

October 2015

## NIEHS Spotlight



### [Nadadur serves in India as first NIEHS U.S. Embassy Science Fellow](#)

Sri Nadadur, Ph.D., an expert on health effects of air pollution, arrived in New Delhi Aug. 25 as the first U.S. Embassy Science Fellow from NIEHS.



### [SRP researchers quickly inform communities near Colorado mine spill](#)

University of Arizona Superfund Research Program scientists provided prompt public information after the recent Gold King Mine Spill.



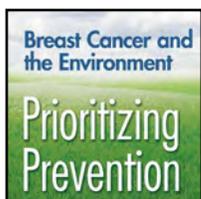
### [Trainees honored during NIEHS Postdoc Appreciation Week](#)

NIEHS celebrated the invaluable contributions of its trainees, with workshops, a trivia game, and activities in individual labs.



### [Council meeting addresses NIEHS and NIH developments](#)

The National Advisory Environmental Health Sciences Council heard new developments at NIEHS and NIH.



### [October is Breast Cancer Awareness Month](#)

In recognition of Breast Cancer Awareness month, NIEHS joins U.S. efforts to raise awareness and highlight research to help fight the disease.

## Clinical Feature



### [Lasker Scholar joins NIEHS](#)

Natalie Shaw, M.D., brings her study of the influences on pubertal development to NIEHS as a Lasker Clinical Research Scholar.

## Science Notebook



### [DeMayo named deputy chief of NIEHS lab](#)

Francesco DeMayo, Ph.D., is the new deputy chief of the NIEHS Reproductive and Developmental Biology Lab and leads the Pregnancy and Reproduction Group.



### [Mutations in mitochondrial DNA lead to disease](#)

Doug Wallace, Ph.D., discussed his theory that many illnesses may result from mutations in mitochondrial DNA, in his September Distinguished Lecture.



### [Advisory committee on alternatives to animal testing looks forward](#)

At its yearly meeting, the Scientific Advisory Committee on Alternative Toxicological Methods discussed recent progress toward alternatives to animal testing.

## NIEHS Spotlight



### [NIEHS trainee begins career in product development](#)

In June, Monica Frazier, Ph.D., began a new career with Rho, Inc., a North Carolina contract research organization.



### [Green Champion awards recognize NIEHS achievements](#)

The Department of Health and Human Services recognized two NIEHS groups with Green Champions awards for promoting sustainable operations.

## Science Notebook



### [New children's health research projects funded by NIH](#)

New National Institutes of Health funding will support research on how environmental exposures affect a child's health and development.



### [NIEHS leads at international epidemiology conference](#)

NIEHS scientists and grantees made key contributions at the 27th annual International Society for Environmental Epidemiology meeting in Brazil.



### [NIH Research Festival celebrates wealth of scientific pursuits](#)

The three-day event in September celebrated research across the institutes and centers that make up the National Institutes of Health.



### [Climate change and environmental exposures challenge announced](#)

NIEHS has challenged innovators to develop tools decision-makers can use to prepare for potential health risks posed by climate change.



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

The October issue of Environmental Health Perspectives explores environmental influences on children's health.

## Inside the Institute



### [Employees' years of service celebrated](#)

The institute's annual Years of Service ceremony recognized 48 employees, commemorating career milestones of 10, 20, 30, and 40 years, and 14 retirees.



### [NIEHS launches 2015 charity drive](#)

You Can Change a Life is the theme of this year's Combined Federal Campaign, which NIEHS launched Sept. 18 with presentations and a bake sale.

## Extramural Research

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

- Researchers pinpoint how mutation increases autism risk
- Lung effects from Deepwater Horizon oil burning
- BPA can adversely affect parenting behavior in mice
- Warmer days may mean more emergency visits and deaths among all ages

## Intramural Research

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

- NTP contributes to the 1000 Genomes High-Throughput Screening Study
- Elevated endotoxin in house dust increases the risk of wheeze
- Enzyme responsible for majority of mutations in certain cancers identified
- Prenatal arsenic exposure induces early onset of puberty and obesity in CD-1 mice
- Crystallography reveals new mechanism of action for polymerase mu

## Calendar of Upcoming Events

- **Oct. 2 (off-site event)**, Duke University Environmental Hall, noon – 1:20 p.m. — Duke University Integrated Toxicology and Environmental Health Program (ITEHP) Fall 2015 Seminar Series presents Vanessa Fitsanakis, Ph.D., from King University, discussing “*C. elegans* Treated With the Glyphosate-containing Herbicide TouchDown Show Mitochondrial Inhibition and Elevated ROS”
- **Oct. 7 (webinar)**, 11:00 a.m. – noon — The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods and the Environmental Protection Agency sponsoring “*In Vitro* to *In Vivo* Extrapolation for High Throughput Prioritization and Decision Making,” [register](#) by Oct. 5.
- **Oct. 9 (off-site event)**, Duke University Environmental Hall, noon – 1:20 p.m. — ITEHP Fall 2015 Seminar Series with John Rawls, Ph.D., from Duke University, exploring “Zebrafish Models for Studying Developmental and Environmental Regulation of Energy Balance”
- **Oct. 16 (off-site event)**, Duke University Environmental Hall, noon – 1:20 p.m. — ITEHP Fall 2015 Seminar Series features Christopher Ward, from Duke University, discussing “Microbial Community Responses to Natural and Anthropogenic Disturbances in Aquatic Systems”
- **Oct. 19 (off-site event)**, National Institutes of Health (NIH), Bethesda, Maryland, 9:00 a.m. – 3:50 p.m. — NIH Digital Summit, “[Optimizing Digital to Reach Patients, Scientists, Clinicians, and the Public](#)”
- **Oct. 23 (off-site event)**, Duke University Environmental Hall, noon – 1:20 p.m. — ITEHP Fall 2015 Seminar Series presentation on “Early-life Exposure to Organophosphate Flame Retardants (OPFRs) Alters Behavior in Zebrafish: A Comparison With Organophosphate Pesticides,” by Anthony Oliveri from Duke University
- **Oct. 28 (off-site event)**, North Carolina Biotechnology Center, 8:30 a.m. – 4:30 p.m. — [Genetics and Environmental Mutagenesis Society fall meeting](#), “The Impact of Environmental Exposures on Genomic Health Across Generations”
- **Oct. 28-29 (off-site event)**, Grand Hyatt Washington, Washington, D.C. — NIEHS/EPA Children’s Centers annual meeting, [register](#) by Oct. 9
- **Oct. 29**, Keystone 1003, 10:00 – 11:00 a.m. — Biomolecular Screening Branch seminar featuring Carole Yauk, Ph.D., from Health Canada and Carleton University, discussing “Towards Implementing Toxicogenomics in Human Health Risk Assessment: Advances in the Application of Benchmark Dose Modeling”
- **Oct. 29**, Rodbell Auditorium, noon – 4:30 p.m. — North Carolina Society of Toxicology fall meeting, “Mouse vs. Man: Where the Differences and Similarities Lie in Today’s Toxicological Research,” [registration required](#)
- **Oct. 30 (off-site event)**, Duke University Environmental Hall, noon – 1:20 p.m. — ITEHP Fall 2015 Seminar, “Mechanisms and Consequences of Evolutionary Adaptation to Polluted Environments: Lessons Learned From PAH-resistant Atlantic Killifish *Fundulus heteroclitus*,” by Nishad Jayasundara, Ph.D., of Duke University
- View More Events: [NIEHS Public Calendar](#)

# NIEHS Spotlight

## Nadadur serves in India as first NIEHS U.S. Embassy Science Fellow

By John Yewell

The [U.S. Embassy Science Fellows Program](#) has provided about 300 scientific and technical experts to U.S. embassies around the world since its inception in 2001. The program enables embassies to host U.S. government scientists and engineers for up to three months, to address science and technology issues and expand cooperation with host country institutions.

Srikanth (Sri) Nadadur, Ph.D., NIEHS program director for Nanotechnology Environmental Health and Safety and the environmental cardiopulmonary health research programs, has become the first NIEHS scientist to participate.

### Focus on air quality

“It’s an exciting opportunity,” said Nadadur, who arrived Aug. 25 in his native India. His 90-day fellowship will focus on research and bilateral consultations on urban air quality. Nadadur will work with interagency colleagues to promote health systems and preparedness, as well as counter antimicrobial resistance. These projects relate to the [Global Health Security agenda](#), an effort to fight infectious diseases and promote health as part of an international security priority.



*Nadadur has more than twenty-five years of research experience in molecular biology and toxicology. (Photo courtesy of Steve McCaw)*

### Ambitious list of goals

Nadadur said the three things he hoped most to accomplish were participation in the Indian public health campaign, interaction with different government ministries, and discussion with the Indian government on global health security. Other priorities he will pursue include:

- Providing technical expertise in outreach activities in northern India.
- Providing technical expertise and promoting interactions with the interagency joint workgroup at the U.S. Embassy.
- Promoting cooperation between the EPA and the Indian, Delhi, and state government pollution control boards.
- Contributing expertise, as needed, on the implementation of research and policy issues for an Indian antimicrobial resistance program.

“It’s a wonderful opportunity for international collaboration,” noted Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, who nominated Nadadur for the fellowship. “Sri brings with him all the strengths of NIEHS, but especially his scientific expertise with air pollution and associated health effects.”

David Boxer, environment, climate, and science unit chief at the U.S. Embassy in New Delhi, said Nadadur’s arrival was eagerly anticipated. “Your expertise will facilitate bilateral cooperation to improve air quality in urban areas, as well as help us move toward a world safe from infectious disease threats,” Boxer wrote.



## **India’s pollution crisis**

Nadadur arrives at his post in New Delhi not a moment too soon. The city heads a list of 25 cities identified by the World Health Organization in 2014 as having the worst average annual ambient air pollution. In fact, the top four cities are in India, as are nine others.

He will meet with Indian government officials and nongovernmental organizations, all while doing considerable public outreach. “Their information on the health affects of air pollution is limited,” said Nadadur. “Education is important.”

One of his goals is to demonstrate that economic progress and a cleaner environment go hand in hand. “You can try to improve living standards, but if you ignore the environment you are never going to solve that [living standards] problem,” Nadadur noted.

## **International context**

President Obama and Indian Prime Minister Narendra Modi released a joint statement Jan. 25 affirming their commitment to cooperation in improving air quality and their pledge to implement the Global Health Security agenda.

Two weeks later, at the 15th Delhi Sustainable Development Summit, the Indian Minister for Environment, Forest, and Climate Change called on citizens of India to assert their right to clean air. These political developments enabled the U.S. Embassy to make a strong case for securing an embassy science fellow, particularly one with Nadadur’s skills and background.

## **Nadadur’s to-do list**

Among the dozen objectives on Nadadur’s to-do list is monitoring exposure to fine particulate matter experienced by U.S. Embassy employees and thousands of U.S. citizens living in India, and educating them on how to reduce the health challenges posed by air pollution. Working with the embassy’s Public Affairs Section, he will also help implement the Combatting Air Pollution in North India program.

Nadadur said that an important early assignment will likely be to support the implementation of a technical collaboration proposal by the U.S. Environmental Protection Agency (EPA) to partner with its Indian counterpart, the Central Pollution Control Board, to improve urban air quality.

Perhaps most importantly, Nadadur will meet with scientists both with, and independent of, the Indian government. Building scientist-to-scientist ties is at the heart of the strategic bilateral relationship between the U.S. and India, according to Boxer. “People-to-people ties nourish our belief in democratic values and sow the seeds for greater collaboration in the future,” he said.

“My goal is to say, you don’t have to reinvent the wheel,” said Nadadur. “The knowledge is here, use this knowledge and see what you can do. It is time to act.”

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



*Shortly after arriving, Nadadur posed with his U.S. Embassy colleagues in New Delhi. From left, Priya Ghose, environmental specialist; Dena Jaques, administrative assistant; Boxer; Nadadur; Beena Achankunju, secretary; and Noopur Singh, science and technology specialist. (Photo courtesy of Sri Nadadur)*

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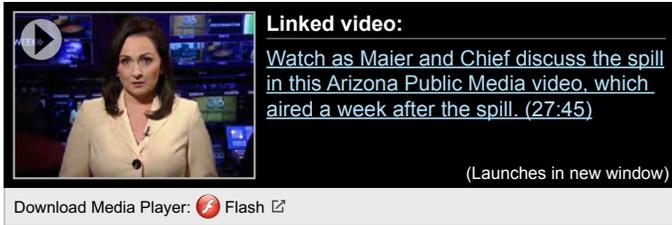
## **SRP researchers quickly inform communities near Colorado mine spill**

*By Sara Mishamandani*

Following the Aug. 5 Gold King Mine spill of about three million gallons of mineral-polluted water into a tributary of the Animas River in Colorado, researchers from the University of Arizona (UA) Superfund Research Program (SRP) moved quickly to inform affected communities about potential health and environmental risks.

A [statement from the U.S. Environmental Protection Agency](#) (EPA) said that an agency cleanup team accidentally caused the spill while excavating above the old entrance to the Gold King Mine, an abandoned mine in southwestern Colorado that had been leaking pollution. In an Arizona Public Media story (see video below), UA SRP Center Director Raina Maier, Ph.D., and researcher Karletta Chief, Ph.D., explained how the spill occurred and the risks it posed.

Maier said it was “a fairly major spill that’s caused a large amount of metals in a highly acidic waste stream to move into the environment.” She explained that metals don’t degrade into less toxic compounds, like oil can after a spill, and that these metals have been settling into river sediment for years as a result of mine waste throughout the region.



### Understanding the risks to Navajo communities

Chief, who works with the [UA Cooperative Extension program](#), is responding to concerns about the spill from Navajo communities downstream, with a focus on human exposure and risk perception.

“The water is very sacred to the Navajo people — not only to sustain their livelihoods, but also culturally and spiritually,” said Chief. The UA program links Arizonans to issues within the Navajo Nation and other tribal groups.

### Concern as the river ran orange

“The Animas River and many other rivers near mines in the region have been heavily polluted and unable to sustain aquatic life since the early 1900s, and EPA is working to fix this problem,” said Christopher Weis, Ph.D., NIEHS senior advisor. “The main difference between this spill and the daily problems with pollution from waste near abandoned mines is that the water turned orange with the relatively short-lived metal release caused by the accident.”

UA SRP researchers put together a brief, [Understanding the Gold King Mine Spill](#), to explain the extent of the accident, the effects of the spill, and what is being done to control it. The brief explains that the orange color of the water coming out of the mine resulted from the presence of highly acidic iron. When it mixes with water, it becomes less acidic and turns yellow. The water has since returned to its normal appearance.

“The mining devastation in this part of the United States is incredible, and it is important to maintain the focus on cleaning it up, even if the water is no longer orange,” said Weis. “This spill has raised awareness about mine waste issues, and we need to continue to work to understand the risks and clean up these problems.”



*Maier leads the UA SRP center, which addresses the health effects of contaminants in the U.S. Southwest, with a focus on mine waste. Researchers at the center study the movement into the environment of mine waste metals, potential health effects, and ways to reduce exposure to mine waste at Arizona’s Iron King Mine and Humboldt Smelter Superfund site. (Photo courtesy of Raina Maier)*



*Chief is a member of the UA SRP Community Engagement Core, which provides science-based information to underrepresented populations, supporting their responses to the health and environmental challenges related to mining. (Photo courtesy of Karletta Chief)*

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

## Educating tribal communities about the effects of mining

Chief and Maier lead an SRP project developing educational modules that focus on mining and its environmental and health effects. The team is collaborating with tribal community college instructors, who incorporate appropriate case studies providing examples of the effects of mining and how exposure to mine waste can be reduced.

In August, they released [Copper Mining and Processing](#), first in a series of planned Mining and Environmental Educational Modules for Tribal Colleges.

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## Trainees honored during NIEHS Postdoc Appreciation Week

By Kelly Lenox

The week of Sept. 21 was packed with activities at NIEHS, celebrating the contributions trainees make to the institute's mission. The variety of events underscored the many roles postdoctoral trainees and all other fellows play at NIEHS, as well as the range of available career options. Postdocs serve a vital role at NIEHS, providing much-needed research support in the labs, while honing their scientific skills.

Organized by the NIEHS Trainees Assembly (NTA; see sidebar), in collaboration with Tammy Collins, Ph.D., director of the NIEHS [Office of Fellows' Career Development](#) (OFCD), the celebration began three days early, as individual labs and research groups held lunches and other smaller gatherings Friday, Sept. 18.

In conjunction with the sixth annual observance of Postdoc Appreciation Day sponsored by the [National Postdoctoral Association](#), NIEHS kicked off the week with an NTA General Assembly meeting, a traditional game of trivia, and pizza provided by the institute's lead researchers.

Collins introduced trivia game emcee Bill Schrader, Ph.D., NIEHS deputy scientific director, making note of his Sept. 30 retirement. "He's done an excellent job for the trainee environment here at NIEHS," she said.



Collins support of NIEHS fellows takes on many forms, including keeping score for the trivia game. (Photo courtesy of Steve McCaw)

## Appreciation Week planning team

To plan the week's activities, Collins collaborated with a team of NTA members, including:

Gary Chan, Ph.D.  
Geoff Feld, Ph.D.  
Sophia Harlid, Ph.D.  
Kiri Hoff, Ph.D.  
Samantha Hoopes, Ph.D.

Linda Birnbaum, NIEHS and National Toxicology Program director addressed the gathering, saying “You play an important and valued role in the success of our research.” She went on to encourage the trainees to seek mentoring advice from other lead researchers, staff scientists, and postdocs throughout the institute.

### Preparing for careers

The week offered trainees several opportunities to jumpstart preparation for the career search they will eventually face. Tuesday afternoon, OFCD sponsored a two-part workshop, Leveraging LinkedIn, with topics that ranged from networking and visibility, to privacy concerns. Collins also conducted an orientation for new fellows, to provide them with information that will help them make the most of their time at NIEHS.

Wednesday saw the launch of a 10-week course, offered via videoconference from the National Cancer Institute, on preparing for careers in the biotechnology and pharmaceutical industries.

And the popular Brown Bag Lunch series kicked off on Thursday, with a choice between two lunchtime talks — one focused on biotech careers, and the other aimed at those interested in academic positions.

The week’s festivities wrapped up with an international potluck meal, to celebrate the diversity of the institute’s trainees. Postdocs brought dishes representing various foreign cuisines, such as China, Israel, and Argentina, as well as some U.S. dishes, including a Kentucky Derby Pie and North Carolina barbecue.



*Schrader emceed the trivia game with both humor and some last words of advice before his retirement. (Photo courtesy of Steve McCaw)*



*NIEHS fellows gathered for a group photo, taking a rare collective break from laboratory research. (Photo courtesy of Steve McCaw)*



Awards were given for winners and losers in the trivia game, as well as best team names. The overall winning team was “Undetermined,” which included, from left, Joey Kolb, Ph.D.; Jennifer Martinez, Ph.D.; Hoopes; NIEHS Scientific Director Darryl Zeldin, M.D.; John House, Ph.D.; Trey Oguin, Ph.D.; and not shown, Matt Edin, Ph.D. (Photo courtesy of Steve McCaw)



The last place team, Game of Testoste-Thrones, celebrated their achievement with enthusiasm. Members included, from left, Barbara Nicol, Ph.D.; Fei Zhao, Ph.D.; Nyssa Adams, Ph.D.; Kathryn McClelland; Margeaux Wetendorf, Ph.D.; Erica Ungewitter, Ph.D.; and Karina Rodriguez, Ph.D. (Photo courtesy of Steve McCaw)



Goldilocks and the Cre Bears won the Most Scientific Team Name award, with members, from left, Elizabeth Denholm, Ph.D.; Mahsa Samadi; Daniel Lustberg; Serena Dudek, Ph.D.; Kelly Carstens; Shannon Farris, Ph.D.; Palmyra Romeo; and not shown, Georgia Alexander, Ph.D.; and Chad Osterlund, Ph.D. (Photo courtesy of Steve McCaw)



The rest of the Bobin’ Hood and His Merry People team, which won the Most Humorous Team Name, had already returned to work in their labs by the time Geoff Feld, Ph.D., accepted the award on their behalf. Team members included Geoff Mueller, Ph.D.; Bart Phillips, Ph.D.; Robert Dutcher; Kathleen McCann, Ph.D.; Tom Stanley; and Bob Petrovich, Ph.D. (Photo courtesy of Steve McCaw)



Birnbaum emphasized the importance of the trainee period, pointing out that she herself had three postdoctoral research positions. “And my third was here at NIEHS,” she said. (Photo courtesy of Steve McCaw)



The Most Environmental Team Name award went to the Toxic Avengers team with, from left, Erin Quist, D.V.M.; Natasha Catlin, Ph.D.; Raj Chhabra, Ph.D.; Kristen Ryan, Ph.D.; Dori Germolec, Ph.D.; Kelly Shipkowski; and Deirdre Tucker. (Photo courtesy of Steve McCaw)



The week closed with perhaps the most festive of all the events — an international potluck, offering a world tour of cuisines and treats. (Photo courtesy of Steve McCaw)

# Council meeting addresses NIEHS and NIH developments

By Ernie Hood

The NIEHS National Advisory Environmental Health Sciences Council meeting Sept. 9-10 highlighted important new developments at NIEHS and the National Institutes of Health (NIH).

## New NIH strategic plan and Common Rule changes

NIH is in the process of formulating a new [strategic plan](#) to guide the agency's mission over the next five years. NIH Deputy Director Lawrence Tabak, D.D.S., Ph.D., briefed the council by phone on the plan's goals and framework and invited feedback from council members. He said that they have received extensive feedback from stakeholders and the final plan will be submitted to Congress in December.

NIH is also involved in a major effort to modernize and reform the federal rules and regulations, known as the Common Rule, which govern the protection of human research subjects. NIH Associate Director for Science Policy Carrie Wolinetz, Ph.D., briefed the council on the project, as well as the [Sept. 8 Notice of Proposed Rulemaking](#).

The changes are designed to improve safeguards and ensure respect for research participants, and to increase the efficiency of the oversight process. The public may comment on the proposal through Dec. 7.

"I see this as a really important step forward in the protection of human subjects, as well as the facilitation of research," said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program.

## Partnerships and innovation

Every [meeting of the council](#) provides an opportunity to update the group on new programs and activities, and this session was no exception.

Liam O'Fallon, Partnerships for Environmental Public Health program lead, updated the council on the tremendous strides made since its inception seven years ago. Today, the program works on a wide variety



Tabak, shown here during a 2014 council talk, described several areas of opportunity in biomedicine. "We are attempting to display the circularity or continuity of the scientific enterprise," he explained. "We'll have a succinct description for each of these opportunities and what NIH needs to do to realize them." (Photo courtesy of Steve McCaw)

## SIRT1 in metabolism, tissue homeostasis, and human diseases

Council members were treated to a science talk by Xiaoling Li, Ph.D., from the NIEHS [Metabolism, Genes, and Environment Group](#), who described her lab's research on a protein called SIRT1. According to Li, who was recently awarded [tenure](#), SIRT1 is a member of a family of proteins known as sirtuins, which regulate the body's metabolism and are believed to play a role in a number of other cellular processes, such as stress response, DNA repair, genome stability, and aging.

Her group's recent work has revealed critical functions of SIRT1 in embryonic stem cell biology, animal development, and cancer cell metabolism. The studies are advancing the understanding of the role of SIRT1 in mediating gene-environment interactions during human development, as well as disease processes, potentially providing the molecular basis for novel therapeutic targets for a number of human diseases.

of issues related to environmental public health, provides an array of educational and outreach resources to the public and scientific community, and communicates information through its newsletter and podcast series.

Daniel Shaughnessy, Ph.D., NIEHS program administrator for the Small Business Innovation Research and Small Business Technology Transfer programs, said that in the near future, these programs will seek to support development of new tools in high priority areas, such as nanomaterial safety and environmental health education. According to Shaughnessy, the two programs saw a significant increase in applications over the past 12 months and will have funded 38 grants by September 30, the close of fiscal year 2015.

Gwen Collman, Ph.D., director of the Division of Extramural Research and Training, provided a detailed rundown of division accomplishments in the past year, and how they related to the 11 goals of the [NIEHS 2012-2017 Strategic Plan](#).

### Evaluating research centers

After intensive work, the subcommittee evaluating the NIEHS Environmental Health Sciences Core Centers program [reported on its findings](#). The team, consisting of four council members and three outside experts, assessed the ability of the centers to produce complex, translational, and emerging environmental health research. Council member Linda McCauley, Ph.D., from Emory University, chaired the subcommittee.



*Li and her colleagues study the SIRT1 protein in a variety of experimental systems, including animal models, cell culture systems, cell-free assays, and human samples. Metabolic syndrome, which affects approximately 25 percent of American adults, is one of several disease states in which SIRT1 is suspected of playing a role. (Photo courtesy of Steve McCaw)*



*Birnbaum applauded outgoing council members Lisa Conti, D.V.M.; Vivian Cheung, M.D.; Randall Kramer, Ph.D.; Edward Postlethwait, Ph.D.; and Howard Hu, M.D., Sc.D. (Photo courtesy of Steve McCaw)*



*Collman presented Division of Extramural Research and Training accomplishments in three categories — raising awareness, building collaborations, and advancing research; moving science forward with programs and initiatives; and building knowledge base with publications and other products. (Photo courtesy of Steve McCaw)*



*Kenneth Fasman, Ph.D., of The Jackson Laboratory, noted the links Collman made between her division's accomplishments and the institute's strategic plan. "I have been involved in a lot of strategic planning exercises over the years, and I have never seen an organization embrace the process and embrace the implementation," he said. Birnbaum agreed, adding, "We're really living the strategic plan, and I think it's making a huge difference in what we do." (Photo courtesy of Steve McCaw)*

The report's conclusions were very positive. "It was readily obvious that the centers create a critical hub of environmental health research," said McCauley, "and there were multiple examples of how centers bring people together, foster interactions, collaborations, training, mentoring, and innovation that would not take place otherwise."

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



Six members of the core center evaluation team discussed their findings. From left are Elaine Collier, M.D., of the National Center for Advancing Translational Sciences; Fasman; council member Phil Brown, Ph.D., from Northeastern University; council member Norbert Kaminski, Ph.D., from Michigan State University; Dan Baden, Ph.D., from University of North Carolina Wilmington; and McCauley. (Photo courtesy of Steve McCaw)



Council members unanimously approved a concept presented by NIEHS health scientist administrator Thad Schug, Ph.D., on environmental influences on placental origins of development. The approach includes collaborating with the NIH [Human Placenta Project](#), led by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and developing a cross-disciplinary project on how environmental exposures affect early stage placental and fetal health. (Photo courtesy of Steve McCaw)

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## October is Breast Cancer Awareness Month

By Kelly Lenox

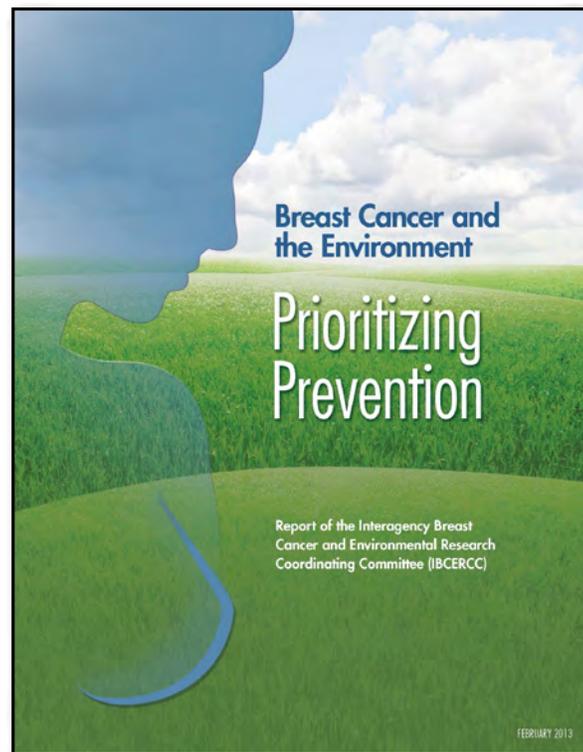
In recognition of Breast Cancer Awareness Month, NIEHS will join efforts across the U.S. to raise awareness, share information, and highlight research to help fight the disease.

Every year, NIEHS funds approximately \$30.6 million in research to help advance our understanding of breast cancer, its causes, mechanisms, and prevention. Research is conducted by in-house scientists, through NIEHS-funded grants, and as part of the National Toxicology Program (NTP), which is headquartered at NIEHS. Across all the institutes and centers at the National Institutes of Health, annual funding totals approximately \$681.6 million.

"Every year, we learn more about the role that environmental exposures may play in triggering this disease," said NIEHS and NTP Director Linda Birnbaum, Ph.D. "Despite decades of research, the number of women diagnosed with breast cancer continues to rise. Since environmental factors can be identified and modified, focusing on these factors presents a tremendous opportunity to prevent breast cancer."

NIEHS offers resources on breast cancer and the environment, aimed at both the general public and researchers, on its [Breast Cancer Awareness: Prevention is the Key](#) Web page. Highlights include:

- [Breast Cancer and the Environment Research Program \(BCERP\)](#), funded by NIEHS and the National Cancer Institute.
- [Breast Cancer and the Environment: Prioritizing Prevention](#), a 2013 report from the BCERP.
- Fact sheet on [breast cancer risk and environmental factors](#), providing an overview of related research efforts funded by NIEHS.
- Updates on the NIEHS-led [Sister Study](#), the only long-term study in the U.S. and Puerto Rico of women ages 35 to 74 whose sisters had breast cancer.
- Summaries of recent NIEHS-funded research.



### Research highlights

New research in the past year by NIEHS scientists and grantees builds understanding of breast cancer, especially with respect to the role of environmental exposures. The Environmental Factor recently highlighted several of these studies.

- NTP reproductive endocrinologist Sue Fenton, Ph.D., [guest edited a special issue of the journal Reproductive Toxicology](#), "Environmental Impact on Breast Development and Disease."
- [NIEHS researchers found that an RNA-binding protein](#) known as LIN28A is an important regulator of processes that play a role in many types of breast cancer, and, as such, is a potential therapeutic target.
- NIEHS grantees and colleagues found that [women who were exposed prenatally to higher levels of the pesticide DDT](#) were nearly four times more likely to develop breast cancer as adults than women exposed to lower levels before birth.

The NIEHS breast cancer awareness page, noted above, contains summaries of these and other research findings.

Breast Cancer Awareness Month is held every October to increase awareness of the disease and to raise funds for research into its cause, prevention, diagnosis, treatment, and cure.

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# NIEHS trainee begins career in product development

By Simone Otto

In June, former NIEHS Intramural Research Training Award (IRTA) fellow Monica Frazier, Ph.D., began a new career as an integrated product development associate at Rho Inc., a contract research organization located in Chapel Hill, North Carolina.

“We are thrilled to have Monica,” said Jack Modell, M.D., senior medical officer at [Rho](#). “She has already made major contributions and is sought out for her knowledge, enthusiasm, and collaborative team spirit.” Frazier’s new position will allow her to use her writing experience while she gains regulatory experience and immerses herself further in science.

Frazier earned her Ph.D. at the University of North Carolina at Chapel Hill, where she studied protein folding. At NIEHS, she researched deoxyribonucleoside triphosphate pools in strains of *E. coli*.

[Roel Schaaper, Ph.D.](#), head of the Mechanisms of Mutation Group within the NIEHS Genome Integrity and Structural Biology Laboratory, mentored Frazier and encouraged her to develop professionally. “One thing that impressed me about Monica is how diligently she worked on improving her skills both inside and outside the lab,” said Schaaper.

## Broadening her goals

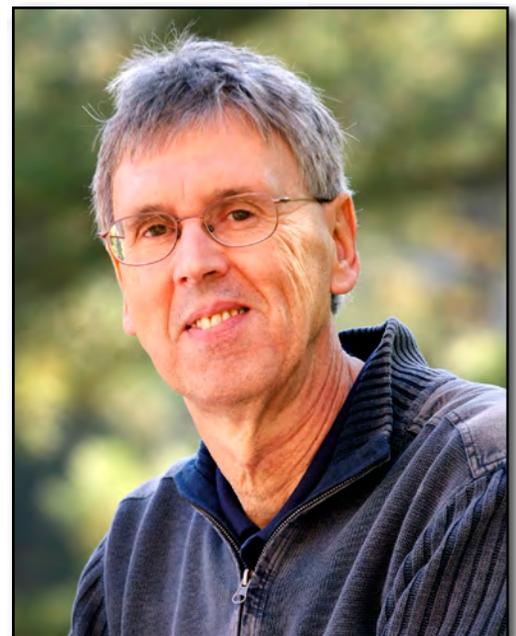
Frazier said she took advantage of the career development opportunities and resources at the institute, including helping plan the NIEHS Biomedical Career Symposium and writing for the Environmental Factor for 2 1/2 years. In addition, she chaired the NIEHS Trainees Assembly from 2014 to 2015 and mentored a student in the NIH Summer Internship Program in Biomedical Research.

Frazier credits peers in the Trainees Assembly for keeping her accountable and on track in her job search. “I worked hard to identify the things I was passionate about and skilled at, then sought out positions where I could combine those,” she said.

Frazier’s attention was drawn to the opening at Rho by friends she met while at NIEHS. She is confident these friendships will last beyond her time at the institute. “I think the key to networking is to build relationships and not to use those contacts only when you need help,” said Frazier.



*Shown with her 2013 NIEHS Science Day award-winning poster, Frazier nurtured her research skills, while enhancing her career development. (Photo courtesy of Steve McCaw)*



*During more than three decades of working with trainees in his lab, Schaaper has encouraged building a solid career skill set that will be useful at or away from the bench. (Photo courtesy of Steve McCaw)*

## The importance of mentoring

Tammy Collins, Ph.D., director of the Office of Fellows' Career Development, played an important role in mentoring Frazier, by helping her explore career paths, develop her curriculum vitae, and practice her interviewing skills. Frazier said Collins also gave her valuable advice on negotiating.

“Thank them for the offer, say what you liked about it, and talk about the part you would like to negotiate,” Collins told her. “It’s important to know your own value, as well as what sets you apart and makes you unique.”

Frazier also credited Environmental Factor Editor in Chief Kelly Lenox and her predecessor, Eddy Ball, Ph.D., with mentoring her. “Writing, leadership, communication, and teamwork were all major talking points in my interviews,” said Frazier. “Having been a writer for the Environmental Factor really helped me stand out.”

Her advice for other NIEHS fellows is to get involved and take advantage of the opportunities available at the institute, especially through the Office of Fellows' Career Development. “I am grateful for the tremendous support I received while at the institute,” said Frazier. “I cannot say enough about it.”

(Simone Otto, Ph.D., is an IRTA fellow in the NIEHS Ion Channel Physiology Group.)

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*Collins oversees a rich program of career awareness and development training that ranges from time management and communication to public speaking, teaching, and presentation skills. (Photo courtesy of Steve McCaw)*

## Green Champion awards recognize NIEHS achievements

*By Kelly Lenox*

NIEHS continued its strong showing this year in the annual Green Champion awards given by the Department of Health and Human Services for sustainability projects. The awards were presented at a National Institutes of Health event on Sept. 11.

“As an institute focused on how our environment affects our health, it is fitting that NIEHS appears in two separate categories of the Green Champions awards,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program.

Jenn Evans, Claire Long, and the Office of Management were named in the Corporate Responsibility category for the NIEHS Transshare and Telework Program. The NIEHS Site Ecology team won an honorable mention in the Environmental Stewardship category.

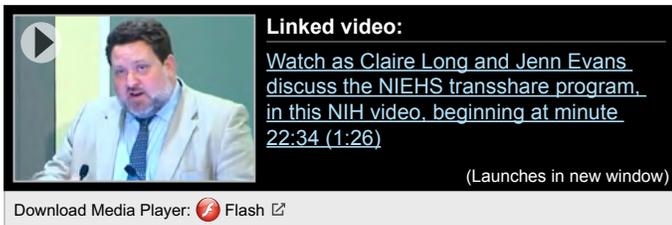


## Innovation and resourcefulness in alternative commuting

The Corporate Responsibility Award acknowledged the NIEHS Transshare and Telework Program for combining innovation and resourcefulness to create successful alternative commuting. The award cited the 2014 NIEHS telework participation rate of more than 50 percent, among other efforts. It also noted that the Triangle J Council of Governments, the multi-county district that includes the NIEHS location, awarded NIEHS the 2014 [Best Workplace for Commuters](#).

“NIEHS has been able to help mitigate traffic congestion and reduce auto emissions that result in greenhouse gases by offering NIEHS employees effective alternative commuting methods such as the use of regional busing, vanpool programs, carpool programs, teleworking, and bike to work programs,” the award stated.

“It’s an honor to work with employees who are so invested in alternative transportation and telework,” said Claire Long, a management analyst with the NIEHS Administrative Services and Analysis Branch (ASAB). “The level of participation has been great.”



## Setting an example for ecosystem protection

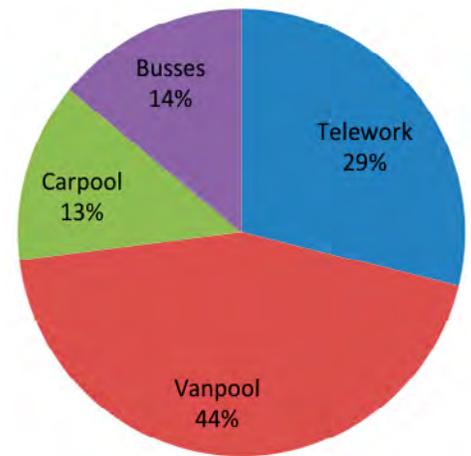
The NIEHS Site Ecology Team (see sidebar) won an honorable mention in the Environmental Stewardship category. The award specifically recognized the team’s innovative strategies to address invasive species and the ecological threats they pose.

“We believe these practices may serve as models for other Operating Divisions within the U.S. Department of Health and Human Services,” the award stated. The team works alongside counterparts at the U.S. Environmental Protection Agency (EPA), which shares the campus.

The team’s strategies include improving habitat, identifying and monitoring invasive plants, monitoring nutrient levels in the lake, and establishing a plan to protect native ash trees from the devastating emerald ash borer beetle. In addition, the group has worked to promote employee awareness.

“The Site Ecology Team provides a way for NIEHS and EPA to work together proactively, to manage campus ecological issues,” explained Bill Steinmetz, NIEHS environmental compliance specialist.

“The team’s actions are not always visible, but it is evident that our efforts to control aquatic weed coverage along the Discovery Lake shoreline, through triploid grass carp reintroduction, were effective,” added Bill Willis, a biologist in the NIEHS Reproductive and Developmental Biology Laboratory.



*In fiscal year 2014, NIEHS employees saved an estimated 871,782 miles using alternatives. Vanpools account for the largest savings, followed by telework, busses, and carpools. (Photo courtesy NIEHS)*

## NIEHS Site Ecology Team members

Bill Steinmetz  
Bill Willis  
Scott Capouch  
Gordon Caviness  
Brian Harris  
Steve Herndon  
Chris Hunt Jr  
Versal Mason  
John McLamb  
Paul Poliachik  
David Sawyer  
Pete Schubert (EPA, ret.)  
Mitch Williams  
Terri Stubblefield (EPA)



*Discovery Lake in 2011, left, before the introduction of triploid grass carp, and in 2015, revealing a dramatic decline in growth of the invasive aquatic weed Ludwigia. (Photos courtesy of Pete Schubert, left, and Bill Steinmetz and Bill Willis, right)*

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# Clinical Feature

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## Lasker Scholar joins NIEHS

*By Robin Arnette*

Hormones control the physical, mental, and emotional changes that accompany adolescence, but scientists who study pubertal development are finding that a child's genes and environment affect the process as well. Natalie Shaw, M.D., is one of those scientists interested in understanding puberty, and she joined NIEHS this fall.

In her previous position as a research fellow at Massachusetts General Hospital in Boston, Shaw examined the interaction between sleep and hormone secretion during puberty. She will continue that work as a member of the NIEHS Clinical Research Program thanks to the National Institutes of Health (NIH) [Lasker Clinical Research Scholars Program](#), which is a joint partnership between NIH and the Lasker Foundation to support a small number of exceptional clinical researchers in the early stages of their careers. The goal of the program is to promote the development of physician-scientists as they transition to fully independent positions. Shaw is the first Lasker Scholar at NIEHS.

### The importance of mentors

Shaw is a native of Binghamton, New York, and said she planned to expand her work by looking at the genetics behind the timing of pubertal development. She hopes to figure out why some teenage girls have irregular menstrual cycles in the years immediately following their first period. She said many people had a hand in her success, but one of the most important is fellow NIEHS clinical researcher Janet Hall, M.D.

"Hall was my mentor when I was in Boston, and she thought that taking a clinical research position at NIEHS would be a great opportunity for me," Shaw said.

Hall is also in the process of heading her own research group at NIEHS, and she is looking forward to collaborating with Shaw on clinical studies that affect children's environmental health.

"Puberty is a key event in human development, yet we know so little about how it occurs normally or in relation to environmental stressors such as obesity, sleep disturbance, and environmental toxins," Hall said. "Despite the inherent difficulties in doing clinical research studies in children, Dr. Shaw has already made important contributions. NIEHS has recruited an extraordinarily talented investigator."

NIEHS Scientific Director Darryl Zeldin, M.D., knows the significance of recruiting highly capable clinical researchers to NIEHS. "Our clinical research program is growing, and the quality of our work is on par with some of the best clinical research programs in the country," he said.



*In addition to her research duties at NIEHS, Shaw is an adjunct faculty member at the University of North Carolina at Chapel Hill School of Medicine. (Photo courtesy of Steve McCaw)*

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# Science Notebook

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## DeMayo named deputy chief of NIEHS lab

By Robin Arnette

In August, Francesco DeMayo, Ph.D., stepped into his new role as deputy chief of the NIEHS Reproductive and Developmental Biology Laboratory (RDBL), and head of the lab's Pregnancy and Reproduction Group.

DeMayo brings a wealth of knowledge and experience to his new positions. During the 32 years he spent at the Baylor College of Medicine in Houston, DeMayo worked his way up from a postdoctoral fellowship to professor and held the Cullen Duncan McAshan Endowed Chair.

“We are extremely fortunate to have been able to attract and recruit someone with Dr. DeMayo’s high scientific stature to NIEHS,” said RDBL Chief Ken Korach, Ph.D. “Dr. DeMayo is one of the few internationally recognized experts in the field of reproductive biology, and his expertise complements and extends the existing strengths in the RDBL and other groups within NIEHS.”

### Two organs, one approach

DeMayo’s research interests include examining the hormonal pathways that regulate uterine function, and how the environment regulates the development of lung cancer. Although these two topics appear to be unrelated, DeMayo explained that the gene called secretoglobin family 1A member 1 (SCGB1A1) produces a uterine protein known as uteroglobin. It also produces the Clara cell 10-kD protein, or CC10, which is secreted in the lung. Both proteins exhibit potent anti-inflammatory properties and make it possible to develop tools to study lung and uterine biology on a molecular level.

“Embryo implantation in the uterus is a controlled inflammatory response, and a switch from inflammatory to noninflammatory says it’s time for the baby to be born,” DeMayo said. “That same inflammation drives a lot of pulmonary diseases, so there’s a core commonality between the two organs.”

For that reason, NIEHS Scientific Director Darryl Zeldin, M.D., thought DeMayo would also be a good fit for the NIEHS [Immunity, Inflammation, and Disease Laboratory](#), so DeMayo holds a secondary appointment in that lab. “We anticipate that while he is at NIEHS, he will continue to make more seminal contributions to the field of reproductive and developmental biology,” Zeldin said.

### Coming home

As a native of Staten Island, New York, DeMayo’s current position at NIEHS is a homecoming of sorts. He is from the town of Stapleton, the place where, in 1887, Joseph Kinyoun, M.D., used his microscope and newly developed research techniques to confirm the identity of the bacterium that caused cholera in the United States.



*“I’ve known people in the Reproductive and Developmental Biology Laboratory for many years,” DeMayo said. “Now, I get to work with them as collaborators. It’s exciting to be here.” (Photo courtesy of Steve McCaw)*

The one-room [Hygenic Laboratory](#) in Stapleton that Kinyoun set up and used for his discoveries eventually became the National Institutes of Health.

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## Mutations in mitochondrial DNA lead to disease

By Robin Arnette

Whether you plug an appliance into a wall outlet, load batteries into an electronic device, or place a solar-powered tool on a windowsill, most of the machines that make life easier in the modern world need energy. The human body is no different in requiring energy for its processes.

One prominent researcher argues that many of the diseases that afflict mankind develop, not as a result of dysfunction in a particular organ, but due to defects in the mitochondria, which are the hundreds of power-producing organelles present in each cell.

Douglas Wallace, Ph.D., specializes in mitochondrial genetics and believes that Alzheimer's disease, cancer, inflammatory illnesses, neuropsychiatric conditions, and other maladies could result from mutations in genes for mitochondrial energy production. Such genes are present in both nuclear DNA and mitochondrial DNA (mtDNA).

He discussed his theory during a Sept. 15 NIEHS Distinguished Lecture Seminar Series talk titled, "Mitochondrial-Cellular Interactions and Pathophysiology of Disease." [Bill Copeland, Ph.D.](#), chief of the NIEHS Genome Integrity and Structural Biology Laboratory and a proponent of studying mitochondria for the origins of disease, hosted the seminar.

### When the power plant goes awry

[Wallace](#) said that mtDNA is similar to nuclear DNA, in that both are constantly making more copies of themselves, a process known as replication. Because replication can be error-prone, damage or mutations may accumulate in mtDNA, leading to problems when it is time for the cell to divide during mitosis.



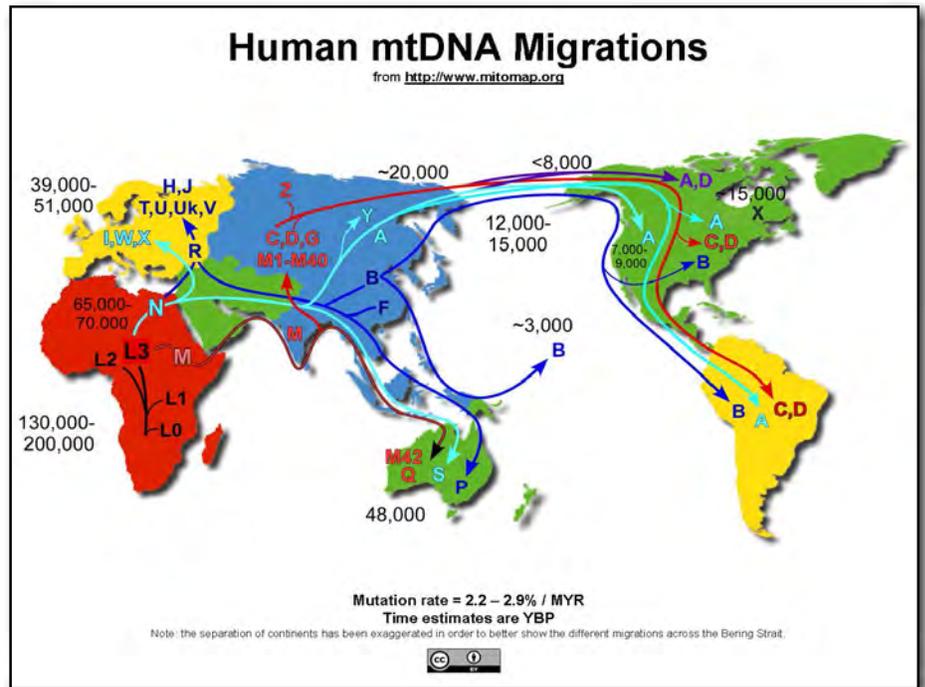
*Wallace is the Michael and Charles Barnett Endowed Chair in Pediatric Mitochondrial Medicine and Metabolic Disease, director of the Center for Mitochondrial and Epigenomic Medicine at the Children's Hospital of Philadelphia Research Institute, and professor of pathology and laboratory medicine at the University of Pennsylvania Perelman School of Medicine. (Photo courtesy of Steve McCaw)*



*"The NIEHS was very fortunate to host Dr. Wallace's visit," Copeland said. "It was refreshing to hear his view of the importance of cellular energy in health and disease processes." (Photo courtesy of Steve McCaw)*

“You end up with something called heteroplasmy, which is when you get cells with normal and mutant mtDNAs,” Wallace said. When the cell divides, he explained, the mutant and normal mtDNAs are randomly distributed into the daughter cells, so that a person can have cells and tissues with different proportions of mutant and normal DNAs.

As the percentage of mutant mtDNAs increases in a cell, the cell’s energy output decreases. According to Wallace, when it drops below a minimum threshold for a given organ, that organ begins to malfunction. As an example, he mentioned that for mutations in one particular protein synthesis gene, 10 to 30 percent heteroplasmy is associated with diabetes and autism, 50 to 90 percent leads to certain neuromuscular diseases, and 100 percent kills an infant, in Leigh’s syndrome.



Wallace and his team reconstructed the migration of women around the globe by examining the mtDNA variation that exists in the human population. According to his studies, women from the Khoisan people of the Kalahari Desert are the original carriers of mtDNAs (L0), with several variants branching off into other African populations. Interestingly, the M and N variants present in Ethiopia were the only 2 mtDNAs that colonized the rest of the world. (Note: MYR, million years; YBP, years before present) (Photo courtesy of Douglas Wallace)

Wallace’s group and others have documented hundreds of mtDNA mutations and have said that toxins from the environment can also inhibit mitochondrial function. These chemical compounds can impair mtDNA maintenance, resulting in more damage and further erosion of cellular energy. He and others suggest mitochondrial decline could be the molecular basis of aging.

## Energy helped colonize the world

Although there appears to be a direct relationship among mutations in mtDNA, changes in cellular energy levels, and disease, Wallace said not all modifications contribute to illness. After he and his team traveled the world to obtain consent and blood samples from indigenous people, they noted that subtle changes in energetic efficiency allowed humans to adapt to new environments. Because mtDNA is only inherited from the mother, the team was able to compare sequence differences between mtDNAs of different groups and reconstruct the origins and ancient migrations of women.

The research found that the original mtDNAs, labelled L0, have the fewest mutations and belong to the Khoisan people of the Kalahari Desert in Africa. L0 mitochondria are the most efficient, meaning that nearly all of the calories ingested go toward making functional energy, with the body generating very little heat. As people moved north, they accumulated functional mutations that made their mitochondria less efficient. They had to eat more calories for the same amount of metabolism, but they generated more heat, which was advantageous in colder climates.

**Linked video:**  
Watch as Wallace explains the movement of mtDNA variants in different lineages of humans from Africa into Europe and Asia. (1:15)  
(Launches in new window)

Download Media Player: Quicktime

Wallace maintains that these variants allowed humans to colonize the world, but they also predisposed people to disease. “In one European lineage, a single A to G nucleotide switch in a particular gene is found in 3 percent of Alzheimer’s disease and 5 percent of Parkinson’s disease, but less than 0.4 percent of the general population,” Wallace said. “This substitution happened about 10,000 years ago, but it predisposes some with this lineage to developing late-onset neurological disease.”

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## Advisory committee on alternatives to animal testing looks forward

By Ernie Hood

At its annual meeting at NIEHS Sept. 2, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) highlighted its recent progress in developing alternatives to traditional animal testing.

The time has now come to take the next step, according to Warren Casey, Ph.D., director of the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM; see [sidebar](#)).

### Creating a 3Rs roadmap

Casey and Brian Berridge, D.V.M., Ph.D., of GlaxoSmithKline, proposed the creation of a national roadmap to replace, reduce, or refine (3Rs) animal use and transform toxicity testing. “This is something much larger than ICCVAM, and much larger than the federal government,” said Casey. “It’s an incredibly complex proposition, but it’s also something that is absolutely necessary if we’re ever going to reach our goal.”

Both speakers cited the need for improved predictability of the effects of drugs and chemicals in humans. They also see opportunities to use computational and high-throughput assays to reduce animal use in some toxicological and drug safety and efficacy testing.

Those opportunities go hand in hand, said Berridge, at least in the drug development arena. “I have no doubt that if we can develop alternative ways of modeling that are more predictive and more efficient than what we do in animals, a decrease in animal dependence will follow,” he noted.

### Upbeat updates

Casey also briefed the committee on many developments over the past year within NICEATM, including the creation of a new database that focuses on toxicants that produce subtle developmental effects. ICCVAM co-chair Anna Lowit, Ph.D., from the U.S. Environmental Protection Agency (EPA) Office of Pesticide Programs, described progress in implementing the priority needs identified in the [2013 ICCVAM reinvention](#).



*Casey explained that the need for a national roadmap and strategy for the 3Rs is driven by public health, economics, and ethics, with each element contributing to reducing and eventually eliminating animal testing. “Development, validation, and adoption of predictive, human-based test methods requires multiple stakeholders all working together with specific intent,” he said. (Photo courtesy of Steve McCaw)*

The priorities include evaluating test methods for acute toxicity, biologics, skin sensitization, and endocrine disruptors. Organizational priorities call for agencies to take a more active role in committee activities, streamline the number of projects, and improve communications and outreach efforts. “We can pat ourselves on the back a little bit, because obviously there’s been an enormous amount of success,” Lowit reported.

The advisory committee also heard updates from four federal agencies that have been very active with ICCVAM-related work — the U.S. Department of Agriculture, EPA, the U.S. Food and Drug Administration, and NIEHS. At EPA, high-throughput and computational methods are contributing to an acceleration of the [Endocrine Disruptor Screening Program](#). At NIEHS, a new [small business cooperative agreements program](#) has been announced to encourage validation and commercialization of approaches to reduce animal use in toxicity testing.

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

## Finding alternatives to animal testing

The term [alternative methods](#) refers to methods of research and testing that use fewer or no animals, or that reduce animal pain and distress. Congress established several groups to ensure the involvement of all stakeholders in development of such methods.

- The [Interagency Coordinating Committee on the Validation of Alternative Methods \(ICCVAM\)](#) coordinates the activities of member federal agencies to replace, reduce, or refine animal use.
- The [NTP Interagency Center for the Evaluation of Alternative Methods \(NICEATM\)](#) is an office within the National Toxicology Program (NTP) that supports ICCVAM activities and NTP high-throughput screening projects. The center is involved with development of novel approaches to testing.
- The [Scientific Advisory Committee on Alternative Toxicological Methods \(SACATM\)](#) advises NICEATM, ICCVAM, and the NIEHS and NTP director. Representatives are drawn from industries regulated by ICCVAM member agencies, animal welfare organizations, academia, test method developers, and regulatory agencies outside of the federal government.



Meeting chair William Janzen, executive director of Lead Discovery at Epizyme, Inc., kept the proceedings moving smoothly. (Photo courtesy of Steve McCaw)



Lowit described EPA’s work with pesticide manufacturers to implement alternative tests or waive acute toxicity tests completely for pesticide reformulations. Such measures, she said, have resulted in significant reductions in the use of animals in testing. (Photo courtesy of Steve McCaw)



At her final meeting as a SACATM member, Tracie Bunton, D.V.M., Ph.D., right, from Eicarte LLC, addressed the challenge of measuring success. “Although we don’t have an edict to determine what the numbers are, I think it would be worthwhile to get a general idea of what the true usage of mice and rats and all of the animals are in the United States,” she said, as Nigel Walker, Ph.D., from NTP, listened. (Photo courtesy of Steve McCaw).



Amy Clippinger, Ph.D., left, and Jeffrey Brown, right, who represent People for the Ethical Treatment of Animals, provided comments during the meeting. (Photo courtesy of Steve McCaw)



David Dix, Ph.D., from EPA, described the Endocrine Disruptor Screening Program’s shift to using high-throughput assays and computational models to rapidly screen chemicals for potential bioactivity and exposure. This approach will increase in the rate of chemical screening from tens to thousands per year. (Photo courtesy of Steve McCaw)



SACATM and ICCVAM members and their NIEHS and NTP hosts had good reason to smile as they gathered for a photograph. “The number of ongoing and planned collaborations among agencies, industry, and our international partners is unprecedented in the 15 years since passage of the ICCVAM Authorization Act of 2000,” said Birnbaum, center front. (Photo courtesy of Steve McCaw)

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# New children's health research projects funded by NIH

By Robin Mackar

Researchers working to improve children's health now have more opportunities to understand the role environmental exposures play in children's health and development, thanks to new funding from the National Institutes of Health (NIH).

NIEHS joined with NIH Sept. 28 in [announcing the recipients](#) of new projects that will provide researchers an expanded range of tools to accurately measure, record, and analyze environmental exposures in children.

"I am thrilled that NIEHS was in a position to mobilize its community to put high quality proposals together and receive this additional funding," said

Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program (NTP). "Our staff deserves a lot of credit for announcing and funding these grants in record time. Healthier children will be the ultimate beneficiaries of all our efforts."



## NIH's three-pronged approach

NIH awarded \$144 million in three specific initiatives, of which NIEHS received \$57 million. The initiatives include developing new tools, understanding the influence of the environment on *in utero* development, and leveraging existing children's environmental health cohorts to look at later child development.

## New tools

In the tool arena, the NIEHS-led [Children's Health Exposure Analysis Resource \(CHEAR\)](#) will provide researchers access to laboratory and statistical analysis.

CHEAR is intended to:

- Expand the number of studies that include environmental exposure analysis in their research.
- Implement the exposome concept in children's health studies.
- Create a public resource of children's exposures across the country.
- Develop data and metadata standards for the environmental health sciences community.

Six researchers received awards as part of CHEAR's National Exposure Assessment Laboratory Network. In addition, the CHEAR Center for Data Science was awarded to the Icahn School of Medicine at Mt. Sinai, and Westat, Inc. will serve as the CHEAR Coordinating Center (see [text box](#)).

## Understanding developmental toxicity

In support of the second NIH initiative, building understanding of the influence of the environment on *in utero* development, NTP, which is housed at NIEHS, will work with the National Center for Advancing Translational Sciences to offer new tools for researchers working to understand human developmental processes.

The two organizations received funds to adapt high-throughput screening and other technologies developed in the [Tox21 predictive toxicology effort](#).

### Ongoing children’s environmental health cohorts

NIEHS provided [supplemental funding](#) to 13 existing research grants, enabling researchers to add or enhance high-dimensional molecular analysis approaches in existing pregnancy, birth, and children’s environmental health populations.

“Technology advances have become a powerful driver in studying and understanding the start and spread of disease,” said NIH Director Francis S. Collins, M.D., Ph.D. “These projects will expand the toolbox available to researchers to improve our ability to characterize environmental exposures, understand how environmental exposures affect *in utero* development and function, and bolster the infrastructure for exposure research.”

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

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## Children’s Health Exposure Analysis Resource

### National Exposure Assessment Laboratory Network

- Kenneth Aldous, Ph.D., Wadsworth Center, New York
- Timothy Fennell, Ph.D., Research Triangle Institute, North Carolina
- John Meeker, Sc.D., University of Michigan
- Gary Miller, Ph.D., Emory University, Georgia
- Lisa Peterson, Ph.D., University of Minnesota
- Robert Wright, M.D., Icahn School of Medicine at Mount Sinai, New York

### Data Repository, Analysis, and Science Center

- Susan Teitelbaum, Ph.D. Icahn School of Medicine at Mt. Sinai, New York

### Coordinating Center

- Barbara O’Brien, Westat Inc., Maryland

## NIEHS leads at international epidemiology conference

*By Virginia Guidry*

NIEHS scientists and grantees made key contributions at the [International Society for Environmental Epidemiology \(ISEE\) 27th annual meeting](#), Aug. 30-Sept. 3 in Sao Paulo, Brazil. Organizers held the meeting in South America to highlight environmental health needs in developing countries, with the theme of Addressing Environmental Health Inequalities.



Environmental epidemiologists and exposure scientists gather each year at the ISEE conference to discuss the latest research on how the environment can help or harm people’s health, and how best to measure these changes. Policy implications of recent findings are also considered. This year’s key topics included air pollution, climate change, and access to green space.

“The annual ISEE meeting is an important opportunity for NIEHS scientists and program staff to discuss new research directions with other environmental health scientists, especially since environmental epidemiology makes up a large part of NIEHS-funded research,” said Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training.

## Health benefits of green space as an emerging topic

Attendees noted the number of scientific presentations that explored the ways that access to green space, such as parks and urban gardens, can improve health. Presenters pointed out that a growing body of literature shows that living near nature and green space benefits cardiovascular health, mental health, obesity, allergies, asthma, neurodevelopment, and birth weight.

NIEHS grantee Patrick Ryan, Ph.D., from the University of Cincinnati, presented new findings about the impact of residential green space on children's respiratory health. He said such green space may reduce the contribution that childhood exposure to traffic-related air pollution makes to asthma development.

"The green space research provided a new interpretation of the built environment," said Kimberly Gray, Ph.D., NIEHS health scientist administrator. "It highlighted how important it is to consider, and measure, the impact of green spaces, tree canopy, and the outdoor features that can impact people's health, or even offset the harmful effects of toxicants in someone's environment."

## NIEHS council member recognized for contributions to environmental epidemiology

Howard Hu, M.D., Sc.D., an outgoing member of the NIEHS advisory council, received the [John Goldsmith Award for Outstanding Contributions to Environmental Epidemiology](#) at the meeting. Now the dean of the Dalla Lana School of Public Health at the University of Toronto, Hu has spent his career investigating environmental contributions to chronic disease and its impacts on child development around the world.

After receiving his award, Hu spoke on "Big Data, Environmental and Social Epidemiology, Power and Politics." He explored the use of big data for epidemiology studies and noted some of the challenges. For example, he said, existing data sources cannot adequately characterize individual environmental exposure levels. Furthermore, marginalized populations are often excluded from existing databases, which might perpetuate health inequities.

## Wide participation from NIEHS

Staff from NIEHS chaired scientific sessions, shared new research findings, and participated in professional development sessions with the ISEE Student and New Researcher Network. Collman chaired a scientific session about gene-environment interactions. Claudia Thompson, Ph.D., chief of the Population Health Branch, chaired a session about indoor air and human health.



*Collman co-chaired a session on gene-environment interactions, which featured research from Taiwan, Canada, South Korea, and the U.S. (Photo courtesy of Steve McCaw)*



*Miller participated in sessions about the evolving National Institutes of Health Disaster Response Research Program, led by NIEHS, and the health response to naturally occurring asbestos and erionite. (Photo courtesy of Steve McCaw)*

Several presentations informed the scientific community about ongoing NIEHS-led efforts. David Balshaw, Ph.D., chief of the Exposome, Response, and Technology Branch, led a poster presentation about the newly funded [Children's Health Exposure Analysis](#) Resource. Larry Engel, Ph.D., an associate researcher in the Epidemiology Branch, provided information from the GuLF STUDY (Gulf Long-term Follow-up Study) regarding cardiovascular findings. Caroline Dilworth, Ph.D., NIEHS health scientist administrator, presented recommendations from the recent NIEHS-hosted [workshop on statistical methods for analyzing exposures to environmental chemical mixtures](#). The recommendations were prepared by NIEHS scientists and grantees.

“The scientific discussions at ISEE are essential for keeping up with the most current scientific findings and moving both research methods and the practice of environmental epidemiology forward,” said Aubrey Miller, M.D., NIEHS senior medical advisor, who gave two presentations at the meeting.

The [next ISEE conference](#) will be held September 1-4, 2016, in Rome, Italy.

(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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*Gray participated in a professional development session on grant preparation, with the ISEE Student and New Researcher Network. (Photo courtesy of Steve McCaw)*

## NIH Research Festival celebrates wealth of scientific pursuits

*By Kelly Lenox*

The National Institutes of Health (NIH) celebrated research across its 27 institutes and centers at the [29th NIH Research Festival](#) Sept. 16-18 on the NIH campus in Bethesda, Maryland. Several NIEHS scientists participated in the event, providing a glimpse into the institute's rich array of in-house researchers and programs.

### FARE award winners celebrated

NIEHS scientists presented eight posters (see [text box](#)) at the festival, representing research in immunology, cancer biology, and molecular biology and biochemistry. Four of the institute's 16 [Fellows Award for Research Excellence \(FARE\) winners](#) were among the group. FARE award winners were recognized in a ceremony on the second day of the festival.

FARE awardee Alisa Suen, a visiting predoctoral fellow in the [Reproductive Medicine Group](#) headed by Carmen Williams, M.D., Ph.D., said this was her first time at the NIH campus, and she especially enjoyed the history tour and tour of the [NIH Clinical Center](#). “The design of the clinical center facility is a true embodiment of bench-to-beside research,” Suen said, “with space for scientists, physicians, and patients to come together in one place for cutting-edge research and care.”

Sylvia Hewitt, senior biologist in the [NIEHS Receptor Biology Group](#) led by Ken Korach, Ph.D., also exhibited a poster at the festival. Visiting the NIH Clinical Center and attending the morning plenary sessions were among the highlights she noted. Referring to the session on Creating NIH Technology Incubators, Hewitt said, “It was really impressive — you’ve got these brilliant young engineer-biologists building amazing microscopes.”

### Focus on public health emergencies

NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., participated in the Responding to Public Health Emergencies plenary session. Speakers focused on the crucial role of the NIH in-house, or intramural, research program in responding to public health emergencies, such as the Ebola crisis and foodborne disease outbreaks.

At NIEHS, such responses include the GuLF STUDY, a long-term study of [workers involved in the Deepwater Horizon oil spill clean up](#). The institute also plays a leading role in the NIH-wide Disaster Research Response project (DR2). “The [DR2 website](#) has some of the materials that have been developed, including fit-for-purpose and ready-to-go protocols that have been pre-approved by the NIEHS IRB [institutional review board] for use in intramural research,” Birnbaum told the audience.

She also called attention to global health issues, especially those related to climate change and projected increases in extreme weather events and other public health emergencies.

Besides the plenary and poster sessions, the festival included workshops on topics such as the microbiome and drug resistance, and RNA biology and therapeutics. It also featured tours of NIH facilities, exhibits on resources for NIH researchers, and a vendor fair.



*Suen was the only predoctoral fellow from NIEHS honored this year with a FARE. She also won best oral presentation at this year’s meeting of the Triangle Consortium for Reproductive Biology in Research Triangle Park, North Carolina. (Photo courtesy of Steve McCaw)*



*Hewitt was impressed with the NIH Clinical Center. “It’s half hospital, half lab,” she said. (Photo courtesy of Steve McCaw)*



*Birnbaum listed extreme heat, severe weather, spread in vectorborne illnesses, and longer allergen seasons as some of the health impacts of climate change. “These are issues we are going to need to be dealing with in emergency response, from a health impact perspective,” she said. (Photo courtesy of NIH)*

## Posters by NIEHS researchers

**“Aberrant uterine SIX1 expression may promote uterine adenocarcinoma following neonatal xenoestrogen exposure”** by AA Suen [FARE Award winner], WN Jefferson, E Padilla-Banks, CE Woods, VL Bae-Jump, CJ Williams.

Excerpt: “These findings indicate that uterine SIX1 expression is a biomarker for exposure and disease, and suggests that SIX1 could play a role in carcinogenesis.”

**“Dendritic and epithelial cell crosstalk in the lung: the impact of cell-specific Myd88 expression on consequent immune response to allergens”** by SY Thomas [FARE Award winner], GS Whitehead, KM Gowdy, M Takaku, X Xu, JM Ward, K Nakano, H Nakano, P Wade, DN Cook.

Excerpt: “These surprising findings reveal that airway eosinophilia and neutrophilia are separable allergic events and suggest that new treatments can be developed to target specific forms of asthma.”

**“Smith-Lemli-Opitz Syndrome reveals requirement for sterol biosynthesis in the innate immune response”** by KA Gabor [FARE Award winner], CA Wassif, PR Bushel, MW Henderson, FD Porter, MB Fessler.

Excerpt: “We propose that deficient innate immunity may be a clinically relevant contributor to SLOS pathogenesis, and that SLOS highlights the importance of cholesterol biosynthesis to innate immunity.”

**“The novel p53 target Tumor Necrosis Factor- $\alpha$ -Induced Protein 8 variant 2 is increased in human cancers and can offset p53-dependent tumor suppression”** by JM Lowe [FARE Award winner], T Nguyen, MA Resnick, SA Grimm, KA Gabor, SD Peddada, CW Anderson, D Menendez, MB Fessler.

Excerpt: “We propose that TNFAIP8 v2 can promote human cancer through p53-independent mechanisms as well as by broadly repressing p53 function, in essence offsetting p53-dependent tumor suppression.”

**“Disruption of endometrial NELF transcriptional pausing complex impairs early pregnancy”** by SC Hewitt, W Winuthayanon, KJ Hamilton, L Donoghue, JF Foley, GW Muse, JP Lydon, FJ DeMayo, K Adelman, KS Korach.

Excerpt: “These findings indicate that Pol II pausing is not necessary to initiate but is required to maintain pregnancy.”

**“Epigenetic Analysis of neonatal diethylstilbestrol (DES) exposure: whole-transcriptome expression and DNA methylation profiles of the adult mouse seminal vesicle (SV)”** by Y Li, KJ Hamilton, T Wang, L Liu, K Gerrish, PA Wade, KS Korach.

Excerpt: “These findings provide a new approach toward further understanding the mechanism during developmental exposure to endocrine-disrupting chemicals in the reproductive system.”

**“Profiling molecular changes in N,N-Dimethyl-p-toluidine-induced nasal cavity toxicity”** by JK Dunnick, BA Merrick, G Flake, J Foley, A Brix, K Gerrish, KR Shockley.

Excerpt: “Cancer is a multistep process, and the early molecular changes in the nasal cavity after DMPT exposure are candidate markers for nasal cavity environmental toxins.”

**“Soluble epoxide hydrolase regulates macrophage phagocytosis and lung bacterial clearance of *Streptococcus pneumoniae*”** by H Li, JA Bradbury, ML Edin, JP Graves, A Gruzdev, J Cheng, SL Hoopes, LM DeGraff, MB Fessler, S Garantiziotis, SH Schurman, DC Zeldin.

Excerpt: “Defining the role of EETs in macrophage function may lead to development of new therapeutic approaches for bacterial diseases.”

# Climate change and environmental exposures challenge announced

*By Kelly Lenox*

NIEHS announced a new challenge Sept. 15 as part of the Climate and Health Innovation Challenge Series. The institute is calling on scientists and other innovators to create tools, such as data visualizations, to support decision-makers whose work may be affected by alterations in environmental exposures associated with climate change.

The goals of the [NIEHS Climate Change and Environmental Exposures Challenge](#) are to raise awareness of how environmental health risks may be worsened by climate change, and to enable decision-makers from local to national levels to take actions to protect their populations.

Winners will be chosen for data visualizations, tools, or applications in two prize categories, one at the multistate or national level, and the other for submissions addressing the local level.

## Improve understanding through innovation

According to the [NIEHS announcement](#), the impacts of climate change on existing environmental health risks, such as hazardous wastes, air pollution, algal blooms, and contaminants in food, are not well understood. At the same time, newly released data and tools, combined with existing data sets, are available for use.

“We’ve made more data available on the [climate data website](#), and this challenge is a way to encourage users to dig into it and create practical tools for the folks who must respond to the environmental health risks presented by climate change,” said John Balbus, M.D., NIEHS senior advisor for public health.

NIEHS issued the challenge to spur the development of innovative approaches to identifying and assessing those risks. The institute hopes public health students and professionals, data and exposure scientists, software developers, and other innovators will find ways to help analyze and convey the potential risks.

Tools may support governments needing to make protective decisions, such as:

- Siting of schools, day care centers, new housing, or critical infrastructure, such as water system intakes.
- Design or siting of urban wastewater drainage or green infrastructure.
- Placement of monitoring equipment or other sensors.
- Prioritizing remediation efforts.
- Permits or regulations that protect environmental health.

Submissions are due by Dec. 4, 2015, and the winners will be announced Jan. 12, 2016.

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## This month in EHP

The October issue of [Environmental Health Perspectives](#) (EHP) explores environmental influences on children's health, from the benefits of visiting parks, to a new study sponsored by the National Institutes of Health (NIH).



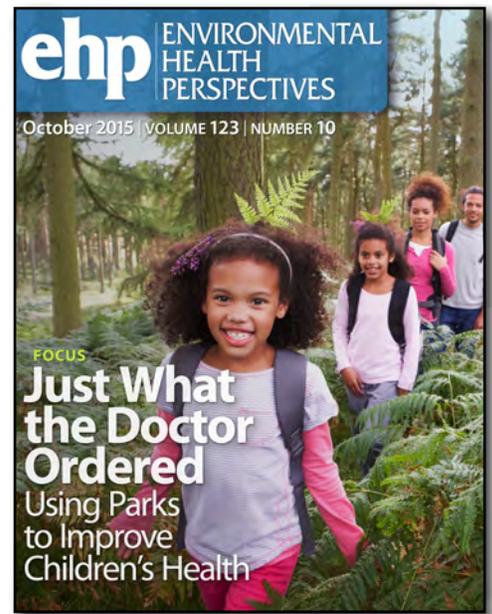
<http://twitter.com/ehponline>

### Just What the Doctor Ordered: Using Parks to Improve Children's Health

In recent years, researchers have dramatically expanded their understanding of health benefits tied to visiting parks and some of the ways these benefits occur. Now, park visits are being integrated into children's health care through park prescriptions and community health programs.

### Growing a New Study: Environmental Influences on Child Health Outcomes

Environmental Influences on Child Health Outcomes (ECHO) is a new NIH study that will focus on four areas of public health concern — respiratory health, obesity and related conditions, pregnancy and birth outcomes, and neurodevelopment.



### Research summaries featured this month include:

**A One–Two Punch to Bone: Assessing the Combined Impact of Lead and a High-Fat Diet** — A new study in mice found that lead exposure combined with a high-fat diet altered metabolic variables and bone quality more than each factor alone.

**Obesogen Holdover: Prenatal Exposure Predicts Cardiometabolic Risk Factors in Childhood** — Researchers examined the link between prenatal exposure to three kinds of persistent organic pollutants and cardiometabolic risk, or the chance of developing diabetes, heart disease or stroke, in young children.

**POPs and Pubertal Timing: Evidence of Delayed Development** — Scientists evaluated three common classes of persistent organic pollutants that affect hormones and found that higher exposures were associated with later puberty in girls, not earlier as might be expected.

**Exploring a Little-Known Pathway: Dermal Exposure to Phthalates in Indoor Air** — Some studies predict that transdermal uptake of chemicals, or absorption through the skin, directly from air may be a potentially important route of exposure. In this human study, researchers confirmed that for some phthalates, dermal uptake from indoor air may be a significant exposure pathway.

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# Extramural papers of the month

By *Nancy Lamontagne*

- [Researchers pinpoint how mutation increases autism risk](#)
- [Lung effects from Deepwater Horizon oil burning](#)
- [BPA can adversely affect parenting behavior in mice](#)
- [Warmer days may mean more emergency visits and deaths among all ages](#)

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

## Researchers pinpoint how mutation increases autism risk

Scientists have identified more than 1,000 gene mutations related to autism, but knowledge of exactly how they work is elusive. An NIEHS grantee and colleagues have found that one of these mutations affects a biochemical pathway that leads to changes in the brain.

The researchers used human cells and mice to study a gene mutation tied to overexpression of the UBE3A enzyme, which previous studies suggested must be tightly regulated for normal brain development. They discovered that protein kinase A (PKA) normally phosphorylates UBE3A, acting as a master switch to disengage UBE3A from substrates to block its activity. In cells derived from an autism patient, the researchers observed that an autism-linked mutation disrupted this phosphorylation site, leading to enhanced UBE3A activity and excessive development of small protrusions, called dendritic spines, on neurons in the brain. A higher than normal density of dendritic spines has been linked with autism.

Using mice with the same mutation, researchers also found excessive dendritic spine development, which persisted into young adulthood. When they treated neurons with agents that stimulate PKA production, levels of UBE3A decreased. This finding has promising therapeutic implications, since drugs already exist to control PKA.

*Citation:* Yi JJ, Berrios J, Newbern JM, Snider WD, Philpot BD, Hahn KM, Zylka MJ. 2015. An autism-linked mutation disables phosphorylation control of UBE3A. *Cell* 162(4):795-807.

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## Lung effects from Deepwater Horizon oil burning

The controlled burning of trapped crude oil on the water surface during the 2010 Deepwater Horizon oil spill released numerous pollutants, including particulate matter. A study, partially funded by NIEHS, revealed that acute exposure to the particulate matter from this burning is associated with lung inflammation and exacerbated allergic asthma in mice.

For the study, the researchers used particulate matter collected from controlled-burn plumes. In cell studies, they found that the particulate matter caused toxicity and generated reactive oxygen species and superoxide radicals. Mice exposed to the particulate matter exhibited significant decreases in body weight gain, systemic oxidative stress, and airway inflammation. The researchers also exposed a mouse model of allergic asthma to the particulate matter and found an exacerbated allergic asthma response via increased T helper 2 cells, lung inflammation, and airway mucus production.

These findings provide valuable information for understanding potential health effects in people, especially those with preexisting lung conditions.

*Citation:* [Jaligama S, Chen Z, Saravia J, Yadav N, Lomnicki SM, Dugas TR, Cormier SA](#). 2015. Exposure to Deepwater Horizon crude oil burnoff particulate matter induces pulmonary inflammation and alters adaptive immune response. *Environ Sci Technol* 49(14):8769-8776.

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## **BPA can adversely affect parenting behavior in mice**

An NIEHS grantee and colleagues have shown that exposure to the endocrine disruptors bisphenol A (BPA) and ethinyl estradiol can negatively affect parenting behavior in mice. This is one of the first studies to show that endocrine disruptors can influence both maternal and paternal care.

The researchers used the California mouse species, a monogamous species in which both parents care for offspring. They exposed female and male California mice in the womb and during suckling, by feeding their mothers a diet containing BPA or ethinyl estradiol. Control mice received a diet free of endocrine disruptors. Male and female offspring were then randomly paired with breeding partners including both controls and those developmentally exposed to the same endocrine disruptors.

The results showed that female California mice developmentally exposed to either BPA or ethinyl estradiol spent less time suckling their pups. Both parents were also absent from the nest more often if they were exposed to the endocrine disruptors. Even females that were not exposed to endocrine disruptors suckled their pups less and spent more time outside the nest if they were paired with a male that was exposed. The researchers believe this is one of the first studies demonstrating that early exposure of the male partner to an endocrine disruptor can disturb normal patterns of care by both partners.

*Citation:* [Johnson SA, Javurek AB, Painter MS, Peritore MP, Ellersieck MR, Roberts RM, Rosenfeld CS](#). 2015. Disruption of parenting behaviors in California mice, a monogamous rodent species, by endocrine disrupting chemicals. *PLoS One* 10(6):e0126284.

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## **Warmer days may mean more emergency visits and deaths among all ages**

An NIEHS-funded study reports that, in Rhode Island, when maximum daily temperatures rose from 75 to 85 degrees Fahrenheit, heat-related emergency department admissions and deaths increased among people of all ages. The study also suggests that the warmer temperatures forecast for the end of the century could increase emergency department visits and deaths even more.

The researchers conducted a statistical analysis of emergency department visits, deaths, and weather data, taking into account possible confounding factors, such as ozone levels. They found that between 2005 and 2012, an increase in maximum daily temperature from 75 to 85 degrees Fahrenheit, in the period from April through

October, was associated with a 23.9 percent higher rate of heat-related emergency visits, which was most pronounced among people ages 18 to 64. The researchers also estimate that if this Rhode Island population were exposed to temperatures projected for 2092 to 2099, there would be 24.4 percent more heat-related emergency department admissions.

The results suggest the need to consider the cumulative benefit of public health educational campaigns and heat warning systems that reflect the potential hazards of even moderate maximum daily temperatures.

*Citation:* Kingsley SL, Eliot MN, Gold J, Vanderslice RR, Wellenius GA. 2015. Current and projected heat-related morbidity and mortality in Rhode Island. *Environ Health Perspect*; doi:10.1289/ehp.1408826 [Online 7 Aug 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, Tara Ann Cartwright, Deacqunita Diggs, Shannon Whirledge, and Qing Xu*

- [NTP contributes to the 1000 Genomes High-Throughput Screening Study](#)
- [Elevated endotoxin in house dust increases the risk of wheeze](#)
- [Enzyme responsible for majority of mutations in certain cancers identified](#)
- [Prenatal arsenic exposure induces early onset of puberty and obesity in CD-1 mice](#)
- [Crystallography reveals new mechanism of action for polymerase mu](#)

## NTP contributes to the 1000 Genomes High-Throughput Screening Study

National Toxicology Program scientists joined researchers from several institutions to conduct the 1000 Genomes High-Throughput Screening Study, a population-wide *in vitro* cytotoxicity screening method that provides rapid estimates of human toxicodynamic variability and data on mechanisms that contribute to variation between individuals.

Researchers tested 1,086 lymphoblastoid cell lines (LCLs) from the 1000 Genomes Project, which represented nine populations from five continents, with diverse geographical and ancestral origins, to assess variation in response to 179 chemicals. Various concentrations for each chemical were applied to the LCLs, and approximately half of the chemicals produced a cytotoxic response. Several of these toxic chemicals were shown to associate with a single nucleotide polymorphism, known as rs13120371, in the solute carrier transporter gene SLC7A11. The gene had previously been implicated in chemoresistance, and the findings suggest a major role for membrane proteins and solute carrier transporters in an individual's susceptibility to environmental chemicals.

This experimental approach can be a model for evaluating individual variability in risk assessment. Although genetic variation accounts for the differences between cell lines, this system can be used to set safety standards for environmental chemicals and determine various mechanisms of toxicity. **(DD)**

*Citation:* [Abdo N](#), [Xia M](#), [Brown CC](#), [Kosyk O](#), [Huang R](#), [Sakamuru S](#), [Zhou YH](#), [Jack JR](#), [Gallins P](#), [Xia K](#), [Li Y](#), [Chiu WA](#), [Motsinger-Reif AA](#), [Austin CP](#), [Tice RR](#), [Rusyn I](#), [Wright FA](#). 2015. Population-based in vitro hazard and concentration-response assessment of chemicals: the 1000 genomes high-throughput screening study. *Environ Health Perspect* 123(5):458-466.

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## **Elevated endotoxin in house dust increases the risk of wheeze**

In a recent study, NIEHS researchers and collaborators found that elevated levels of bacterial endotoxin in house dust were linked with increased risk of wheeze, and that this exposure was higher in homes with poor living conditions. The findings may provide guidance on how to reduce the number of asthma-related medical visits that result from high endotoxin exposure.

This research is the largest study of endotoxin exposure to date. The scientists analyzed data for nearly 7,000 participants in the 2005-2006 National Health and Nutrition Examination Survey. Endotoxin levels were measured in dust samples collected from bedding and bedroom floors. Asthma-related outcomes were obtained by interviewing participants using questionnaires.

The analysis shows that endotoxin exposure is significantly associated with wheeze in the past 12 months, wheeze during exercise, doctor's office or emergency room visits, and use of prescription drugs for wheeze. Higher endotoxin exposure was linked to lower family income, older homes, carpeted floors, and the presence of cockroaches, pets, younger children, or smokers in the home. The authors propose that reducing poverty and improving living conditions may help alleviate house endotoxin-induced wheeze. **(QX)**

*Citation:* [Thorne PS](#), [Mendy A](#), [Metwali N](#), [Salo P](#), [Co C](#), [Jaramillo R](#), [Rose KM](#), [Zeldin DC](#). 2015. Endotoxin exposure: predictors and prevalence of associated asthma outcomes in the U.S. *Am J Respir Crit Care Med*; doi:10.1164/rccm.201502-0251OC [Online 10 August 2015].

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## **Enzyme responsible for majority of mutations in certain cancers identified**

Scientists were aware that the apolipoprotein B mRNA editing enzyme catalytic polypeptide-like (APOBEC) cytidine deaminases were capable of inducing DNA damage and mutations, but a team led by NIEHS researchers determined that mutations made by APOBEC3A were more frequently found in certain cancers. Other researchers previously named APOBEC3B as the deaminase primarily responsible for a majority of DNA mutations in cancerous cells. The study may help scientists further determine the mechanism of genome instability in cancer.

APOBEC3A and APOBEC3B prefer distinct DNA motifs, which allowed the researchers to follow their signatures in The Cancer Genome Atlas, a cancer sequence database. The authors mined 15 recently published cohorts of cancer whole-genome mutations and found that five cancer types — bladder, breast, head and neck, lung adenocarcinoma, and lung squamous cell carcinoma — had a significant presence of APOBEC signatures. In these cancers, APOBEC3A caused 10 times more DNA sequence changes than APOBEC3B. These distinct signatures may prove useful when determining the course of treatment for patients, while the presence or absence of either mutagen may be useful for cancer screening. (SW)

*Citation:* Chan K, Roberts SA, Klimczak LJ, Sterling JF, Saini N, Malc EP, Kim J, Kwiatkowski DJ, Fargo DC, Mieczkowski PA, Getz G, Gordenin DA. 2015. An APOBEC3A hypermutation signature is distinguishable from the signature of background mutagenesis by APOBEC3B in human cancers. *Nat Genet* 47(9):1067-1072. (Story)

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## Prenatal arsenic exposure induces early onset of puberty and obesity in CD-1 mice

NIEHS researchers have investigated the impact of prenatal exposure to arsenic at two levels — the U.S. Environmental Protection Agency drinking water standard of 10 parts per billion and the tumor-inducing level of 42.5 parts per million — on reproductive and metabolic functions. Female CD-1 mice were exposed *in utero* via drinking water during the second half of gestation, which was between 10 days after fertilization and birth, and monitored through adulthood.

The study demonstrated that CD-1 females exposed to arsenic *in utero* exhibited early onset puberty. Females in the 42.5 parts per million treatment group had fewer litters and a shorter fertile period compared to the 10 parts per billion treatment group. Both arsenic-exposed groups also exhibited higher body weight and fat content. In addition to increasing the incidence of obesity, exposure to arsenic also impaired glucose tolerance.

Taken together, these data suggest that arsenic-induced weight gain, glucose intolerance, and early onset puberty could derive from epigenetic changes as a consequence of *in utero* exposure. These epigenetic changes can occur at cellular or systemic levels, influencing metabolism and hormone production. Future studies are needed to shed light on the mechanism underlying arsenic-associated complications and are of foremost importance to understanding the possible health outcomes in humans. (TAC)

*Citation:* Rodriguez KF, Ungewitter EK, Crespo-Mejias Y, Liu C, Nicol B, Kissling GE, Yao HH. 2015. Effects of in utero exposure to arsenic during the second half of gestation on reproductive end points and metabolic parameters in female CD-1 mice. *Environ Health Perspect*; doi:10.1289/ehp.1509703 [Online 21 August 2015]. (Story)

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## Crystallography reveals new mechanism of action for polymerase mu

NIEHS researchers discovered a novel aspect of the DNA repair mechanism for polymerase mu (Pol mu) utilized in the repair of double strand DNA breaks.

Researchers determined X-ray crystal structures of Pol mu with a 2-nucleotide gapped DNA substrate and an incoming nucleotide, to clarify the steps involved in its catalytic DNA strand break repair cycle. Scientists found that Pol mu uses the last unpaired template base on the 5' end of the DNA break to direct nucleotide binding and incorporation. This mechanism of action is in stark contrast to the canonical mechanism described for other template-dependent DNA polymerases, which involves using the first available 3' template base to direct strand elongation.

This report highlights the importance of understanding the structure and function relationships of this polymerase and provides critical insights into its behavior within the context of DNA strand break repair. **(RB)**

*Citation:* [Moon AF](#), [Gosavi RA](#), [Kunkel TA](#), [Pedersen LC](#), [Bebenek K](#). 2015. Creative template-dependent synthesis by human polymerase mu. *Proc Natl Acad Sci U S A* 112(33):E4530-E4536.

(Robert Brown, Ph.D., is an Intramural Research and Training Award (IRTA) fellow in the NIEHS Cell Biology Group. Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group. Deacquita Diggs, Ph.D., is a National Health and Environmental Effects Laboratory fellow in the U.S. Environmental Protection Agency Developmental Toxicity Branch. Shannon Whirledge, Ph.D., is an IRTA fellow in the NIEHS Molecular Endocrinology Group. Qing Xu is a biologist in the NIEHS Metabolism, Genes, and Environment Group.)

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# Inside the Institute

## Employees' years of service celebrated

*By Ian Thomas*

NIEHS staff gathered Sept. 16 in Rodbell Auditorium for the institute's annual Years of Service ceremony. The event was hosted by NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., and recognized 48 employees, commemorating career milestones of 10, 20, 30, and 40 years, and 14 retirees.

"As federal employees, we work directly for the American people," said Birnbaum. "Here at NIEHS, that means funding and supporting groundbreaking research into the causes of disease and disability. It's a big job, and it takes a very special type of person to choose it for a career."

Assisted by NIEHS Deputy Director Richard Woychik, Ph.D., Birnbaum presented each honoree with a framed certificate noting their milestone and thanked them for their service.

In all, this year's event recognized 850 years of Federal service. "It's not every year that we get to celebrate this much collective experience," noted Birnbaum. "That's a lot of dedication, both to our institute and our mission."

Awardees were joined afterward by colleagues, peers, and members of NIEHS leadership for a reception in the lobby.



*Ten-year awardee Dutcher is a biologist with the NIEHS Macromolecular Structure Group. (Photo courtesy of Steve McCaw)*



*Beard, who received a 20-year award, is an industrial hygienist with the NIEHS Worker Education and Training Program. (Photo courtesy of Steve McCaw)*



*Mauil, of the NTP Biomolecular Screen Branch, was recognized for 20 years of service as a toxicologist. (Photo courtesy of Steve McCaw)*



From left, Zhang, Yang, and Chao enjoy refreshments at the reception. (Photo courtesy of Steve McCaw)



From left, John Bucher, Ph.D.; Darryl Zeldin, M.D.; Janet Hall, M.D.; Sharon Evans, and Kay Tierney were happy to serve ice cream at the reception. (Photo courtesy of Steve McCaw)

10 Years		
Karen Adelman	Susan Elmore	Paul Wade
Tracy Aiken	Kristina Filardo	Laura Wharey
Frank Chao	Richard Kwok	Gregory Whitehead
Honglei Chen	Yin Li	Pinkney Wilder
Wei Chen	Robert Oakley	Jason Williams
Donald Cook	Uduwage Perera	Jun Yang
Elizabeth Denholm	Min Shi	Dmitri Zaykin
Robert Dutcher	Ryan Snyder	Leilei Zhang

20 Years		
Sharon Beard	Christine Jewell	Edward Mosley
Trisha Castranio	Stephanie London	Alyson Scoltock
John Cidlowski	Jason Malphus	Laura Watson
Julie Horton	Elizabeth Maull	Leroy Worth

30 Years		
Gwen Collman	James Mastin	John Roberts
Scott Gabel	Bruce Merrick	Roeland Schaaper
Dori Germolec	David Miller	Diane Wilson

40 Years		
Barbara Dietz	Fred Mitchell	

Retirees		
Wanda Boggs	Susan Hart	Michael Resnick
Hamilton Brown	Sharon Hite	William Schrader
Adolphus Caviness, III	Robin Jones	Velvet Torain
Mary Gant	Scott Merkle	Diane Wilson
Clarence Gibson	Georgina Pagan	



40-year honoree Mitchell indulges his sweet tooth after the ceremony. (Photo courtesy of Steve McCaw)

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

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# NIEHS launches 2015 charity drive

By Ian Thomas

On Sept. 18, NIEHS launched its annual charity drive, known as the Combined Federal Campaign (CFC). Centered on the theme, “You Can Change a Life,” this year’s campaign started in style with a well-attended event and a morning-long bake sale with tasty treats for attendees.

“The CFC is our chance to band together as federal workers in support of those that support our local community,” said Mark Miller, Ph.D., who is co-chairing this year’s drive along with NIEHS colleagues Debbie Wales and Mary Jacobson.

All proceeds from the bake sale went toward this year’s overall fundraising goal of \$116,000 in charitable pledges by Dec. 1.

## A legacy of caring

Founded in 1961, the mission of the CFC has been to promote and support philanthropy through a program that is employee-focused, cost-efficient, and effective in providing all federal employees the chance to help improve life for all.

“Since its inception more than fifty years ago, CFC has evolved into the leading employee giving program in the country,” said NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D. “In that time, federal employees have donated more than \$193 million to charities across the nation — \$1.3 million of that right here at home through CFC of North Carolina.”

Today, donors can pledge to more than 24,000 charities nationwide. Some love the range of options; Birnbaum considers it awe-inspiring. “We host dozens of charities on our campus every year through events like Fall Fest,” Birnbaum said, referring to the first in a series of upcoming events (see [sidebar](#)). “Those are priceless opportunities because they put us face-to-face with the causes we’re supporting. If you’re unsure where to give, that’s a great way to narrow down your choices.”

The two charities present at this year’s kickoff were Durham-based [Independent Animal Rescue \(IAR\)](#) and the [United Service Organizations of North Carolina \(USO-NC\)](#).

More information on giving to CFC is available from the [Greater North Carolina Area CFC](#).

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



*Birnbaum thanked donors, past, present, and future, for their generosity. (Photo courtesy of Steve McCaw)*



*“Supporting USO-NC is not only changing a life, but saving a life,” said Kathy Bull, development director for USO of North Carolina, as she detailed some of the many ways USO supports U.S. servicewomen and servicemen. (Photo courtesy of Steve McCaw)*



NIEHS employees lined up for sweets donated by staffers to support CFC. (Photo courtesy of Steve McCaw)



IAR Director Elaine Bardes discussed her organization's commitment to animal care, sharing several animal rescue stories. (Photo courtesy of Steve McCaw)

## 2015 CFC Events

**Fall Fest/Charity Fair**, Oct. 20, Building 101.

**Fun Run/Walk with EPA**, Oct. 21 (Rain Date October 23). More details to follow.

**Pumpkin Carving Contest**, Oct. 29. More details to follow.

**Book Sale**, Nov. 10-13, Building 101 C-Mall and Keystone Lobby

**Bake Sale**, Nov. 24, Building 101 Lobby and Keystone Lobby.

**Silent Auction**, Dec. 1, Building 101 Lobby and Keystone Lobby.

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