environmental exposures — with the exception of lead — affect children. "The only other environmental agents with data available from human children were radiation, methylmercury, and hexachlorobenzene," he said. Furthermore, all the data were from children who were ill, and there were no control groups, he added.

"The data, by and large, were not used by the regulatory agencies, who preferred data from grown-ups or, better yet, grown-up mice," he said. That began to change as Rogan and NIEHS colleague Beth Gladen, Ph.D., previously of the NIEHS Statistics and Biomathematics Branch, embarked on studies of the potential consequences of polychlorinated biphenyls in breast milk.

Rogan continued to break new ground in research on the environment and children's health throughout his NIEHS career. "We've come a long way," he observed, "but there is a long way to go." As evidence, Rogan noted that, typically, an influential paper in adult cardiology or cancer might be cited by other researchers 3,000 times, but an important paper in children's environmental health is cited about 300 times.



*Last year, Rogan received the 2014 Zena Stein and Mervyn Susser Award for Lifetime Achievement at the National Maternal and Child Health Epidemiology Conference. (Photo courtesy of Steve McCaw)*

## A pioneering researcher

Honoring Rogan upon his retirement, Allen Wilcox, M.D., Ph.D., head of the NIEHS Reproductive Epidemiology Group, listed some of the firsts Rogan holds at NIEHS.

- The first epidemiologist hired at NIEHS — in 1976 — before there was an epidemiology program, branch, or section.
- Lead researcher for the first epidemiologic study at NIEHS — a study of PCBs in breast milk.
- The first NIEHS in-house researcher to publish a paper in the journal *Science*, and the first to publish in the *New England Journal of Medicine*.
- The founder and first chair of the NIEHS Institutional Review Board, which reviews and approves protocols for all in-house research.

## A crowning achievement

“This award from CEHN is a fitting capstone to a successful and influential career of many firsts,” said Dale Sandler, Ph.D., head of the NIEHS Epidemiology Branch (see [sidebar](#)). She noted that Rogan also represented the National Institutes of Health at the American Academy of Pediatrics Council on Environmental Health for an unprecedented 36 years, and wrote four of their policy statements. “The American Academy of Pediatrics recognized him by making him an honorary fellow in 2012,” she said.

“I am really thrilled that Walter will be honored by CEHN,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program. “It’s well deserved.” Birnbaum and William Suk, Ph.D., director of the NIEHS Superfund Research Program, have also received recognition from CEHN.

Rogan joins an illustrious group of honorees, including Sen. Frank Lautenberg, Philadelphia Mayor Michael Nutter, Sanjay Gupta, M.D., and two former administrators of the U.S. Environmental Protection Agency, Lisa Jackson and Carol Browner, J.D.

CEHN is a multidisciplinary organization working to protect the developing child from environmental health hazards and promote a healthier environment.

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## Three NIEHS Scholars Connect students win travel awards

*By Simone Otto*

Three NIEHS labs are pleased to count among their members winners of student travel awards from the Annual Biomedical Research Conference for Minority Students (ABRCMS).

The winners (see [sidebar](#)) are Alanna Burwell, in the NTP Molecular Pathogenesis Group, headed by Darlene Dixon, D.V.M., Ph.D.; Carri Murphy, in the Chromosome Stability Group, headed by Michael Resnick, Ph.D.; and Porscha Walton, in the National Toxicology Program (NTP) Office of Health Assessment and Translation, led by Kris Thayer, Ph.D.

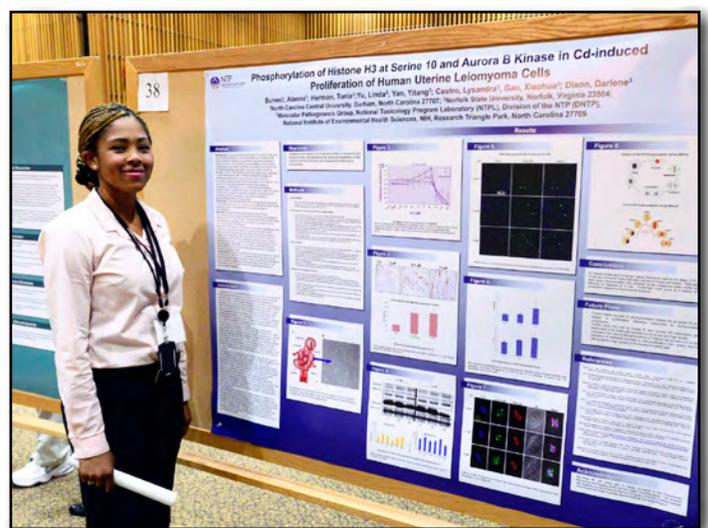
The awards enabled the three participants in the NIEHS Scholars Connect Program (NSCP) to travel to the ABRCMS, Nov. 11-14 in Seattle. ABRCMS bills itself as the largest professional conference for underrepresented minority students, military veterans, and persons with disabilities.



**Linked audio:**  
[Listen to Rogan discuss his research on use of the drug succimer to remove lead and mercury from children in this NIH podcast. \(3:16\)](#)

(Launches in new window)

Download Media Player: [Quicktime](#)



*Burwell, shown during an NIEHS poster session in July, presented her work at the ABRCMS conference. (Photo courtesy of Steve McCaw)*

## A transformative experience

Attending the conference was a transformative experience for these young scholars. “My experience at the conference was amazing,” said Murphy. “I had the opportunity to meet Desmond Tutu’s daughter, Dr. Naomi Tutu, who gave a wonderful speech about being black in the sciences, and it inspired me. The conference motivated me to strive for excellence, step outside my comfort zone, try new things, and to never stop asking questions.”

As participants in NSCP, Murphy and the other two winners will be able to put the conference experience to practical use. “Scholars Connect gives the scholars a chance to meet with top leadership at NIEHS, have guidance in career development, and three opportunities to present throughout the year,” said Erica Rogers, Ph.D., who coordinates the program for the NIEHS Office of Science Education and Diversity (OSD).

“We started in 2012 and are extremely pleased that three of our six scholars this year received travel awards,” added Ericka Reid, Ph.D., director of OSD. Rogers and Reid staffed an NIEHS booth at the conference.

NSCP opens the door for undergraduate students interested in a career in science, technology, engineering, or mathematics (STEM) disciplines. Juniors and seniors from academic institutions in the local area spend three semesters on a single research project, under the guidance of a lead scientist, as well as a postdoctoral fellow or staff scientist mentor.

## Meaningful contributions

The NSCP lasts an entire year, providing opportunities for the scholars to contribute in a meaningful way to the research in their laboratories. “I have been impressed with the seriousness of the [students in the] NSCP,” said Resnick.

Resnick’s high opinion of the program was shared by Dixon. “This program is a good opportunity for our staff to interact with, and mentor, students interested in biomedical careers,” she said.

Kembra Howdeshell, Ph.D., mentor for Walton, added, “We can often get caught up in the jargon of our specialties. Working with Porscha has helped me improve my ability to explain the science we do.”



Walton also presented her poster at the conference, gaining valuable experience by discussing her research with attendees from a wide range of specialties. (Photo courtesy of Ericka Reid)

## Scholars contribute vital research

**Alanna Burwell**, a senior at North Carolina Central University (NCCU), is studying the basic mechanisms of tumor growth in uterine fibroid cells, induced by a low and environmentally relevant dose of cadmium. Burwell works under the direction of Yitang Yan, Ph.D., and Linda Yu.

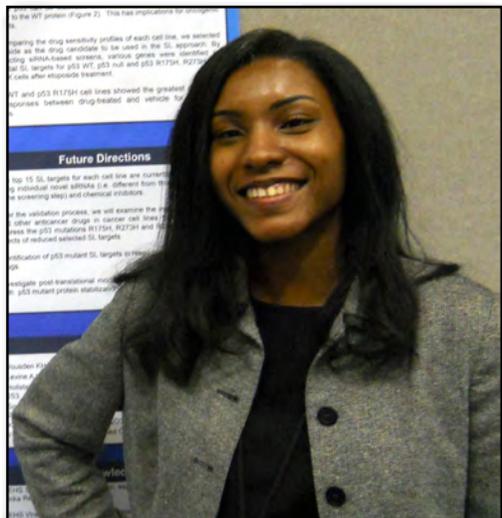
**Carri Murphy**, is also a senior at NCCU. She is conducting research on the p53 tumor suppressor gene, under the guidance of mentor Daniel Menendez, Ph.D. Her research helped establish a new role for p53 in inflammation and immunity.

**Porscha Walton**, a senior at St. Augustine’s University, is identifying various uses of synthetic progesterone drugs and categorizing adverse outcomes, specifically as a result of exposure during development. She is mentored by Kembra Howdeshell, Ph.D., and Abee Boyles, Ph.D.

David Menendez, Ph.D., mentor to Murphy, agrees. “Having a student to mentor also pushes you,” he said. “They start with naive questions, but that pushes you towards thinking about your project. Over the course of the year, the transformation the students’ experience is fantastic. In addition, they are able to apply what they learn here to their university experience, and we are able to use their results in the next project.”

“Alanna’s project will help us understand how environmentally relevant concentrations of cadmium cause fibroid tumor cells to grow,” said Yitang Yan, Ph.D., one of her mentors. “This work is of interest to both lay and scientific communities.”

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



Murphy is a returning scholar and, in April, was the winner of the first *NSCP Outstanding Scholar Award*. (Photo courtesy of Ericka Reid)



From left, Walton, Murphy, Burwell, and Tobias Flow took a moment from the packed conference schedule to pose at the NIEHS booth. Flow, an NCCU senior, is another NSCP participant who attended the conference. (Photo courtesy of Ericka Reid)

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## Generation Public Health takes over Chicago meeting

By Robin Mackar

To create the healthiest nation in one generation, or what the American Public Health Association (APHA) is calling Generation Public Health, was the key theme of this year’s APHA meeting in Chicago.

At the opening session, speakers including U.S. Surgeon General Vivek Murthy, M.D.; the president of the University of Maryland, Baltimore County; the APHA president; actor and environmentalist Ed Begley Jr.; and others called on the public health community to leverage their passion and expertise to [improve our nation’s health](#).

“There are three elements central to our work as public health leaders — information, inspiration, and equality,” said Murthy. “When we in public health can inform and inspire the people we serve, we can empower them to improve not only their health, but their community as well. This is how we can create a movement around health.”

The Oct. 31-Nov. 4 meeting, with more than 1,000 scientific sessions, offered attendees the breadth of knowledge needed to build a healthier nation. Sessions focused on the power of prevention, establishing health equity, and the role that emphasizing health in all policies can play in reducing health disparities.



**Linked video:**  
[Watch a video highlighting the key messages at the opening general session of the 2015 APHA meeting \(1:46\)](#)  
(Launches in new window)

Download Media Player:  Flash [↗](#)

## NIEHS-led sessions

About a dozen NIEHS staff from across the institute helped lead pivotal sessions. Joseph (Chip) Hughes and Sharon Beard from the NIEHS [Worker Training Program](#), and NIEHS Senior Medical Advisor Aubrey Miller, M.D., moderated and organized many of the occupational health and safety offerings. They discussed issues such as protecting disaster response workers in a variety of settings, including from biological threats like ebola; integrating mental health training into worker training programs; and doing more to protect vulnerable populations.

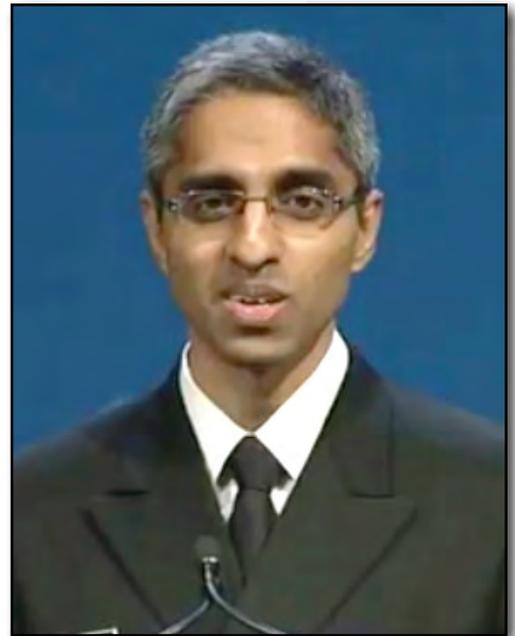
Liam O’Fallon, coordinator of the NIEHS [Partnerships for Environmental Public Health](#) program, led several sessions on health disparities and environmental justice. The connection between [climate change and human health](#) was a theme that permeated the conference, with John Balbus, M.D., NIEHS senior advisor for public health, and Kimberly Thigpen Tart, J.D., program analyst in the NIEHS Office of Policy, Planning, and Evaluation, both leading sessions on the topic. The choice of climate change and health for the focus of the 2017 APHA meeting in Atlanta received an enthusiastic response from conference-goers.

Sally Perreault Darney, Ph.D., new editor in chief of [Environmental Health Perspectives](#), attended the meeting and joined Thigpen Tart and others on several career panels. The [National Toxicology Program](#) (NTP) also had a presence. Mary Wolfe, Ph.D., NTP deputy division director for policy, showcased ways in which the work of NTP helps shape public health policies.

## Former NIEHS colleagues continue public health work

The APHA conference provided the perfect venue to catch up with former colleagues and hear about their new public health adventures.

Former NIH health disparities trainee [Rosemarie Ramos, Ph.D.](#), visited several NIEHS panels, as well as the exhibit, to share information about her role as an assistant research program director in the Department of Emergency Medicine at the University of Texas Health Science Center at San Antonio.



*Murthy, shown during his opening talk, was confirmed as Surgeon General Dec. 15, 2014, and said his highest priority is improving the health of the American people and our neighbors around the world. (Photo courtesy of APHA)*



*Ramos continues to work on health disparities. She said she is especially interested in getting more people involved in the NIH Precision Medicine Initiative. (Photo courtesy of Robin Mackar)*

Brenda Weis, Ph.D., formerly with the NIEHS Division of Extramural Research and Training and NIEHS Office of the Director, is doing well in her role as director of the [New Bedford Health Department](#) in Massachusetts, where she oversees a number of innovative health programs.

Former NIEHS Associate Director William Martin, M.D., also stopped by to catch up and share how much he is enjoying his role as professor and [dean of the Ohio State University College of Public Health](#).

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



*Weis stopped by the NIEHS booth after her talk. She said she loves doing public health work in her Massachusetts community. (Photo courtesy of Robin Mackar)*



*From left, Lynae Thomas and Joan Packenham, Ph.D., both from the NIEHS Office of Human Research Compliance, talked to O'Fallon about involvement in next year's Women's Health Awareness Day in Durham, North Carolina. (Photo courtesy of Robin Mackar)*

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## **NIEHS Science Days celebrate excellent trainees and mentors**

*By Kelly Lenox*

Each year, NIEHS researchers gather during the first week of November to share their work, explore collaborations, and celebrate excellence with awards. The NIEHS Science Days event Nov. 5-6 included recognition for the trainee and mentor of the year, as well as the best trainee poster and talk.

“Science Days is, in part, a training exercise — it gives trainees a forum to develop their technique in giving poster and oral presentations,” said Joel Abramowitz, Ph.D., special assistant to the NIEHS scientific director. “No other institute has the breadth of the types of science that we do here, so the trainees have to explain themselves to a broad audience.”

### **Fellow and mentor of the year**

The NIEHS Trainees Assembly (NTA) names a mentor of the year based on nominations from trainees and researchers alike. In 2012, the NIEHS Office of Fellows Career Development (OFCD) began selecting a fellow of the year, awarding travel funds to attend a conference.

Tammy Collins, Ph.D., OFCD director, said the fellow award was created to recognize a trainee with the outstanding qualities necessary for a well-rounded independent research career. A panel of scientists evaluated the nominees and selected Miranda Bernhardt, Ph.D., an Intramural Research Training Award fellow (IRTA) in the Reproductive Medicine Group, headed by Carmen Williams, M.D., Ph.D.

“Miranda has a passion for reproductive biology,” said Williams. “And she’s an intellectual powerhouse.” She cited Bernhardt’s successful demonstration of a novel calcium channel involved in egg fertilization (see [related story](#)). Williams also noted Bernhardt’s commitment to service, especially science education, among her qualifications for the prize.

In a fitting surprise, Kristin Gabor, Ph.D., announced that the NTA choice for mentor of the year was Williams. Bernhardt and Williams returned to the podium. “I’ve been able to accomplish so much more than I would have without her leadership and guidance,” Bernhardt said.

Other nominators cited Williams’ commitment to training the next generation of reproductive scientists and clinicians. One noted the possible key to Williams’ success. “She listens to all ideas, no matter how outside the box they are,” the letter read.

### Excellent science presentations in talks and posters

Continuing the robust showing of recent years, Science Days featured 92 posters, representing research across all divisions of the institute. Scientists stood by on Nov. 5 to discuss their research with participants.

Organizers planned to recognize the top nine posters and award travel funds to the top five. But when the judges’ scores were tallied, there was a six-way tie for fourth place, and the Division of Intramural Research stepped up and provided all nine winners with cash awards (see [text box](#)).

Trainees presented nine of the [scientific talks](#) featured in the festival. Mitoki Takaku, Ph.D., won the best oral presentation award. Takaku, a visiting fellow in the Eukaryotic Transcriptional Regulation Group, headed by Paul Wade, Ph.D., discussed the mechanism of chromatin reprogramming by GATA3, a pioneer transcription factor that has been implicated in the progression of breast cancer.

“The science is of a really high quality. We have a magnificent group of people here doing important work, and it’s really important to acknowledge it,” Abramowitz said afterward.



*Abramowitz, left, presented Henriques with the best poster award. Judges included eight from outside of NIEHS and sixty from within the institute. (Photo courtesy of Steve McCaw)*



*It may be no coincidence that Fellow of the Year Bernhardt, left, works for Mentor of the Year, Williams, center, who received her award from NTA representative Gabor, right. “The mentors here are taking bright people, who are very knowledgeable, and leading them in a way that enables them to do their best in conducting science,” Abramowitz said of the NIEHS training environment. (Photo courtesy of Steve McCaw)*



Judges voted the presentation by Takaku, right, to be the best trainee talk. "I want to thank the organizers for giving me the opportunity to talk about my research," he said. "GATA3 is one of the most frequently mutated genes in breast cancer." (Photo courtesy of Steve McCaw)



Jonathan Hollander, Ph.D., right, of the Division of Extramural Research and Training (DERT), talked with Neurobiology Lab research fellow Chen about his poster, "Environmental Factors in the Development of Parkinson's Disease: Recent Trends and NIEHS Funding Efforts" (Photo courtesy of Steve McCaw)



Juhee Haam, Ph.D., left, of the Neurobiology Lab, enlightened Hong about her poster, "Cholinergic Regulation of the Hippocampal Output to Entorhinal Cortex." (Photo courtesy of Steve McCaw)



Stavros Garantziotis, M.D., right, from the Clinical Research Branch, learned about the promotion of allergic asthma from biologist Greg Whitehead, from the Immunogenetics Group. (Photo courtesy of Steve McCaw)



Postdoctoral fellow Seddon Thomas, Ph.D., left, explained her research on dendritic and epithelial cell crosstalk in the lung to Leping Li, Ph.D., head of the Biostatistics and Computational Biology Branch. (Photo courtesy of Steve McCaw)



IRTA fellow Shannon Farris, Ph.D., from the Neurobiology Lab, explained her study of plasticity in hippocampal area CA2 to Cindy Lawler, Ph.D., head of the DERT Genes, Environment, and Health Branch. (Photo courtesy of Steve McCaw)



*Makia, left, discussed his award-winning research with toxicologist Kristine Witt, also of the National Toxicology Program. (Photo courtesy of Steve McCaw)*



*Hideki Nakano, Ph.D., staff scientist in the Immunogenetics Group, discussed his poster, "Inhaled House Dust Programs Pulmonary Dendritic Cells to Initiate Allergic Responses by Inducing Secretion of an Endogenous Factor Into the Airway," with Michelle Heacock, Ph.D., left, from DERT. (Photo courtesy of Steve McCaw)*

## Winning Posters

**First place** — Telmo Henriques, Ph.D., postdoctoral fellow in the Transcriptional Responses to the Environment Group, led by Karen Adelman, Ph.D., for "Probing Co-transcriptional RNA Processing."

**Second place** — Sonika Patial, D.V.M., Ph.D., visiting fellow in the Polypeptide Hormone Action Group, led by Perry Blackshear, M.D., D.Phil., for "Genetic Deletion of an Instability Motif in the 3' Untranslated Region of Tristetraprolin mRNA Increases TTP mRNA Stability and Protein Expression and Protects Against Immune-mediated Inflammatory Diseases."

**Third place** — David Chen, Ph.D., research fellow in the Neuropharmacology Group, led by Jau-Shyong Hong, Ph.D., for "Reactive Microgliosis Is Essential in Driving Chronic Neuroinflammation-related Neurodegeneration: Role of the MAC1-NOX2 Signaling Pathway."

### **Fourth place, six-way tie**

**Joanne Damborsky, Ph.D.**, IRTA fellow in the Ion Channel Physiology Group, led by Jerry Yakel, Ph.D., for "Interplay Between Cholinergic and Galaninergic Modulation of GABA Release in the Basal Forebrain."

**Douglas Ganini da Silva, Ph.D.**, research fellow in the Free Radical Metabolism Group, led by Ron Mason, Ph.D., for "Human Mitochondrial SOD2 and Bacterial SOD A Incorporated With Iron Become Prooxidant Peroxidases."

**Samantha Hoopes, Ph.D.**, IRTA fellow in the Environmental Cardiopulmonary Disease Group, led by NIEHS Scientific Director Darryl Zeldin, M.D., for "Transgenic Mice Expressing CYP4F2 in Endothelial Cells Exhibit Altered Retinal Angiogenesis In Vivo."

**Julie Lowe, Ph.D.**, IRTA fellow in the Clinical Investigation of Host Defense Group, led by Michael Fessler, M.D., for "The Novel p53 Target TNFAIP8 Variant 2 Is Increased in Cancer and Offsets p53-dependent Tumor Suppression."

**Ngome Makia, Ph.D.**, visiting fellow in the Stem Cell Toxicology Group, led by Erik Tokar, Ph.D., for "Cadmium and Arsenic Transformed Human Peripheral Lung Cells Expressing CD34 Display Stem Cell-like and Malignant Properties."

**Dan Su, Ph.D.**, IRTA fellow in the Environmental Genomics Group, led by Doug Bell, Ph.D., for "Tobacco-smoke Associated DNA Methylation and Gene Transcription in Human Blood Cell Lineages."

# Summit addresses safe drinking water from private wells

By Sara Mishamandani

NIEHS staff and grantees joined the Research Triangle Environmental Health Collaborative (EHC) Oct. 26-27 for its 2015 Environmental Health Summit, [Safe Water from Every Tap](#), which examined the quality of drinking water from private wells in North Carolina. EHC is a regional nonprofit focused on strengthening global environmental health.

According to EHC, approximately 25 percent of North Carolina residents rely on private wells for their water, which are not regulated by the Safe Drinking Water Act, leaving some residents without access to clean drinking water.

The summit, held in Research Triangle Park, North Carolina, brought together scientists, community members, and public health professionals, with representatives from industry, local health departments, and local, state, and federal agencies to develop recommendations for improving access to safe drinking water from private wells.

## Showcasing SRP water research innovation

During a plenary talk, Heather Henry, Ph.D., health scientist administrator with the NIEHS Superfund Research Program (SRP), highlighted SRP-funded research, nationwide, related to detecting and measuring contaminants in water, and treating it to meet safe drinking water standards.

Henry discussed research by SRP grantees, many of whom attended the meeting. For example, [a study by Rebecca Fry, Ph.D.](#), University of North Carolina (UNC) SRP center director, linked exposure to high concentrations of manganese in North Carolina well water, during pregnancy, to birth defects. Later in the day, Fry gave a presentation to a community education working group, which was organized by NIEHS grantees Kathleen Gray and Neasha Graves of UNC.

SRP is also funding research on technologies to detect and clean up contaminants in water. For example, Henry said that Duke University SRP center researchers are developing membranes, using nanomaterials, to treat water contaminated with chemicals, such as brominated flame retardants. Henry pointed out that a former Duke SRP center trainee who worked on the project, Alexis Carpenter, Ph.D., was present at the summit.



*Henry spoke about the federal perspective on improving drinking water. (Photo courtesy of Steve McCaw)*



*Rep. David Price, right, who represents the North Carolina 4th Congressional District, provided a congressional perspective on issues related to private drinking wells in North Carolina. He is shown speaking with Birnbaum during a break. (Photo courtesy of Steve McCaw)*

## Moving forward to improve water quality

After the plenary presentations, participants broke into four working groups to focus on community education, governance and policy, pollution prevention, and user-friendly technologies. Each working group raised concerns and discussed potential solutions for problems related to private well contamination in North Carolina. EHC will lead development of recommendations and solutions from the four working groups.

During a community impacts panel, Mark Borsuk, Ph.D., discussed the work of the Dartmouth SRP center to test well water in New Hampshire for arsenic, and inform well owners of their risks and ways to reduce arsenic exposure. Reaching out to well owners that have a higher probability of contamination, and engaging communities to encourage them to have their wells tested, were important topics discussed at the meeting. In North Carolina, citizens can contact their [county health department](#) to request testing.

“This is a beautiful example of how state, federal, and other organizations get together to fill the well of knowledge regarding safe drinking water,” said NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., during her talk. She described the long history of NIEHS in North Carolina, and its mission of advancing science to improve public health.

Birnbaum also discussed NIEHS research on water contaminants, and emerging areas of study, such as climate change and hydraulic fracturing, and the need for chemical testing and development of tools to better understand how contaminants affect health.

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

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## NIH honors nine NIEHS scientists at Director’s Awards ceremony

*By Eddy Ball*

At its annual Director’s Awards ceremony Nov. 17 in Bethesda, Maryland, the National Institutes of Health (NIH) conferred its highest honors on nine outstanding NIEHS scientists (see [sidebar](#)). The nine were among some 850 people recognized for contributions in the fields of biomedical research, administration, mentoring, and clinical care that have served to advance the NIH mission.

The winners from NIEHS included eight scientists from three trans-NIH teams working on gene expression, innovative models of human disease, and promotion of diversity and inclusion in the workforce. Veteran lead researcher Samuel Wilson, M.D., was recognized for his years of mentoring.

NIEHS Senior Medical Advisor Aubrey Miller, M.D., represented the institute, and served as the co-presenter, along with NIH Deputy Director Lawrence Tabak, D.D.S., Ph.D., for awards given to Wilson, and to Kimberly McAllister, Ph.D., and members of the Epigenomics Road Map team.



*For Wilson, this was the second round of celebration for his mentoring award. He was also honored in July (see [story](#)) during a gathering of NIEHS colleagues and trainees. (Photo courtesy of Steve McCaw)*

## Gravitas and levity

Following an introduction by emcee John Burklow, associate director of the NIH Office of Communications and Public Liaison, NIH Director Francis Collins, M.D., Ph.D., delivered opening remarks.

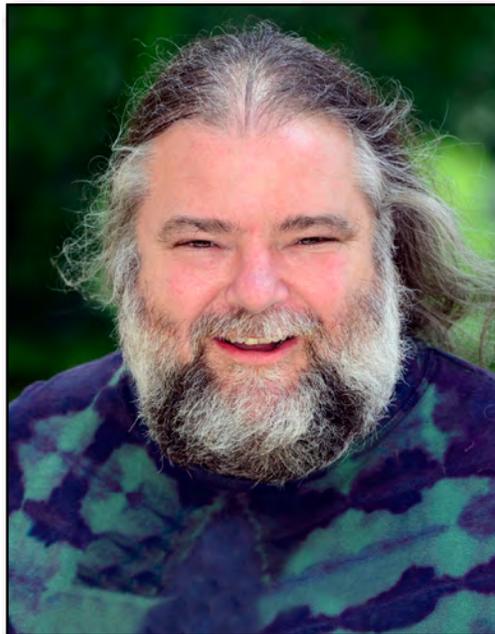
“It’s perfectly fitting today to recognize members of the NIH Ebola response teams,” Collins noted. As with all of the awards, he added, “We’re only scratching the surface [of an organization of outstanding individuals].”

Collins led the audience in a moment of silence to recall those who died Nov. 13 in the terrorist attack in Paris. “We join in solidarity today with all the French people ... and all of those victims of terrorism around the world,” he said, as attendees rose in respect.

During his overview of the many exceptional employees receiving the highest honor NIH has to offer, Collins singled out two people for special mention — Clinical Center receptionist Annie Harrison, for her commitment to the provision of exceptional customer service to guests staying at the Edmond J. Safra Family Lodge; and Kenneth Stith, in posthumous recognition of extraordinary leadership as the NIH Office of Financial Management director and deputy chief financial officer.

## And the NIEHS winners are ...

- **David Balshaw, Ph.D.**, and **Les Reinlib, Ph.D.**, of the NIH Microphysiological Systems (Tissue Chip) Program Team, in recognition of outstanding contributions managing and providing oversight to the Microphysiological Systems Program, recognized worldwide as innovative technology in therapy development and disease modeling.
- **Lisa Chadwick, Ph.D.; Astrid Haugen; Pat Mastin, Ph.D.; Kimberly McAllister, Ph.D.; and Fred Tyson, Ph.D.**, of the NIH Epigenomics Roadmap Program, for exceptional efforts in guiding the Common Fund Epigenomics Program and enhancing community use of the epigenomics resource to support and inspire scientific discoveries worldwide.
- **William (QB) Quattlebaum**, of the Sexual and Gender Minority (SGM) Research Coordinating Committee, for catalyzing the advancement of SGM health research, including the creation of the first NIH SGM Health Research Strategic Plan.
- **Samuel Wilson, M.D.**, with a Ruth L. Kirschstein Mentoring Award, for exemplary performance while demonstrating significant leadership, skill, and ability in serving as a mentor.



*Quattlebaum was recognized for his work advancing initiatives of the NIH Office of Equity, Diversity, and Inclusion. (Photo courtesy of Steve McCaw)*



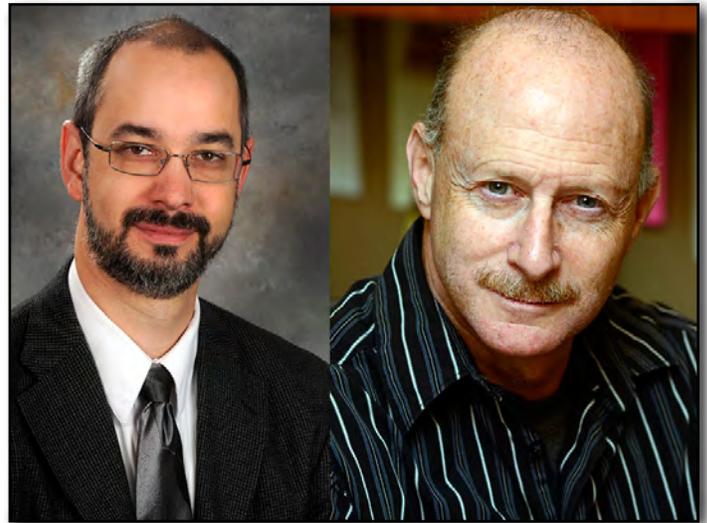
*Chadwick is one of the program directors of the NIH Roadmap Epigenomics Program (see [story](#)), and is one of the scientific contacts for NIEHS-funded epigenetics studies. (Photo courtesy of Steve McCaw)*

Although he was in some pain and discomfort from emergency back surgery the previous week and unable to stay for the rest of the ceremony, Collins, known for breaking out his guitar and singing a song, quipped, “Any threat of a musical outburst from the NIH director has been removed this year.

(Eddy Ball, Ph.D., is a contract writer with the NIEHS Office of Communications and Public Liaison.)



From left, Mastin, Haugen, McAllister, and Tyson administer NIEHS grants in the NIH Epigenomics Roadmap Program. NIEHS is the lead institute for the program. (Photo courtesy of Steve McCaw)



Two NIEHS scientists, Balshaw, left, and Reinlib, administer grants for development of organs and systems on a chip (see [story](#)), as part of the NIH Microphysiological Systems (Tissue Chip) Program Team, led by the National Center for Advancing Translation Sciences. (Photo courtesy of Steve McCaw)

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## Innovative research and collaboration at SRP Annual Meeting

By Sara Mishamandani

The NIEHS Superfund Research Program (SRP) annual meeting brought together SRP researchers, trainees, administrators, and partners to share findings and discuss research translation, community engagement, and training. The theme of the meeting, SRP Collaboration for Innovation, encouraged participants to find ways to work across disciplines and with different SRP grantees and partners from the U.S. Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry.

The meeting Nov 18-20 in San Juan, Puerto Rico, was hosted by the [Puerto Rico Testsite for Exploring Contamination Threats \(PROTECT\) SRP Center](#). The PROTECT Center studies exposure to environmental contaminants and preterm birth in Puerto Rico, which, according to the Centers for Disease Control and Prevention, has one of the highest rates of preterm birth among U.S. states and territories.



Suk discussed the importance of training the next generation of scientists and highlighted several SRP trainee accomplishments from the past year. He emphasized the importance of tackling data challenges and integrating multidisciplinary research. (Photo courtesy of Northeastern University)

SRP Director William Suk, Ph.D., and NIEHS Deputy Director Rick Woychik, Ph.D., kicked off the meeting with opening remarks that emphasized the multidisciplinary nature of SRP. Scientific sessions throughout the meeting included talks by graduate students and postdoctoral researchers. The five 2014 [K. C. Donnelly Externship Award winners](#) described experiences and results from their SRP-funded externships at other SRP centers and federally-supported laboratories.

### **A focus on big data**

NIH Associate Director for Data Science Philip Bourne, Ph.D., was invited to give a talk on big data as a catalyst for collaboration and innovation. He described community, policy, and infrastructure as the three elements of the digital enterprise. Bourne also emphasized the need for sustainability, collaboration, and training when using big data to move biomedical research forward.

Bourne's talk was followed by a session on SRP applications of big data and data science, where six SRP grantees discussed their work related to data management and modeling, reporting exposure data to participants, and developing computational frameworks to better understand biological effects of exposures and susceptibility.

### **Emphasizing the importance of technology advances**

Several scientific sessions featured grantees that are developing technologies and methods to detect and clean up environmental contaminants in the environment. They discussed ways to clean up contaminants, like mercury, and chlorinated compounds, such as trichloroethylene, and how to move their methods into the field. Presentations on detection technologies included identifying contaminants in the environment, such as those in estuaries, as well as measuring biomarkers in humans, such as in blood.

Jeff Heimerman, associate director for the EPA Technology Innovation and Field Services Division, gave a talk on opportunities to support hazardous waste sites with science and technology advances. He discussed considerations that researchers should be aware of in applying their work to the field. According to Heimerman, roughly 51 percent of the U.S. population lives within three miles of a Superfund site, underlining the importance of research related to Superfund contaminants.



*"We are entering a period of disruption in biomedical research and we should all be thinking about what this means," said Bourne. He described the tremendous potential that big data offers and explained the need for new methodologies, skills, and cultures in biomedical research. (Photo courtesy of Northeastern University)*



*Akram Alshawabkeh, Ph.D., professor at Northeastern University and PROTECT Center director, served as the meeting's scientific coordinator. The PROTECT Center involves researchers and staff from Northeastern University, the University of Puerto Rico Medical Sciences Campus, University of Michigan, and University of Puerto Rico at Mayaguez. (Photo courtesy of Northeastern University)*

## Community engagement and building sustainable communities

During the main meeting, speaker Rachel Morello-Frosch, Ph.D., professor at the University of California, Berkeley, discussed her work linking citizen science, or scientific research conducted in whole or part by amateur or nonprofessional scientists, and social equity to advance public health. She described her work with partners to develop the Environmental Justice Screening Method to examine cumulative impacts and social vulnerability within regions in California.

The scientific session that followed featured researchers who are working with communities affected by environmental exposures, such as asbestos, vapor intrusion, and arsenic. They described their work with community members to assess exposure to environmental contaminants, overcome barriers to testing, and identify health effects.

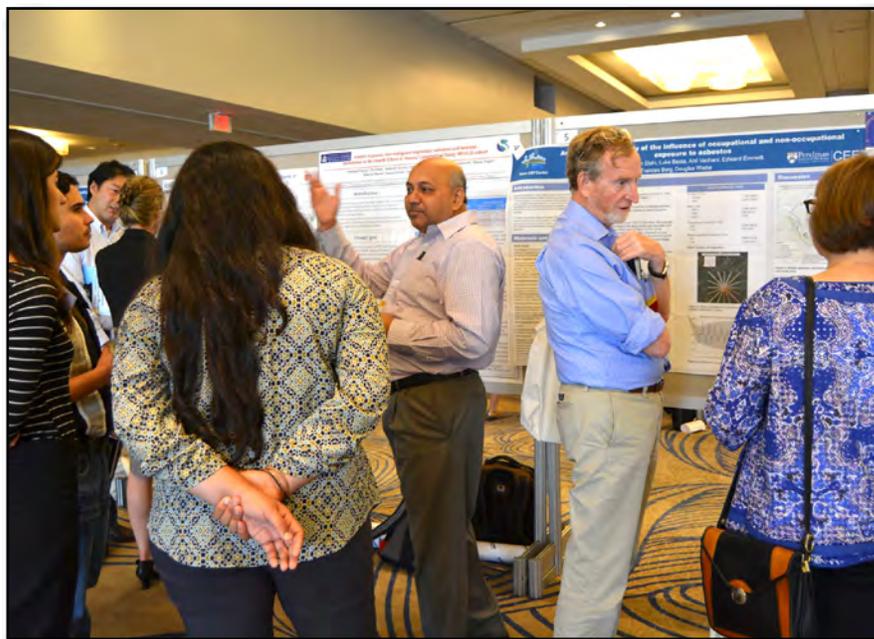
(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)



*Suk, left, congratulated Nishad Jayasundara, Ph.D., the 2015 Karen Wetterhahn Memorial Award winner. Jayasundara, a postdoctoral researcher at Duke University, is the 18th recipient of the award. His research focuses on how rapid and profound changes in the environment affect the health of ecosystems and, in turn, the health and well-being of humans. (Photo courtesy of Northeastern University)*



*Woychik discussed how the SRP aligns well with the NIEHS strategic plan and helps bridge the gap between health research and environmental science research. (Photo courtesy of Northeastern University)*



*Two poster sessions were held after the scientific sessions. The posters exhibited work from grantees all over the country and highlighted collaboration. (Photo courtesy of Northeastern University)*



*Suk, left, posed with the four students who won poster awards. In the environmental sciences and engineering category, the winners were Andrew Cooper, right, from the University of California, San Diego, and Jing Sun, second from left, from Columbia University. In the health sciences category, the winners were Oluwadamilare Adebambo, center, from North Carolina State University and the University of North Carolina at Chapel Hill SRP Center, and William Klaren, second from right, from the University of Iowa. (Photo courtesy of Northeastern University)*



*The PROTECT Research Translation Core and Community Engagement Core held a joint session with SRP trainees focused on environmental contamination in Puerto Rico. The session included a panel, shown above, that shared the diverse perspectives of local community organizations. Using case studies, participants shared challenges the organizations face and brainstormed ways to address them. (Photo courtesy of Northeastern University)*



*In a separate session for trainees, a panel of SRP alumni discussed where they are now and answered questions. From left, Xabier Arzuaga, Ph.D., a University of Kentucky SRP alumnus and EPA toxicologist; Andres Cardenas, Ph.D., a University of Oregon SRP alumnus and Harvard University postdoctoral fellow; Ingrid Padilla, Ph.D., a University of Arizona SRP alumna, professor at the University of Puerto Rico, and PROTECT Center researcher; and Veronica Vieira, D.Sc., a Boston University SRP alumna and professor at the University of California, Irvine. (Photo courtesy of Northeastern University)*



*SRP Research Translation and Community Engagement Cores showcased successes from the year and identified ways centers could collaborate and learn from each other. During the session, participants broke into workgroups to address topics such as evaluating community outreach and research translation activities. (Photo courtesy of Northeastern University)*

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# Duke symposium addresses toxicity of energy production

By Kelly Lenox

Several scientists and grantees from NIEHS participated in the Duke University Integrated Toxicology and Environmental Health Program 2015 fall symposium Nov. 13 in Durham, North Carolina. The event's theme, "The Toxicity of Power," addressed toxicological issues caused by energy production and highlighted ways to reduce public health impacts.

Public health implications of mountaintop coal mining, hydraulic fracturing, mercury emissions from power plants, and wastes from energy production were addressed in morning presentations. The 2010 Deepwater Horizon oil spill was the focus of the afternoon talks.

Power production is associated with environmental health challenges at every stage of the process, according to Ed Levin, Ph.D., a researcher with the [Duke Superfund Research Center's](#) Neural and Behavioral Toxicity Assessment Core. Levin and Richard Di Giulio, Ph.D., director of the Duke Integrated Toxicology and Environmental Health Program, and the Duke Superfund Research Center, hosted the symposium.

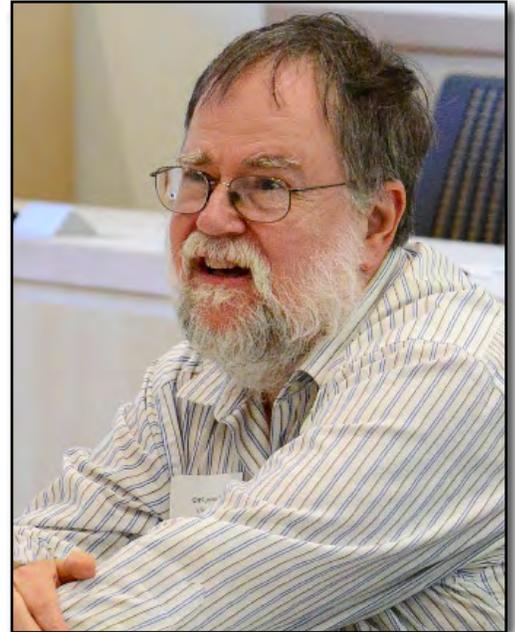
"We wanted to highlight both the threats posed by various types of power exploration and production, as well as ways researchers are finding to reduce health impacts, whether through technology, training and behavior, or policy."

## Worker protection and disaster response

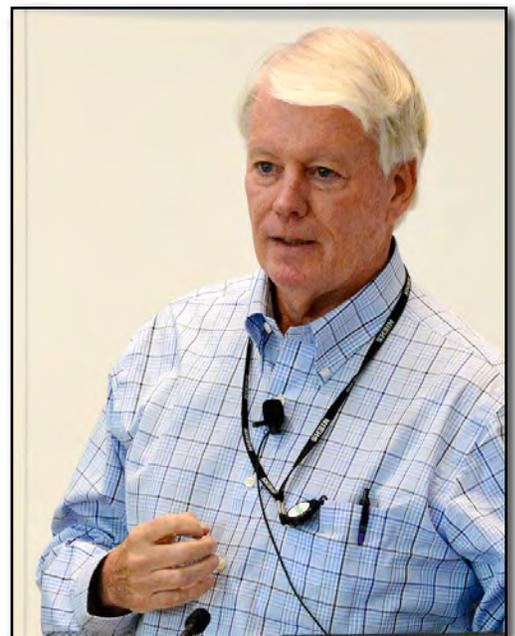
Joseph "Chip" Hughes, director of the NIEHS [Worker Training Program](#), discussed how, in the wake of the devastating Deepwater Horizon oil spill, NIEHS mobilized staff, experts, and grantees to set up training in personal protection for cleanup workers. Building a cadre of Vietnamese, Spanish, and Cajun-speaking instructors was key to the outreach effort. "We distributed more than 35,000 guides in multiple languages," Hughes said.

"We thought about all the types of exposures that might be happening and what medical surveillance should be put in place afterwards," he continued. The effort became the basis for developing a scientific approach to address the health impact of the spill.

Hughes said it also influenced development of the NIH [Disaster Research Response](#) program, to enhance the timely collection of human data during and after disasters.



*Levin is also the head of the Neurobehavioral Research Lab in the Psychiatry Department of Duke University Medical Center. (Photo courtesy of Steve McCaw)*



*Hughes described NIEHS-sponsored tabletop exercises, including a tsunami hitting a California oil refinery, designed to help regional leaders better prepare for scenarios posing environmental health threats. (Photo courtesy of Steve McCaw)*

## GuLF STUDY challenges

The scientific approach Hughes described became the **GuLF STUDY**, an NIEHS effort to assess whether long-term health impacts were associated with working on the oil spill cleanup, according to Richard Kwok, Ph.D., staff scientist in the NIEHS Epidemiology Branch and one of the study's lead researchers.

Scientists were challenged to get the study underway very quickly. "There was no precedent for how do to this study," Kwok said. "The context is unlike a traditional occupational setting, and very few individuals were cleanup workers before the spill." The researchers have now collected health data and exposure information on the more than 32,000 individuals enrolled in the study.

Preliminary results indicate that increased exposure to oil is associated with greater incidence of wheeze. Kwok said there also appears to be an increased prevalence of depression and post-traumatic stress disorder, but work is ongoing to determine whether that can be associated with exposures to the oil and other chemicals, or is a consequence of living through the trauma of the spill.

## Mercury emissions and seafood contamination

Aquatic ecologist Celia Chen, Ph.D., researcher at the NIEHS-funded **Dartmouth Toxic Metals Superfund Research Program**, discussed mercury pollution in coastal and ocean waters, and mercury contamination in aquatic species. She described international efforts to reduce emissions worldwide and shared research indicating that changes in emissions, especially from coal-fired power plants and industrial boilers, are well-correlated with changes mercury concentrations observed in water and fish.

According to Chen, atmospheric sources of mercury will be addressed by national and global policies in the near future, but the effectiveness of these policies needs to be evaluated.



**Linked video:**  
[Watch as Chen and others discuss how mercury builds up in foodchains in this video from Dartmouth College, with funding from NIEHS. \(11:57\)](#)  
(Launches in new window)

Download Media Player:  Flash 

## Generating power and protecting health

Besides Hughes, Kwok, and Chen, other scientists addressed environmental health concerns associated with power generation.

- **Tracy Collier, Ph.D.**, from the University of Washington, presented "Lessons in Toxicity Learned From the Deepwater Horizon Oil Spill."
- **Michael Hendryx, Ph.D.**, from Indiana University, discussed "Mountaintop Mining and Public Health."
- **Heileen Hsu-Kim, Ph.D.**, from Duke University, gave a talk on "Environmental and Human Health Effects of Conventional and Unconventional Energy Exploration: A Comparison of Wastewater From Oil and Gas Production and Coal Ash Disposal."
- **Rob Jackson, Ph.D.**, from Stanford University, presented "The Environmental Implications of Hydraulic Fracturing."



*Kwok said that results of the GuLF STUDY are shared with participants through newsletters and interviews with local media. (Photo courtesy of Steve McCaw)*



*“Mercury pollution is widespread in our coastal and ocean waters, and dominant sources are artisanal-scale gold mining and coal-fired EGUs [electric generating units],” Chen said. (Photo courtesy of Steve McCaw)*



*Kim Gray, Ph.D., left, and Annette Kirshner, Ph.D., center; health scientist administrators in the NIEHS Division of Extramural Research and Training, were among the scientists closely following the talks. (Photo courtesy of Steve McCaw)*



*Collier said there is little evidence of oil exposure in shellfish from spill-affected areas of the Gulf of Mexico. In contrast, in the same area, researchers are documenting more dolphin strandings and decreases in dolphin survival. “This work on cetaceans in the northern Gulf of Mexico is helping us develop our knowledge of the impacts of oil on wildlife,” he said. (Photo courtesy of Steve McCaw)*

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## **NTP highlights new technologies to protect health and environment**

*By Catherine Sprankle*

Twenty National Toxicology Program (NTP) scientists and contractors joined about 300 other researchers to assess how high throughput laboratory methods and big data analysis techniques could be applied to chemical safety testing. A keynote lecture at the meeting focused on using use these approaches to identify endocrine disruptors.

[FutureTox III: Bridges for Translation](#) focused on “Transforming 21st Century Science Into Risk Assessment and Regulatory Decision-making.” The meeting, held Nov. 19-20 in Arlington, Virginia, was the third in a series organized by the Society of Toxicology to bring together a diverse group of stakeholders to consider how new technologies can be applied to protect human health and the environment.



### **New technology to identify endocrine disruptors**

In his keynote address, Jim Jones, U.S. Environmental Protection Agency (EPA) assistant administrator of the Office of Chemical Safety and Pollution Prevention, noted how high throughput screening and computational toxicology tools are used in the [EPA Endocrine Disruptor Screening Program](#) to identify chemicals that could affect the estrogen pathway. He also announced an aggressive timeline to begin use of such tools for androgen pathway testing.

The announcement was met with enthusiasm by attendees, including Nicole Kleinstreuer, Ph.D., senior computational toxicologist for ILS, a contractor supporting the [NTP Interagency Center for the Evaluation of Alternative Toxicological Methods](#) (NICEATM). “It’s exciting to see diverse groups collaborating on projects leading to real progress towards regulatory applications,” she noted. Kleinstreuer, who moderated a breakout group at the meeting, [contributed to developing the testing approaches](#) described by Jones.

### NTP research showcased in poster session

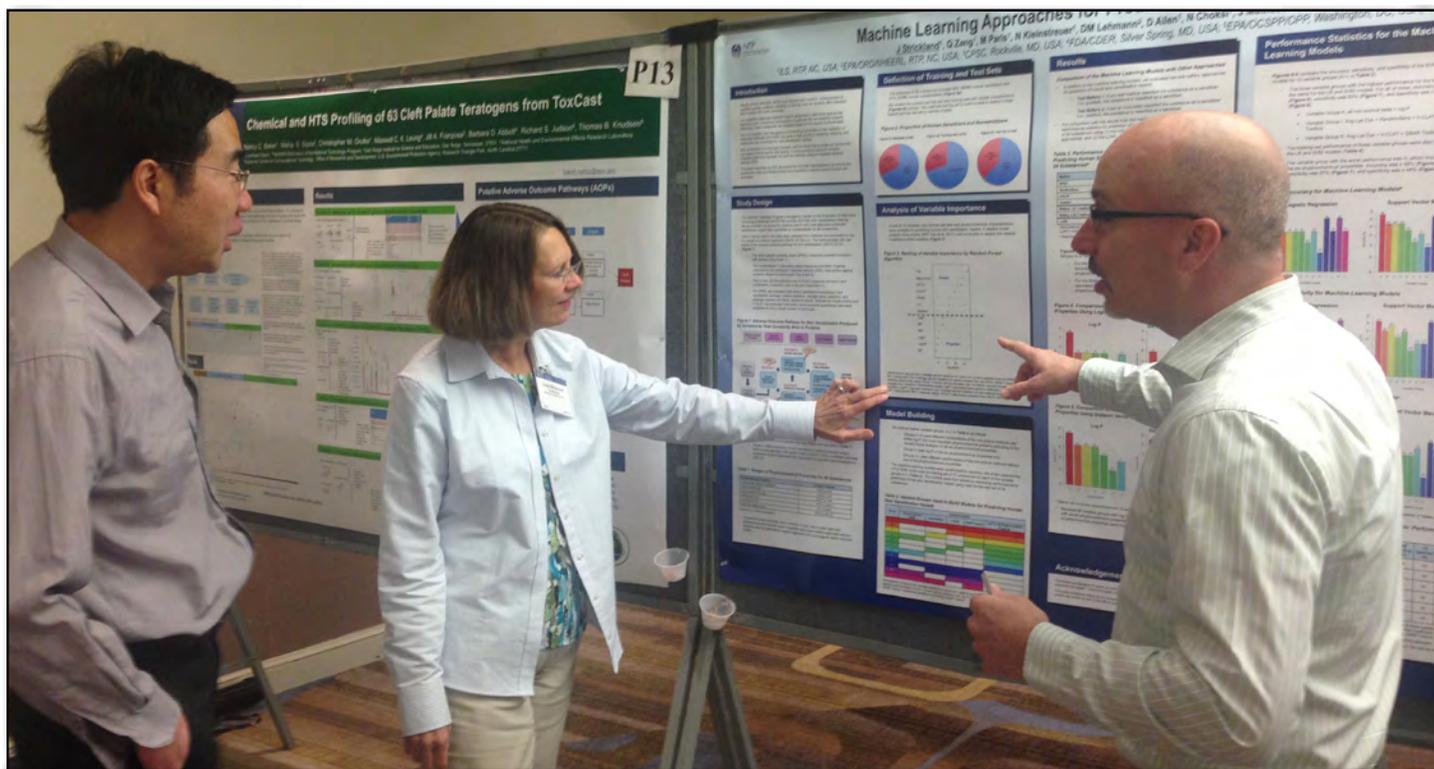
NTP scientists co-authored 15 of the more than 80 posters presented at the meeting’s poster session. Of these, [five focused on NICEATM projects](#) to develop alternative methods for identifying potential endocrine disruptors and skin sensitizers. Other NTP posters described use of high throughput assays and computational approaches applications such as prioritizing compounds for future testing and identifying substances likely to cause DNA damage or birth defects.

Several presentations discussed using high throughput and computational methods to assess toxicity and exposure, as well as the use of such methods by EPA and the U.S. Food and Drug Administration, to regulate labeling and handling of chemicals, drugs, and medical devices.

Four breakout groups considered the regulatory applications of high throughput screening and computational toxicology tools in more detail. The group moderated by Kleinstreuer focused on identification of endocrine disruptors. Other groups considered the topics of drug development, proposals for reform of chemical safety regulation, and issues affecting international trade.

Speakers and moderators at the workshop will co-author a report for publication in 2016.

(Catherine Sprankle, is a communications specialist with ILS, who supports NICEATM.)



*Judy Strickland, Ph.D., center, senior toxicologist from ILS, discussed her poster with John Reichard, Ph.D., right, of the Toxicology Excellence for Risk Assessment Center at the University of Cincinnati, and ILS colleague Qingda Zang, Ph.D. (Photo courtesy of Xiaoqing Chang)*

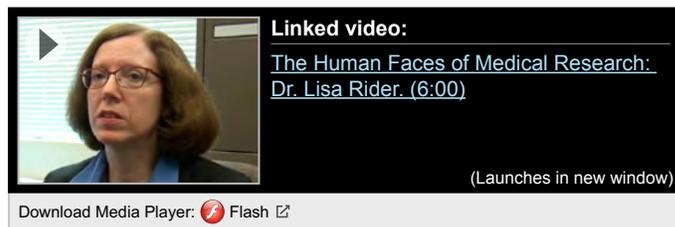
# Clinical Feature

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## LabTV focuses on NIEHS clinical researcher

*By Kelly Lenox*

In late October, Lisa Rider, M.D., deputy chief of the NIEHS Environmental Autoimmunity Group, was featured on LabTV, a video series created by the National Institutes of Health (NIH). The series highlights the biographies and careers of NIH scientists, as a way to interest young people in pursuing careers in biomedical research.



Rider speaks about her studies of myositis, in particular juvenile myositis (JM), a disease characterized by chronic muscle inflammation and weakness. JM includes both juvenile dermatomyositis and the very rare juvenile polymyositis.

In the video, Rider described myositis and how her interest in it developed. She also shared some clinical aspects of her research, as she works with children to follow their JM progression. She is particularly interested in pinpointing environmental and genetic factors that may contribute to the disease.

Rider noted the importance of collaborations with other researchers, within the United States and internationally, in helping to advance the understanding of these rare diseases. Noting that there are currently no approved therapies for JM, she said, "In my lifetime, I'm really hoping we'll have approved treatments."

For those considering a career in research, Rider listed some important steps, including "... getting a solid education and then keeping your mind open to all the opportunities that come through ... always asking questions ... always trying to be on the cutting edge."

The video is currently featured on the NIH Clinical Center [Researcher Stories: Why We Became Scientists](#) page.

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# Science Notebook

## Distinguished lecturer advances nuclear receptor field

By Shannon Whirlledge

As key regulators of hormone action, nuclear receptors are targeted in the treatment of many human diseases. Bert O'Malley, M.D., is a pioneer of nuclear receptor biology, having devoted more than 50 years to the field. He discussed current advances in the understanding of nuclear receptors during a Nov. 10 NIEHS Distinguished Lecture Seminar Series talk titled, "Deciphering the Structure of a Biologically Active Nuclear Receptor-Coactivator Complex on DNA."

### Coactivators hold the key

O'Malley began his seminar by explaining that the key to gene expression comes from the recruitment of coactivators to DNA. Coactivators enhance gene expression by binding to proteins known as transcription factors. O'Malley discovered the first steroid receptor coactivator (SRC-1) in 1995 and has since revolutionized the understanding of how gene expression is regulated.

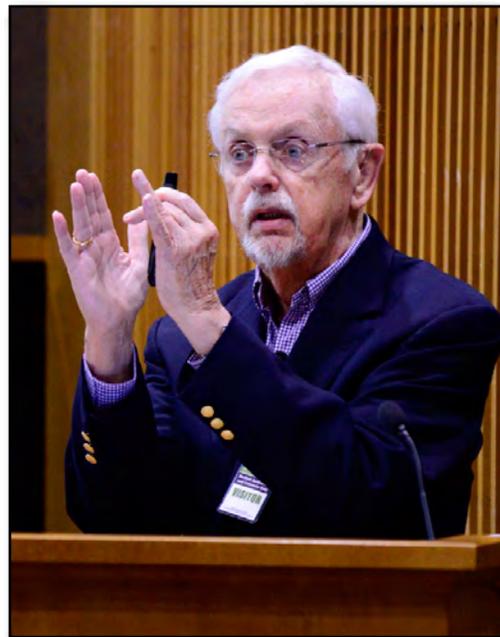
He is currently using new techniques to visualize the recruitment of receptors and coactivators, and the conformational changes, or changes in the structure or shape of a molecule, that occur as gene transcription begins. O'Malley believes that understanding how this process occurs will lead to novel, targeted therapies for cancer. Fellow nuclear receptor researcher Kenneth Korach, Ph.D., chief of the Reproductive and Developmental Biology Laboratory, hosted O'Malley's talk.

### Novel approaches to answer long-standing questions

Nuclear receptors play a major role in determining cell fate by regulating development, differentiation, and maintenance of cells. Scientists have long sought to determine how nuclear receptors bind to coactivators at sites of transcription.

Baylor College of Medicine, where O'Malley is chair of molecular and cellular biology, has one of the select few labs that use cryo-electron microscopy (Cryo-EM), via the lab of [Wah Chiu, Ph.D.](#) Resolving the structure of protein complexes by Cryo-EM, which images frozen samples, is an additive approach.

O'Malley and his group have been able to image each protein alone and then reconstruct each shape as a piece of the protein complex puzzle. He claimed it was entirely a coincidence that the structure of SRC-3 resembles Texas, the state in which it was discovered.



O'Malley completed his training at the University of Pittsburgh and the National Cancer Institute, before heading his own research group at Baylor College of Medicine in Houston, Texas. He was awarded a National Medal of Science in 2007. (Photo courtesy of Steve McCaw)

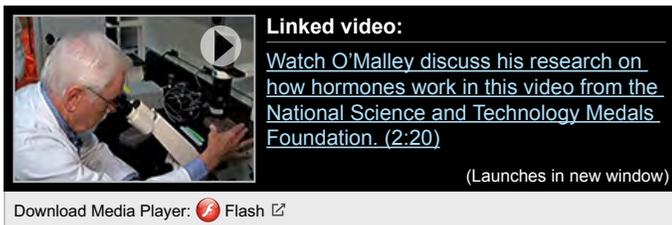


Acknowledging O'Malley's many accomplishments, Korach joked during his introduction that he had never seen a 98-page curriculum vitae. (Photo courtesy of Steve McCaw)

## New insights from unique visualizations

In an approach not possible using conventional techniques, researchers were able to visualize new regions of the estrogen receptor, by further refining the data using antibodies that target specific regions of the protein. With this approach, O'Malley determined that the receptor complex functions as a flexible platform in which coactivator proteins may be exchangeable.

He said that the same approach can be used to determine how protein complex formation changes in the presence of endocrine disruptors, which often have their own unique gene expression signature.



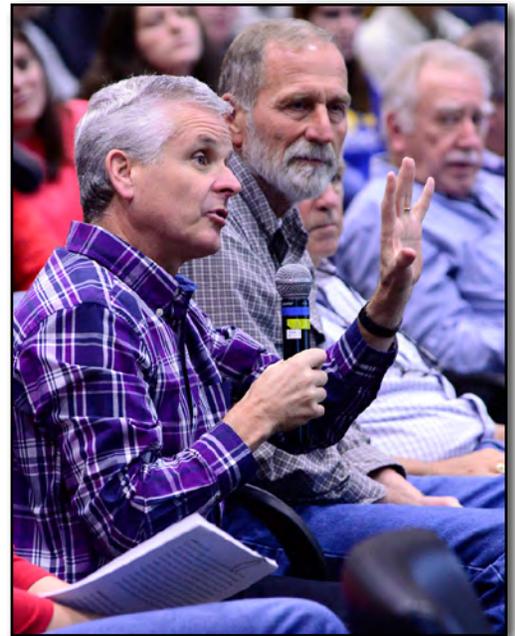
## Mentoring advice from a giant in the field

Following his seminar, O'Malley sat down with NIEHS trainees to discuss their projects and offer advice. He stressed the need to be adaptable in science by illustrating that at the beginning of his career in reproductive biology, the focus in the field was on contraception, but now it is on infertility. "It's the same question, just flip the switch," he said. In addition to being adaptable, O'Malley said researchers need to be aware, investigative, and industrious in finding funding.

O'Malley shared a frank perspective on beginning a tenure-track career. "The good news is you are on your own. The bad news is you are on your own," he said. However, he pointed out that the risk is worth the reward. "Biological research is the best job in the world. There are not many jobs where you don't mind coming home late, working at home, or just thinking about work while away from the job," he said. That passion for research has driven his long and distinguished career.

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

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*Donald McDonnell, Ph.D., left, chairman of the Duke University Department of Pharmacology and Cancer Biology, also studies nuclear receptor signaling and did not miss the opportunity to hear O'Malley's talk. He is seated next to John Cidlowski, Ph.D., head of the NIEHS Signal Transduction Laboratory and lead researcher for the Molecular Endocrinology Group. (Photo courtesy of Steve McCaw)*



*Darryl Zeldin, M.D., right, NIEHS scientific director, looked on as Trevor Archer, Ph.D., left, head of the NIEHS Epigenetics and Stem Cell Biology Laboratory, asked O'Malley about the applications of his discoveries. (Photo courtesy of Steve McCaw)*

# Asian Pacific autism conference includes focus on the environment

By Kelly Lenox

The first regional meeting of the International Society for Autism Research was held Nov. 6-8 in Shanghai. Organized to extend the global reach of the society, it drew more than 700 participants from 31 countries, primarily from Asia and the Pacific region. Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, was invited to give a plenary talk at the meeting. Several NIEHS-funded scientists also participated.

The [Asia Pacific Regional International Meeting for Autism Research](#) brought together health care professionals, researchers studying autism and related conditions, and families of children with autism. Organizers included the Children’s Hospital of Fudan University, Autism Speaks, China Women’s Development Foundation, and Shanghai Disabled Persons’ Federation.

The meeting opened with welcomes from a number of Chinese dignitaries, followed by [Geraldine Dawson, Ph.D.](#), president of the [International Society for Autism Research](#) and a professor at Duke University, who provided opening comments. In a later plenary talk, Dawson presented her research on brain imaging in siblings of children with autism. “The hope is, that by intervening very early in life, the course of early brain and behavioral development can be modified, and the disabling symptoms of autism can be significantly reduced or even prevented,” she wrote in a summary of her talk.

## NIEHS and the role of environmental exposures

Collman’s talk focused on early environmental exposures and the risk of autism spectrum disorders (ASD). She provided research updates on environmental chemicals, such as pesticides, metals, endocrine disrupting chemicals, and air pollution, as risk factors.

Collman also discussed strategies for improving environmental exposure assessments in human studies.



*Collman and Rahbar posed after adding their signatures to those of other attendees at the International Meeting for Autism Research in Shanghai. (Photo courtesy of Gwen Collman)*

## Plenary talks by other researchers

Plenary talks featured researchers from across the globe.

- [Francesca Happe, Ph.D.](#), from King’s College London, provided an overview of current challenges and questions in ASD research.
- [Catherine Lord, Ph.D.](#), from Weill Cornell Medicine, presented findings on early intervention strategies that suggest ASD is both a disorder of learning, as well as of social motivation and processing.
- [Mu-Ming Poo, Ph.D.](#), from the Shanghai Institutes for Biological Sciences, spoke on the China Brain Project and autism.
- [Matthew State, M.D., Ph.D.](#), from the University of California, San Francisco, spoke about the genetics of autism.
- [Helen Tager-Flusberg, Ph.D.](#), from Boston University, discussed strategies for detection and diagnosis of autism, and language development and therapy needs in children and adults with autism.
- [Yi Wang, M.D., Ph.D.](#), from [Children’s Hospital of Fudan University](#) discussed a national epidemiological study of ASD in China.

One such strategy is to use interdisciplinary teams that include members of autism advocacy groups. “These partnerships are important for incorporating the concerns of the affected community and translating the research results back to families of persons with ASD,” she said.

Her presentation was well-received and prompted a number of thoughtful questions from participants of the discussion session. “It was a sophisticated audience and their questions raised important points,” she said. Collman took the opportunity to meet with scientists from the region, answering their questions about how to study environmental exposures in the context of children’s health research.

### Grantees discuss air pollution and gene-environment interactions

A panel on the environment, biomarkers, and risk factors featured two NIEHS-supported researchers, as well as two researchers from Chinese institutions. [Jim Zhang, Ph.D.](#), of Duke University, presented an in-depth analysis of studies linking air pollution exposure and autism risk. He discussed evidence of a causal link and its biological likelihood, and recommended that future studies examine exposure levels, biomarkers, and their relationships with ASD clinical measures.

[Mohammad Rahbar, Ph.D.](#), from the University of Texas Health Science Center at Houston, described results of metal biomonitoring in a case control study of autism he is conducting in Jamaica. Rahbar described an interesting gene-environment interaction between genes involved in the production of glutathione-S-transferases, or GSTs, and blood levels of manganese, a heavy metal, in the children studied. GSTs are a major group of detoxification enzymes, especially involved in removal of heavy metals.



Collman’s talk on the NIEHS mission and research into environmental impacts on public health was translated into Chinese at the fully bilingual event. (Photo courtesy of Gwen Collman)

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# NIEHS Science Days offers insights on inflammation

By Robin Arnette

Inflammation is a protective response the body uses to fight off infection from foreign organisms and to respond to injury caused by the environment. However, when the process persists over a long period of time, illness usually follows.

Attendees at the 2015 NIEHS Science Days were treated to a mini-symposium that discussed connections between inflammation and disease, with insights suggesting that inflammation could be a major player in the origins of certain human diseases.

## The role of cholesterol trafficking

The first speaker was [Michael Fessler, M.D.](#), deputy chief of the NIEHS Immunity, Inflammation, and Disease Laboratory and head of the Clinical Investigation of Host Defense Group. Fessler discussed how oxysterols, an oxidized form of cholesterol, play a role in clearing inflammation in the lungs. He made the case that oxysterols may be important in acute respiratory distress syndrome, a lung condition with a mortality rate of 25 to 40 percent. Patients with this condition require a ventilator to breathe.

Fessler said cells, including macrophages that destroy invading organisms, avoid cholesterol overload by relying on a transporter called ABCG1 to export cholesterol from the cell. The absence of functioning ABCG1 leads to the inability to remove cholesterol, driving macrophages into a hyperinflammatory state and toward cell death.

Research performed by Fessler's group found that an oxysterol, called 25-hydroxycholesterol, activates a protein, named liver X receptor (LXR), that is involved in clearing lung inflammation and promoting cholesterol export from cells. "25-hydroxycholesterol seems to be required to activate anti-inflammatory properties of LXR in the lung," Fessler said.

## Peripheral nerves in environmental sensing

[Sven-Eric Jordt, Ph.D.](#), is interested in how sensory neurons become sensitized during injury and chronic pain conditions, such as inflammation. Jordt is an associate professor in anesthesiology at Duke University School of Medicine and studies transient receptor potential (TRP) channels, a superfamily of proteins involved in the senses of sight, smell, taste, touch, and hearing.

TRPs exist in the trigeminal nerves of the head and connect to the eyes, nose, and mouth. When a person is exposed to an airborne irritant, such as smoke, these nerve endings become excited. TRPs also exist in the dorsal nerves connecting to the skin, where heat and chemical stimuli are sensed.



*Fessler studied a line of mice that lack ABCG1. Their lung cells, which were unable to export cholesterol effectively, were transformed into lipid-laden foam cells, similar to those found in the blood vessels of heart disease patients. (Photo courtesy of Steve McCaw)*



*Jordt said that TRPs allow humans to experience a range of sensations in food. TRPV1 is the receptor for capsaicin, the pungent ingredient in chili peppers. He and others also determined that TRPA1, which is closely related to TRPV1, is the receptor for mustard oil, the ingredient in wasabi and mustard responsible for their intense flavor. (Photo courtesy of Steve McCaw)*

Jordt said that in cases of chemically-induced inflammation, TRPA1 and sensory nerves promote an inflammatory response. His work has demonstrated that the lungs make peptides that rely on sensory nerves to provide biochemical cues.

“Our hypothesis is that inflammation activates pulmonary neuroepithelial cells, so that they produce neural peptides. The sensory neurons become more sensitive to these peptides, inducing coughing and other symptoms during a pulmonary infection from a pathogen that produces the endotoxin lipopolysaccharide,” Jordt said.

### **Fungi are everywhere**

According to [Dori Germolec, Ph.D.](#), head of the Systems Toxicology Group in the Toxicology Branch of the National Toxicology Program, mold spores are ubiquitous and are not a concern in healthy individuals unless they reach extremely high levels.

Germolec studies the inflammatory responses that occur after long-term exposure to the mold *Aspergillus fumigatus*. Colleagues at the National Institute for Occupational Safety and Health in Morgantown, West Virginia built an enclosed exposure system that provides a real-life inhalation exposure scenario. The system, which can be precisely controlled, is used to evaluate potential health effects following mold exposure.

The researchers exposed mice to one of three conditions — an air control, viable spores from *A. fumigatus*, and heat-inactivated spores, which are considered nonviable. They found that nonviable spores generate some inflammatory responses in rodent lungs, but the viable spores produced a much more potent inflammatory response, which appears to be related to spore germination in the lungs. Germolec explained that the life stages of mold are dependent on temperature and humidity, and spore germination can occur when conditions are optimum for growth.

“Everything we’ve looked at indicates that germination is critical to the development of the allergic response in mice,” Germolec said.



*Germolec said natural disasters, such as Hurricane Katrina and Superstorm Sandy, have heightened our awareness about the health impacts from exposure to high levels of mold. (Photo courtesy of Steve McCaw)*



*Block’s research group has shown that protein radicals, reactive oxygen species, and the process of aging each can reprogram mouse microglial cells to be hypersensitive to innocuous stimuli. She is still looking for several specific factors that initiate this reprogramming. (Photo courtesy of Steve McCaw)*

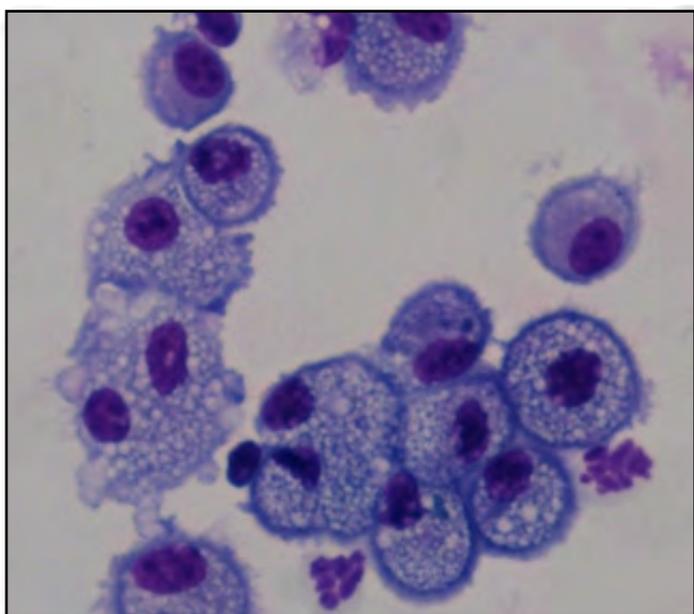
## Neuroinflammation and the aging brain

The NIEHS Science Days committee typically invites a former trainee back to the institute to give a talk, and this year's speaker fit right in with the presentations on inflammation. [Michelle Block, Ph.D.](#), is an associate professor in the Department of Anatomy and Cell Biology at Indiana University School of Medicine. At NIEHS, she worked with [Jau-Shyong \(John\) Hong, Ph.D.](#), in the Neuropharmacology Group.

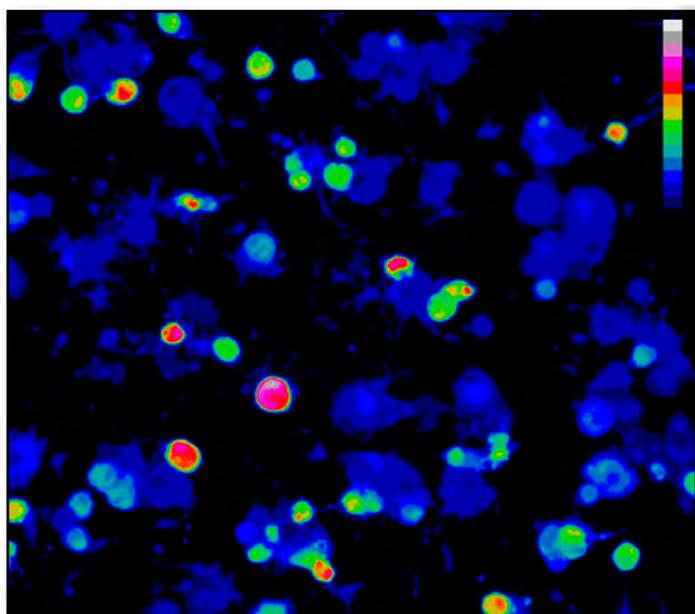
Block explained that microglia, the main immune cells in the brain, act as sentinels that detect and respond to pathogens or environmental toxicants once they reach the brain. However, sometimes microglial cells stop being a neuronal police force, and instead become a source of chronic inflammation and oxidative stress.

Block said the switch is an important one, because neuroinflammation is a common denominator in several central nervous system (CNS) disorders, such as autism, Parkinson's and Alzheimer's diseases, stroke, multiple sclerosis, and traumatic brain injury.

"My obsession with understanding how and why microglia damage brain neurons started when I was at NIEHS," Block said. "We call the process neurotoxic reactive microgliosis, and we believe it underlies the chronic nature of CNS diseases, particularly many of those associated with aging."



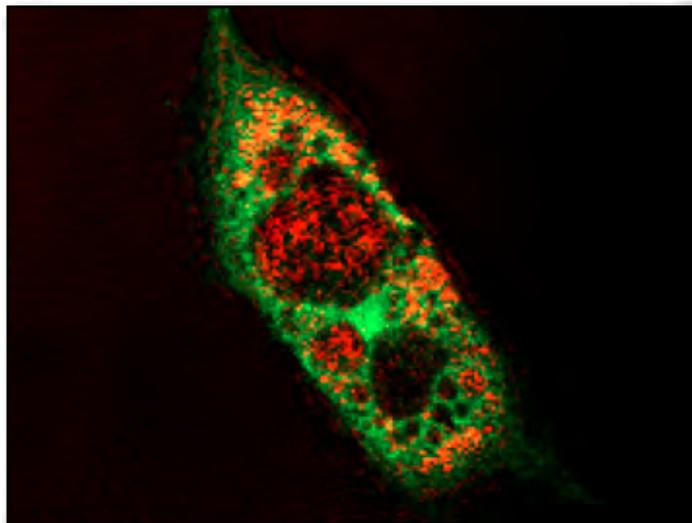
*Fessler's group demonstrated that alveolar macrophages in mice that lack the *Abcg1* gene transform into lipid-laden foam cells. (Photo courtesy of Michael Fessler)*



*Exposure to chlorine gas stimulates TRPs in human trigeminal nerves. As a result, the neurons become activated. In this image, shading from blue to pink corresponds to increasing amounts of calcium uptake, an indicator of cellular activity. (Photo courtesy of Bret Bessac)*



*A house affected by Hurricane Katrina shows contamination with molds, such as *Stachybotrys chartarum*, also known as toxic black mold. Germolec and her colleagues are using their exposure system to test the effects of these spores on mice. (Photo courtesy of Dori Germolec)*



*When a microglial cell is activated by proinflammatory triggers, reactive oxygen species modify the DNA and proteins inside of the cell, forming highly reactive molecules known as radicals. Protein and DNA radicals are shown in red, whereas nitric oxide synthase, an enzyme that produces the signaling molecule nitric oxide, is shown in green. (Photo courtesy of Michelle Block)*

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## Simmons speaks on the origins of obesity

*By Virginia Guidry*

The tendency toward obesity may originate before conception, according to research that Rebecca Simmons, M.D., presented in an Oct. 26 seminar.

“We invited Dr. Simmons to speak because of her expertise in many priority areas for NIEHS, including the developmental origins of adult disease, epigenetics, and obesity,” said Jerry Heindel, Ph.D., NIEHS health scientist administrator and host of the talk. Simmons’ talk, “Programming of Obesity for Life: Is It Over Before Conception?” was part of the Keystone Science Lecture Seminar Series.

According to [Simmons](#), a professor at the Perelman School of Medicine at the University of Pennsylvania, 66 percent of women of reproductive age are overweight and 35 percent are obese. Obesity has been linked to abnormalities in reproduction, such as difficulty getting pregnant, increased rate of miscarriages, and smaller babies than normal. She also cited research showing that obese parents are more likely to have obese children. Simmons and her group are studying when the tendency toward obesity begins.



*“For public health policy, we need to think about counseling girls at a young age to pay attention to their weight, because their weight as it occurs during and after puberty appears to have a profound influence, independent of lifestyle factors, on their offspring,” said Simmons. (Photo courtesy of Steve McCaw)*

## Metabolic changes passed to offspring

Simmons' team showed that mice fed a higher carbohydrate, higher fat Western diet became visibly obese and had abnormal metabolic functioning at the cellular level. The abnormal metabolic profiles observed by the researchers suggested that the diet, which was started immediately after puberty in the mice, triggered oxidative stress and inflammation.

Importantly, the scientists also found that these metabolic changes could be passed down to offspring. The team used metabolomics studies to look at the biochemical differences between Western diet and control diet groups. When mice that were obese from eating the Western diet became pregnant, their embryos showed the same altered biochemical profiles, predisposing the offspring to obesity.

## Preconception environment influences obesity

In their next series of experiments, Simmons' lab found that the tendency toward obesity is influenced by the maternal environment before conception and the environment in the womb.

The scientists saw differences between obese and normal weight mice at several developmental stages. There were noticeable deficiencies in the placentas of obese mice, even very early in pregnancy. They also found that oocytes, or eggs, from obese mice were of lower quality than those from control mice. This has been established by other research, but Simmons' lab demonstrated the presence of important genetic and epigenetic differences that contributed to these changes and enabled them to be passed down to offspring.

“There are multiple windows of exposure that affect developmental programming of adult disease, and these intersect and interact,” Simmons said in summary. “The pregestational environment, the preconception environment, the gestational environment, as well as a period of time during lactation, all interact to produce obesity-related changes in the offspring. It is very important now to recognize that these windows have been pushed back to include preconception.”

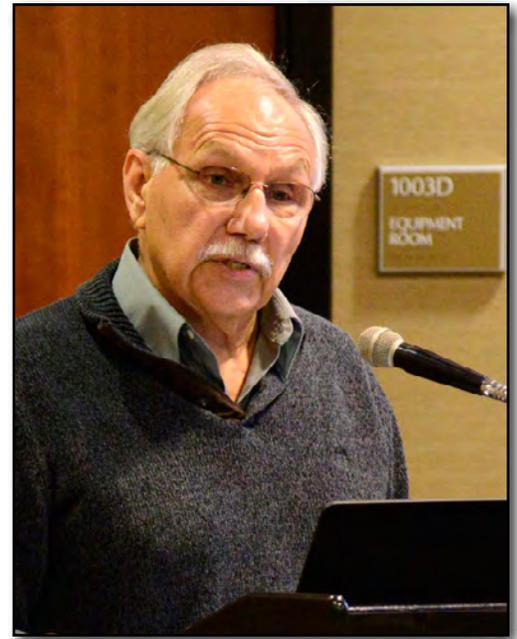
(Virginia Guidry, Ph.D., is a technical writer and public information specialist in the NIEHS Office of Communications and Public Liaison.)

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## 3-D print fest inspires innovation at NIEHS

*By Kelly Lenox*

People from all divisions of NIEHS flocked to an Oct. 22-23 showcase of 3-D print technology. Transforming Your Science: Innovations with 3-D Printing featured representatives from the National Institute of Allergy and Infectious Diseases (NIAID), which leads development of the National Institutes of Health (NIH) 3D Print Exchange, local universities, and Betabox Labs, a Raleigh company with a mobile prototyping lab.



*Heindel noted that Simmons' research is related to the second goal of the NIEHS strategic plan, regarding key windows of susceptibility to environmental factors. "Her presentation and visits with staff will help us consider potential research funding in these areas," he said. (Photo courtesy of Steve McCaw)*

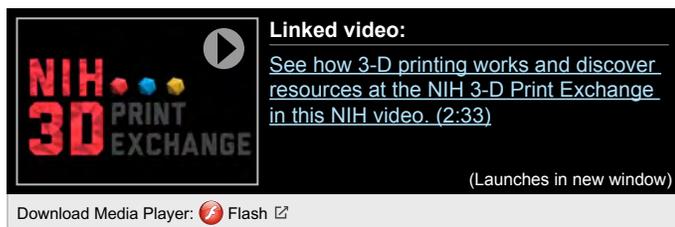
Gary Bird, Ph.D., staff scientist in the NIEHS Calcium Regulation Group, co-hosted the event with NIEHS data scientist Rebecca Boyles, reference librarian Sandra Chambers, and Geoffrey Mueller, Ph.D., staff scientist with the Nuclear Magnetic Resonance Group.

“The ideas and capability behind 3-D printing can be harnessed to create and support a vast range of applications,” Bird said. “From custom-fit lab equipment to molecular modeling, or even print your own liver, the possibilities are limitless.”

### “Changing the way that we think”

Representatives from the [NIH 3D Print Exchange](#) described the center resources, and advances NIH researchers have made using the technology. Darrell Hurt, Ph.D., head of the Bioinformatics and Computational Biosciences Branch in the NIAID Office of Cyber Infrastructure and Computational Biology, said that researchers studying the influenza virus had worked with online visual models. But upon examining a physical model, they gained a powerful insight into how it binds with other molecules.

“It’s not about the 3-D printing,” Hurt emphasized. “It’s about changing the way that we think and work to take advantage of technology, to make life easier and work more efficient.”



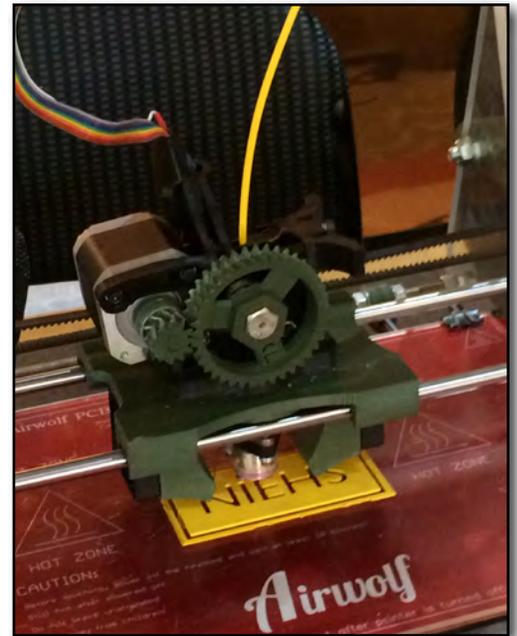
3-D printers feed material — plastics, calcium carbonate, silver, and even cells suspended in a gel — through a nozzle that applies it in a process similar to inkjet printing. Design software directs the nozzle to make repeated passes, building a three-dimensional structure. “It’s a robotic hot glue gun,” Hurt quipped.

### From information to inspiration

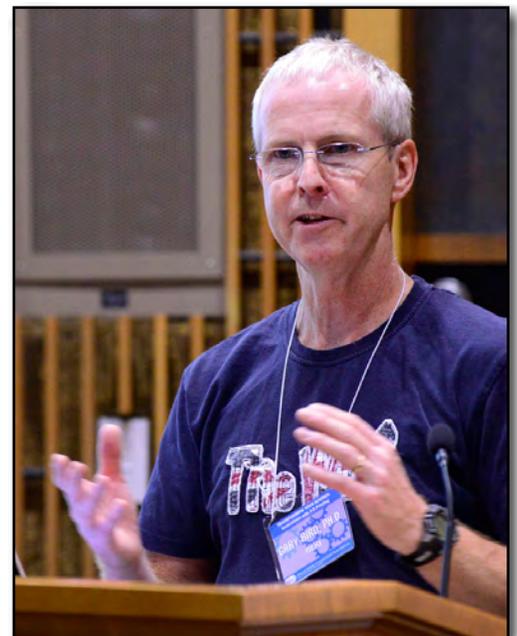
Researchers and staff from North Carolina State University (NCSSU) and the University of North Carolina at Chapel Hill (UNC) shared diverse applications of 3-D printing, such as animal prostheses and models that simulate movement of blood through a tumor.

BetaBox, a mobile prototyping lab provided by [BetaBox Labs](#), allowed NIEHS participants to brainstorm problems and design solutions on the spot. Several prototypes were produced on site, including a clamp that serves as a one-handed lid opener, and goggles to protect the eyes of mice during exposure to ultraviolet light.

Print designs generated during the event were uploaded by Mueller to the NIH 3D Print Exchange website and are publicly available.



*An NIH demonstration machine printed out an NIEHS plaque in less than an hour. (Photo courtesy of Kelly Lenox)*



*“The dynamics of the groups working in the BetaBox are fascinating,” said Bird during the event. “The groups are mixed [from different labs and divisions], so there is cross-pollination going on. That is key to the creative dynamic.” (Photo courtesy of Steve McCaw)*

## Easily accessible and low cost

The NIH 3D Print Exchange includes a virtual collection of scientific and biomedical 3-D models, as well as printing tutorials. It also offers tools to upload data from public databases — such as the molecular structure of a protein — and convert it to a 3-D print design.

“It’s really very easy to use the online software,” Hurt said. “For a protein structure, you type in the [primary database] accession code, wait two minutes, and you’ve got your model design.”

The exchange does not do the printing. Hurt said the technology is developing so fast that many users, rather than investing in machinery, prefer to send designs to a commercial printer, much like the way one uploads photo files to a site for printing.

## A resource for NIEHS

“We have to figure out what the resource is going to look like here at NIEHS,” Chambers said. “We held this event to make people aware of what is available now.” She created an internal wiki site to help NIEHS staff explore 3-D printing.

“I’d like to see a space where people can gather and brainstorm to create and learn — our very own NIEHS makerspace — but what should it look like here?” asked Bird. Makerspaces at UNC and NCSU are generally housed in libraries and provide a variety of resources, including 3-D printers, software, machine tools, electronics, and hardware supplies.



*From right, Tracy Clement, Ph.D., from the NIEHS Reproductive and Developmental Biology Lab, along with Patricia Lamb and JuHee Haam, Ph.D., both from the Neurobiology Lab, talk with NIH representatives about their 3-D printed objects, from bone models made with calcium carbonate, to models of organisms responsible for infectious diseases. (Photo courtesy of Steve McCaw)*



*Hurt, shown above, quoted NIH Director Francis Collins, M.D., Ph.D., who said, “We hope that 3-D printing machines will expand interest and participation in this new and exciting field among scientists, educators, and students, including people at the NIH.” (Photo courtesy of Steve McCaw)*



*A simulated tumor made from paper and wax intrigued Humphrey Yao, Ph.D., center, from the NIEHS Reproductive and Developmental Biology Lab, and Chip Romeo, Ph.D., right, director of the NIEHS Viral Vector Core Lab, who learned more about it from a UNC representative, left. (Photo courtesy of Steve McCaw)*



*Michael Hobgood, left, Betaversity chief design officer, and Meredith Ingrassia (not shown), program director, led prototyping sessions in the BetaBox. The laptop is sitting on a stand made onsite using a laser cutter. (Photo courtesy of Kelly Lenox)*



*The printer is completing a device designed by one of the NIEHS groups to enable six test tubes to be filled at the same time from a single beaker. The large green piece was designed to hold vacuum tubing on a lab bench. The small collar will allow pipetting the contents of the tubing. (Photo courtesy of Kelly Lenox)*

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## Genetics society celebrates history and prepares scientists for the future

*By Kelly Lenox*

The [Genetics and Environmental Mutagenesis Society](#) (GEMS) held its 33rd annual fall meeting, The Impact of Environmental Exposures on Genomic Health Across Generations, Oct. 28 in Research Triangle Park, North Carolina. The event looked forward, with trainees presenting posters and talks, as well as back, by honoring two founding members with lifetime achievement awards.

NIEHS and National Toxicology Program (NTP) scientists from across the institute, many of whom have been longtime members of GEMS, participated as invited speakers, poster presenters, and attendees. This year's president-elect [Stephanie Smith-Roe, Ph.D.](#), is a genetic toxicologist in the NTP Biomolecular Screening Branch.

### Focus on mutagenesis

One of the inspirations for establishing the society in 1982 was to enable junior scientists who study mutagenesis, or changes to genetic information that result in a mutation, to interact with more seasoned researchers, said Tom Hughes, of the U.S. Environmental Protection Agency (EPA).

Hughes and David DeMarini, Ph.D., also of EPA, were presented with lifetime achievement awards by Channa Keshava, Ph.D., GEMS president and EPA senior scientist. Among their achievements, Keshava noted DeMarini's success in attracting early-career scientists, from a variety of organizations, to the society.

As a local society focused on mutagenesis, the group is unique in the United States. "We have academic, industry, and government scientists — a broad spectrum," Smith-Roe said. In her opening remarks, she underlined the excellence of the local scientific community, citing the high quality of the abstracts submitted by trainees.

### Talks, posters, and awards

Meeting planners invited three senior researchers and an assistant professor to discuss their work (see [text box](#)), including [Carole Yauk, Ph.D.](#), head of the genomics laboratory for Health Canada. Her long list of achievements includes a 2006 Health Canada Most Promising Scientist award.

Yauk uses next-generation approaches to measure mutagenesis in germ cells, or egg and sperm cells. Each germ cell contains only one set of chromosomes — half the number of chromosomes in somatic cells, or all other cells in the body. Yauk's findings showed that benzo[a]pyrene, an environmental contaminant, causes germ cell mutagenesis. Exposure produced different kinds of mutations in germ cells than it did in somatic cells, and the mutations suggested that exposure to benzo[a]pyrene could have a significant impact on disease burden in future generations.

Another invited speaker was NIEHS Deputy Director Rick Woychik, Ph.D., who heads the [Mammalian Genome Group](#). His talk examined how repetitive elements, once referred to as junk DNA, or DNA believed to be non-functional, may influence gene expression in a variety of ways.

Talks by the invited speakers were complemented by presentations by four trainees, including two from NIEHS. The Best Talk award went to Jose Zavala, Ph.D., a postdoctoral fellow at the EPA National Health and Environmental Effects Research Laboratory. The award provides travel funding to attend the 2016 national meeting of the [Environmental Mutagenesis and Genomics Society](#) (EMGS). Smith-Roe noted that his award is partially funded by a generous gift from Hughes and the EMGS Emerging Scientist Award.



From left, Keshava, Hughes, DeMarini, and Smith-Roe celebrated the lifetime achievements of those who helped found the unique organization. "I appreciate the collegiality and friendship that GEMS has helped foster among so many of us," DeMarini said. (Photograph courtesy of Steve McCaw)



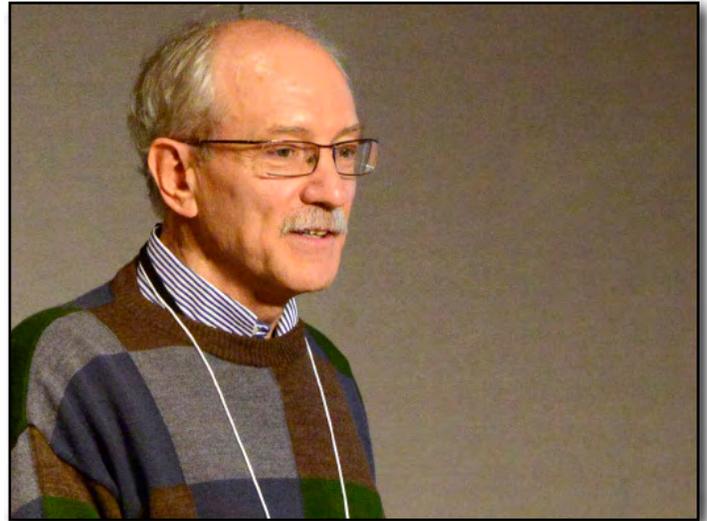
Yauk said prenatal exposures should be studied more in regulatory genetic toxicology, because they happen during a highly sensitive developmental window. "Our group is working internationally ... towards the long-term objective of developing a stronger regulatory paradigm to identify and assess germ cell mutagens," she said. (Photo courtesy of Steve McCaw)

Of the dozen or so posters on display, three won cash prizes from the Burroughs Wellcome Fund. First place went to NIEHS visiting predoctoral fellow Alisa Suen, who works in the [NIEHS Reproductive Medicine Group](#) under Carmen Williams, M.D., Ph.D. Suen is currently a Ph.D. candidate at the University of North Carolina at Chapel Hill (UNC).

Zachary Messenger, a graduate student in the North Carolina State University (NCSU) toxicology program, won second place. Third place went to Maureen Pittman, a UNC undergraduate studying environmental sciences and quantitative biology.



*UNC assistant professor Ideraabdullah also works at the UNC Nutrition Research Institute in Kannapolis, North Carolina. Her talk focused on epigenetics as the interface between genetics and the environment in influencing health outcomes. "I'm very interested in the different nutritional requirements of different individuals, and the role of genetics in that," she said. (Photo courtesy of Steve McCaw)*



*Woychik noted the abundance of the repetitive elements in the genome, as well as the difficulty of studying them. "I hope to convince you today that if you don't pay attention to these repetitive elements, you're potentially missing a major component of the biology within the cell," he said. (Photo courtesy of Steve McCaw)*



*Zavala, left, winner of the Best Talk Award, shared a light moment with his mentor, DeMarini. Zavala's findings suggest that the mutagenic effects of smog are due less to the individual components of smog, such as particulate matter, ozone, and nitrous oxides, and more to the hundreds of products formed when ultraviolet light interacts with those components. (Photo courtesy of Steve McCaw)*



*First place poster prize winner Suen, center, talked with attendees about her findings that indicate uterine expression of the transcription factor SIX1 is a biomarker for exposure and disease. SIX1 may also play a role in the development of uterine cancer in both mice and women. Suen shared her work in September at the National Institutes of Health Research Festival (see [related story](#)). (Photo courtesy of Steve McCaw)*



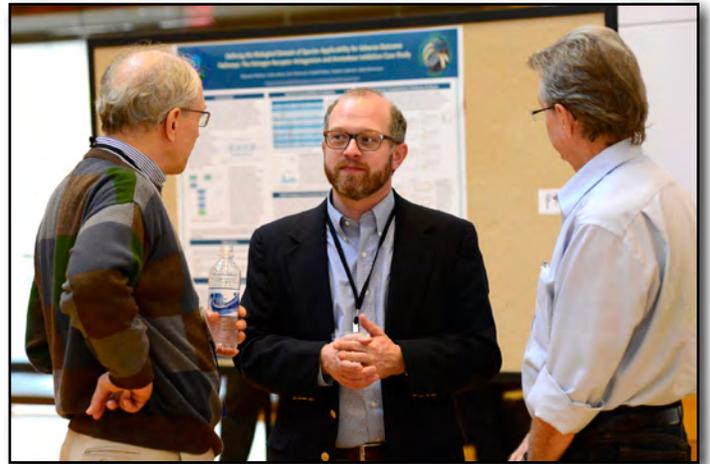
*Doug Bell, Ph.D., head of the NIEHS Environmental Genomics Group, took an avid interest in the proceedings. NIEHS fellows Su and Wan, who gave talks, both work in his lab, as does GEMS councilor Michelle Campbell. (Photo courtesy of Steve McCaw)*



*NTP toxicologist Kristine Witt, center, talked with retired NTP toxicologist Barbara Shane, Ph.D., left, and Smith-Roe, who said Witt is a dedicated champion of GEMS. Shane is secretary of the Environmental Mutagenesis and Genomics Society. (Photo courtesy of Steve McCaw)*



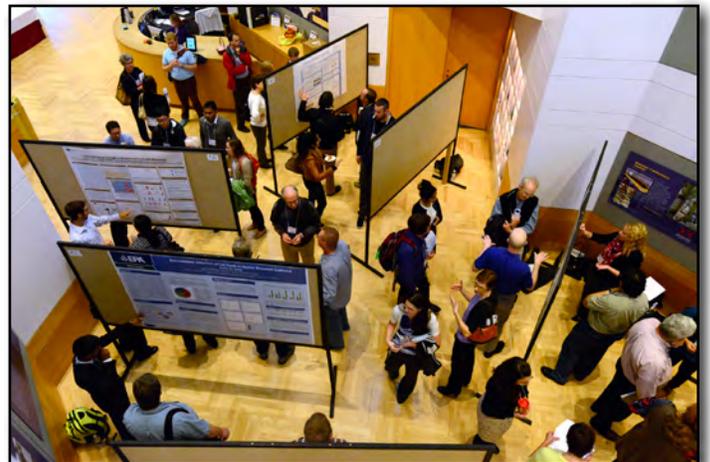
*Chuan Gao, a graduate student at Wake Forest University, conferred with Yauk during a break, in an example of the collaboration between junior and senior researchers that characterizes GEMS. (Photo courtesy of Steve McCaw)*



*NCSU assistant professor David Aylor, Ph.D., center, shown here with Woychik, left, and retired NIEHS researcher Jef French, Ph.D., runs a relatively new lab specializing in mouse genomics, hybrid sterility, and stem cells. (Photo courtesy of Steve McCaw)*



*As one of the founders of GEMS, Hughes, left, has a lot of society history to share with incoming president-elect Brian Chorley, Ph.D., from EPA. Chorley was a postdoctoral fellow at NIEHS. (Photo courtesy of Steve McCaw)*



*Attendees flocked to the poster session in the atrium of the North Carolina Center for Biotechnology where the meeting was held. (Photo courtesy of Steve McCaw)*

## GEMS Fall Meeting talks

The meeting featured presentations by four invited speakers, as well as four postdoctoral researchers.

**David DeMarini, Ph.D.**, from EPA — “Are There Human Germ-Cell Mutagens? We May Know Soon”

**Carole Yauk, Ph.D.**, from Health Canada — “The Future of the Future: Next-Generation Analyses of Germ Cells to Protect the Next Generation”

**Richard Woychik, Ph.D.**, from NIEHS — “The Broad Impact of Repetitive Elements on Protein Coding Gene Expression in the Brain and Other Tissues”

**Folami Ideraabdullah Ph.D.**, from UNC — “Dissecting Mechanisms of Epigenetic Inheritance Using Mouse Models”

## Trainee Presentations

**Jenna Currier, Ph.D.**, from EPA — “What’s in a Tipping Point? Using Systems Biology to Characterize Adverse Oxidative Responses in Human Lung Cells”

**Dan Su, Ph.D.**, from NIEHS — “Tobacco Smoke-associated DNA Methylation and Gene Transcription in Human Blood Cell Lineages”

**Ma Wan, M.D., Ph.D.**, from NIEHS — “Genome-wide DNA Methylation Changes Link Cigarette Smoke to Atherosclerosis in Human Circulating Monocytes”

**Jose Zavala, Ph.D.**, from EPA, winner of the Best Talk Award — “Two Simulated-Smog Atmospheres with Different Chemical Compositions Produce Contrasting Mutagenicity in Salmonella”

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## Toxicologists explore mouse versus man, award postdoc researchers

*By John Yewell*

The North Carolina chapter of the Society of Toxicology (NCSOT) held its annual fall meeting Oct. 29 at NIEHS. This year’s theme was “Mouse vs. Man: Where the Differences and Similarities Lie in Today’s Toxicological Research.”

NCSOT President MaryJane Selgrade, Ph.D., opened the meeting with the presentation of the 2015 President’s Award for Research Competition (PARC). “We try to promote activities for students and postdocs that will benefit their careers,” said Selgrade, technical director at ICF International.

“The quality and relevance of the work done by postdoctoral fellows in the local area is evident by the three-way tie we had for third place,” said NIEHS health scientist administrator Danielle, Carlin, Ph.D., vice president of NCSOT and an organizer of the event. “It’s a great showing this year.”

## First place for NTP postdoc

First place was awarded to Ntube Olive Ngalame, Ph.D., a postdoctoral fellow in the Stem Cell Toxicology Group of the National Toxicology Program (NTP). Her work focuses on the carcinogenic effects of inorganic compounds on stem cells, and the microenvironment.

“Olive is a highly-motivated and innovative postdoc and we are very fortunate to have her in our group,” said lead researcher Erik Tokar, Ph.D. “She has a bright future ahead of her.” As part of the PARC, Ngalame received a cash award and the opportunity to present her research at the meeting.

## Differences in human and mouse models of toxicity

Organizers invited three guest speakers to the event, each of whom addressed the differences between human and mouse responses in toxicological research.

David Threadgill, Ph.D., director of the Whole Systems Genomic Initiative at Texas A&M University, spoke on population-based animal models. Threadgill uses the Collaborative Cross mouse as a genetic model to understand individual differences in cancer susceptibility and the role of genetic variation in response to environmental stimuli.

“We’re on the verge of rethinking how we do a lot of experimental work,” he said. “What we can do in the lab that we can’t do in humans is actually distinguish how much of that susceptibility was the environment and how much of it was genetic.”

Beverly Koller, Ph.D., associate professor in the Department of Genetics at the University of North Carolina at Chapel Hill (UNC) School of Medicine takes a different approach to using mice to research human disease. Koller’s talk, “Humanization of Mouse Metabolic Pathways: Increasing the Translational Value of Rodent Toxicological Screens,” explored the use of human genes in mice to achieve a pattern of gene expression that more closely matches that of humans.

The third speaker was Brian Bennett, Ph.D., assistant professor in the Department of Genetics at UNC, who discussed “Differences Between the Man and Mouse Microbiomes.” Bennett’s current research focuses on the genetic components of chronic metabolic diseases.

(John Yewell is a contract writer for the NIEHS Office of Communications and Public Liaison.)



*Selgrade is also the former head of the Cardiopulmonary and Immunotoxicology Branch at the U.S. Environmental Protection Agency. (Photo courtesy of Steve McCaw)*



*“The mouse population actually matches the variance in human populations very nicely,” said Threadgill. “There are cases where they will conform to human biology in situations where we can’t do the studies in humans.” (Photo courtesy of Steve McCaw)*



*Bennett, left, is also on the faculty of the UNC Nutrition Research Institute. His work includes research on systems genetics, cardiovascular disease, and nutrigenomics. Koller, center, said that her research is yielding human gene function in the liver, kidney, and lung. (Photo courtesy of Steve McCaw)*



*The five award winners took a break from the proceedings to pose for a photo with Selgrade. From left are Ngalame, Catlin, Selgrade, Makia, Achanta, and Sollome. (Photo courtesy of Steve McCaw)*

## 2015 PARC winners

**First place** — Ngalame submitted the winning abstract, “Molecular characterization of exosomes released by arsenic-malignantly transformed prostate epithelial cells and their potential role in the recruitment of nearby, but noncontiguous normal stem cells into an oncogenic phenotype.”

**Second place** — James Sollome, Ph.D., postdoctoral fellow at UNC working with Rebecca Fry, Ph.D., secured second place with his abstract on “Environmental contaminants and microRNA regulation: transcription factors as master regulators of toxicant-altered microRNA expression.”

**Third place, three-way tie** —

- Natasha Catlin, Ph.D., Intramural Research Training Award fellow in the NTP Developmental and Reproductive Toxicology Group, led by Barry McIntyre, Ph.D., tied for third with her abstract on “*In utero* exposure to the dietary supplement vinpocetine is associated with rat and rabbit embryo-fetal toxicity.”
- Satya Achanta, D.V.M., Ph.D., postdoctoral research associate at Duke University in the lab of Sven-Eric Jordt, Ph.D., submitted his winning abstract on “TRPV4 inhibitor improves pulmonary function and oxygen saturation in a pig translational model of chemically induced acute lung injury.”
- Ngome Makia, Ph.D., visiting postdoctoral fellow in Tokar’s group, won with his abstract on “Cadmium and arsenic transformed human peripheral lung cells expressing CD34 display stem cell-like and malignant properties.”

# Quist wins young investigator award

By John Yewell

NIEHS postdoctoral fellow Erin Quist, D.V.M., has added to her growing list of awards and official recognitions, winning first place in the Young Investigator in Toxicologic and Industrial Pathology competition. The award was presented at the October combined meeting of the Society of Toxicologic Pathology, American Society of Veterinary Clinical Pathology, and American College of Veterinary Pathologists (ACVP) in Minneapolis.

Quist is an Intramural Research and Training Award fellow in the National Toxicology Program (NTP). She works in the Reproductive Endocrinology Group, led by Sue Fenton, Ph.D., and is also a member of the NTP Pathology Group, headed by David Malarkey, D.V.M., Ph.D. Quist is pursuing a Ph.D. from North Carolina State University (NCSU).

“I have nominated her for every postdoc and graduate student award that she is qualified for,” said Fenton. “She certainly deserves the awards she has received. Erin has a lot of positive energy and works hard on her projects.” Quist was the [winner of the Roger O. McClellan Student Award](#) at the March meeting of the Society of Toxicology, and the society recently honored her with a travel support award to attend the society’s 2016 meeting.

## Searching out mechanisms of PFOA liver toxicity

Quist’s winning poster, “Potential modes of action for perfluorooctanoic acid (PFOA)-induced hepatocellular hypertrophy in mice,” described progress on her Ph.D. research. “I am looking at a developmental toxicity model of prenatal PFOA exposure, using a mouse model,” she explained. PFOA is used as a stain repellent, flame retardant, lubricant, and is in many other products.

“In the livers of prenatally exposed mice, we see hepatocellular hypertrophy, which can lead to tumor development, and we are seeing it as early as 21 days old,” she explained. “I am looking for a mechanism that might drive that response, and it looks like mitochondrial proliferation plays an important role. That hasn’t been described before. But I haven’t connected all the dots yet.”

## Collaboration at NIEHS and beyond

Quist’s association with NIEHS began during a 2010 visit when she met Malarkey, who encouraged her to pursue her Ph.D. in the NCSU Comparative Biomedical Sciences program.



*In their poster, Quist and colleagues wrote that low doses of PFOA induced significant alterations in genomic expression patterns of prenatally exposed mice. The alterations affected key proteins involved in lipid metabolism, cellular proliferation pathways, and mitochondrial function. (Photo courtesy of Steve McCaw)*



*Fenton’s group focuses on the developmental impacts of numerous environmental chemicals. (Photo courtesy of Steve McCaw)*

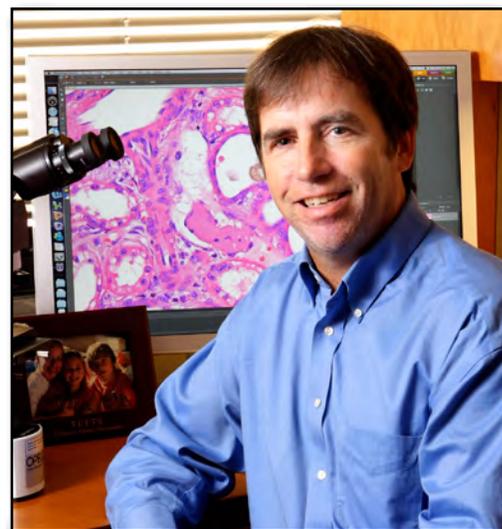
“Erin is a star in our [toxicological pathology training program](#) and has taken full advantage of the opportunities at both NIEHS and NCSU to develop into an ACVP-certified veterinary pathologist, a researcher, and collaborator,” Malarkey said. “She is also conscientious where others are concerned and is the one of the first to volunteer to organize a holiday or birthday party.”

Reflecting on her experience at NIEHS, Quist said, “One of the things I love about NIEHS is that the environment feels like a family dynamic. We are a really collaborative, collegial bunch. I love it.”

Quist is preparing to defend her dissertation in April 2016. After that, she would like to stay at NIEHS. Eventually Quist would like to return to academia.

(John Yewell is a contract writer for the NIEHS Office of Communications and Public Liaison.)

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*Malarkey's group supports NTP and NIEHS researchers, and oversees pathology-related issues in rodent toxicology and carcinogenesis studies. (Photo courtesy of Steve McCaw)*

## This month in EHP

The December issue of [Environmental Health Perspectives](#) (EHP) highlights the decline of fruit trees in Africa, and the need for greater racial diversity in health studies.

### **Africa's Indigenous Fruit Trees: A Blessing in Decline**

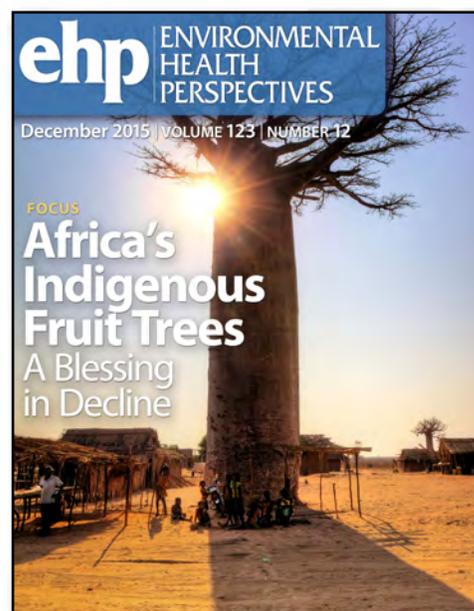
The indigenous fruits of sub-Saharan Africa, including baobab, desert date, black plum, and native varieties of mango, have long provided essential nutrients and other ecosystem services, including soil stability and carbon storage. Farmers have never needed to cultivate these once-bountiful wild trees. But as the trees' natural habitats are lost, questions arise over where they will grow in the future and whether they will continue to provide the same wide range of benefits.

### **Racial Disparities in Research Studies: The Challenge of Creating More Diverse Cohorts**

Minority populations are more likely to deal with pollution, poor housing, and certain other environmental factors than their white counterparts, yet are much less likely to be included in studies on environmentally related diseases that disproportionately affect minority communities. A failure to create more racially diverse research cohorts, some experts say, could worsen existing health disparities.



<http://twitter.com/ehponline>



## Research summaries featured this month include:

- **Unexpected Activity: Evidence for Obesogenicity of BPA Metabolite** — A new study indicates that the metabolite beta-D-glucuronide, like its parent compound bisphenol A (BPA), can induce pre-adipocytes to develop into mature fat cells.
- **Low-Dose BPA and DNA Damage: Examining Mechanisms of Action** — Previous studies have connected BPA exposure to molecular events in breast cells that are characteristic of cancer development. New research implicates a gene involved earlier in the molecular pathway than earlier studies have shown.
- **Identifying Potential Breast Carcinogens: A New Approach** — A team of researchers used a novel framework to identify appropriate tests for disease-specific chemical risk assessment. They worked backward from a specific health outcome — in this case, breast cancer — through its associated biological mechanisms, to determine the right test.
- **Folic Acid and Reduced Blood Arsenic: Nutritional Remediation for a Toxic Exposure?** — Researchers report that folic acid supplementation is associated with reduced average blood arsenic levels in Bangladeshi residents who drank arsenic-contaminated water.

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## Extramural papers of the month

*By Nancy Lamontagne*

- [Green office environments linked with higher cognitive function](#)
- [Lead exposure can cause multigenerational epigenetic changes](#)
- [Maternal and fetal exposure to parabens](#)
- [Prenatal exposure to PBDEs associated with later attention problems](#)

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

## Green office environments linked with higher cognitive function

People who work in well-ventilated offices with below-average levels of indoor pollutants and carbon dioxide showed significantly higher cognitive functioning scores than those working in offices with typical levels, according to a new study funded in part by NIEHS. The findings suggest that improving air quality could greatly increase the cognitive performance of workers.

The double-blind study included architects, designers, programmers, engineers, creative marketing professionals, and managers who worked in a controlled office environment for six days. Participants performed their normal work while exposed to one of four simulated building conditions per day. The indoor environmental quality conditions were conventional, with relatively high concentrations of volatile organic compounds (VOCs), green conditions with low VOC concentrations, green conditions with enhanced ventilation, and conditions with artificially elevated levels of carbon dioxide, independent of ventilation. At the end of each day, participants underwent cognitive testing.

On average, cognitive scores were 61 percent higher on days the participants experienced green conditions with low VOC concentrations and 101 percent higher on the days they experienced green conditions with enhanced ventilation, compared with the conventional building day (p less than 0.0001). VOCs and carbon dioxide were independently associated with cognitive scores. The researchers, who measured nine types of cognitive function, found that the green conditions with low VOCs and green conditions with enhanced ventilation showed the largest improvements in the areas of crisis response, strategy, and information usage.

*Citation:* [Allen JG](#), [MacNaughton P](#), [Satish U](#), [Santanam S](#), [Vallarino J](#), [Spengler JD](#). 2015. Associations of cognitive function scores with carbon dioxide, ventilation, and volatile organic compound exposures in office workers: a controlled exposure study of green and conventional office environments. *Environ Health Perspect*; doi:10.1289/ehp.1510037 [Online 26 October 2015].

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## Lead exposure can cause multigenerational epigenetic changes

An NIEHS-funded study showed that high neonatal blood levels of lead in mothers — indicating that the mothers experienced lead exposure themselves while in the womb — can cause epigenetic changes in their unborn children. This study is one of the first to show that an environmental exposure in pregnant mothers can have an epigenetic effect on DNA methylation in their grandchildren.

Epigenetic changes, such as DNA methylation, are chemical modifications that change how DNA is expressed without altering the genetic code. For this study, researchers measured methylation at more than 450,000 DNA locations, or loci, as well as lead levels in blood and neonatal dried blood spots in 35 mother-infant pairs. The samples came from the Michigan Neonatal Biobank, which contains most of the neonatal dried blood spots from children born in Michigan since 1984.

The researchers found that mothers whose own neonatal blood spots showed high lead levels were correlated with DNA methylation changes at 564 loci in their children's neonatal blood. These results suggest that lead exposure during pregnancy affects the DNA methylation status of the fetal germ cells, which leads to altered DNA methylation in grandchildren's neonatal dried blood spots. The study also showed that the altered DNA methylation status detected in the grandchildren's blood is apparently normalized during postnatal development.

*Citation:* [Sen A](#), [Heredia N](#), [Senut MC](#), [Land S](#), [Hollocher K](#), [Lu X](#), [Dereski MO](#), [Ruden DM](#). 2015. Multigenerational epigenetic inheritance in humans: DNA methylation changes associated with maternal exposure to lead can be transmitted to the grandchildren. *Sci Rep* 5:14466.

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## Maternal and fetal exposure to parabens

An NIEHS grantee and colleagues report that paraben exposure varies greatly among communities and countries, as well as by individual paraben. The new study emphasizes the need to monitor exposure to parabens as individual chemicals and at a community level.

Parabens, which are used as preservatives in personal care products, pharmaceuticals, and some foods, have been shown to act as endocrine disruptors in animal studies. The researchers investigated exposure using 181 maternal urine and 38 umbilical cord blood plasma samples from 185 pregnant women, predominantly of Caribbean- and African-American descent, in Brooklyn, New York. They examined exposure to methyl- (MePB), ethyl- (EtPB), propyl- (PrPB), butyl- (BuPB), and benzylparaben.

Compared to levels reported for the general U.S. population, the study group showed a 4.4 times higher median concentration for MePB and 8.7 times higher concentration for PrPB. The researchers detected MePB in 97.4 percent of the cord blood plasma samples. Upon comparing their findings to data for other communities and countries, the researchers found that the Brooklyn study participants ranked the highest in the world for MePB and PrPB exposure in pregnant women, whereas they ranked among the lowest for EtPB and BuPB.

The authors said that future work should examine the cultural- and country-specific factors that may be responsible for the substantial differences observed between communities and countries, both in the spectrum and degree of paraben exposures.

*Citation:* [Pycke BF](#), [Geer LA](#), [Dalloul M](#), [Abulafia O](#), [Halden RU](#). 2015. Maternal and fetal exposure to parabens in a multiethnic urban U.S. population. *Environ Int* 84:193-200.

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## **Prenatal exposure to PBDEs associated with later attention problems**

NIEHS grantees reported that prenatal exposure to polybrominated diphenyl ethers (PBDEs), which are used as flame retardants, are associated with attention problems in children 3 to 7 years old. This is one of the first studies to examine prenatal PBDE exposure effects on both preschool and school age development.

Researchers followed 210 mother-child pairs from birth through early childhood. This cohort showed cord plasma PBDE concentrations consistent with exposure levels detected elsewhere in the United States. The researchers used cord blood samples to assess prenatal exposure to PBDEs and then assessed child behavior yearly from age 3 to 7 years using a standardized rating scale.

The researchers detected four types of PBDEs in more than half of the samples, with BDE-47 showing the highest concentrations. After adjusting for factors associated with PBDE exposure levels or neurodevelopment in other studies, the researchers observed an association between childhood attention problems and increasing levels of blood plasma concentrations of BDE-47, -99, -100, and -153, for ages 3, 4, and 7 years. The authors stated the behavior instrument used might not effectively capture behavior patterns at ages 5 and 6 years because the test transitions from a preschool- to school-aged version at those ages.

*Citation:* [Cowell WJ](#), [Lederman SA](#), [Sjodin A](#), [Jones R](#), [Wang S](#), [Perera FP](#), [Wang R](#), [Rauh VA](#), [Herbstman JB](#). 2015. Prenatal exposure to polybrominated diphenyl ethers and child attention problems at 3–7 years. *Neurotoxicol Teratol*; doi:10.1016/j.ntt.2015.08.009 [Online 5 Sept. 2015]

(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 Robert Brown, John House, Mahita Kadmiel, Emily Mesev, and Qing Xu

- NTP finds toxicity associated with organophosphorus flame retardants
- High resolution structure of the APE1-DNA complex
- Role of a T-type Ca<sup>2+</sup> channel in fertility
- Mechanism of nuclear uptake of a DNA repair scaffold protein revealed
- Refined mining of GWAS data reveals new insights into airway disease

## NTP finds toxicity associated with organophosphorus flame retardants

A team led by National Toxicology Program scientists found that many organophosphorus flame retardants (OPFRs) might pose health hazards similar to those from brominated flame retardants (BFRs). Manufacturers are turning away from the latter, because of their toxicity and environmental persistence. This study suggests that many OPFRs might have comparable toxicity and must be further evaluated if they are to be considered safe replacements.

OPFRs share structural similarities with organophosphate insecticides, which raise concerns about their effects in the human body. Researchers in this study used cell-based *in vitro* assays and *in vivo* model systems using lower organisms, such as the zebrafish and the roundworm *C. elegans*. They evaluated the potential for developmental toxicity and neurotoxicity among eight OPFRs, covering a wide range of structures, and compared their activities with two well-characterized BFRs, tetrabromobisphenol A and tetrabromodiphenyl ether.

Assays revealed that exposure to many OPFRs caused adverse effects at equal or greater potency than BFRs. For example, many of the compounds led to developmental deaths and malformation of zebrafish embryos; decreased growth and larval development in *C. elegans*; decreased proliferation of human neuroprogenitor cells and decreased neurite outgrowth in human neurons; and decreased spontaneous electrical firing in primary rat neuronal cells.

However, not all OPFRs were active in the assays used to test these chemicals. Notably, tris(2-chloroethyl) phosphate was negative for activity up to the maximum concentration tested. These findings suggest that OPFRs differ in their health effects and lays the groundwork for further characterization of these compounds. **(EM)**

*Citation:* Behl M, Hsieh JH, Shafer TJ, Mundy WR, Rice JR, Boyd WA, Freedman JH, Hunter ES 3rd, Jarema K, Padilla S, Tice RR. 2015. Use of alternative assays to identify and prioritize organophosphorus flame retardants for potential developmental and neurotoxicity. *Neurotoxicol Teratol*; doi:10.1016/j.ntt.2015.09.003 [Online 16 September 2015].

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## High resolution structure of the APE1-DNA complex

Using X-ray crystallography, NIEHS researchers have generated a molecular snapshot that shows how noncoding DNA apurinic-apyrimidinic (AP) sites are recognized and cleaved by AP endonuclease 1 (APE1), an enzyme involved in DNA base excision repair. Since the expression of APE1 is increased in some aggressive tumors, the findings may provide insights into targeting APE1 for cancer treatment.

AP sites are DNA locations without a purine or a pyrimidine. They frequently occur in cells either spontaneously or from oxidative DNA damage. APE1 prepares the DNA lesions to be patched by DNA polymerases, by incising, or nicking, the AP sites. Previous studies provided limited information about the nicking process, but in this study, the researchers identified the molecular features that contribute to APE1 cleavage.

By characterizing the crystallized structure of the APE1-DNA complex, the researchers determined the metal-binding site that stabilized the complex, the water molecule that acted as the donor of electrons required for DNA strand incision, and the arginine sites that facilitated DNA binding. More importantly, they found that a thymine-guanine (T-G) mispair, which often arose from methylated CpG islands within mammalian promoters, distorted the neighboring AP site and reduced the activity of APE1. These results imply a crucial role of APE1 in DNA repair and genome stability. **(QX)**

*Citation:* [Freudenthal BD](#), [Beard WA](#), [Cuneo MJ](#), [Dyrkheeva NS](#), [Wilson SH](#). 2015. Capturing snapshots of APE1 processing DNA damage. *Nat Struct Mol Biol* 22(11):924-931.

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## Role of a T-type Ca<sup>2+</sup> channel in fertility

NIEHS scientists and their collaborators were the first to demonstrate that the T-type Ca<sup>2+</sup> channel CaV3.2 has an essential role in oocyte maturation and embryonic development in mice. Ca<sup>2+</sup> acts as an important second messenger during oocyte maturation, fertilization, and embryonic development for mammals. Prior to this report, the ion channels responsible for the fertilization-induced influx of Ca<sup>2+</sup> were entirely unknown.

To demonstrate the importance of CaV3.2 for Ca<sup>2+</sup> homeostasis in the oocyte and fertilized egg, researchers used genetically modified mice, as well as pharmacological inhibitors that target the CaV3.2 Ca<sup>2+</sup> channel. These studies revealed that a loss of CaV3.2 function resulted in oocytes with reduced cellular stores of Ca<sup>2+</sup> and fertilized eggs with less Ca<sup>2+</sup> response. Not only do these findings document an important and previously unrecognized function of a T-type channel, but they also have further implications for infertile couples, because the therapeutic use of Ca<sup>2+</sup> channel blockers in women could negatively impact fertility. **(RB)**

*Citation:* [Bernhardt ML](#), [Zhang Y](#), [Erxleben CF](#), [Padilla-Banks E](#), [McDonough CE](#), [Miao YL](#), [Armstrong DL](#), [Williams CJ](#). 2015. CaV3.2 T-type channels mediate Ca<sup>2+</sup> entry during oocyte maturation and following fertilization. *J Cell Sci*; doi:10.1242/jcs.180026 [Online 19 October 2015].

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# Mechanism of nuclear uptake of a DNA repair scaffold protein revealed

NIEHS scientists used X-ray crystallography to identify and characterize the nuclear localization signal (NLS) of XRCC1, a scaffold protein involved in DNA repair. Cooperative binding of the NLS major and minor motifs helps explain how it meets the inherently conflicting requirements of high affinity and high flux that are needed for efficient nuclear import.

Due to the complexity of DNA damage, repair often requires involvement of several repair enzymes, which bind to a scaffold protein such as XRCC1. The XRCC1 protein enters the nucleus due to its NLS and also co-transport other repair enzymes, such as DNA ligase 3-alpha. Classical nuclear import involves binding of the XRCC1 NLS to Importin alpha, enabling it to translocate into the nucleus.

In addition to X-ray crystallography, the authors used fluorescence imaging and peptide binding assays to show that certain regions in the NLS sequence major and minor motifs were critical for efficient nuclear import of XRCC1. The researchers also suggested a model in which partial dissociation of XRCC1 NLS from Importin alpha facilitates unloading of the XRCC1 cargo from Importin alpha, allowing other proteins to bind. This action allows a more efficient nuclear transport system. **(MK)**

*Citation:* Kirby TW, Gassman NR, Smith CE, Pedersen LC, Gabel SA, Sobhany M, Wilson SH, London RE. 2015. Nuclear localization of the DNA repair scaffold XRCC1: uncovering the functional role of a bipartite NLS. *Sci Rep* 5:13405.

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# Refined mining of GWAS data reveals new insights into airway disease

Genome-wide association studies (GWAS) for pulmonary function and airway obstruction have identified numerous associated single nucleotide polymorphisms (SNPs). Yet, combined, these SNPs explain a small fraction of the variability seen. To utilize the oft-ignored information in GWAS from SNPs with moderate association, the researchers combined GWAS data with gene-ontology (GO) methodology. They analyzed discovery and replication meta-GWAS data sets for pulmonary function, to identify 131 overlapping enriched gene sets. These gene-enrichment sets mapped to distinct biological modules, such as development, cell adhesion, cell migration, tissue remodeling, and immunity, and surprisingly, were driven by SNPs below genome-wide significance thresholds.

They next analyzed airflow obstruction with a combined GWAS data set to reveal, as expected, significant overlap with lung function GO categories, as well as new GO categories, including extracellular matrix (ECM) remodeling, collagen processing, and integrins. Further analysis of the ECM module revealed MMP10 as a candidate for follow-up, and subsequent work in a mouse emphysematous smoking model demonstrated the module's involvement in the pathogenesis of cigarette smoke-induced airway disease.

This work provides a novel way to use information below significance thresholds, usually discarded from GWAS, to gain additional understanding of critical biological processes involved in the pathogenesis of complex traits. **(JH)**

*Citation:* Gharib SA, Loth DW, Soler Artigas M, Birkland TP, Wilk JB, Wain LV, Brody JA, Obeidat M, Hancock DB, Tang W, Rawal R, Boezen HM, Imboden M, Huffman JE, Lahousse L, Alves AC, Manichaikul A, Hui J, Morrison AC, Ramasamy A, Smith AV, Gudnason V, Surakka I, Vitart V, Evans DM, Strachan DP, Deary IJ, Hofman A, Glaser S, Wilson JF, North KE, Zhao JH, Heckbert SR, Jarvis DL, Probst-Hensch N, Schulz H, Barr RG, Jarvelin MR, O'Connor GT, Kahonen M, Cassano PA, Hysi PG, Dupuis J, Hayward C, Psaty BM, Hall IP, Parks WC, Tobin MD, London SJ, CHARGE Consortium, SpiroMeta Consortium. 2015. Integrative pathway genomics of lung function and airflow obstruction. *Hum Mol Genet* 24(23):6836-6848.

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# Inside the Institute

## NIEHS staff cleans up local highway

By Ian Thomas

NIEHS employees celebrated America Recycles Day Nov. 4 by picking up trash from a 1.2-mile stretch of Hopson Road in Research Triangle Park, bordering the institute campus. The lunchtime outing was part of the North Carolina [Adopt-A-Highway Program](#), a long-standing effort to reduce litter on local roadsides and preserve the natural beauty of the Tar Heel State.

“NIEHS has been involved with the Adopt-A-Highway program for nearly twenty years, and I’m proud to say it’s one our people take very seriously,” said NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., one of ten employees to brave the rain and muddy conditions. “Come rain or shine, they always show up, and as legacies go, that’s a great one to have in our community.”

Established in 1988 as a response to growing concerns from local citizens about litter, the Adopt-A-Highway Program volunteers include representatives from government and private-sector entities across the state.

“Our team gathered everything from soda cans to hot dog wrappers, and even an old sweatshirt from the roadside today,” said Paul Johnson, co-chair of the NIEHS Environmental Awareness Advisory Committee and an organizer of the cleanup. “We do this every year. I only wish we could do it more often.”

[America Recycles Day](#) is an initiative of Keep America Beautiful. It is the only nationally recognized day of events dedicated to promoting recycling.

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



Popovich, left, and Rice share trash and recycling bags.  
(Photo courtesy of Steve McCaw)

### Fall 2015 NIEHS Adopt-A-Highway participants

**Linda Birnbaum, Ph.D.** — NIEHS and National Toxicology Program Director

**Laura Hall** — NTP Program Operations Branch

**Maggie Humble** — NIEHS Genomic Integrity and Structural Biology Laboratory

**Cindy Innes** — NIEHS Clinical Research Branch

**Paul Johnson** — NIEHS Health and Safety Branch

**Nicole Popovich** — NIEHS Division of Extramural Research and Training

**Bill Steinmetz** — NIEHS Health and Safety Branch

**Ian Thomas** — NIEHS Office of Communications and Public Liaison

**Julie Rice** — NTP Laboratory



Johnson, left, and Steinmetz go deep into the brush after trash. (Photo courtesy of Steve McCaw)



Humble, left, and Birnbaum make a final pass over Hopson Road for loose trash. (Photo courtesy of Steve McCaw)



From left, Rice, Innes, Birnbaum, Humble, Popovich, Steinmetz, Thomas, and Johnson show off the fruits of their labors. (Photo courtesy of Steve McCaw)



Birnbaum celebrates another successful cleanup. (Photo courtesy of Steve McCaw)

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