

May 2015

NIEHS Spotlight



[Tribal forum forges new connections](#)

Environmental and health workers representing more than 20 tribes joined researchers and NIEHS in a tribal forum in Tucson, Arizona.



[Five years after oil spill, NIEHS continues work in Gulf region](#)

NIEHS researchers continue work with Gulf region partners to study human health effects and establish a plan for research response to future disasters.



[Spotlight on air pollution and health](#) 🏆

NIEHS scientists and grantees highlight air pollution and health in exciting new findings, educational webinar presentations, and award-winning research.



[NIEHS supports White House event on climate change and health](#)

The White House held a live webcast April 7 to launch the new climate data initiative, helping communities minimize health impacts of climate change.



[Scholars Connect Program shares outstanding results](#) ▶ Video

The NIEHS program celebrated its third year of research experience for local students, with a symposium including an Outstanding Scholar Award.

Clinical Feature



[Women's Health Awareness Day serves Durham area](#) ▶ Video

On April 11, women from the Durham, North Carolina area enjoyed events to enhance their health, cosponsored by the NIEHS Clinical Research Program.

Science Notebook



[Distinguished lecturer examines the biology of Alzheimer's disease](#) ▶ Video

Scott Small, Ph.D., discussed his use of functional imaging to study the role of the hippocampus in Alzheimer's disease and other illnesses.



[Zeldin inducted into Association of American Physicians](#) 🏆

NIEHS Scientific Director Darryl Zeldin, M.D., was inducted into the 130-year-old Association of American Physicians in April.



[Fessler elected to American Society for Clinical Investigation](#) 🏆

Michael Fessler, M.D., joined an elite group of physician scientists during the annual meeting of the American Society for Clinical Investigation.



[Exposome research highlighted at Duke symposium](#)

The April 3 symposium explored the impact of environmental exposures on biological pathways involved in cancer.

NIEHS Spotlight



[Public Health Service officers from NIEHS welcomed home from Ebola mission](#)

Lt. Debra King and Lt. Cmdr. John McLamb deployed to Liberia for two months to serve in the Monrovia Medical Unit, and both would do it again.



[NIEHS postdoc lands big pharma job in Europe](#)

Christopher Campos, Ph.D., landed a job at Roche in Switzerland, as a trainee scientist specializing in bimolecular drug delivery to the brain.



[UNC Environmental Resource Program recognized for partnerships and community service](#)

The NIEHS-funded program won a UNC engaged partnership award for its work to protect people consuming fish caught in PCB-contaminated waters.



[St Charles transitions into project management](#)

In March, NIEHS trainee Jordan St Charles, Ph.D., began a new position as a clinical trials project manager at LabCorp.



[NIH names Goldstein scientist emeritus](#)

NIH awarded emeritus status to NIEHS scientist Joyce Goldstein, Ph.D., in honor of her contributions to biomedical research and her worldwide reputation.

Science Notebook



[New tenure-track researcher joins NIEHS](#)

Jennifer Martinez, Ph.D., heads the Inflammation and Autoimmunity Group, focusing on responses of the innate immune system.



[Bushel honored with career achievement award](#)

UMass-Amherst honored Pierre Bushel, Ph.D., with a Distinguished Alumni Award for his substantial influence in the field of toxicogenomics.



[Arsenic linked to blood pressure increases during pregnancy](#)

K.C. Donnelly award-winner Shohreh Farzan, Ph.D., reported links between arsenic in drinking water and elevated blood pressure in pregnant women.



[Gordenin talk featured at 2015 Lineberger Symposium](#)

NIEHS scientist Dmitry Gordenin, Ph.D., was a featured speaker at the 39th annual Lineberger Symposium at the University of North Carolina.



[Spring Neuroscience Meeting is a resounding success](#)

NIEHS cosponsored the spring meeting of the Triangle Society for Neuroscience and was well represented by NIEHS scientists and fellows.



[This month in EHP](#)

This month's Environmental Health Perspectives looks at personal care products, and use of chemical footprinting to manage liabilities.

Inside the Institute



[Administrative professionals event recognizes heavy lifters behind the scenes](#) Video

NIEHS continued its tradition of celebrating contributions of administrative professionals with a special event and ice cream social May 22.



[NIEHS team cleans local roadway for Earth Day](#)

NIEHS continued its weeklong celebration of Earth Day on April 21 by cleaning up a stretch of Hopson Road near the institute.

Extramural Research

[Extramural papers of the month](#)

- Children's lungs grew stronger as pollution declined in California
- Prenatal window of susceptibility for genetic damage
- More evidence that lead plays a role in schizophrenia
- MRI reveals how early life air pollution exposure affects the brain

Intramural Research

[Intramural papers of the month](#)

- NTP researchers demonstrate common drinking water disinfection by-product is carcinogenic
- NELF mediated Pol II pausing in ESCs controls signaling pathways necessary for development
- Genetic and environmental factors interact to affect the severity of infant RSV bronchiolitis
- Leading the way in ribonucleotide excision repair
- Inhibition of NADPH oxidase halts disease progression in Parkinson's disease models

Calendar of Upcoming Events

- **May 6-7 (off-site event)**, May 6, 8:30 a.m. – 5:00 p.m.; May 7, 8:30 a.m. – 3:30 p.m., at RTI headquarters in Research Triangle Park, North Carolina — NIEHS Centers for Nanotechnology Health Implications Research Consortium Grantee Meeting
- **May 7**, 9:00 a.m. – 5:00 p.m., in Rodbell AB — NIEHS Genomics Day
- **May 7**, 1:00 – 2:00 p.m., in Keystone 1003 — Keystone Science Lecture Seminar Series talk by Jack Gilbert, Ph.D., from the Argonne National Laboratory, on “Adventures in Our Microbial World”
- **May 11-12 (off-site event)**, May 11, 8:00 a.m. – 5:00 p.m.; May 12, 8:00 a.m. – noon, at the NIH Natcher Conference Center in Bethesda, Maryland — NTP Expert Panel on Identifying Research Needs for Assessing Safe Use of High Intakes of Folic Acid, register to attend [in person](#) or via [webinar](#)
- **May 14**, 9:30 – 11:00 a.m., in Rodbell C — the Embryonic Stem Cell Biology Laboratory welcomes Guoliang Xu, Ph.D., from the Shanghai Institutes for Biological Sciences, speaking on “Enzymatic DNA Oxidation in the Control of Mammalian Development”
- **May 14 (webinar)**, 11:00 a.m. – 12:30 p.m. — NIEHS Exposure Science and the Exposome Webinar Series with John Wambaugh, Ph.D., from the U.S. Environmental Protection Agency, discussing “EPA Exposure Research and the ExpoCast Project: New Methods and New Data”, register
- **May 15**, 11:00 a.m. – noon, in Rodbell Auditorium — Distinguished Lecture Seminar Series featuring John Hogenesch, Ph.D., from the University of Pennsylvania, speaking on “The Landscape of Circadian Gene Expression: Implications for Biology and Medicine”
- **May 17-19 (off-site event)**, at the Carolina Inn in Chapel Hill, North Carolina — 9th Congress of the International Society of Nutrigenetics and Nutrigenomics, [register to attend](#)
- **May 27 (off-site event)**, 9:00 a.m. – noon, at the NIH Natcher Conference Center in Bethesda, Maryland — Interagency Coordinating Committee on the Validation of Alternative Methods public forum, register to attend [in person](#) or via [webinar](#)
- **May 28**, 10:00 – 11:00 a.m., in Rodbell AB — Keystone Science Lecture Seminar Series talk by Graham Walker, Ph.D., from the American Cancer Society, on “Translesion DNA Polymerases: From Cancer Chemotherapy to Bactericidal Antibiotics”
- **June 2-3**, 8:00 a.m. – 3:30 p.m., in Rodbell Auditorium — NAEHS Council meeting
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Tribal forum forges new connections

By Kelly Lenox

Representatives of more than 20 tribes joined the University of Arizona [Southwest Environmental Health Sciences Center](#) (SWEHSC) and NIEHS April 16 in Tucson, Arizona for a tribal forum. NIEHS regularly holds community forums around the country to learn about local environmental health concerns and to share NIEHS research.

Linda Birnbaum, Ph.D., NIEHS and National Toxicology Program director, accepted the suggestion to invite tribal partners to the forum, made by Marti Lindsey, Ph.D., director of the SWEHSC Community Outreach and Education Program. An outreach committee with representatives from SWEHSC, the Inter Tribal Council of Arizona (ITCA), and the Environmental Protection Offices of the Tohono O'odham Nation, and Ak-Chin Indian Community developed the program, [Tribal Stories of Health and the Environment](#).

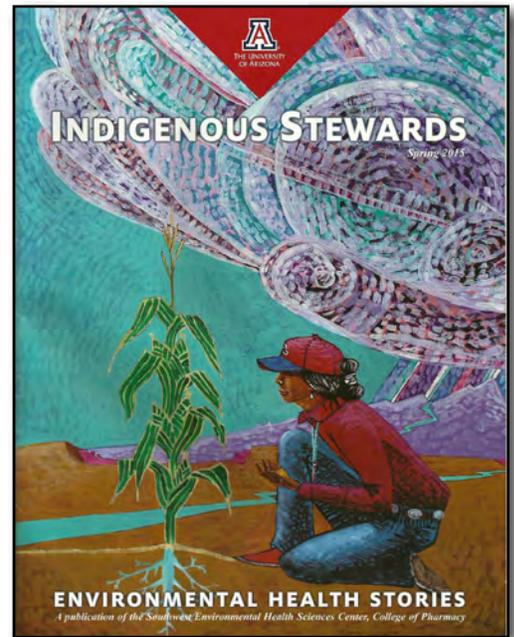
With a focus on environmental health challenges faced by Native Americans, the forum drew more than 115 tribal community members. "The event was the largest forum yet," said John Schelp, NIEHS special assistant for community engagement and outreach.

Numbers were not the only sign of success, according to Lindsey. She said the outreach partnership and the center had been trying for six years to bring environmental and health professionals and university researchers together at a conference. "This is the first time health and environmental workers met in the same room at the same time," Lindsey said. "I expect the ripples from the forum will last for many years."

Forging stronger ties and new connections

According to event planners, Birnbaum's presence helped achieve a high level of participation from regional tribes, as did her approach of treating the event as a dialogue, with a focus on listening to what tribal members had to say.

Marc Matteson, representing the Ak-Chin Indian Community of Maricopa, Arizona, served on the planning committee. "[We saw] a lot of freedom in putting together this conference — which you don't see that much," he said. Lindsey agreed, emphasizing the wisdom of asking tribal leaders and researchers to work together on setting priorities. "The planning committee was able to inform each other and seek collaboration across Indian Country," she said.



The first issue of [Indigenous Stewards](#), published by SWEHSC, reflects the center's holistic approach to environmental health, which respects interconnections with water, air, food, and land. (Artwork courtesy of Patrick Tso)



Gilbert Rivera Jr., left, tribal liaison for SWEHSC, worked closely with NIEHS on the forum. "We need to understand the problem before pushing for solutions," said Birnbaum, right. (Photo courtesy of Gilbert Rivera Jr.)

Putting needs of tribes first

Souta Calling Last, water systems environmental specialist with ITCA, articulated the theme of the forum in her keynote address, saying participants were “lashed together, bundled throughout life.” That interconnection was reflected by the day’s sessions.

- **Water and Human Health** — presentations addressed drinking water exposures from arsenic, uranium, cryptosporidium, and other contaminants.
- **Air Quality and Respiratory Health** — speakers discussed dust, pesticide use in agriculture and communities, and indoor air quality.
- **Climate Change and Epidemiology** — speakers focused on health effects of climate change and epidemiological perspectives on tribal issues.
- **Environment and Health** — presenters shared concerns ranging from health disparities and cancer prevalence, to health education and children’s health.
- **Resources for Addressing Environmental Health Disparities** — staff from SWEHSC, NIEHS, and other groups discussed resources available to address tribal health disparities.

Each session provided time for feedback and discussion. “Every table mixed Native American representatives with NIEHS scientists and University of Arizona researchers,” said Schelp. “At the end of the day, each of us shared what had struck us most,” he continued. “It was a powerful way to end the gathering.”

Planning for the future

NIEHS staff also visited the University of Arizona to speak with graduate students. Ericka Reid, Ph.D., director of the NIEHS Office of Science Education and Diversity; Mike Humble, Ph.D., health scientist administrator in the NIEHS Division of Extramural Research and Training; and Schelp discussed topics ranging from NIEHS research to career opportunities within the National Institutes of Health.

Addressing the near term, Birnbaum announced a December 2015 workshop to focus on the concept of tribal ecological knowledge. “Workshop goals are to explore ways to improve trust in academic-tribal research; to identify methods for incorporating community-acquired data and local tribal ecological knowledge into environmental health and biomedical research studies; to consider ethical approaches for tribal-specific data collection; and to build capacity to respond to long-term and immediate disaster events,” she said.

Joint meeting of NIEHS core centers and training directors

While in Arizona, Birnbaum also participated in the NIEHS Environmental Health Sciences Core Centers and Training Directors annual meeting April 14-15, hosted by SWEHSC at the University of Arizona.

As with other core center meetings (see [story](#)), the agenda offered a vast array of scientific talks and poster sessions, meetings on administrative needs, and presentations by new investigators, combined with opportunities for informal discussions.



While in Arizona, Birnbaum toured sites on Tohono O’odham Nation lands, where cliffs like these are formed when land gives way due to groundwater extraction. (Photo courtesy of John Schelp)



Inside a greenhouse on a Tohono-O’odham cooperative farm, Bob Sotomayor, left, San Xavier Co-op Farm coordinator, discussed agricultural water use with Birnbaum. (Photo courtesy of John Schelp)



After the greenhouse tour, Sotomayor, center, spoke with, from left, Schelp; Serrine Lau, Ph.D., director of SWEHSC; Clark Lantz, Ph.D., deputy director of SWEHSC; Lindsey; Birnbaum; and Liam O’Fallon, who oversees the NIEHS Community Outreach and Engagement Cores. Of the tribe’s agricultural practices, Sotomayor said the coop uses only things from the land when cultivating their crops. (Photo courtesy of Gilbert Rivera Jr.)



From right, Phyllis Valenzeula, San Xavier Co-op Farm catering coordinator, shows Lau, Lantz, and Birnbaum one of the edible cactus fruits that grow in the area. (Photo courtesy of Gilbert Rivera Jr.)



Sally Pablo, right, director of natural resources for the San Xavier District, described to Birnbaum the successful restoration of riparian wetlands carried out by the Tohono O’odham Nation. (Photo courtesy of John Schelp)



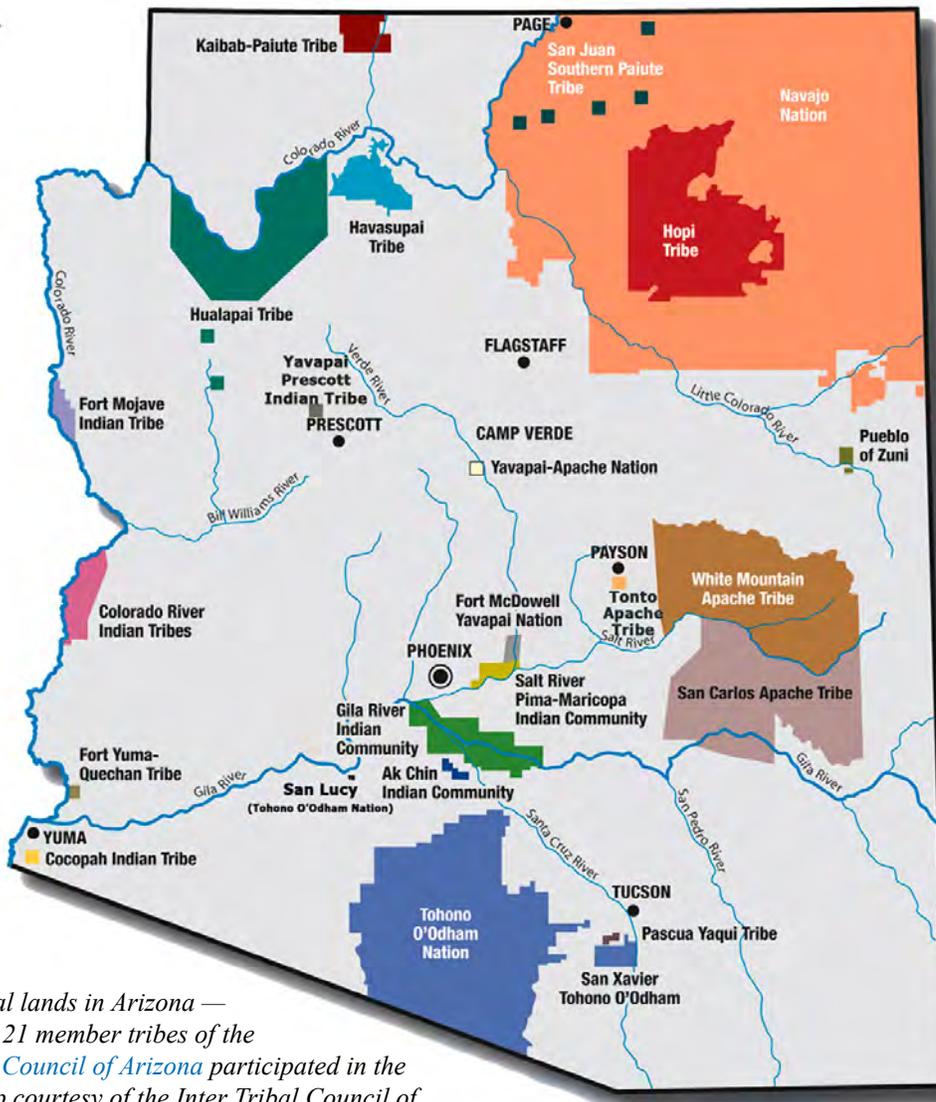
Students from Ha:san Preparatory and Leadership School in Tucson, Arizona, opened the forum with traditional songs. (Photo courtesy of Gilbert Rivera Jr.)



On a visit to Mission San Xavier del Bac, Birnbaum, left, listened as Lindsey, center, and Lau discussed area health concerns. (Photo courtesy of John Schelp)



Forum organizers assigned seats to participants, to ensure stakeholder groups would mix with each other and encounter new points of view. (Photo courtesy of Gilbert Rivera Jr.)



Map of tribal lands in Arizona — many of the 21 member tribes of the [Inter Tribal Council of Arizona](#) participated in the forum. (Map courtesy of the [Inter Tribal Council of Arizona](#)) [Click for larger image](#)

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Five years after oil spill, NIEHS continues work in Gulf region

By Robin Mackar

Five years after the Deepwater Horizon oil rig explosion, researchers supported by NIEHS and the National Institutes of Health (NIH) continue work in three related areas — a study of oil spill cleanup workers called the GuLF STUDY, research partnerships between Gulf-area universities and community organizations, and an NIH disaster research response effort.

“Ever since the oil spill in 2010, we’ve been working to understand if the disaster caused health problems among Gulf Coast residents,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program. “Health research takes a long time, but we are making progress, thanks in large part to the continued and dedicated efforts of community partners.”

GuLF STUDY

Preliminary results from the NIH-led [GuLF STUDY](#) show that oil spill cleanup workers reported increased physical symptoms, including cough and wheeze, and mental health symptoms, such as depression and anxiety, compared to nonworkers.

The research team developed a job-exposure matrix for specific cleanup jobs at different times and locations. The matrix enabled scientists to characterize exposures of workers participating in the study and assess possible links between reported health symptoms and the chemicals each worker was exposed to.

“Starting with total hydrocarbons as a marker of oil exposure, we are beginning to see that levels of chemical exposure vary across jobs and differ with the time period of the spill,” said Dale Sandler, Ph.D., lead researcher for the GuLF STUDY. “Exposure levels were higher for those working closest to the spill, and while the well was leaking. Many of the measurements taken on land were at or close to normal exposure levels. This should be good news for many in the Gulf community.”

Gulf university-community partnerships

NIEHS has also taken the lead in funding the [Deepwater Horizon Research Consortia](#). As part of the consortia, four Gulf-area universities are working with dozens of community organizations to conduct health research and communicate results. These university-community partnerships focus on health concerns identified by communities after the oil spill, including pregnancy and birth outcomes, general physical and mental health of coastal residents, and seafood safety.



“Communities know who they are, know what concerns them, and want to work with researchers to be part of the program,” Birnbaum said in her keynote presentation at the 2015 Gulf of Mexico Oil Spill and Ecosystem Science Conference. (Photo courtesy of Steve McCaw)



Sandler leads the GuLF STUDY, which includes adults ages 21 and over who helped with the oil spill cleanup, took training, signed up to work, or were sent to the Gulf to help in some way. (Photo courtesy of Steve McCaw)

“The consortium exemplifies an equitable academic-community partnership and shows how community engagement can support research as well as address local needs,” said Claudia Thompson, Ph.D., head of the NIEHS Population Health Branch and lead of the consortia.

Preliminary findings indicate that the social environment may affect a person’s ability to cope with disasters or negative health outcomes. For example, people who have strong social support systems, with networks of families, friends, and neighbors that offer psychological, physical, and financial support, tend to be more resilient and able to cope with multiple stressors in post-disaster situations.

Researchers have also determined that the seafood in the Gulf is not contaminated by the oil spill — an important finding for food supply and economics of the region.

Lesson learned — plan for disaster research response

An important lesson of the Gulf oil spill and other recent disasters is that researchers need to be involved in response efforts early, so they can collect vital health information and samples of air, water, and other materials. They also need off-the-shelf, customizable research tools to quickly launch studies that will meet all guidelines for protecting the rights of study volunteers.

To meet these needs, NIEHS is collaborating with other agencies on the [NIH Disaster Research Response Project](#). Key elements of this project include publicly accessible, field-tested data collection tools, research protocols, training materials and exercises, and development of a network of trained research responders.

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

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Spotlight on air pollution and health

By Kelly Lenox

This month, the Environmental Factor takes a look at activities by NIEHS researchers and grantees related to air pollution and health, including exciting new findings, educational webinar presentations, and award-winning research.

Prenatal exposure to air pollution linked to effects on brain development

A study published March 25 in [JAMA Psychiatry](#) and funded in part by NIEHS reports links between prenatal exposure to air pollution and effects on children’s brain structure. [Frederica Perera, Ph.D., Dr.P.H.](#), and colleagues tested pregnant women for exposure to polycyclic aromatic hydrocarbon (PAH), a component of air pollution, in their third trimester of pregnancy, then followed their babies from birth until 7 to 9 years of age, when they assessed the cognitive and behavioral development of the children.



The consortia headed by Thompson bring together Louisiana State University Health Sciences Center, Tulane University, University of Florida, and University of Texas Medical Branch at Galveston in partnership with about four dozen community organizations to conduct health research and communicate results. (Photo courtesy of Steve McCaw)

Using MRI, the researchers found that children of mothers with the highest PAH exposure had the greatest reductions of the white matter surface in the brain's left hemisphere. This reduction was associated with slower information processing speed and more severe attention deficit hyperactivity disorder symptoms.

The new results are consistent with earlier studies linking air pollution exposure and neurodevelopmental impacts. "Our findings raise important concerns about the deleterious effects of air pollutants, and PAH in particular, on brain development in children," the authors wrote. Perera is a professor of environmental health sciences at the Columbia University Mailman School of Public Health and directs the [Columbia Center for Children's Environmental Health](#).

Webinar explores reproductive health and air pollutants

The Center for Environmental Health, in collaboration with the [Reproductive Health Technologies Project](#), is sponsoring a [six-week webinar series](#) on energy development and reproductive health. NIEHS researcher [Sue Fenton, Ph.D.](#), and Perera launched the series April 6 by sharing their research on reproductive and developmental health effects of exposures to pollutants, including substances released by burning fossil fuels.

Fenton, who leads the Reproductive Endocrinology Group in the National Toxicology Program, spoke on "Chemical Exposures and Life-Long Reproductive Health Impacts." Using breast cancer as an example of the vulnerability of early life stages to chemical exposures, Fenton described the prenatal and pubertal development of breast tissue, especially its vulnerability to the effects of endocrine disruptors, carcinogens, and pollutants such as dioxins and the pesticide DDT.

Perera's talk, "The Case for an Integrated Assessment and a Sharper Focus on Children as the Moral Lever for Policy Change," broadly addressed scientific findings on the effects of emissions from fossil fuel combustion, highlighting impacts on the health of children. She explained why children and fetuses are more vulnerable to pollutants and chemicals, then reviewed numerous effects of exposures, including those on neurodevelopment, asthma, obesity, and cancer risk. "Children, especially in low-income communities, are disproportionately affected," Perera said.

She also shared good news regarding the success of interventions. Collaborating with researchers in China, Perera and colleague Deliang Tang, M.D., Dr.P.H., also from the Mailman School of Public Health, found that closure of a coal-fired power plant was linked to improvements in indicators of brain development among study participants.



Perera delivered the NIEHS Distinguished Lecture Seminar Series in January, discussing her findings related to prenatal exposures and child development. (Photo courtesy of Steve McCaw)

Perera wins Heinz Award

The [Heinz Family Foundation](#) announced April 23 that Perera is the winner of its Environment Award for 2015. The foundation said she is "a tireless champion of children's health whose research has revealed how prenatal and childhood exposures to common environmental toxicants can cause neurodevelopmental problems, cancer, and other diseases."

Perera is one of five winners of the prestigious award this year, recognizing those who have made outstanding contributions in the arts and humanities, the environment, the human condition, public policy, and technology, the economy, and employment.

Jason West wins Airkeeper Award

NIEHS grantee [Jason West, Ph.D.](#), of the University of North Carolina at Chapel Hill, was presented with the [Airkeeper Award](#) March 25. Clean Air Carolina presents these awards annually to honor individuals and organizations for leadership in air quality protection.

West's NIEHS-funded research seeks to quantify the effects of climate change on health through changes in air quality. He is also working to quantify the benefits of actions to slow climate change. According to Clean Air Carolina, West led the first study to use global atmospheric models and future scenarios to analyze the co-benefits of greenhouse gas (GHG) mitigation for air quality and human health. "Results showed that the monetized co-benefits exceeded previous co-benefits estimates and exceeded the global costs of GHG mitigation in 2030 and 2050."

Citations:

[Peterson BS, Rauh VA, Bansal R, Hao X, Toth Z, Nati G, Walsh K, Miller RL, Semanek D, Perera F.](#) 2015. Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood. *JAMA Psychiatry*; doi:10.1001/jamapsychiatry.2015.57 [Online 25 Mar 2015].

[Macon MB, Fenton SE.](#) 2013. Endocrine disruptors and the breast: early life effects and later life disease. *J Mammary Gland Biol Neoplasia* 18(1):43–61.

[Tang D, Lee J, Muirhead L, Li TY, Qu L, Yu J, Perera F.](#) 2014. Molecular and neurodevelopmental benefits to children of closure of a coal burning power plant in China. *PLoS One* 9(3):e91966.

[West JJ, Smith SJ, Silva RA, Naik V, Zhang Y, Adelman Z, Fry MM, Anenberg S, Horowitz LW, Lamarque JF.](#) 2013. Co-benefits of global greenhouse gas mitigation for future air quality and human health. *Nat Clim Chang* (3):885–889.

Save the date – virtual forum on near roadway exposure

On July 10, from 2:00 to 3:00 p.m. EDT, NIEHS will present a virtual forum on near roadway exposures and health. Moderator Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, will direct questions from online and local participants to a panel of experts from across the country. Check the [NIEHS Community Forum](#) page in the coming weeks for more information.



According to Fenton, it is important to evaluate the effects of mixtures of chemicals, because biological effects appear to differ when more than one exposure is involved. (Photo courtesy of Steve McCaw)



"Air pollution is underappreciated for its widespread health effects. It is truly satisfying to know that my research, and that of my colleagues, makes a difference in understanding the health effects of air pollution and leads to action to address this important threat," West said of his award. (Photo courtesy of the University of North Carolina)

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NIEHS supports White House event on climate change and health

By Kelly Lenox

The White House held a live webcast April 7 in Washington, D.C., to highlight data and innovation related to health and climate change. The event was part of a [broader White House effort](#) to raise awareness of the health implications of climate change, in recognition of National Public Health Week.

NIEHS Senior Advisor for Public Health John Balbus, M.D., was on hand to demonstrate new online resources and to chair a panel on climate change and infectious diseases. “Today is a great step forward, as we release these resources to support learning about and responding to the health effects of climate change,” Balbus said.

According to the National Climate Assessment [Section on Human Health](#), which NIEHS helped develop, climate change threatens health through impacts such as decreased air quality, greater exposure to allergens, and increased illnesses transmitted by disease carriers, such as mosquitoes and ticks. In addition, hospitals and other health care facilities may be threatened by extreme weather events.

New online tools

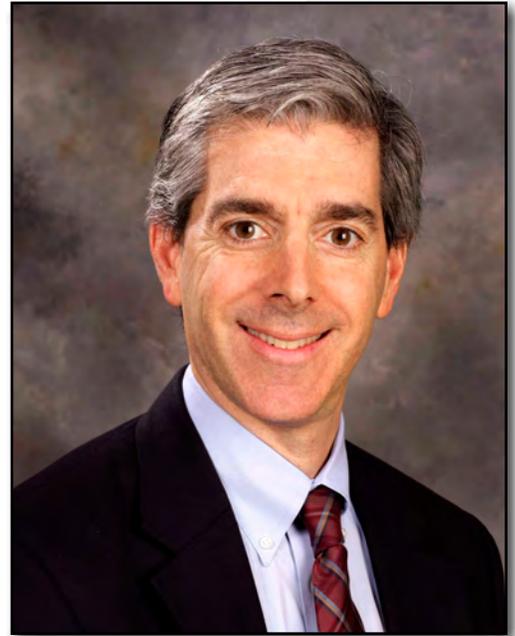
NIEHS played a substantial role in several of the initiatives announced during National Public Health Week. During the webcast, Balbus demonstrated the [Building Health Care Sector Resilience](#) toolkit. He led its creation, with the goal of helping the health care sector better respond to extreme weather events and other impacts of climate change.

This resource is part of the larger [U.S. Climate Resilience Toolkit](#) website, which provides public health officials, city planners, researchers, and others with information and decision-making tools. Balbus and Kimberly Thigpen Tart, J.D., NIEHS program analyst, led the team that developed the health topic section of the site.

Free public data sets

The webcast included the unveiling of the health topic on [Climate.Data.Gov](#), which provides free access to more than 150 data sets to help communities, public health providers, and businesses make science-based decisions to lessen the effects of climate-related health impacts.

The Centers for Disease Control and Prevention (CDC) took the lead in assembling the data sets. NIEHS provided consultation through the participation of Balbus, Thigpen Tart, and Caroline Dilworth, Ph.D., who is the NIEHS program officer for research grants related to climate change and health, in the [Interagency Crosscutting Group on Climate Change and Human Health](#).



Balbus emphasized the new data sets and toolkits are just the beginning, and that organizers are seeking additional data sets. (Photo courtesy of Steve McCaw)



Thigpen Tart serves as the NIEHS contact for the National Climate Assessment, which was released in May 2014 (see [story](#)). (Photo courtesy of Steve McCaw)

Innovation and empowerment

Representatives from the [White House Office of Science and Technology Policy](#) and leaders from academia, government, and the private sector gathered for the event in the Indian Treaty Room of the Eisenhower Executive Office Building. Many speakers highlighted the innovations that are expected to result from supporting people and communities in activities that promote climate resilience.

“We should work together to empower [people] with tools and opportunities to bring [to bear] the rich contextual information that they have ... as we try to understand the impact of climate change on their individual lives, their neighborhoods, their communities, and our nation,” said [Ernesto Ramirez](#), program director at Quantified Self Labs and one of the panelists at the event.

Beyond the data

On the same day, the White House released the draft [Climate and Health Assessment](#) for peer review by the National Academies and for public comment. Public health officials and policy makers are especially encouraged to submit comments. Balbus and Thigpen Tart served as co-authors and members of the steering committee.

“This is an unprecedented level of substantive activity on the health implications of climate change,” said Balbus. “It represents the culmination of years of effort and a huge team that has developed across HHS [the Department of Health and Human Services] and the federal government to support this work.”

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Scholars Connect Program shares outstanding results

By Kelly Lenox

Scholars, mentors, family, and friends celebrated the third year of the NIEHS Scholars Connect Program (NSCP) April 17 with a symposium featuring research presentations by each scholar. For the first time, one student was named the program’s Outstanding Scholar.

“NSCP is a concerted effort to connect with surrounding colleges and universities and take further steps toward increasing the number of students from underrepresented groups in the sciences,” said Ericka Reid, Ph.D., director of the NIEHS Office of Scientific Education and Diversity (OSD).



“I’ve learned this is what I want to do, and I learned a lot about myself,” said Outstanding Scholar Carri Murphy, center, with her mentors from left, Resnick, Thuy-Ai Nguyen, Ph.D., Menendez Rendon, and Snipes. (Photo courtesy of Steve McCaw)

Linked video:
[Watch NCSP students at work and hear what the program offers. \(3:23\)](#)

(Launches in new window)

Download Media Player: Quicktime [↗](#)

From classroom to laboratory and back

The six students in this year's cohort hail from St. Augustine's University (SAU), North Carolina Central University (NCCU), and North Carolina State University (NCSSU). Organizers began the program with a boot camp in laboratory techniques, so that the students, who have a range of laboratory and academic experience, would start with the necessary skills (see [story](#)).

The scholars worked full time in their laboratories through the summer, continuing part time when classes resumed in the fall. Their training was enhanced with opportunities to attend scientific seminars, give informal presentations of their projects, and attend information sessions on topics such as ethics and resume writing.

The program is proving its reach beyond the students directly involved. "[My experience] has carried over to my lab at school, and it helped me learn how to mentor others," said Carri Murphy, a senior at NCCU.

Outstanding Scholar Award

Organizers added an award to this year's program, recognizing one scholar for outstanding work, based on performance evaluations by mentors and the scholars themselves, as well as ratings of professional demeanor, communication skills, and enthusiasm.

Murphy was chosen as Outstanding Scholar. "Thank you very much for being part of this program and for doing your absolute best at all times," Reid said, presenting the award.

Poise and presentation

The students showed poise and expertise in their presentations. The diversity of research topics reflected their interests and backgrounds, as well as the range of scientific endeavors within NIEHS and the National Toxicology Program (NTP) (see [text box](#)).

The strengths of the NIEHS scientific community were also celebrated. Several scholars spoke of the high standards set by their mentors. "[My mentor] did not settle for anything less than excellence.

If it was good, she would say it was good, but not good enough," said DeAsia Lewis of her mentor, Natalie Ren, Ph.D. "I've been able to carry that to school with me — in writing assignments, I can always hear her in the background saying it can be better."

Several students underscored the value of the extended practical experience. "I discovered that I am still not a scientist in spite of being in a bachelor's of science program for three and a half years," laughed Aaron Manning. Besides scientific insights and shared humor, a few tears also marked the afternoon, reflecting the collegiality and connections formed among the students, and between students and the scientists they worked with so closely.



"Today is an opportunity for you to hear more about the research these scholars have been involved with since joining us last June," Reid said. (Photo courtesy of Steve McCaw)



From left, DeAsia Lewis thanked Xiaoling Li, Ph.D. and Natalie Ren, Ph.D. "I had the best experience here as a scholar," Lewis said. Speaking of Ren's high standards, she added, "and she learned that from Dr. Li." (Photo courtesy of Steve McCaw)



Angela King-Herbert, D.V.M., leader of the NTP Laboratory Animal Medicine Group, continued her strong tradition of mentoring by serving as the session chair for the third year of the NSCP. (Photo courtesy of Steve McCaw)



"I would like to give a personal thanks to my mentor Geoffrey Mueller, who has been very patient with me," said Manning, a senior at SAU. "Coming from a public health background, [Mueller] put in the time to give me the extra push I needed." (Photo courtesy of Steve McCaw)



Brianda Elzey, a student at SAU, echoed the appreciation other scholars expressed for the hard work and patience of their mentors. (Photo courtesy of Steve McCaw)



"I would really like to thank [my mentors] for letting me come into their lab. I learned a lot," said Nichole Flynn. (Photo courtesy of Steve McCaw)



"Coming from a chemistry background ... it was a big transition, but [they] really worked with me on my project. Thank you so much," said Nicole Sciortino of her mentors. (Photo courtesy of Steve McCaw)



Erica Rogers, Ph.D., of OSED, is the coordinator of the NIEHS Scholars Connect Program. (Photo courtesy of Steve McCaw)

Scholar research presentations

- **Brianda Elzey** (SAU) — “Immunohistochemical Characterization of Pulmonary Alveolar/Bronchiolar Carcinomas in Mice and Rats.” Mentored by Ron Herbert, D.V.M., Ph.D., head of the NTP [Pathology Support Group](#), and biologist Natasha Clayton, Elzey explored ways to determine the cell of origin for mice and rat carcinomas of the lung.
- **Nichole Flynn** (NCSU) — “Improved Immunofluorescence of PARP-1 for DNA Repair Studies.” Working with Sam Wilson, M.D., head of the [DNA Repair and Nucleic Acid Enzymology Group](#), postdoctoral fellow Natalie Gassman, Ph.D., and staff scientist Julie Horton, Flynn explored techniques to improve immunofluorescence of the abundant nuclear protein PARP1, to support research for correction of single-base lesion repairs.
- **DeAsia Lewis** (SAU) — “The Role of SIRT 1 in Tumorigenesis.” Xiaoling Li, Ph.D., head of the [Metabolism, Genes, and Environment Group](#), and postdoctoral fellow Shunxiang (Natalie) Ren, Ph.D., mentored Lewis in her analysis of the role of the SIRT1 protein in cancer, where it can act to both suppress and promote tumors.
- **Aaron Manning** (SAU) — “NSCP Final Presentation.” Mentored by Geoff Mueller, Ph.D., staff scientist in the [Nuclear Magnetic Resonance Group](#), Manning researched antibodies to allergens from the German cockroach and two species of dust mites, comparing populations in the U.S. and Colombia.
- **Carri Murphy** (NCCU) — “Synthetic Lethality of p53 Deficient and Mutant Cells.” Working in the [Chromosome Stability Group](#), mentored by group leader Mike Resnick, Ph.D., staff scientist Daniel Menendez Rendon, Ph.D., and biologist Joyce Snipe, Murphy worked to establish a cell model that would shed light on synthetic lethality in cells deficient in the tumor suppressor p53.
- **Nicole Sciortino** (SAU) — “The Effects of Bisphenol S (BPS) on Cell Proliferation and Estrogen Receptor Alpha 36 Signaling in Human Uterine Leiomyoma Cells.” Working with mentors Darlene Dixon, D.V.M., Ph.D., head of the NTP [Molecular Pathogenesis Group](#), and biologist Linda Yu, Sciortino studied how exposure to BPS affects proliferation of cells and cell signaling in uterine fibroids.

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Public Health Service officers from NIEHS welcomed home from Ebola mission

By Eddy Ball

The work was physically demanding and the hours were long, but for NIEHS staffers Lt. Debra King and Lt. Cmdr. John McLamb, deployment to Liberia was something they'd do again. Now back in the U.S. with a clean bill of health, the two volunteers have returned to their regular jobs.



Linked video:
[Watch a November 2014 video about the Monrovia Medical Unit \(06:46\)](#)

(Launches in new window)

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Looking back on their two months at the Monrovia Medical Unit in Liberia, neither had any regrets. When asked if he'd return if the opportunity arose, McLamb simply said, "In a heartbeat." King added, "That is what I signed up for [as a commissioned officer in the U.S. Public Health Service]."

NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., spoke for all staff in an April 2 message. "The entire NIEHS family appreciates the service that John and Debra provided during this public health crisis," she wrote.

Establishing an infrastructure for the Ebola response

Initially an emergency response facility, the 25-bed treatment center expanded its scope to become a site for clinical trials for a National Institutes of Health experimental treatment known as ZMapp, a candidate therapeutic with antibodies produced in specially grown tobacco plants.

The efforts of staff involved in the response not only saved lives, but also helped create a safety net for care providers. Assuring healthcare workers that they would be provided the best care possible if they contracted the disease helped alleviate the shortage of health care workers.

King, a medical technologist in the NTP Cellular and Molecular Pathology Branch, was the lead for the on-site clinical laboratory, where she performed testing for basic chemistry, hematology, malaria, and HIV, in collaboration with nearby off-site facilities where Ebola testing was performed. As part of her duties, King reviewed and updated standard operating procedures, developed quality control measures, and submitted daily updates.

McLamb served as an infection control officer for the unit, ensuring that individuals who entered the hot zone were properly trained and outfitted in personal protective equipment. He was responsible for decontamination of workers and overseeing infectious waste disposal, as well as air monitoring related to chlorine disinfection and heat stress.

Sacrifice and physical discomfort

As part of what U.S. Ebola responders in Liberia designated team three, King and McLamb worked many long hours in watertight protective gear. The gear was unavoidable, because their work involved the possibility of direct contact with infected patients and their biological samples.

During their first weeks in Liberia, the volunteers worked six days straight each week and often ate military MREs — meals ready-to-eat. To help deal with the heat and struggles of putting on their gear and taking it off — a process that took at least forty minutes each time — King and McLamb both shaved their heads.



Lt. Debra King (Photo courtesy of Steve McCaw)



Lt. Cmdr. John McLamb (Photo courtesy of John Maruca)

Support at home and abroad

They enjoyed the full support of their supervisors and colleagues at NIEHS and NTP, as well as their spouses and families, who assumed extra duties during the deployment.

Despite the long days at the unit, King and McLamb appreciated the reception they received in Liberia. They also managed to enjoy the tropical wildlife, especially the rich variety of insects and lizards. King went a step further into West African culture, by sampling the local delicacy of fried termites, during a termite swarm.



Not all work required full protective gear, but all was conducted in the challenging environment of the medical unit. (Photo courtesy of John McLamb)

Protected from head to toe

Writing in an HHS.gov [blog post](#), Capt. Calvin Edwards, a member of an earlier deployment with team one, described his experience in the outfits. “We worked 12-hour shifts in 90 degree heat and 90 percent humidity, often wearing head-to-toe layers of plastic gear that left us soaked in sweat within minutes,” he said.

Living conditions had improved somewhat by the time McLamb and King arrived in Liberia. But the need to follow protocol remained, and they had to be just as safety conscious as Edwards had months earlier. “A single slip in protocol could expose us to a deadly virus ...” Edwards wrote.



King's desk is typical of workspace in the tents that made up the Monrovia Medical Unit. (Photo courtesy of John McLamb)

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

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NIEHS postdoc lands big pharma job in Europe

By Vijay More

In February, former NIEHS postdoctoral fellow Christopher Campos, Ph.D., began work as a trainee scientist at the Hoffman-La Roche World Headquarters in Basel, Switzerland. After five years in the NIEHS [Intracellular Regulation Group](#), led by David Miller, Ph.D., Campos accepted a position that focuses on biomolecular drug delivery to the brain.

Novel work and specialized training

According to Campos, a novel aspect of his work in the Signal Transduction Laboratory involved establishing a protocol for isolating rodent spinal cord capillaries. He also described the first molecular signaling mechanism for transporter regulation at the blood-spinal cord barrier. Campos said his specialized training in rodent carotid artery cannulation, which allows for use of radioactive tracers to study the brain's uptake of drugs, earned him several coauthor publications and helped him land the job at Roche. As a postdoctoral fellow at NIEHS, Campos published nine papers, and he has five more in the pipeline.

“Chris has been one of the most interesting trainees in my lab,” said Miller. “He functioned as a technical wizard, improving existing procedures and developing new ones. He took full advantage of the opportunities that NIEHS and the [Research Triangle Park] area had to offer.”

While still a trainee, Campos presented invited talks at the Gordon Research Conference for Barriers of the CNS, in 2012 and 2014. In addition, he won a Fellows Award for Research Excellence, also known as a FARE award.

Beyond the lab

Campos was involved beyond his own lab as well. “The best thing about working at NIEHS is the ample exposure to a variety of science, through seminars from internal and external speakers,” Campos said. He encourages fellows to attend more talks organized by the institute. “Even if they appear less relevant to your own work, they develop your aptitude as a comprehensive scientist,” he said.

As a social chair for the NIEHS Trainees Assembly, he organized special events, including the annual trainee dinner, the Chinese New Year celebration, and the monthly fellows happy hour. He also planned informal meetings between postdoctoral fellows at local universities to foster regional networking and research collaborations.

Campos also suggested fellows take advantage of local networking opportunities, including [Triangle Biotech Tuesdays](#) and [RTP180](#). And he credited his resume and interview preparation sessions with Tammy Collins, Ph.D., head of the NIEHS Office of Fellows' Career Development, and Denise Saunders, Ph.D., career counselor with the National Institutes of Health [Office of Intramural Training and Education](#) for vital assistance in his job search.

“I firmly believe that in today's job market, networking is almost as essential as publishing papers for a postdoctoral fellow,” Campos said.

(Vijay More, Ph.D., is a visiting fellow in the NIEHS Intracellular Regulation Group.)



In addition to conducting his own research, Campos trained more than 10 postbaccalaureate and postdoctoral fellows during his fellowship. (Photo courtesy of Christopher Campos)

UNC Environmental Resource Program recognized for partnerships and community service

By Sara Mishamandani

The NIEHS-funded Environmental Resource Program (ERP) at the University of North Carolina at Chapel Hill (UNC) was honored for its partnerships with North Carolina organizations and its project to communicate fish consumption advisories to people who may eat fish caught in contaminated waterways. The program was presented with the 2015 UNC Office of the Provost Engaged Scholarship Award for Engaged Partnership on April 7.

The Office of the Provost Engaged Scholarship Award recognizes faculty members and other university groups for exemplary engaged scholarship in service to the state of North Carolina, in engaged teaching, research, and partnership. [ERP Director Kathleen Gray](#) accepted the award on behalf of the program at the UNC Public Service Awards ceremony, which is sponsored by the Carolina Center for Public Service.

With funding from the NIEHS Superfund Research Program (SRP) and Environmental Health Core Centers Program, as well as other governmental agencies and private foundations, the ERP connects UNC environmental work to North Carolina communities, classrooms, and businesses. The award highlighted its partnerships and engagement work with the Upper Neuse RIVERKEEPER Foundation, Lake Crabtree County Park (LCCP), the North Carolina Division of Public Health (DPH), and the NIEHS-funded Center for Human Health and the Environment at North Carolina State University (NCSU).

Communicating with vulnerable populations

Working with DPH, program staff and graduate students informed anglers around Badin Lake in North Carolina of advisories against consuming fish caught there because of polychlorinated biphenyl (PCB) contamination from industrial activities. With NCSU researchers Gregory Cope, Ph.D., and Catherine LePrevost, Ph.D., they also helped DPH identify more effective ways to inform anglers of potential risk to vulnerable groups they may share the fish with, such as pregnant women and children.



Gray, center, accepted the award with UNC Chancellor Carol Folt, Ph.D., left, and UNC Provost James Dean Jr., Ph.D. (Photo courtesy of Kathleen Gray)



“We felt it was crucial to involve the target audience in the process of both developing educational material and generating ideas for future outreach and education projects,” explained SRP Research Translation Core community engagement coordinator Kat Bawden, left, shown surveying an angler at Lake Crabtree. “Recreational anglers know fishing and their community’s resources better than we do.” (Photo courtesy of Sarah Yelton)

Collaborating with the Neuse RIVERKEEPER Foundation and LCCP, ERP staff and students are also developing low-literacy messages and interventions to help communicate the potential risks of eating PCB-contaminated fish caught in Lake Crabtree, another North Carolina Lake, with a special emphasis on Spanish-speaking populations. SRP Research Translation Core staff are piloting these English and Spanish educational materials at four Lake Crabtree fishing locations. They survey anglers to better understand their perception of PCB risk and receive feedback on the educational materials, including whether the materials affect the angler's intent to reduce consumption of contaminated fish.

“According to the Neuse RIVERKEEPER Foundation and LCCP, the efforts to protect vulnerable populations from consuming contaminated fish had direct and immediate benefits to those who previously had been consuming or sharing such fish,” said Gray. “Other outcomes included better understanding of how people access information on fish advisories and how or whether they factor such information into their decision making.”

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

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St Charles transitions into project management

By Monica Frazier

In March, NIEHS trainee Jordan St Charles, Ph.D., began a new position as a clinical trials project manager at [LabCorp](#) in Research Triangle Park, North Carolina. LabCorp provides comprehensive laboratory services to sponsors who are conducting clinical trials.

While at NIEHS, St Charles studied various aspects of DNA replication fidelity using budding yeast as a model system, as part of the [DNA Replication Fidelity Group](#), which is led by Tom Kunkel, Ph.D. “[Jordan] made seminal contributions to our research on three projects, the first of which has just been provisionally accepted for publication,” he said.

Using NIEHS and NTA resources

St Charles said that the NIEHS Brown Bag Lunch series was instrumental in identifying her new career as one she was interested in. “The Brown Bag Lunch events were the first place that I considered trying to work in clinical trials,” she said.

In addition to attending events like the Brown Bag Lunch series, St Charles participated in a variety of career development opportunities available at NIEHS, including the Trainees Action Committee within her laboratory branch, the NIEHS Trainees Assembly (NTA) Steering Committee, as well as writing stories for the Environmental Factor. “Being a part of the steering committee gave me more communication experiences, which should help with the more client-focused aspects of my new job,” St Charles said.



For trainees hoping to move into a similar career, St Charles gave this suggestion, “Diversify your experiences as much as possible, because those experiences can show your adaptability and bridge gaps in your resume.” (Photo courtesy of Steve McCaw)

Kunkel also recognized the contributions St Charles made throughout the institute in preparation for her future career. “Her organizational and people skills contributed greatly to the whole scientific enterprise in the Division of Intramural Research, and they were a valuable component of her training,” he said.

Preparing for a career away from the bench

St Charles took steps to help prepare for a career away from the lab bench, a move many trainees consider but are unsure how to achieve. Once she identified the career path she wanted to take, she researched important qualifications that could make her a better candidate and then followed through.

“I would recommend the Regulatory Affairs Certification study course that the [North Carolina Regulatory Affairs Forum](#) runs during evenings in the summer as a good way to learn about clinical trials in the U.S.,” St Charles noted. “It is also a great networking opportunity. I met several people who got internships or jobs through people they met there,” she added.

St Charles got additional experience by taking on an internship with Camargo Pharmaceutical Services, an opportunity she found out about through the NIEHS [Office of Fellows Career Development](#), headed by Tammy Collins, Ph.D.

Kunkel emphasized the importance of the translatable skills St Charles strengthened at NIEHS. “By the time she left for her new position, I was very confident that she had the critical thinking skills, work ethic, positive attitude, and persistence needed for success in her new position, regardless of the exact scientific context,” he said.

(Monica Frazier, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Mechanisms of Mutation Group.)

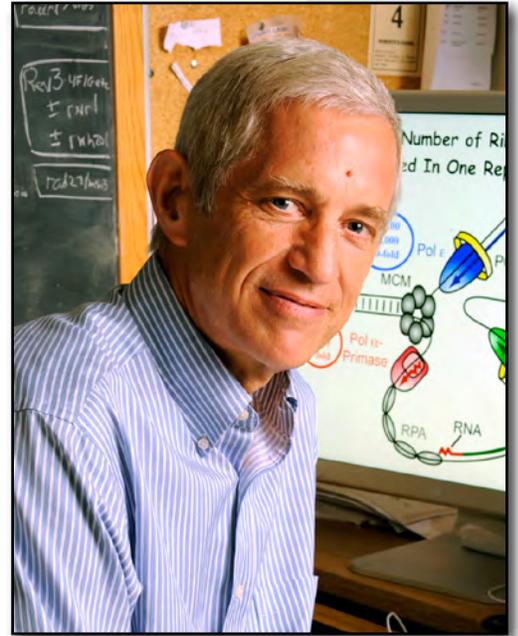
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NIH names Goldstein scientist emeritus

By Eddy Ball

Joyce Goldstein, Ph.D., became the latest National Institutes of Health (NIH) scientist emeritus appointed at NIEHS, as part of a recent wave of retirements by senior scientists. On April 3, she joined colleagues Lutz Birnbaumer, Ph.D., and Thomas Eling, Ph.D., who also followed this more indirect path to retirement. Her emeritus status honors the importance of her contributions to biomedical research and her worldwide reputation in her field.

In his announcement of Goldstein’s appointment, Scientific Director Darryl Zeldin, Ph.D., praised her groundbreaking scientific discoveries and enviable productivity. “Dr. Goldstein has published over 160 papers and 25 books and chapters during her illustrious career, and her work has been cited over 12,000 times.”



“I very much admired the fact that Jordan always took the larger view, by constantly networking as she planned for her future,” Kunkel said. (Photo courtesy of Steve McCaw)

The culmination of a 46-year career as a federal scientist

Following appointments at the Centers for Disease Control and Prevention and the U.S. Environmental Protection Agency, Goldstein accepted a position in 1977 as group leader of the NIEHS Systemic Biology Branch. She became one of the first women scientists to achieve tenure at the institute.

By the 1990s, Goldstein's research had evolved beyond her original interests in toxicology and animal studies, to center on the identification and characterization of polymorphisms, or variations in a specific DNA sequence, in the human cytochrome P450 family, which metabolizes a number of widely used pharmaceutical drugs. Over the past 25 years, her findings have helped lay the foundation for the development of personalized, precision medicine.

Looking back at her decades of mentoring biomedical researchers, Goldstein said modestly, "I had some good postdocs." Many of her former students and trainees now hold high-profile positions with government, academic, and private-sector scientific institutions.

Honor and a chance to continue research

As a scientist emeritus, Goldstein no longer receives pay for her work, but she will continue to have office space, library privileges, and network access, as well as limited technical and supply support to continue her research and service. She maintains her position as a member of the NIEHS scientific community, now with the Signal Transduction Laboratory.

Goldstein will continue to write manuscripts and reviews, contribute to editorial boards, and serve on the Faculty of 1000 as a reviewer of outstanding research in her areas of expertise. Her most immediate goal, however, is helping the scientists and trainees in her [Human Metabolism Group](#) take the next step in their careers.

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

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The package Zeldin submitted to NIH for Goldstein's emeritus appointment included glowing letters of recommendation from leading scientists at universities in the U.S., Asia, and Europe. (Photo courtesy of Steve McCaw)

Clinical Feature

Women's Health Awareness Day serves Durham area

By Robin Arnette and Kelly Lenox

On April 11, women of Durham, North Carolina and surrounding counties enjoyed Women's Health Awareness Day 2015 — a full day of activities to promote women's health awareness and provide helpful services and tools. Organizers welcomed more than 400 participants to the free program on the campus of North Carolina Central University (NCCU) in Durham. The NCCU Department of Public Health Education sponsored the event, along with the NIEHS Office of Human Research Compliance (OHRC) and Delta Sigma Theta Sorority, Inc.

Because the month of April is set aside for recognition of public health, domestic violence, and minority health and health disparities, planners placed special emphasis on serving women of color as well as the underserved, uninsured, and underinsured. "If you ask, Why women," said Joan Pakenham, Ph.D., director of OHRC and an active member of Delta Sigma Theta, "NIEHS knows that women are the core of the family, and when you promote women's health, it leads to a healthier family, which leads to healthy communities."



Linked video:
[Watch as Pakenham explained the importance of promoting women's health in this ABC news clip. \(2:13\)](#)
(Launches in new window)

Download Media Player: Flash [↗](#)

Everything in one place

The event offered four major health components in one centralized location — seminars, information sessions, health services, and on-site screenings and resources. Seminars, such as "Chronic Obstructive Lung Disease, the Overlooked Women-Killer" and "Diabetes 101 and the Durham Diabetes Coalition," and activities, such as healthy cooking demonstrations and screenings for diabetes and coronary artery blockage, were well-attended (for full list, see [text box](#)).

Clinical research booths provided information about active clinical research studies in the local area, including those being conducted at NIEHS. To help participants better understand participation in clinical studies, NIEHS sponsored a performance titled, "Trials, Not Tribulations: Judging Which Clinical Trial Fits You Best."



Pakenham, who chaired the planning and steering committee, said the hard work was put to good use, helping women focus on their health needs and learning ways to lead a healthier life. (Photo courtesy of Veronica Robinson)

Community engagement

Community engagement is an important component of clinical research at the institute, according to Pakenham. “Since NIEHS is actively carrying out clinical research studies, it is important that the community know who we are and that we are genuinely interested in working with them as an actual partner and not merely as scientists who need research participants for our clinical studies,” she said. “This event also helped NIEHS gauge the health and research needs of the community.”

Community-engaged research requires collaboration, cooperation, and negotiation with community partners, and a commitment by researchers to address local health issues. NIEHS has a long history of supporting this type of research through its grants program and the 2009 opening of the Clinical Research Unit on the NIEHS campus. As a further commitment to community engagement, in 2012, OHRC cosponsored the South Atlantic National Research Conference, “Engaging the Community for Research Success: What Scientists and IRBs [Institutional Review Boards] Need to Know” (see [story](#)).



NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., joined Durham Mayor Pro Tem Cora Cole-McFadden, Durham Public Health Director Gayle Harris, and Wake County, North Carolina, Human Services Director Regina Petteway in welcoming participants. (Photo courtesy of Veronica Robinson)



NIEHS industrial hygienist Vee Vee Shropshire, right, demonstrated the proper techniques for the Heimlich maneuver. She later joined Lindia Engram, R.N., and Harold Morcombe of Health and Safety Consultants of N.C., not shown, to demonstrate other basic first aid skills. (Photo courtesy of Veronica Robinson)



From left, Annette Rice, Sharon Beard, Pakenham, and Terry Lewis, members of the Women's Health Awareness Day committee, took a quick break from the busy, yet informative and productive day. (Photo courtesy of Veronica Robinson)



Shawn Jeter, right, is a technical information specialist in the NTP Program Operations Branch, and a fitness instructor at the Durham YMCA. She and dozens of event-goers got their heart rates up during the session on dancing for fitness and fun. (Photo courtesy of Veronica Robinson)



Blood pressure checks were just one of the many health screenings available at the event. (Photo courtesy of Veronica Robinson)



The Durham Senior Divas 'N Dude cheerleaders showed the crowd that it's never too late to get active and stay healthy. All of the members are in their 60s and 70s. (Photo courtesy of Robin Arnette)



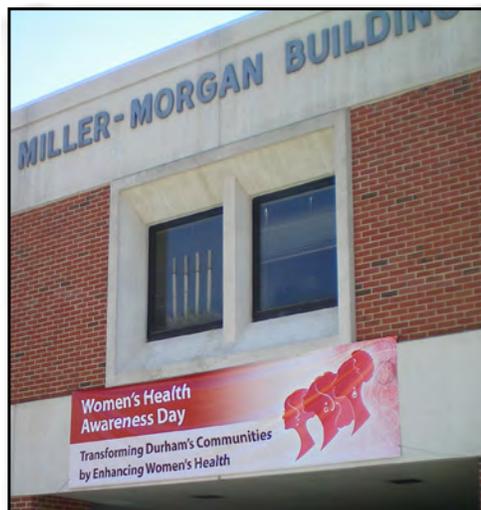
Journalist and visual artist [Anita Woodley](#) performed a one-woman show, explaining what clinical trials are and how volunteers can determine which study is right for them. (Photo courtesy of Robin Arnette)



Grace Isshiki, right, [NHALES](#) study coordinator, provided information on the NIEHS-led clinical study, which offers free treatment and medications for people with moderate to severe asthma. (Photo courtesy of Veronica Robinson)



[Stavros Garantziotis, M.D.](#), pulmonary specialist and medical director of the NIEHS Clinical Research Unit, gave a seminar on chronic obstructive lung disease. (Photo courtesy of Veronica Robinson)



All of the Women's Health Awareness Day activities took place at the Miller-Morgan building on the NCCU campus. (Photo courtesy of Robin Arnette)

Health Seminars

- Empowering Women to Love Their Heart
- Diabetes 101 and the Durham Diabetes Coalition
- My Breast Cancer Came Out of Nowhere: What Happened?
- Alzheimer’s Disease and Women’s Health
- Chronic Obstructive Lung Disease, the Overlooked Women-killer
- Eye Health
- HIV 101
- Superwoman Schema, Stress, and Self-Care: Implications for Mental Health and Wellness Among Women
- “Trials, Not Tribulations: Judging Which Clinical Trial Fits You Best”
- Risk, Awareness, Prevention of Sickle Cell Disease

Health Informational Sessions

- A Need for Change: Better Outcomes for Moms and Babies of Color
- A Journey to Breast Awareness: From Screening to Treatment
- Protecting Women’s Preventative Health Services Under the Affordable Care Act
- Human Papillomavirus: The Infection, Cancers, and the Vaccines
- Balancing Act: The Eating and Exercise Equation
- Hormones 101
- When Loving You Is Wrong: Red Flags of an Unhealthy Relationship

Health Services

- Basic First Aid Skills for the Lay Person
- Breast Self-awareness
- Healthy Cooking Demonstrations
- Myths and Realities of Organ Donation
- When You Are Unemployed: Community Access to Resources
- Holistic Practices for Improved Health and General Well-being
- Line Dancing for Fitness and Fun
- Stress Relief: N.C. Foreclosure Prevention Program

On-site Health Screenings

- Breast Mammography Screening
- Blood Pressure Checks
- Lung Capacity Testing
- Diabetes Screening
- Vision Screening
- Dental Screening
- HIV Screening
- Cholesterol Screening
- Mobile Veterans Health Center

Science Notebook

Distinguished lecturer examines the biology of Alzheimer's disease

By Robin Arnette

The hippocampus is a small structure in the brain primarily involved in learning and memory, but a growing body of research suggests it is also implicated in several illnesses, such as Alzheimer's disease, cognitive aging, depression, and schizophrenia. These disorders are mechanistically distinct, so how can the same structure be associated with such a diverse range of conditions?

Scott Small, M.D., is one of several neurologists interested in that question. His work with functional imaging has shown that part of the answer is due to the hippocampus being made of several different cell types, rather than one. Small presented his findings April 14 during his NIEHS distinguished lecture titled, "Isolating Pathogenic Mechanisms Embedded Within the Hippocampal Circuit Through Regional Vulnerability." David Armstrong Ph.D., of the NIEHS Neurobiology Laboratory, served as seminar host.

Functional imaging reveals earliest signs of illness

Small is the Boris and Rose Katz Professor of Neurology and Director of the Alzheimer's Disease Research Center at Columbia University in New York. He said the imaging technology that allows his group to study the hippocampus has only been around since the beginning of this century.

The term functional imaging means that the cameras used in this research are sensitive to changes in the metabolism of neurons. Cerebral blood volume functional magnetic resonance imaging, or CBV-fMRI, is not the only tool that can measure neuronal metabolic changes, but it is the only one that offers submillimeter resolution of hippocampal cells, which allows the ability to quantify measurements. It is also applicable to a variety of species.

"CBV-fMRI allows us to generate spatial maps in patients versus controls and ask what part of the hippocampus is linked to different disorders," Small said.

According to Small, Alzheimer's disease progresses through four major stages — preclinical; prodromal, or the earliest indication of symptoms; mild cognitive; and dementia. The areas of the hippocampus that show a loss of cerebral blood volume or loss of function show up in color on images from CBV-fMRI cameras. Small's research was able to determine that cells in a part of the brain called the lateral entorhinal cortex (LEC) start to show signs of sickness during the preclinical stage, perhaps several years before cell death and symptoms of Alzheimer's begin.



Although the majority of Small's talk focused on Alzheimer's disease, he said mapping patterns of brain dysfunction could lead to clues about other diseases. (Photo courtesy of Steve McCaw)



Linked video:
[Watch as Small explains the complexity of Alzheimer's disease in this video from Columbia University. \(2:46\)](#)

(Launches in new window)

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Alzheimer's may result from dysfunction in cellular transport

The brain mapping work also found that another part of the brain called the dentate gyrus (DG) becomes dysfunctional during the normal process of aging. However, it was relatively resistant to Alzheimer's. Analysis of both the LEC and DG highlighted a molecule, called retromer, that is involved in the origin of Alzheimer's disease.

Small explained that retromer is a multimodule protein complex involved in the transport of molecules from the endosome, which is a cellular sac that sorts particles moving into and throughout the cell. He said that amyloid precursor protein, which is the progenitor of the amyloid plaques that form in the brains of Alzheimer's patients, gets chopped up after it leaves the endosome. If retromer does not remove these fragments, they become neurotoxic to the cells. Studies in which retromer was knocked out showed an increase in brain plaques, and an increase in retromer showed a decrease in brain plaques.

Because retromer is made up of several modules, Small and his team thought that increasing the modules' ability to stick to each other would be a viable approach to drug design. "We developed chaperones, or proteins that bind two of the modules very tightly, and it increased retromer stability," Small said. "The chaperone also decreased amyloid formation."

Small discussed two other pathologies associated with Alzheimer's, which included the contribution of microglia cells and a protein called tau. Because retromer also plays a role in these pathologies, Small and his colleagues are a little closer to understanding the disease.



"Dr. Small has uncovered a fundamental insight into the relationship between aging and Alzheimer's disease, which affect different areas of the hippocampus, but together produce one of our most devastating afflictions," Armstrong said. (Photo courtesy of Steve McCaw)



"The seminar was a really nice combination of brain imaging with a molecular understanding of the results," said Geoffrey Mueller, Ph.D., a staff scientist in the NIEHS Nuclear Magnetic Resonance Group. (Photo courtesy of Steve McCaw)

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Zeldin inducted into Association of American Physicians

By Robin Arnette

NIEHS Scientific Director Darryl Zeldin, M.D., manages scores of in-house researchers that make up the institute's intramural division, but it is his pursuit of basic and clinical research that led to his nomination to the Association of American Physicians (AAP). Zeldin and several other physician-scientists were inducted into the 130-year-old association April 24 in Chicago during a joint meeting of the AAP and the American Society for Clinical Investigation.

When asked about his feelings on being inducted into the association, Zeldin said, "To be elected as a member of this association is a great honor. Members have included Nobel laureates, and members of the National Academy of Sciences and the Institute of Medicine. I am humbled to be considered part of this prestigious group of physician-scientists."

Advancing science and improving public health

AAP was founded by seven physicians in 1885 and now has more than 1,300 active members, as well as approximately 600 emeritus and honorary members around the world. The contributions of AAP members have always advanced science and improved public health. With his induction, Zeldin joins several other physician-scientists at the National Institutes of Health (NIH), including NIH Director Francis Collins, M.D., Ph.D.; Clinical Center Director John Gallin, M.D.; and Michael Gottesman, M.D., deputy director for intramural research.

"Darryl's election to membership in the Association of American Physicians recognizes both his important work on the causes of inflammation in the lung and his leadership role as scientific director of NIEHS," Gottesman said. "His studies showing that cytochrome P450s metabolize arachidonic acid to specific eicosanoids with a role in a variety of pulmonary inflammatory disorders, including asthma, have important public health implications. NIH is proud to have a scientist of Darryl's caliber, and this recent recognition is well-deserved."

Opportunities for translational research

In addition to his duties as NIEHS scientific director, Zeldin leads the Environmental Cardiopulmonary Disease Group in the Immunity, Inflammation, and Disease Laboratory, and holds a secondary appointment in the Clinical Research Branch. His research focuses on three major areas:

- Understanding the environment's role in the origins of respiratory and cardiovascular diseases.
- Identifying molecules that may be used to treat respiratory and cardiovascular disease.
- Examining the potential risk factors associated with the development and exacerbation of allergic diseases, including asthma.



Zeldin, center, shown with fellow AAP members and NIEHS colleagues Janet Hall, with the Clinical Research Program, and Perry Blackshear, M.D., D.Phil., lead investigator in the Signal Transduction Laboratory, has published more than 275 peer-reviewed articles in leading biomedical journals, as well as numerous reviews and book chapters. (Photo courtesy of Lauren Myers)

He serves as an attending physician at Duke University Medical Center and the Durham Veterans Affairs Medical Center. He also regularly sees research participants at the NIEHS Clinical Research Unit.

Zeldin earned a B.A. in chemistry from Boston University in 1982 and an M.D. from the Indiana University School of Medicine in 1986. He completed a residency in internal medicine at Duke University in 1989 and a fellowship in pulmonary/critical care medicine at Vanderbilt University in 1993.

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Fessler elected to American Society for Clinical Investigation

By Eddy Ball

NIEHS lead researcher Michael Fessler, M.D., joined an elite group of physician-scientists when he was elected to the American Society for Clinical Investigation (ASCI). Fessler was introduced as a new member April 24 at the joint meeting of ASCI and the Association of American Physicians in Chicago.

Each spring, [ASCI](#) welcomes up to 80 new early-career physicians to its membership, which now numbers more than 3,000. The society elects physicians, from all medical specialties, who have demonstrated outstanding records of scholarly achievement in biomedical research.

ASCI bylaws stipulate that to be considered for membership, “[A prospective member must be a] physician who is 50 years of age or less [and] has accomplished meritorious original, creative, and independent investigations in the clinical or allied sciences of medicine and enjoys an unimpeachable moral standing in the medical profession.”

When [Fessler](#) was awarded tenure in 2013, NIEHS Scientific Director and fellow member of ASCI Darryl Zeldin, M.D., described his colleague’s commitment to research. “He’s a great example of a translational investigator who learns about diseases at the bedside, goes back to the lab and tries to understand basic mechanisms using cell systems and animal models, and then takes what he learns in the lab back to humans, to develop novel approaches to treat or prevent disease.”

Merging basic and clinical research

Fessler is a respiratory biologist and critical care physician who serves as deputy chief of the NIEHS Immunity, Inflammation, and Disease Laboratory and heads the Clinical Investigation of Host Defense Group. His team investigates the role of cholesterol in immunity, and uses advanced laboratory analysis and translational approaches to discover and validate novel insights into the innate, or immediate, immune response.

Along with his basic research, Fessler holds a secondary appointment in the NIEHS [Clinical Research Branch](#). Using human specimens from the NIEHS Clinical Research Unit, Fessler’s group translates hypotheses and experimental observations into practical applications for human disease.



“I am honored, but also greatly humbled, to join the ranks of the ASCI,” said Fessler, center; shown with members Perry Blackshear, M.D., D.Phil, head of the NIEHS Post-Transcriptional Gene Expression Group and NIEHS Scientific Director Darryl Zeldin, M.D. (Photo courtesy of Anne Fessler)

Even at this early stage in his career, Fessler has published more than 60 studies in leading peer-reviewed journals, including the Journal of Experimental Medicine, Cell Metabolism, and the Journal of Biological Chemistry.

Fessler received an A.B. from Princeton University in 1992, and an M.D. from Harvard Medical School in 1996. He trained in internal medicine at Massachusetts General Hospital and pulmonary and critical care medicine at the University of Colorado, before joining NIEHS in 2006 as a physician-scientist specializing in immunology.

Election to ASCI is the latest of several awards Fessler has received, which include the NIEHS Early Career Award, NIEHS Intramural Research Award, and the American Thoracic Society Carol Basbaum Award. He serves on the editorial board of the journal PLOS ONE and is a member of the [Faculty of 1000](#).

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

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Exposome research highlighted at Duke symposium

By Eddy Ball

A symposium April 3 at Duke University explored the impact of environmental exposures on biological pathways involved in cancer. Organized and hosted by Duke's Integrated Toxicology and Environmental Health Program, the event highlighted NIEHS-supported efforts on the exposome, which refers to the theoretical totality of internal and external exposures implicated in health and disease over an organism's lifespan. [Steven Patierno, Ph.D.](#), codirector of the Duke Cancer Institute, moderated the symposium.

The symposium opened with a keynote presentation by exposome pioneer [Stephen Rappaport, Ph.D.](#), "The Exposome and EWAS [Exposome-wide Association Studies]: Finding Causes of Cancer." In 2010, Rappaport and his colleague, Martyn Smith, Ph.D., of the University of California at Berkeley, authored what is considered a seminal statement of the exposomic approach to disease research (see [story](#)).

NIEHS program manager David Balshaw, Ph.D., concluded the symposium with an outline of major new funding mechanisms for developing infrastructure to advance exposome research (see [sidebar](#)). "This is really encouraging, to see NIEHS embracing this [exposome] concept to this level," Patierno said during the final discussion of the day.

Taking next steps in exposome research

Attendees also heard reports on new directions in research by two NIEHS Outstanding New Environmental Scientist awardees, environmental chemist [Heather Stapleton, Ph.D.](#), and molecular geneticist [Joel Meyer, Ph.D.](#), who are both faculty members in the Nicholas School of the Environment at Duke.



"Poverty is a carcinogen," Patierno said in his introduction, underscoring the role of intangibles such as socioeconomic stress in the matrix of exposures that can influence health. (Photo courtesy of Steve McCaw)

Stapleton, who studies the health effects of exposure to fire retardant chemicals, has teamed up with Duke Cancer Institute surgeon [Julie Sosa, M.D.](#), to study connections to thyroid cancer. Meyer, who investigates the role of mitochondrial regulation, is working with Duke Medical Center molecular physiologist [Matthew Hirsche, Ph.D.](#), to expand understanding of the role of disrupted mitochondrial function in promoting cancer. A generous donation from Duke alumni Fred and Alice Stanback is promoting these transdisciplinary collaborations.

Also on the program was neurobiologist Gary Miller, Ph.D., director of the NIEHS-funded Health and Exposome Research Center: Understanding Lifetime Exposures ([HERCULES](#)) Center at Emory University. The initiative, which is a collaboration between researchers at Emory and the Georgia Institute of Technology, is funded by the first exposome center grant awarded in the U.S.

Because the exposome includes all exposures related to health outcomes, symposium organizers invited Patricia Matthews-Juarez, Ph.D., and Paul Juarez, Ph.D., social scientists at the University of Tennessee Health Science Center, to present the work of their center on community environmental assessment. Their talk outlined “The Public Health Exposome: A Systems Approach Towards Understanding the Spatial/Temporal Dynamics of Environmental Exposures, Adverse Health Outcomes, and Cancer Health Disparities.”

Qualified successes point to tremendous potential

Basic questions about exposome research remain to be answered, such as what biomarkers can offer insight into meaningful exposures and whether the ambitious goal of measuring the totality of those exposures can even be accomplished. But as the presentations made abundantly clear, innovative transdisciplinary collaborations and advances in exposome assessment are helping researchers take novel approaches to addressing questions about host susceptibility and the health effects of multiple, simultaneous exposures.

National Institutes of Health support for meeting the challenges ahead

The new Children’s Health Exposure Analysis Resource, administered by NIEHS, resulted from termination of the National Children’s Study and redirection of its funds into support for exposome research to advance understanding of environmental impacts on children’s health. The three-part initiative will build infrastructure by providing researchers access to laboratory and statistical analyses to increase the study of environmental exposures.

NIEHS-administered grants will fund a National Exposure Assessment Laboratory Network; a Data Repository, Analysis, and Science Center; and a Coordinating Center. NIEHS is also one of six institutes participating in an additional initiative to develop sensor systems for characterizing the external environment for children’s health studies. The Pediatric Research Using Integrated Sensor Monitoring Systems (PRISMS) program is led by the National Institute of Biomedical Imaging and Bioengineering.

“If we’re successful, many of the people coming into the program will not be [traditional] environmental health scientists,” Balshaw said of the transdisciplinary exposome infrastructure he envisions.



Balshaw, center was part of the audience as well as a speaker at the well-attended event. (Photo courtesy of Steve McCaw)

Attendee Rick Woychik, Ph.D., NIEHS deputy director, noted, “This exposome framework is a way for us to address the issue of mixtures.” Better understanding of an individual’s matrix of exposures will also help answer the longstanding question of why some people react differently than others to their shared environments.

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



Juarez, above, and Mathews-Juarez integrate enormous amounts of data from different sources to map patterns of health disparities across the U.S. (Photo courtesy of Steve McCaw)



“I want to get as many people thinking about this as possible,” Miller said, as he described the textbook he authored for his course at Emory, “[The Exposome: A Primer](#).” (Photo courtesy of Steve McCaw)



“Mitochondrial metabolism is altered in cancer cells,” Meyer said, discussing his research into whether that alteration is a causal factor or an effect of cancer metabolism. (Photo courtesy of Steve McCaw)



Balshaw invoked goal three of the NIEHS strategic plan as he opened his discussion of new funding to help transform exposure science. “You need to measure as much as you can,” he said of the push for better assessment tools. (Photo courtesy of Steve McCaw)

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New tenure-track researcher joins NIEHS

By Robin Arnette

The institute welcomed a new tenure-track scientist to its growing list of in-house researchers. Jennifer Martinez, Ph.D., joined NIEHS this spring to head the Inflammation and Autoimmunity Group. Her work focuses on how the innate immune system, or the body's first line of defense against infection, deals with pathogens, environmental toxins, and the accumulation of dead cells.

Martinez is an immunologist and completed her postdoctoral fellowship at St. Jude Children's Research Hospital in Memphis, Tennessee. Her lab at St. Jude studied the mechanisms of how cells die, so when she began her research there, she became interested in what happens to the cells afterwards.

"I learned at St. Jude that every 7 years you make a new skeleton, because of the turnover of cells, but where do those cells go?" Martinez wondered. "A lot of autoimmune diseases are characterized by an inability to get rid of cells, so I want to understand the immune response to these cells and how the body determines if they are a danger or part of normal processes."

Busy at the bench

Martinez has been busy doing experiments in her new lab space and will continue to work at the bench after her staff members arrive. She does it because she loves doing research, but more importantly, she knows her commitment may eventually lead to therapies to help millions with autoimmune disorders.

"Jennifer Martinez is a great addition to the laboratory," said Anton Jetten, Ph.D., head of the NIEHS Immunity, Inflammation, and Disease Laboratory. "Her focus on the study of autophagy — the breakdown of cellular components — and its role in inflammation and immunity brings a new perspective, and one that will help us better understand inflammatory and autoimmune disease."

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Martinez is a native of Hattiesburg, Mississippi and earned her doctorate at Duke University in Durham, North Carolina. She and her dog, Winston, are back in familiar surroundings now that she is part of NIEHS. "I enjoyed my time when I was here," Martinez said. "We are both glad to be in an area where there are so many beautiful forests and trails." (Photo courtesy of Jennifer Martinez)

Bushel honored with career achievement award

By Shannon Whirledge

NIEHS researcher Pierre Bushel, Ph.D., was honored at the Massachusetts State House on April 23 with the Distinguished Alumni Award from the University of Massachusetts (UMass) at Amherst for his substantial influence in the field of toxicogenomics. The Distinguished Alumni Award is the most prestigious award conferred by the UMass Amherst Alumni Association upon its alumni, faculty, and friends, and is presented to those who have translated their UMass Amherst experience into distinguished achievement in their field of study.

Going back to where it started

Bushel began his career in bioinformatics and toxicogenomics with a bachelor's degree in zoology from UMass Amherst. "You can't predict the path your undergraduate degree will take you," Bushel said. In addition to biology coursework, Bushel was mentored by several professors in the school's highly regarded chemistry department. During his undergraduate studies, Bushel reinforced the principles he learned in the classroom through laboratory instruction on actual research projects. "A firm foundation in both the physical and biological sciences and a knack for experimental procedures," Bushel said, crediting these as major contributing factors in his success.

Bushel explained that the Distinguished Alumni Award caught him by surprise. In addition to the great honor, Bushel learned that [Brian O'Connor, Ph.D.](#), professor emeritus of biology at UMass Amherst and Bushel's undergraduate advisor, would host his visit. The opportunity to thank the people who set him on his path to achievement underscored the unique nature of this award for Bushel.

Putting bioinformatics to good use

After leaving UMass Amherst, Bushel earned a master's degree in molecular and cellular biology from Long Island University-Brooklyn and a doctorate in bioinformatics from North Carolina State University. In 2000, Bushel joined NIEHS as a biologist and is now a staff scientist in the Biostatistics and Computational Biology Branch. He also leads the institute's microarray and genome informatics efforts.

At NIEHS, Bushel has been awarded the Merit Award four times and received the National Institutes of Health (NIH) Director's Award in 2002 for his role in conceptualizing and implementing the NIEHS Toxicogenomics Research Consortium. His research using bioinformatics and computational biology to investigate the biological effects of toxicants led to a collaboration that may help better predict toxicity of anticancer therapies (see [story](#)).

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



Bushel, right, with Andrew MacDougall, president of the UMass-Amherst Alumni Association. In addition to his scientific accomplishments, Bushel has enhanced the NIEHS community by mentoring students in the NIEHS Scholars Connect Program, the NIH Summer Internship Program, and as an external advisor for Ph.D. students. (Photo courtesy of Thom Kendall)

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Arsenic linked to blood pressure increases during pregnancy

By Sara Mishamandani

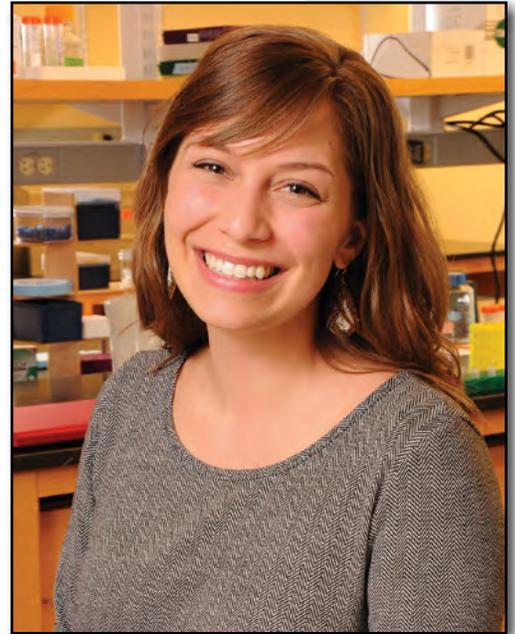
Arsenic exposure is associated with greater increases in blood pressure over the course of a pregnancy, according to a new NIEHS-funded study of U.S. pregnant women. These findings may have important implications, because even modest increases in blood pressure can affect future cardiovascular disease risk for mothers and their children. Published online March 20 in the journal *Environmental Health Perspectives*, this is the first long-term study to examine the association between arsenic and blood pressure during pregnancy in the U.S.

Focusing on a susceptible population

Lead author Shohreh Farzan, Ph.D., postdoctoral fellow at Dartmouth College, collaborated with researchers from the [Dartmouth Toxic Metals Superfund Research Program \(SRP\) Center](#), the [Columbia University SRP Center](#), and New York University (NYU). Her study involved the analysis of longitudinal, or repeated long-term, blood pressure and urinary arsenic measurements for participants in the New Hampshire Birth Cohort Study, which is funded by the Dartmouth SRP and the [Children's Environmental Health and Disease Prevention Research Center](#). The group of pregnant women who were studied live in New Hampshire and drink water from private wells, which are not regulated by state or federal governments. In some parts of the state, approximately one in five private wells contains levels of naturally occurring arsenic above the U.S. Environmental Protection Agency limit for drinking water.

Researchers found that women with higher levels of urinary arsenic during pregnancy had increases in systolic blood pressures and pulse pressures higher than those that normally occur over the course of a pregnancy. Systolic blood pressure normally increases an average of approximately 3.7 millimeters of mercury (mmHg) for systolic blood pressure between the first and third trimesters. The new study found, on average, that each increase in urinary arsenic of 5 micrograms per liter was associated with additional monthly increases in systolic blood pressure and pulse pressure of 0.15 and 0.14 mmHg, respectively.

According to the authors, the potential risk of later life cardiovascular diseases in mothers and children who are exposed to arsenic during pregnancy makes this a critical area of investigation.



Farzan received an SRP K.C. Donnelly Externship Award Supplement in 2013 and currently has a Pathway to Independence Award, known as a K99/R00 grant. (Photo courtesy of Shohreh Farzan)



Karagas leads the NIEHS-funded New Hampshire Birth Cohort Study at Dartmouth. (Photo courtesy of Margaret Karagas)

Fostering collaboration — the K.C. Donnelly Externship

In 2013, Farzan was awarded a [K.C. Donnelly Externship Award Supplement](#) to complete a three-month externship with Yu Chen, Ph.D., NYU professor and Columbia SRP Center co-investigator (see [story](#)). At the time, Farzan was a postdoctoral fellow at the Dartmouth SRP Center, under the guidance of Margaret Karagas, Ph.D.

“With Chen’s help, I learned to analyze longitudinal blood pressure measurements using data from the Health Effects of Arsenic Longitudinal Study (HEALS) in Bangladesh,” Farzan said of her externship. “I was able to apply what I learned to the Dartmouth study, examining arsenic exposure in relation to blood pressure data over the course of pregnancy.”

“I used a lot of what I learned and the preliminary data that I generated during my K.C. Donnelly Externship to write a Pathway to Independence Award application to continue studying the effects of arsenic on cardiovascular disease outcomes, which was funded by NIEHS last summer,” said Farzan. She is currently in the training phase of that grant with mentors Chen and Karagas. “It’s been great to be able to continue my work with the Dartmouth SRP and continue to collaborate with the Columbia SRP, too,” she said.

Citation: [Farzan SF, Chen Y, Wu F, Jiang J, Liu M, Baker E, Korrick SA, Karagas MR.](#) 2015. Blood pressure changes in relation to arsenic exposure in a U.S. pregnancy cohort. *Environ Health Perspect* [Online 20 March 2015].

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

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Gordenin talk featured at 2015 Lineberger Symposium

By Eddy Ball

NIEHS lead researcher Dmitry Gordenin, Ph.D., was one of fifteen speakers featured at the 39th annual Lineberger Symposium April 8-9 in Chapel Hill, North Carolina.



Each year organizers at the University of North Carolina School of Medicine Comprehensive Cancer Center invite leading experts in cancer research and treatment to participate in the themed symposium, highlighting exciting new developments in the field. This year’s conference focused on “[Personalized Medicine, the Cancer Genome Atlas, and the Future of Cancer Care](#).”

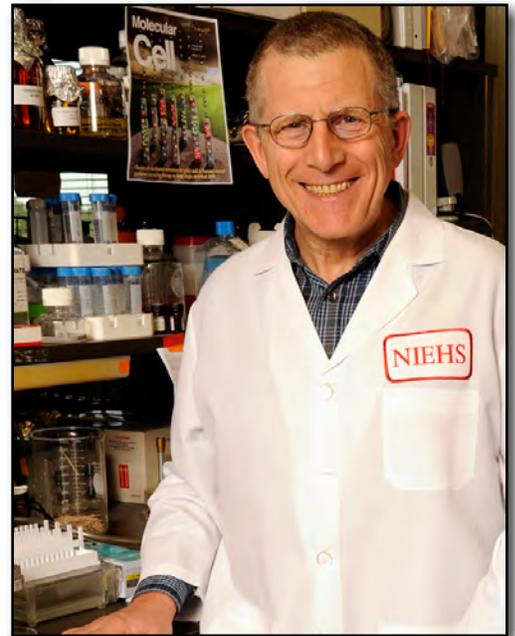
[Gordenin](#), who leads the NIEHS Mechanisms of Genome Dynamics Group, discussed his team’s groundbreaking discoveries in experiments with a yeast model, during a talk titled “Pan-Cancer Analysis of APOBEC Mutagenesis.” APOBEC refers to a specific family of proteins. The researchers, including Kin Chan, Ph.D., an NIEHS Intramural Research and Training Award fellow, confirmed the findings in human tumor samples, with follow-up bioinformatic analyses performed in collaboration with Les Klimczak, Ph.D. Klimczak is an NIEHS contract scientist who developed and maintains the [analytical package](#) that was recently integrated into The Broad Institute TCGA Genome Data Analysis Center Firehose pipeline, which performs pan-TCGA analysis on a regular basis.

A newly discovered mechanism involved in cancer

Gordenin presented results of work that became a part of The Cancer Genome Atlas (TCGA) Network, indicating that APOBEC cytidine deaminases, which are enzymes that normally act in antiviral immune responses, can be a powerful source of mutations linked to cancer initiation and disease progression. Gordenin said these hypermutational patterns, or mutation clusters, stemmed from infrequent, long single-strand DNA regions.

The clusters helped to identify APOBEC enzymes as a powerful source of hypermutation in several cancer types. For example, APOBEC hypermutation is observed in more than half of urinary bladder cancers, a common malignancy that causes approximately 150,000 deaths per year worldwide. The discovery of this new type of carcinogenic mutagenesis presents an exception to the traditional view that mutations occur randomly across the genome and accumulate over time.

Bladder cancer is not the only cancer in which APOBEC hypermutation is robust, Gordenin explained. The pattern is also abundant in cancers of the cervix, head, neck, breast, and lung. “It’s probably in the background of many other cancers,” he said. “In some of these samples [examined by the team], APOBEC mutagenesis was the dominant mutational force, producing 300 mutations per exome (300,000 per whole genome) and constituting up to 70 percent of total mutations.”



Gordenin joined researchers from institutions in the U.S. and U.K., who presented findings of genomic abnormalities in a variety of cancers. (Photo courtesy of Steve McCaw)



Chan combined genetic analysis of APOBEC mutagenesis in a yeast model and in cancer genomes to further detail APOBEC mutagenic mechanisms. (Photo courtesy of Steve McCaw)

Linked audio:

[Listen to Gordenin discuss clustered mutations in this NIEHS podcast \(2:16\)](#)

(Launches in new window)

Homing in on molecular targets in cancer

During the course of three major studies that combined mechanistic and bioinformatics approaches to better understand mutation processes operating in cancer, cited below, Gordenin and his collaborators identified molecular targets that may ultimately revolutionize treatment for cancers with the APOBEC mutational signature.

Greater understanding of the factors that regulate APOBEC activity may also lead to the development of cancer therapies and prevention strategies aimed at minimizing the negative effects of these proteins, while maintaining their normal functions in immunity.

Citations:

Roberts SA, Sterling J, Thompson C, Harris S, Mav D, Shah R, Klimczak LJ, Kryukov GV, Malc E, Mieczkowski PA, Resnick MA, Gordenin DA. 2012. Clustered mutations in yeast and in human cancers can arise from damaged long single-strand DNA regions. *Mol Cell* 46(4):424-435. ([Story](#))

Roberts SA, Lawrence MS, Klimczak LJ, Grimm SA, Fargo D, Stojanov P, Kiezun A, Kryukov GV, Carter SL, Saksena G, Harris S, Shah RR, Resnick MA, Getz G, Gordenin DA. 2013. An APOBEC cytidine deaminase mutagenesis pattern is widespread in human cancers. *Nat Genet* 45(9):970-976. ([Story](#))

[Cancer Genome Atlas Research Network](#). 2014. Comprehensive molecular characterization of urothelial bladder carcinoma. *Nature* 507(7492):315-322. ([Story](#))

(Eddy Ball is a contract writer for the NIEHS Office of Communications and Public Liaison)

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Spring Neuroscience Meeting is a resounding success

By *Simone Otto*

The Triangle chapter of the Society for Neuroscience (Triangle SfN) held its first Spring Neuroscience Meeting April 10 at Research Triangle Park headquarters in North Carolina. NIEHS was one of the sponsors of this event, which was well-attended by members of the NIEHS Neuroscience Laboratory and other area researchers in the field of neuroscience.

The meeting included presentations by local scientists, a keynote address, and a poster session. In between talks and during the poster session, attendees had opportunities to visit with sponsors.

Local speakers impress

The event began with presentations from three area scientists. [Regina Carelli, Ph.D.](#), with the University of North Carolina at Chapel Hill (UNC), focused on the “Dynamics of Rapid Dopamine Signaling During Decision Making.” Her lab studies how dopamine release balances the cost of getting a reward with the size of the reward.

[Stephen Lisberger, Ph.D.](#), with the Duke University School of Medicine, focused on discovering “Mechanisms of Motor Learning by Just Listening to the Cerebellum While It Works.” According to Lisberger, he meant his title to be both a philosophical statement and a scientific statement. “The art of listening carefully to the brain seems to be dying,” he said. “[We can] discover mechanisms by just listening.”

[Emilio Salinas, Ph.D.](#), of the Wake Forest School of Medicine, spoke on “Cognitive Manipulation of Oculomotor Activity in the Frontal Cortex of Monkeys Performing a Simple Reaction-time Task With Reward Bias.” Salinas studies the relationship between variability in behavior and variability in neural activity.



Carstens, left, was presented with an award for her poster, “Perineuronal Nets in Hippocampal Area CA2: A Role in Restricting Synaptic Plasticity?” by lab mate Farris. (Photo courtesy of Leah Townsend)

Poster award winners

Undergraduate or graduate students

Leslie Wilson, NCSU
Kelly Carstens, NIEHS and UNC
Chris Foster, UNC
Leah Townsend, UNC

Postdoctoral

Georgia Alexander, Ph.D., NIEHS
Ryan Bell, Ph.D., UNC

Internationally known scientist gives keynote address

[Adron Harris, Ph.D.](#), director of the Waggoner Center for Alcohol and Addiction at the University of Texas at Austin, presented the keynote address. “Adron received his Ph.D. from UNC Chapel Hill, and from there he’s gone on to a most distinguished career as evidenced by his numerous publications,” said Patricia Jensen, Ph.D., head of the NIEHS Developmental Neurobiology Group, in her introduction.

Harris fascinated the audience by discussing what reviewers of one of his scientific papers termed more of a hallucination than a moment — namely, his discovery of the ability of alcohol to enter into a small pocket between alpha helices and stabilize an otherwise fluid channel, which leads to either enhancement or inhibition, depending on the channel involved.

Poster session buzzed with activity

Poster awards were given to both undergraduate and postdoctoral fellows. Two winners, predoctoral fellow Kelly Carstens and research fellow Georgia Alexander, Ph.D., work in the NIEHS Synaptic and Developmental Plasticity Group, led by [Serena Dudek, Ph.D.](#)

The session buzzed with the energy of the attendees as they discussed posters and networked with scientists from Duke University, East Carolina State University, NIEHS, North Carolina Central University, North Carolina State University (NCSU), and UNC.

The Triangle SfN was reinstated less than one year ago with the help of members of NIEHS, particularly Shannon Farris, Ph.D. (see related [story](#)). “The Triangle is home to some of the top universities and research institutes in the country, and it is my hope that through Triangle SfN individuals from each of these institutions will be able to form a tight and collaborative network,” wrote [Amir Rezvani, Ph.D.](#), president of Triangle SfN and professor at the Duke Institute for Brain Sciences, in his welcome letter. Judging by the success of the spring meeting, the network is well underway, and organizers are already looking toward next year’s event.

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



Shown from right, Harris received a commemorative plaque from Jensen, Farris, and Rezvani, after giving his keynote address, “Alcohol and the Brain: From Binding States to Gene Expression.” (Photo courtesy of Juhee Haam)



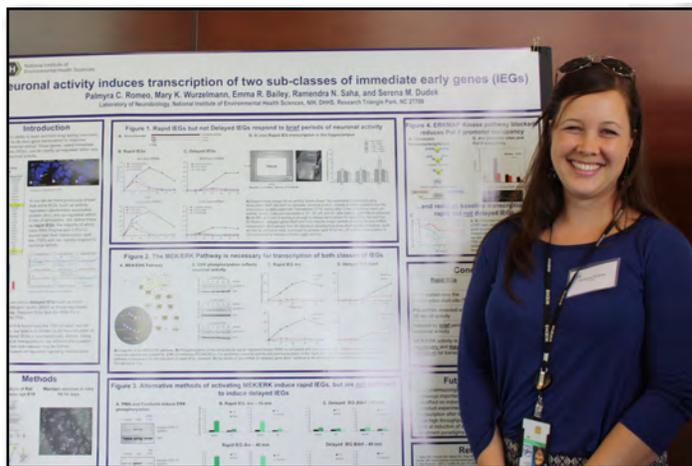
The packed audience took full advantage of the question and answer time following Harris’s talk. (Photo courtesy of Juhee Haam)



Alexander, left, shown with her lead researcher Dudek, won an award for her poster, “Firing Properties and Immediate Early Gene Mapping in Hippocampal Area CA2.” (Photo courtesy of Leah Townsend)



Rezvani, right, and Farris, left, presented awards to featured speakers, from left, Carelli, Salinas, and Lisberger (Photo courtesy of Juhee Haam)



Palmyra Romeo, a baccalaureate fellow in Dudek's lab, discussed her poster, "Neuronal Activity Induces Transcription of Two Sub-Classes of Immediate Early Genes" with attendees. (Photo courtesy of Leah Townsend)



Some of the organizers of the SfN event included from left, Jensen; Chintan Oza, Ph.D., a postdoctoral student at Duke; Alex Marshall, Ph.D., a postdoctoral fellow at UNC; Farris; NIEHS toxicologist Mamta Behl, Ph.D., with the National Toxicology Program; Rezvani; John Meitzen, Ph.D., assistant professor at (NCSU); and Charlotte Boettiger, Ph.D., assistant professor at UNC. (Photo courtesy of Mahsa Samadi)

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This month in EHP

The May issue of Environmental Health Perspectives (EHP) looks into reformulation of personal care products, and manufacturers' use of chemical footprinting to manage hidden chemical liabilities.

Beyond Cosmetic Changes: Taking Stock of Personal Care Product Safety

Under mounting pressure from advocacy groups, a number of major manufacturers and retailers have begun eliminating controversial ingredients from the personal care products they produce and sell. Companies are investing considerable resources to reformulate their products, even as they universally defend the questioned ingredients as safe.

Chemical Footprinting: Identifying Hidden Liabilities in Manufacturing Consumer Products

Corporate policies for chemicals management have traditionally focused on making sure certain chemicals are not found in products in amounts greater than a mandated threshold. Manufacturers are now going a step farther, using chemical footprinting to identify and manage hidden chemical liabilities in products and supply chains.

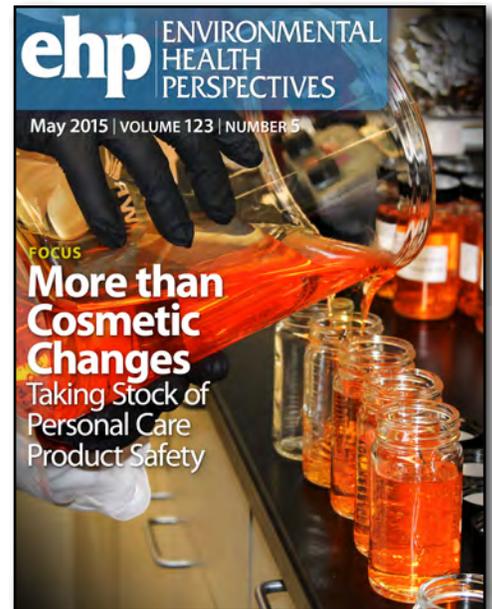
Featured research and related news articles this month include:

- **Air Pollution and Diabetes Risk: Assessing the Evidence to Date** — Vascular and respiratory diseases associated with diabetes may be worsened by exposure to air pollution. A team of European scientists has now evaluated whether air pollution is also associated with development of diabetes.
- **Assessing Long-term Dietary Exposure to OP Pesticides: Study Affirms the Utility of Urinary Biomonitoring** — Investigators describe a new noninvasive method for characterizing long-term dietary exposures to organophosphate pesticides.
- **Profiles in Cytotoxicity: A First Step Toward Chemical-specific Adjustment Factors** — A new study demonstrates that high-throughput, cell-based screening assays are useful in estimating the range of human responses to individual chemicals.
- **Arsenic Exposure in Infancy: Estimating the Contributions of Well Water and Human Milk** — A new paper from the New Hampshire Birth Cohort Study reports that infants fed powdered formula mixed with private well water were at greater risk of arsenic exposure than breast-fed infants.

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Extramural papers of the month

By Nancy Lamontagne

- [Children's lungs grew stronger as pollution declined in California](#)
- [Prenatal window of susceptibility for genetic damage](#)
- [More evidence that lead plays a role in schizophrenia](#)
- [MRI reveals how early life air pollution exposure affects the brain](#)

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

Children's lungs grew stronger as pollution declined in California

New research from NIEHS grantees found that as air quality improved in the Los Angeles basin, children's lung health also improved. Improving lung function during developmental years could lead to better lung function in adulthood, and potentially reduce risk for adverse health outcomes.

The improving air quality of the Los Angeles basin, over the last several decades, provided an opportunity to study its potential benefits to human health. As part of the Children's Health Study, researchers measured lung function in 2120 children, from three different cohorts, who lived in the same five communities. Measurements were taken each year between the ages of 11 and 15, but during different calendar periods — 1994-1998, 1997-2001, and 2007-2011. After adjusting for age, gender, ethnicity, height, respiratory illness, and other variables, the researchers found large improvements in lung development for children studied in 2007-2011, compared to children studied in 1994-1998 or 1997-2001. Regional air quality improved dramatically over the course of the study, and lung function gains strongly correlated with lower levels of particulate matter (PM2.5 and PM10) and nitrogen dioxide in the communities studied. For example, lung growth was more than 10 percent greater for children breathing the lower levels of nitrogen dioxide in 2007-2011, compared to those breathing higher levels in 1994-1998.

Citation: [Gauderman WJ, Urman R, Avol E, Berhane K, McConnell R, Rappaport E, Chang R, Lurmann F, Gilliland F.](#) 2015. Association of improved air quality with lung development in children. *N Engl J Med.* 372(10):905-913. ([Story](#))

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Prenatal window of susceptibility for genetic damage

A new mouse study, funded in part by NIEHS, quantitatively links prenatal DNA damage from the liver carcinogen aflatoxin B1 (AFB1) with risk of cancer later in life. The new results point to the prenatal period as a critical window of susceptibility to genetic damage from toxins.

AFB1, a toxin produced by fungi that contaminate food supplies, is a potent carcinogen that leads to a type of liver cancer known as hepatocellular carcinoma. It is especially problematic in the developing world. To quantify the link between AFB1 damage and later development of cancer, the researchers exposed mice embryos to AFB1 and compared the rates of cancer-causing mutations in these mice with adult mice exposed to the same dose.

The data revealed that the DNA adducts produced in the livers of exposed embryos were twentyfold more likely to lead to mutations than in adults that received the same dose of aflatoxin. These results correlated with Ki67 staining of the liver, which indicated that the fetal liver cells were dividing much faster than adult liver cells.

Based on these findings, the researchers noted that it is especially important to prevent maternal exposures to aflatoxins. They also pointed to the need to explore preventive measures that improve maternal pathways of metabolism and detoxification, to prevent effects from unavoidable exposures to food contaminated with aflatoxins.

Citation: [Chawanthayatham S, Thiantanawat A, Egner PA, Groopman JD, Wogan GN, Croy RG, Essigmann JM](#). 2015. Prenatal exposure of mice to the human liver carcinogen aflatoxin B1 reveals a critical window of susceptibility to genetic change. *Int J Cancer* 136(6):1254-1262.

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More evidence that lead plays a role in schizophrenia

An NIEHS grantee and colleagues report strong similarities between the brains of people with schizophrenia and the brains of rats chronically exposed to lead from the prenatal period through adolescence, adding evidence that early lead exposure primes the brain for schizophrenia later in life.

The researchers found that rats with chronic lead exposure during development showed detriments in three brain areas known to be involved in schizophrenia — the medial prefrontal cortex, hippocampus, and striatum. Compared to control rats that were not exposed to lead, the exposed rats showed a decrease of approximately one-third in the density of parvalbumin-positive GABAergic interneurons (PVGI), which are critical to cognitive function. Using imaging technology, the researchers identified higher levels of D2-dopamine receptor, a hallmark of schizophrenia, in the striatum of lead-exposed rats.

Psychosis, a characteristic symptom of schizophrenia, has been linked to subcortical dopaminergic hyperactivity. To determine whether lead-exposed animals expressed this hyperactivity, the researchers administered cocaine to both control and lead-exposed rats and measured their locomotor response. The lead-exposed rats showed hyperactivity in the subcortical dopaminergic system.

Overall, the study in rats showed that developmental lead exposure reproduces the specific neuropathology and dopamine system changes seen in people with schizophrenia.

Citation: [Stansfield KH, Ruby KN, Soares BD, McGlothan JL, Liu X, Guilarte TR](#). 2015. Early-life lead exposure recapitulates the selective loss of parvalbumin-positive GABAergic interneurons and subcortical dopamine system hyperactivity present in schizophrenia. *Transl Psychiatry* 5:e522.

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MRI reveals how early life air pollution exposure affects the brain

In one the largest MRI studies to date, NIEHS grantees report how prenatal and postnatal exposure to polycyclic aromatic hydrocarbon (PAH) air pollutants disturbs the developing brain. If confirmed, the findings have important public health implications, as PAHs are widespread in the environment.

The researchers used MRI to study the brains of 40 children from minority communities in New York City that had been followed from before birth until 7 to 9 years of age. The researchers previously reported that prenatal exposure to airborne PAHs during gestation in this cohort was associated with multiple neurodevelopmental problems, including development delay by age 3, reduced verbal IQ at age 5, and symptoms of anxiety and depression at age 7.

The new study showed a dose-response relationship between increased prenatal PAH exposure and later childhood reductions in the white matter surface of the left hemisphere of the brain, which is associated with slower processing of information and externalizing behavioral problems, including ADHD and aggression. For postnatal PAH exposure measured at age 5, the researchers found additional disturbances in development of white matter in the dorsal prefrontal region of the brain, which is associated with concentration, reasoning, judgment, and problem-solving ability. The postnatal affects were spatially distinct and statistically independent from those for prenatal PAH exposure. The researchers are currently undertaking a much larger study to confirm and extend their findings.

Citation: Peterson BS, Rauh VA, Bansal R, Hao X, Toth Z, Nati G, Walsh K, Miller RL, Semanek D, Perera F. 2015. Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood. *JAMA Psychiatry*; doi:10.1001/jamapsychiatry.2015.57 [Online 25 March 2015]. ([Story](#))

(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 Greg Buchhold, Tara Ann Cartwright, Geoffrey Feld, Deepa Singh, and Qing Xu

- [NTP researchers demonstrate common drinking water disinfection by-product is carcinogenic](#)
- [NELF mediated Pol II pausing in ESCs controls signaling pathways necessary for development](#)
- [Genetic and environmental factors interact to affect the severity of infant RSV bronchiolitis](#)
- [Leading the way in ribonucleotide excision repair](#)
- [Inhibition of NADPH oxidase halts disease progression in Parkinson's disease models](#)

NTP researchers demonstrate common drinking water disinfection by-product is carcinogenic

Several haloacetic acids are already regulated by the U.S. Environmental Protection Agency as carcinogens, and this National Toxicology Program study argues that bromodichloroacetic acid (BDCA) should also be considered a potential human environmental health hazard. The authors say that BDCA is one of the most common byproducts of water disinfection, formed by the reaction of oxidizing agents containing chlorine with naturally occurring organic material and bromide ions in source water. They estimated that exposure risk to the public could be substantial.

Exposing rats to BDCA caused the animals to develop a hormone-dependent (ERalpha+/PR+) mixed ductal-basal breast cancer. The malignancy was similar to human breast cancer, displaying several distinct molecular features, indicating a more aggressive capacity compared to the spontaneous breast tumors that arose in the untreated animals.

The chemical produced mutations in genes frequently altered in human breast cancer, including p53, PTEN, and EGFR. The tumors also showed increased levels of the hereditary breast cancer gene BRCA2 and TGFbeta. Notably, gene expression changes in the tumors indicated a cluster of genes likely elevated by the increased TGFbeta signaling, promoting new blood vessel growth (VEGFA), degradation of the extracellular matrix (MMP9, MMP2, THBS1, ID1), and epithelial-to-mesenchymal transition (TWIST), changes that promote cancer growth and invasion. **(GB)**

Citation: [Harvey JB, Hong HH, Bhusari S, Ton TV, Wang Y, Foley JF, Peddada SD, Hooth M, DeVito M, Nyska A, Pandiri AR, Hoenerhoff MJ. 2015. F344/NTac rats chronically exposed to bromodichloroacetic acid develop mammary adenocarcinomas with mixed luminal/basal phenotype and Tgfbeta dysregulation. Vet Pathol; doi:10.1177/0300985815571680 \[Online 2 March 2015\].](#)

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NELF mediated Pol II pausing in ESCs controls signaling pathways necessary for development

A paradigm got a makeover as scientists at NIEHS reported that plasticity of embryonic stem cells (ESCs) is facilitated by pausing of RNA polymerase II (Pol II). Surprisingly, pausing did not occur on developmental genes, as has been observed in Drosophila embryos. Instead, it occurred on genes regulating cell cycle and signal transduction. The study improves understanding of mechanisms that underlie the pluripotency of stem cells, which is necessary for the development of regenerative medicines.

Researchers used high-resolution genomic analysis to investigate distribution of paused Pol II and gene expression in ESCs that were specifically maintained in a nondifferentiated state. The finding highlights that Pol II pausing is enriched at cell cycle regulators and at genes involved in signal transduction. Moreover, this observation was consistent in ESCs studied in different conditions and methodologies. To evaluate the functional significance of Pol II pausing, the authors genetically deleted the pause-inducing factor, NELF. In the absence of NELF, ESCs were resistant to differentiation through inhibition of key developmental signaling pathways. Together these studies contribute to a rapidly developing potential for ESC reprogramming for the benefit of human health. **(DS)**

Citation: [Williams LH, Fromm G, Gokey NG, Henriques T, Muse GM, Burkholder A, Fargo DC, Hu G, Adelman K. 2015. Pausing of RNA polymerase II regulates mammalian developmental potential through control of signaling networks. Mol Cell 58\(2\):311–322. \(Story\)](#)

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Genetic and environmental factors interact to affect the severity of infant RSV bronchiolitis

NIEHS researchers and collaborators have discovered that living conditions and toll-like receptor 4 (TLR4) genotypes interact in infants to determine the consequence of respiratory syncytial virus (RSV) infection. The findings open new avenues for interventions in RSV disease.

Severe RSV infection is the leading cause of infant hospitalization worldwide. Activation of TLR4, an endotoxin lipopolysaccharide (LPS)-sensing receptor, has been implicated in RSV pathogenesis. The researchers studied hospitalized babies with RSV bronchiolitis in rural and urban regions of Argentina. They found that among rural children with high LPS exposure, TLR4 mutations correlating with reduced response to LPS are found more frequently in mild cases, but in urban children with low LPS exposure, the mutations are found more frequently in severe cases.

Interestingly, RSV titers were not associated with disease severity or the interaction between TLR4 and LPS. Patients from rural homes had suppressed inflammatory cytokines, suggesting environmental conditioning of the immune system. In addition, high GATA3/T-bet and IL-4/IFN γ ratios, indicators of Th2 polarization, are present in severe RSV cases. The researchers also confirmed these findings in a mouse model of RSV bronchiolitis. Molecules identified in this study could help develop better treatments for illness from RSV. **(QX)**

Citation: Caballero MT, Serra ME, Acosta PL, Marzec J, Gibbons L, Salim M, Rodriguez A, Reynaldi A, Garcia A, Bado D, Buchholz UJ, Hijano DR, Coviello S, Newcomb D, Bellabarba M, Ferolla FM, Libster R, Berenstein A, Siniawski S, Blumetti V, Echavarría M, Pinto L, Lawrence A, Ossorio MF, Grosman A, Mateu CG, Bayle C, Dericco A, Pellegrini M, Igarza I, Repetto HA, Grimaldi LA, Gudapati P, Polack NR, Althabe F, Shi M, Ferrero F, Bergel E, Stein RT, Peebles RS, Boothby M, Kleeberger SR, Polack FP. 2015. TLR4 genotype and environmental LPS mediate RSV bronchiolitis through Th2 polarization. *J Clin Invest* 125(2):571-582. [\(Story\)](#)

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Leading the way in ribonucleotide excision repair

NIEHS researchers and colleagues reveal how the enzyme topoisomerase 1 (Top1) mediates ribonucleotide excision repair (RER) only on the leading strand and not the lagging strand during DNA replication. The erroneous incorporation of ribonucleotides into the genome overwhelmingly represents the most common form of DNA damage, often resulting in several mutagenic consequences, including the autoimmune disorder Aicardi-Goutieres syndrome.

Using a yeast model, the team previously reported on a mutant variant of the DNA polymerase responsible for leading strand extension, pol2-MG, which incorporates high levels of ribonucleotides into DNA. This construct enabled the identification of RNase H2 as the critical enzyme responsible for removing the incorporated ribonucleotides. In this study, the authors examined lagging strand polymerase variants, pol1-LM and pol3-LM, using yeast genetics, radiolabeling, and a new method developed in their lab, called hydrolytic 5'-DNA end-sequencing, or HydEn-seq. The pol1-LM and pol3-LM enzymes also incorporate ribonucleotides into genomes, and these ribonucleotides are removed in an RNase H1-dependent manner.

Top1 also catalyzes RER activity, but requires additional post-processing that often leaves the genome susceptible to further damage. When RER-defective yeast strains lacking Top1 are considered, only pol2-MG, not pol1-LM or pol3-LM, results in an increase in DNA damage. The authors propose three, non-exclusive testable models to explain Top1's preference for leading strand RER, and future work is geared towards pinning down the correct model. **(GF)**

Citation: Williams JS, Clausen AR, Lujan SA, Marjavaara L, Clark AB, Burgers PM, Chabes A, Kunkel TA. 2015. Evidence that processing of ribonucleotides in DNA by topoisomerase 1 is leading-strand specific. Nat Struct Mol Biol 22(4):291-297.

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Inhibition of NADPH oxidase halts disease progression in Parkinson's disease models

Scientists from the NIEHS Neurobiology Laboratory and the National Toxicology Program showed that post-treatment of an ultra-low dose of the nicotinamide adenine dinucleotide phosphate (NADPH) inhibitor, diphenyleneiodonium (DPI), reduces both neuroinflammation and neurotoxicity in rodent Parkinson's disease (PD) models by systemic injections of either endotoxin lipopolysaccharide (LPS) or 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Since PD is a progressive disabling disorder characterized by dopaminergic degeneration, the findings provide a promising therapeutic strategy for stopping the progression of the disease and other neurodegenerative disorders.

The study, published in the journal *Brain*, demonstrated that subcutaneous infusion of ultra-low dose DPI to both LPS and MPTP rodent models reduced microglia-mediated chronic neuroinflammation by selectively inhibiting NADPH oxidase activation. Inhibiting NADPH oxidase attenuated the progression of dopaminergic neuron degeneration and motor deficits. Additionally, mice treated with ultra-low dose DPI did not display overt organ toxicity or any effects on body weight. Results also indicated that DPI in low concentrations did not influence peripheral immune cell function. Taken together, these findings show that ultra-low dose DPI is an excellent drug candidate for future clinical trials. **(TAC)**

Citation: Wang Q, Qian L, Chen SH, Chu CH, Wilson B, Oyarzabal E, Ali S, Robinson B, Rao D, Hong JS. 2015. Post-treatment with an ultra-low dose of NADPH oxidase inhibitor diphenyleneiodonium attenuates disease progression in multiple Parkinson's disease models. *Brain* 138(Pt 5):1247-1262.

(Greg Buchold, Ph.D., is a former postdoctoral fellow in the NIEHS Reproductive and Developmental Biology Laboratory. Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group. Geoffrey Feld, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Genome Stability Structural Biology Group. Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Mechanisms of Mutation Group. Qing Xu is a biologist in the NIEHS Metabolism, Genes, and Environment Group.)

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Inside the Institute

Administrative professionals event recognizes heavy lifters behind the scenes

By Eddy Ball

NIEHS continued its long-standing annual tradition of celebrating the contributions of its administrative professionals May 22 with a special presentation and ice cream social.

The star of the high-energy event was motivational speaker [Earl \(Dr. Earl\) Suttle, Ph.D.](#), who was so well received two years earlier (see [story](#)) that organizers invited him back for an encore.



Linked video:
Watch a video of Dr. Earl wowing the crowd at a 2014 inspiration talk in Atlanta (02:14)

(Launches in new window)

Download Media Player:  Flash 

Showing their support for administrative professionals were NIEHS leaders Linda Birnbaum, Ph.D., NIEHS and National Toxicology Program director; Deputy Director Rick Woychik, Ph.D.; and Associate Director of Management Joellen Austin. They were later joined by other members of leadership to serve ice cream and cake at the social.

Dealing with sources of stress to improve quality of life

Suttle told the audience, “If you don’t laugh 14 times a day, you’re under-laughed.” As he punned his way through messages about self-worth and the importance of dealing constructively with stress, Suttle made sure those in the room got at least their daily dose of mirth during the two hours they spent together.

What Suttle had to say wasn’t new, but the way he presented his messages kept his listeners hanging on every word. “Your chance of dying is 100 percent,” he said, “and probably stress is going to do it.” With his candid discussion of stressors in his own life, Suttle helped others open up about their own challenges.



Central to Earl’s message is the idea that people need to trust in themselves and commit to working to make their lives at home and on the job more satisfying. His running conversation engaged the audience with rhythms borrowed from the evangelical church and the rapid-fire repartee of hip-hop. (Photo courtesy of Steve McCaw)



Birnbaum opened the celebration by reminding participants that their contributions should never be taken for granted. “The scientists here at NIEHS could not do their work without the work that you do.” (Photo courtesy of Steve McCaw)

If the administrative professionals in the audience thought this talk would end in a conventional way, they were very wrong. In the last of many hands-on exercises, Suttle asked them to write a letter of love and commitment to themselves that included at least five ideas from a 20-point wellness and growth plan he had distributed.

Five volunteers shared their letters, which were addressed to themselves and signed with love. Participants left the workshop reenergized, holding a tangible reminder of their commitment to insights for making life, love, and work more rewarding.

(Eddy Ball is a contract writer for the NIEHS Office of Communications and Public Liaison)



Suttle helped people look at the strengths and weaknesses of their work styles. (Photo courtesy of Steve McCaw)

Word play to surprise listeners and refresh basic truths

Suttle made sure he kept the audience engaged every step of the way, as he worked the floor and addressed individuals by their given names. He put familiar words, such as under and laughed, together in new ways, and inverted well-known sayings to make obvious truths refreshingly new again.

“Dress the way you want to be addressed,” he said of grooming for success. “You don’t get a second chance to make a first impression.”

Suttle used the same number play in his rule of four for first impressions. He told the group that it takes four seconds to make a first impression, four minutes for others to confirm it, and four years to undo a bad one.

“Learn to work harder on you than you do on your job,” Suttle said of an enlightened, self-interested approach to life and work. “Give yourselves to yourselves, before you give yourselves away.”



Suttle’s winning formula kept people moving, laughing, and interacting, often in team exercises. Above, left to right, Mary Jacobson, Benny Encarnacion, and Barbara Dietz worked as a group to brainstorm different working styles for team efforts. (Photo courtesy of Steve McCaw)



Like many of her colleagues, Jenn Evans, center, managed to build up her reserve of daily smiles, as Suttle entertained while he taught. (Photo courtesy of Steve McCaw)



As the workshop progressed, Suttle created an accepting environment that encouraged Tonya Stonham, left, and Marva Wood to share details of their love and commitment letters. (Photo courtesy of Steve McCaw)



One of Suttle's tactics for empowering the audience involved showing them how they could do what seemed to be completely impossible. In this example, volunteers, from left, Peggy Mooring, Diana Callender, and Michelle Owens learned they could drive a plastic straw through a raw potato. (Photo courtesy of Steve McCaw)



Birnbaum, second from left, joined other members of leadership to cut cake and scoop ice cream for the administrative professionals. (Photo courtesy of Steve McCaw)

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NIEHS team cleans local roadway for Earth Day

By Ian Thomas

NIEHS continued its weeklong celebration of Earth Day on April 21 by cleaning up the 1.2-mile stretch of Hopson Road between Davis Drive and N.C. Highway 55 in Research Triangle Park. The lunchtime cleanup was part of North Carolina's [Adopt-A-Highway Program](#), a long-standing effort to reduce litter on local roadsides and preserve the natural beauty of the Tar Heel State.

“NIEHS has a rich history with the Adopt-A-Highway Program, dating all the way back to the mid-1990s,” said Paul Johnson, co-chair of the NIEHS Environmental Awareness Advisory Committee and an organizer of the cleanup team. “Not a lot of organizations hold that kind of legacy within their community, but it’s fantastic to know that ours does.”

Established in 1988 as a response to growing public concern about litter along the roadways, the Adopt-A-Highway Program currently hosts representatives from government and private sector entities across the state.

“It’s always a treat to get out here on a sunny day and do my part to keep the Triangle beautiful,” said NIEHS biologist Cindy Innes. “After all, isn’t that what Earth Day is all about?”

Earth Day is an annual event, first celebrated on April 22, 1970, to demonstrate support for environmental protection. Now, Earth Day is globally recognized, and many organizations have expanded it to a full week.

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

2015 NIEHS Adopt-A-Highway participants

Laura Hall — National Toxicology Program, Program Operations Branch

Maggie Humble — Division of Intramural Research (DIR) Genomic Integrity and Structural Biology Laboratory

Mike Humble, Ph.D. — Division of Extramural Research and Training (DERT) Genes, Environment, and Health Branch

Cindy Innes — DIR Clinical Research Branch

Paul Johnson — NIEHS Health and Safety Branch

Nicole Popovich — DERT Office of the Director

VeeVee Shropshire — NIEHS Health and Safety Branch

Bill Steinmetz — NIEHS Health and Safety Branch

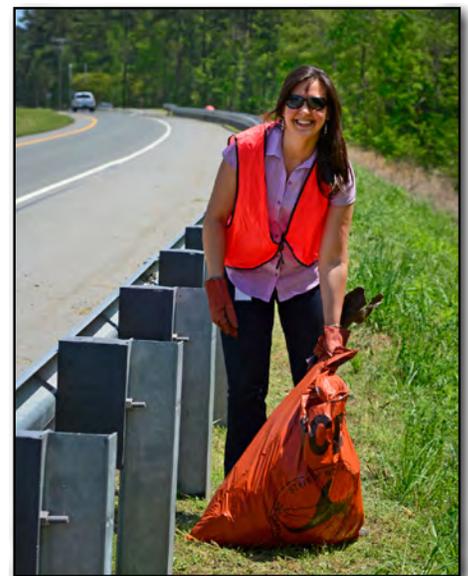
Bill Willis — DIR Laboratory of Reproductive and Developmental Toxicology



Mike Humble braved the outer guardrail to help clean up Hopson Road. (Photo courtesy of Steve McCaw)



Willis, left, and Steinmetz worked together to maximize their efforts. (Photo courtesy of Steve McCaw)



Popovich brings another load of trash to the pile. (Photo courtesy of Steve McCaw)



The Adopt-A-Highway Program is managed by the N.C. Department of Transportation. (Photo courtesy of Steve McCaw)



From left, Steinmetz, Popovich, Maggie Humble, Mike Humble, Hall, Johnson, and Willis displayed the results of their labor. Innes and Shropshire, not shown, also participated in the cleanup effort. (Photo courtesy of Steve McCaw)

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