

September 2014

NIEHS Spotlight



[Alaska community forums highlight tribal health disparities](#)

NIEHS and NTP Director Linda Birnbaum, Ph.D., visited St. Lawrence Island and Chickaloon, working to reduce tribal health disparities.



[Birnbaum reflects on life-changing experience](#)

Birnbaum reflects on her immersion in Native Alaskan life and describes the environmental health challenges tribal communities face.



[NTP to conduct testing on chemicals from West Virginia spill](#)

NTP will conduct further toxicity testing on chemicals spilled into the Elk River, to determine possible health effects.



[Forum explores environmental impacts on women's health](#)

▶ Audio

Birnbaum was the featured speaker at a forum July 28 at the Dobbs Ferry campus of Mercy College in Westchester County, New York.



[NIH associate director for prevention outlines strategic plan](#)

David Murray, Ph.D., director of the NIH Office of Disease Prevention, engaged a supportive audience of policy and program leadership Aug. 20 at NIEHS.

Clinical Feature



[NIEHS receives human research accreditation, launches training programs](#)

A new series of seminars and training programs follows NIEHS accreditation for human research and helps ensure protection of human research subjects.

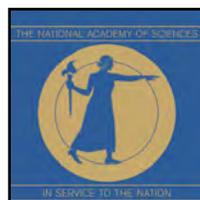
Science Notebook



[NTP symposium examines indoor air pollution from biomass fuels](#)

▶ Video

An interdisciplinary team of speakers surveyed the state of the science, policy, and future directions of research on adverse health effects of indoor solid fuel combustion.



[NAS agrees with NTP Report on Carcinogen listing decisions](#)

The National Academy of Sciences reviewed and agreed with NTP decisions listing formaldehyde and styrene in the Report on Carcinogens.



[Symposium features talks on NIH core support and metabolomic profiling](#)

▶ Video

NIEHS Health Scientist Administrator Daniel Shaughnessy, Ph.D., led a lineup of eight speakers at the Aug. 22 Metabolomics Symposium at RTI International.

NIEHS Spotlight



[Robin Stanley joins NIEHS Signal Transduction Laboratory](#)

Stanley brings her interest in ribosome development to her new position as an NIH Earl Stadtman Tenure-Track Investigator and head of the Nucleolar Integrity Group.



National Institute of Environmental Health Sciences

[NIEHS fellows set record for Pathway to Independence Awards](#)

Two more NIH Pathway to Independence Awards, or K99/R00 grants, given to NIEHS trainees, raise the number of successful applicants to six in 2014.



[New study reviews needs for research on health effects of fracking](#)

A new paper by a working group of NIEHS grantees echoes prior recommendations for fracking research, but adds a new twist with a call for community engagement.



[NIEHS-funded summer student wins President's award](#)

High schooler May Wing's summer research, funded by NIEHS, won her a President's Environmental Youth Award, given at an Aug. 12 White House ceremony.



[Arizona internship program marks ninth year](#)

Funded in part by NIEHS, this summer the University of Arizona gave 45 more high school interns an intensive 7-week enrichment experience in science.

Science Notebook



[A new approach to determine cancer risk of chemicals](#)

The NIEHS-funded study, led by Boston University computational biologist Stefano Monti, Ph.D., is a step toward simpler and cheaper tests to screen chemicals.



[Special seminar highlights global impact of air pollution](#)

A special seminar Aug. 1 at NIEHS featured Jinming Gao, M.D., Ph.D., professor of medicine and chief physician at Peking Union Medical College Hospital in Beijing.



[Putting data on the map — data science seminar highlights synthetic populations](#)

Synthetic data populations can provide realistic information for public health decision makers, according to Bill Wheaton of RTI International.



[Webinars highlight European advances in exposome research](#)

Researchers from two European studies — the HEALS integrated methodology and HELIX — focus on developmental exposures in NIEHS webinars.



[Peer reviewers support NTP listing recommendation for TCE](#)

A panel of experts spent Aug. 12 peer reviewing an NTP draft monograph on trichloroethylene, a chemical once prominently used as a degreaser for metal parts.

NIEHS Spotlight



[ONES awardee honored by Oregon State University](#) 🏆

Oregon State University has selected NIEHS grantee Stacey Harper, Ph.D., as the recipient of its 2014 Savery Outstanding Young Faculty Award.



[Postdoctoral fellows use proximity to help land local academic positions](#)

The stories of two NIEHS postdoctoral fellows who secured positions in local universities provide useful insights for other trainees.



[Teachers give NIEHS an A-plus rating](#)

The evaluations have been compiled, and teachers who participated in this summer's STaRs Institute gave the NIEHS program excellent marks.

Inside the Institute



[Birnbaum visits First Environments Early Learning Center](#)

Birnbaum toured the gardens and met staff and children at the NIEHS and EPA daycare center, which shares the NIEHS interest in a healthy start to life.



[2014 Feds Feed Families campaign helps knock out local hunger](#)

NIEHS employees donated more than 2,500 pounds of food and personal hygiene items for area food banks.

Science Notebook



[This month in EHP](#)

In September, Environmental Health Perspectives examines environmental influences on aging brains and health impacts of e-cigarettes.



[Phillip Beachy to present upcoming distinguished lecture](#)

Beachy, a leader in adult stem cell biology and regenerative medicine focusing on the Hedgehog signaling pathway, will speak Sept. 26.

Extramural Research

[Extramural papers of the month](#)

- Perinatal DDT exposure linked to later risk of metabolic syndrome
- DDT alternative linked to transgenerational inheritance of disease
- Marine bacteria produce polybrominated diphenyl ethers
- Combined action of Srs2 and Exo1 enzymes helps maintain DNA

Intramural Research

[Intramural papers of the month](#)

- NTP research finds low doses of inorganic arsenic cause lung tumors in male mice
- Maternal smoking linked to altered DNA in newborns
- Control of histone expression by phosphorylation of an mRNA processing protein
- Retinoic acid-related orphan receptors involved in novel signaling pathway
- Crystal structure of an important inositol phosphate kinase

Calendar of Upcoming Events

- **Sept. 3, (Offsite event)**, NIH campus in Bethesda, Maryland 3:00-4:00 p.m. — NIH Wednesday Afternoon Lecture Series, featuring Andrew Feinberg, M.D., addressing “The Epigenetic Basis of Common Human Disease,” [webcast](#)
- **Sept. 9-10**, Rodbell Auditorium 8:30 a.m.-5:00 p.m. — National Advisory Environmental Health Sciences Council, [webcast](#)
- **Sept. 10**, Rodbell Auditorium 1:30-2:30 p.m. — Inflammation Faculty Seminar Series with Tomas Guilarte, Ph.D., exploring “TSPO in Brain Injury and Inflammation: A Biomarker With Therapeutic Potential”
- **Sept. 15-16 (Offsite event)**, James B. Hunt Jr. Library at North Carolina State University 8:30 a.m.-5:00 p.m. — Workshop for the Development of a Framework for Environmental Health Science Language, [webcast Sept. 15](#) and [Sept. 16](#)
- **Sept. 16**, Rodbell Auditorium 8:30 a.m.-5:00 p.m. — Scientific Advisory Committee on Alternative Toxicological Methods (SACATM), [register](#) to attend or view [webcast](#)
- **Sept. 17**, in Keystone 1003AB 9:00 a.m.-noon — Data Science and Keystone Symposium
- **Sept. 19 (Offsite event)**, Pew Charitable Trusts in Washington, D.C., 8:00 a.m.-5:00 p.m. — Mid-Atlantic Center for Children’s Health and the Environment [Annual Conference](#), [register](#)
- **Sept. 22-24**, Rodbell Auditorium 8:00 a.m.-5:00 p.m. — Partnerships for Environmental Public Health Annual Meeting: Communication Research in Environmental Health Sciences — Environmental Health Literacy, [register](#) to attend.
- **Sept. 26**, Rodbell Auditorium 11:00 a.m.-noon — Distinguished Lecture Series, featuring Philip Beachy, Ph.D.
- **Sept. 26 (Offsite event)**, Environment Hall Field Auditorium at Duke University, noon-1:30 p.m. — Integrated Toxicology and Environmental Health Program Fall 2014 Seminar Series, featuring Nicole Kleinstreuer, Ph.D., discussing “Computational Toxicology Tools: Constructing and Evaluating an Adverse Outcome Pathway for Embryonic Vascular Disruption”
- **Sept. 29-30 (Offsite event)**, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina — ToxCast Data Summit: Beginning the dialogue about using new data to transform chemical safety evaluations, [register](#) to attend
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Alaska community forums highlight tribal health disparities

By Kelly Lenox

NIEHS and NTP Director Linda Birnbaum, Ph.D., traveled to the far north July 20-25 for community forums in Alaska, where she heard firsthand the unusually severe environmental health challenges faced by tribal communities. In addition, Birnbaum met with health care providers to discuss ways to improve environmental public health in the region (see [side bar](#)).

Vi Waghiyi, Alaska Community Action on Toxics (ACAT) Environmental Health and Justice Program director and member of the NIEHS National Advisory Environmental Health Sciences Council, invited Birnbaum to St. Lawrence Island, Alaska. Waghiyi noted that Alaska is home to 231 federally recognized tribes, including some of the most highly contaminated populations on the planet.

“It’s not a question of whether you will get cancer, but when,” Waghiyi said. She herself is Yupik, an Alaska Native tribe whose numbers on St. Lawrence Island were far higher before the coming of European whalers, missionaries, and archaeologists. “Help is not coming fast enough,” she said.

“We’re part of the ecosystem”

Birnbaum has held numerous [community forums](#) and other meetings in places facing environmental health disparities (see related [story](#)). The exchanges allow NIEHS to bring research to bear on public health concerns shared by tribal leaders, regional health care providers, and community organizations.

The Alaska visit underscored how changes in the environment, both local and global, threaten the health of people living traditional lifestyles. “Northern peoples are an indicator for the world,” said an elder in the St. Lawrence Island community of Savoonga. “We’re part of the ecosystem,” he said.



Lisa Wade, left, of the Chickaloon Village Traditional Council, showed Birnbaum the site of a proposed surface coal mine. (Photo courtesy John Schelp)



Waghiyi, a Yupik mother and grandmother, explained that ACAT enables communities like Savoonga to be involved in designing research to address their needs. (Photo courtesy of Samarys Seguinot-Medina of ACAT)

Triple threat on St. Lawrence Island

The Yupik on St. Lawrence Island face a triple threat — air pollutants transported from Asia and North America by global air currents; polychlorinated biphenyls (PCBs), organochlorine pesticides, and other chemicals in marine mammals, which constitute their major food source; and contaminants from a former military installation.

With funding from NIEHS, ACAT conducts community-based participatory research with the island leaders. According to early [results](#) of one study, blood serum in residents of the island, which is closer to Siberia than to the Alaska mainland, showed elevated levels of PCBs. The levels in those exposed to environmental degradation around the closed military site at Northeast Cape, an area that is an important source of traditional foods, were up to 10 times higher than the average American.

Elders and leaders shared their concerns with Birnbaum, and she participated in a women's listening circle, as well as a lunch discussion with elders. Immersion into local life through meals and festivities gave the forum a unique flavor.

Coal mining in Chickaloon

Chickaloon Village, northeast of Anchorage, is located on the mainland, in contrast to the island setting of Savoonga, and while residents face some of the same environmental health concerns, there are differences, as well.

Notably, Chickaloon lies near an area of historical coal mining operations, which have led to underground fires and stream pollution. At meetings with tribal elders and members of the Chickaloon Village Traditional Council, Birnbaum heard concerns about a proposal for new mining operations adjacent to the community, and shared recommendations for responding to health challenges.

The events ended with visits to grantees at the University of Alaska Anchorage, and a wrap-up meeting with ACAT staff. The NIEHS Office of Science Education and Diversity has already begun planning for the next community forum in Tucson, Arizona, in the spring of 2015.

Closing the loop with health care providers

Birnbaum met with health care providers for both tribal areas. In Nome, more than 150 miles northeast of St. Lawrence Island, Birnbaum spoke with Angie Gorn, president and CEO of the Norton Sound Health Corporation, sharing what she learned in the women's listening circle — that the community faces serious public health concerns, including a high prevalence of cancers, reproductive problems, and developmental disabilities. By the time residents receive evaluation and treatment, cancers and other health issues are often far advanced. Gorn agreed to send evaluation teams out to the island to assess health status.

In Anchorage, Birnbaum met with representatives of the Alaska Native Tribal Health Consortium, which serves Alaska Natives statewide, and the Southcentral Foundation, which serves Chickaloon and Alaska Natives in the south-central region. Birnbaum again emphasized the need for addressing environmental health, such as PCB contamination, in addition to traditional concerns with water, sanitation, and rabies. The health care providers agreed, sharing their focus on prevention and use of culturally based approaches.



Living on the northern coast of St. Lawrence Island — thought to be a remnant of the land bridge that once connected Asia and North America — Savoonga's residents rely on traditional sources of food — mostly marine mammals. (Photo courtesy of John Schelp)



The unique health challenges of living on permafrost, or permanently frozen soil, have been met with creative solutions, such as the above-ground heated water and sewer system in Savoonga. (Photo courtesy of John Schelp)



In Savoonga, the community leadership spoke frankly with Birnbaum about the environmental health threats they face. (Photo courtesy of John Schelp)



Lunch with the Savoonga elders was one of the rich opportunities Birnbaum had to hear from local residents. (Photo courtesy of John Schelp)



Savoonga residents played traditional drums during the atuq, a celebration to welcome Birnbaum. (Photo courtesy of Samarys Seguinot-Medina of ACAT)



Lodging in Savoonga reflected the remote locale. Birnbaum, right, is shown with John Schelp, NIEHS special assistant for community engagement and outreach. (Photo courtesy of John Schelp)



Birnbaum met with local residents in a variety of settings, such as this lunch with the Chickaloon elders. (Photo courtesy of Samarys Seguinot-Medina of ACAT)



Birnbaum answered questions and shared environmental health research findings relevant to local concerns. (Photo courtesy of John Schelp)



Birnbaum met with local residents in a variety of settings, such as this lunch with the Chickaloon elders. (Photo courtesy of Samarys Seguinot-Medina of ACAT)



The Matanuska Glacier feeds the Matanuska River; which flows past Chickaloon, eventually reaching Anchorage on its way into the Gulf of Alaska. (Photo courtesy of Samarys Seguinot-Medina of ACAT)

Alaska community forum events

Savoonga, St. Lawrence Island

- Dialogue with tribal leaders and community members
- Lunch and listening session with elders
- Women's listening circle, with women and girls from the island, on women's and children's health

Nome

- Meeting with marine biologist on connections between human health and marine mammal health
- Roundtable discussion with Norton Sound Health Corporation, the regional health care provider

Chickaloon Village

- Meeting with tribal chief, village council, and health department staff
- Lunch and discussion with elders
- Visit to site of proposed mine

Anchorage

- Meeting with University of Alaska Anchorage grantees, faculty, and students
- Roundtable discussion with Alaska Native Tribal Health Consortium and Southcentral Foundation
- Wrap-up with ACAT staff and research collaborators

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Birnbaum reflects on life-changing experience

By Kelly Lenox

After NIEHS and NTP Director Linda Birnbaum, Ph.D., returned from the Alaska community forums, the Environmental Factor (EF) had a rare opportunity to speak with her at length of her experiences and lasting impressions. In the excerpts below, Birnbaum (LB) reflects on what she learned of life in the far north, as well as on her thoughts after 30 years of studying chemicals, exposures, and underserved populations.

EF: You've done community forums all over the country since coming to NIEHS, and recently returned from holding community forums in Alaska. How do these forums play a part in designing environmental health research?

LB: Before I came to NIEHS, I had no involvement in community-based research at all, but I have learned that we can't do environmental health sciences without involving the community. People know what their problems are, and if we listen to them, we will better understand the processes at work.

EF: What are some of the ways your community meetings in Alaska were different from previous forums?

LB: No doubt it was the intensity. Normally, a community forum is two to four hours long and involves other community leaders. Presentations focus on a specific topic, with time for dialogue.

In Alaska, we spent five days immersed in tribal issues and health disparity concerns. That included meeting with a marine biologist, and with some of our grantees at the University of Alaska. We set up a meeting with one of the health providers for one hour, and we talked for more than two hours. I think that enabled us to open their eyes to environmental health needs and get specific commitments to do things that hadn't yet been done.

EF: How do environmental health challenges in Native American tribal areas in the far north compare with those in other tribal areas you've visited?

LB: This trip had a real impact on my understanding of what some of our indigenous peoples must confront. The traditional lifestyles that remain are threatened in Alaska and in the lower 48.

In Savoonga, they are subsistence hunters, and their traditional diet is now heavily contaminated. That is partly due to global pollution, including PCBs, organochlorine pesticides, and other compounds that are produced in temperate climates, and then are taken up in the atmosphere and deposited in polar regions. Others bioaccumulate up the food chain and the Yupik are eating at the top of the food chain. And then there's the military base there.

In Chickaloon, the traditional diet is salmon and other fish from the stream, and hunting. Coal mining has affected those activities.

At an environmental justice meeting in 1994, a woman — she was Lakota Sioux, I believe, and an attorney — said, "I don't think you understand that the spirits of my ancestors live in the stream that runs next to my house, and in the trees that shade my house, and I can't move because I am part of the continuity of the earth and the land."

Most European Americans are descendants of people who chose to come here, and we don't have the same integral connection to the land, even if we love our homes or have been living on the same land for generations.



Bad weather meant Birnbaum had to wait nearly a full day in Nome before boarding her flight for Savoonga on St. Lawrence Island. (Photo courtesy John Schelp)



Birnbaum, center, with a community member, right, and Pamela Miller, director of Alaska Community Action on Toxics, which conducts NIEHS-funded community participatory research in Savoonga. (Samaris Seguinot-Medina, of ACAT)

EF: Prevention is a persistent theme of your talks at community forums. What realistic steps can a community that relies heavily on traditional food sources take to protect its members?

LB: Prevention is challenging. First is the good news. Some of the levels of persistent organic pollutants in seals and fish are starting to decline, though they are still very high.

On St. Lawrence Island, for full medical care, the residents have to go to Nome, or even Anchorage. The health care organizations are largely focused on smoking and alcohol use. We urged them to think more about the health impact of environmental issues, and we got a commitment for a medical team to go out for several days to study the health of everyone on the island.

For subsistence tribal communities, you can educate people to, for instance, avoid the skin and fat. Certain species of fish can be avoided. But it's a change from traditional practices. Blubber, for instance, is a mainstay, but it's highly contaminated. You can also look at the individuals who are at enhanced risk. For instance, women of childbearing age and young children can be encouraged not to eat certain foods.

Working from another direction, we urged the islanders to get their young people trained to provide medical care. It's very hard for them to go off the island to medical school and leave their families and environment. But that's another way to address the disparities.

EF: With so many environmental contaminants originating elsewhere, how does the Alaska experience speak to the global nature of environmental public health?

LB: Our environment is global, but also local. The air pollution in Beijing reaches California in four to five days and may reach Alaska even sooner. So it's not only the persistent compounds that undergo global transport, but also the nonpersistent ones. They may not accumulate in our bodies, but that doesn't mean we're not impacted by a daily onslaught.

EF: Is there anything else you'd like to add?

LB: The trip was amazing, maybe even life changing. I'm already looking forward to visiting the Tohono O'odham in Arizona next April.

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The events on St. Lawrence Island allowed Birnbaum and others to deepen their understanding of how the island's environment shapes local life. (Photo courtesy of John Schelp)



A community meal in Savoonga heightened Birnbaum's (second table, left, in blue shirt) sense of immersion in local culture. (Photo courtesy John Schelp)

NTP to conduct testing on chemicals from West Virginia spill

By Robin Mackar

John Bucher, Ph.D., associate director of the National Toxicology Program (NTP), met July 23 with colleagues from the Centers for Disease Control and Prevention (CDC), a member of Congress, and West Virginia state and local health officials, to discuss plans for conducting additional studies related to a chemical spill earlier this year into West Virginia's Elk River.

Bucher outlined a series of short-term toxicity studies that NTP would conduct on 4-methylcyclohexanemethanol (MCHM) and other chemicals known to be involved in the spill.

In January, approximately 10,000 gallons of chemicals used to process coal spilled from a storage tank into the Elk River. The river is a municipal water source that serves about 300,000 people in the Charleston area.

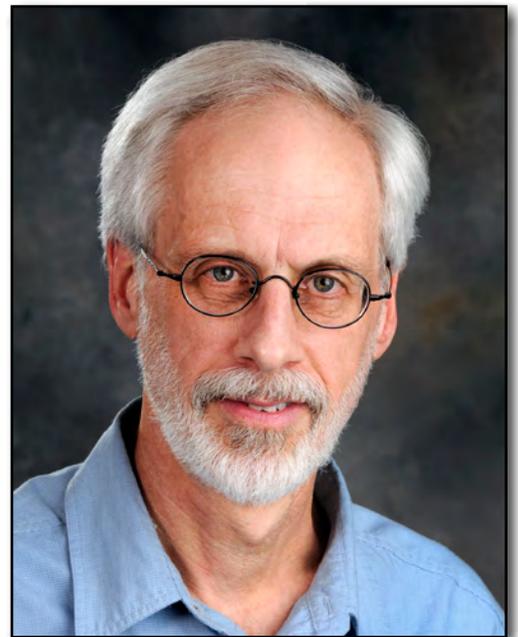
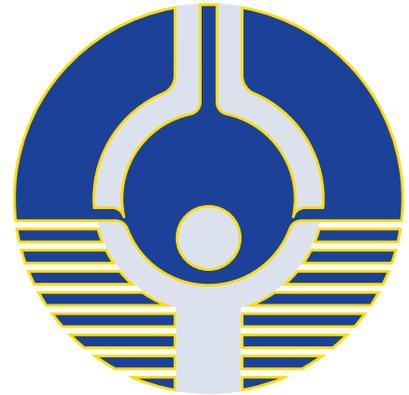
Based on the limited toxicology information available at the time, scientists judged an MCHM level of 1 part per million unlikely to be associated with any long-term adverse health effects, and recommended that as the screening level. More details are available on the [CDC website](#).

Federal agencies have continued working to learn more about the chemicals. Since the early days of the incident, NTP has conducted computer modeling to predict potential adverse effects from the chemicals. This summer, NTP received a request from the CDC Agency for Toxic Substances and Disease Registry to conduct additional toxicity studies.

NTP has published a [fact sheet](#) discussing the proposed efforts. Results from the NTP studies should be available within a year.

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

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Bucher announced that NTP will conduct additional research to more clearly understand the potential for long-term health effects of the Elk River spill. (Photo courtesy of Steve McCaw)

Forum explores environmental impacts on women's health

By Eddy Ball

NIEHS and NTP Director Linda Birnbaum, Ph.D., was the featured speaker at a forum July 28 at the Dobbs Ferry campus of [Mercy College](#) in Westchester County, New York. Mercy College, founded by the Sisters of Mercy in 1950 to educate members of the order, began in the 1960s to evolve into a non-sectarian coeducational institution with strong programs in the health sciences.

The forum, "Silent Dangers: Environmental Impacts on Women's Health," helped raise awareness of environmental influences on public health and the importance of biomedical research in developing effective preventive initiatives.



Linked audio:
[Listen to WAMC Northeast Public Radio reporter Allison Dunne's report on the forum with interviews of Birnbaum and Lowey \(03:51\)](#)

(Launches in new window)

Download Media Player:  Quicktime [↗](#)

Key messages about public health and biomedical research

"Gaining a better understanding of how the environment affects our health will lead to healthier lives," Birnbaum told the audience. "NIEHS' work is centered around important environmental health research, focusing on prevention as opposed to expensive treatment."

"Investments in environmental health research lead to lower health care costs, greater economic growth, and improved quality of life," said U.S. Representative Nita Lowey, D-N.Y., who also spoke at the forum. "I've seen, firsthand, NIH's impact on improving health."

Women with a commitment

Birnbaum has led the world's premier environmental sciences research organization and the leading public health institute at NIH since 2009. Lowey, who has represented New York's 17th congressional district since 1988, has taken a leadership role in such areas as equal opportunity and biomedical research. Both are firsts in their fields.

Birnbaum is the first woman and first toxicologist to serve as director of NIEHS and NTP, as well as the first director to have served as a lead researcher for both NIEHS and the U.S. Environmental Protection Agency.



"We know that at least two-thirds of cancer cases are, in part, caused by environmental factors," Birnbaum said. "If we know what it is in our environment that's impacting our health, we should be able to do something about it." (Photo courtesy of Steve McCaw)



Lowey told attendees that biomedical research is not only essential for advancing public health, but also a stimulant for economic development. (Photo courtesy of Nita Lowey)

Lowey is the first woman and the first New Yorker to chair the Democratic Congressional Campaign Committee, as well as the first woman to lead either party on the powerful U.S. House of Representatives Committee on Appropriations, also known as the House Appropriations Committee.

(This story was adapted from a July 28 [story](#) by Danny LoPriore in the Pleasantville [New York] Daily Voice and a July 30 [report](#) by Allison Dunne of WAMC Northeast Public Radio.)

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NIH associate director for prevention outlines strategic plan

By Eddy Ball

David Murray, Ph.D., director of the NIH Office of Disease Prevention (ODP) and associate director for prevention, engaged a supportive audience of policy and program leadership Aug. 20 at NIEHS, during a presentation that was also webcast. Hosted by NIEHS and NTP Director Linda Birnbaum, Ph.D., [Murray](#) outlined his challenges and accomplishments to date, in a talk on “Developing a Strategic Plan for the NIH Office of Disease Prevention.”

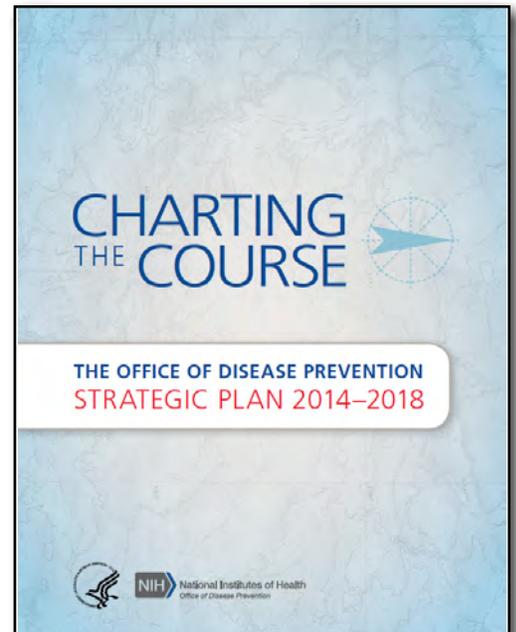
As the head of a trans-NIH programmatic [office](#), Murray is responsible for assessing, facilitating, and stimulating research on disease prevention and health promotion, and disseminating results of the research to improve public health. The goal of ODP is to further raise the visibility of such research throughout NIH, and collaborate with NIH and other public and private partners to achieve the office’s mission and goals.

Murray assumed office in September 2012 with a small permanent staff and budget, along with the Herculean task of redirecting business as usual among many levels of activity at NIH. Needs ranged from developing the metrics and taxonomy for monitoring investments and making refinements in training, to setting future directions by identifying best practices in programming and [prevention research](#), as well as experts who can serve on related grant review panels.

Murray understood the importance of engaging directors and leaders at the NIH Institutes and Centers (ICs), along with nonprofit and partner agency stakeholders, about prevention research and its place in the scientific culture at NIH. “I realized early on that we needed to develop a strategic plan,” he noted with modest understatement, “to frame the increase in staff, technology, and sheer activity required to accomplish the ODP mission.”

Charting the course

“I was naive,” Murray said of his early weeks in office. But nearly two years later, he can point to significant progress toward meeting the first three of six priorities outlined in the ODP [strategic plan](#) for fiscal years 2014-2018, as he ramps up work on the last three priorities (see [text box](#)).



“We’ll increase our staff by 50 percent in the next six months,” Murray told the audience. “We’re optimistic that this can work,” he said of efforts to develop machine-learning tools for portfolio analysis and the experts database. “It’s infinitely expandable,” he said of the database. “It will be Web-based.”

Not surprisingly, a lively question and answer session followed Murray’s talk, which included policy and planning leaders from the NIEHS divisions of the National Toxicology Program (NTP); Extramural Research and Training (DERT); and Intramural Research (DIR), as well as the Office of the Director (OD).

Birnbaum moderated the session, but let other members of leadership dominate the conversation. She and Murray had enjoyed a breakfast meeting, and there were other opportunities for conversation during his daylong visit to NIEHS.

ODP is one of nine offices in the NIH [Division of Program Coordination, Planning, and Strategic Initiatives \(DPCPSI\)](#), directed by James Anderson, M.D., Ph.D. The division works to identify emerging scientific opportunities, rising public health challenges, and knowledge gaps that merit further research or deserve special emphasis.



Along with his experience sitting on review panels for several ICs, Murray served as the first chair of the NIH Community-Level Health Promotion Study Section. (Photo courtesy of Steve McCaw)



Birnbaum, right, introduced Murray, and described the extensive experience in prevention research and methodology that made him a natural choice to lead ODP. She also monitored questions from the audience. (Photo courtesy of Steve McCaw)



Intrigued by plans for a database of experts, NTP Deputy Division Director for Policy [Mary Wolfe, Ph.D.](#), wondered about using what Murray called an electronic Rolodex of experts to help find members for NTP expert panels. (Photo courtesy of Steve McCaw)



DERT Director Gwen Collman, Ph.D., who had participated in developing the ODP strategic plan, asked about the integration of basic research into the ODP vision. “Prevention research can operate at several levels,” she said. (Photo courtesy of Steve McCaw) DERT Director Gwen Collman, Ph.D., who had participated in developing the ODP strategic plan, asked about the integration of basic research into the ODP vision. “Prevention research can operate at several levels,” she said. (Photo courtesy of Steve McCaw)

OD Office of Policy, Planning, and Evaluation Director Sheila Newton, Ph.D., asked about dissemination of ODP Tobacco Regulatory Science Program research and translation into public policy. (Photo courtesy of Steve McCaw)

Priorities of the ODP strategic plan

- Systematically monitor NIH investments in prevention research and assess the progress and results of that research.
- Identify prevention research areas for investment or expanded effort by NIH.
- Promote the use of the best available methods in prevention research and support the development of better methods.
- Promote collaborative prevention research projects and facilitate coordination of such projects across NIH and with other public and private entities.
- Identify and promote the use of evidence-based interventions and promote the conduct of implementation and dissemination research in prevention.
- Increase the visibility of prevention research at NIH and across the country.

Those interested in progress on the six priorities can receive notifications about ODP programs and activities, by signing up for the [ODP mailing list](#).

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Robin Stanley joins NIEHS Signal Transduction Laboratory

By Robin Arnette

The NIEHS Laboratory of Signal Transduction welcomed a new researcher to the fold in July. Robin Stanley, Ph.D., joined the institute as a National Institutes of Health Earl Stadtman Tenure-Track [Investigator](#) and head of the Nucleolar Integrity Group. She will examine the regulation and molecular mechanisms that govern the development of ribosomes, the primary sites of protein synthesis in cells.

Prior to her appointment at NIEHS, Stanley was a postdoctoral fellow at the National Institute of Diabetes and Digestive and Kidney Diseases, where she studied autophagy, a cellular process that literally means self-eating. A cell activates autophagy in response to nutrient starvation. Stanley said she wanted to switch her research focus to how ribosomes form, because it is one of the most taxing processes in the cell, using up to 80 percent of a cell's energy. In addition, the signaling pathways involved in ribosome biogenesis take their cues from the environment, so doing her research at NIEHS was a perfect fit.

“I really wanted to come to NIEHS when I started looking for permanent positions,” Stanley said. “Not only would I get to collaborate with some of the top scientists in environmental health research, but I’d also have an opportunity to enjoy the wonderful recreational and cultural activities that take place in the Raleigh-Durham area.”



Stanley said her older brother was a runner, so she started running in high school to keep up with him. (Photo courtesy of Steve McCaw)

Having the best of both worlds

When Stanley graduated from high school in Lumberton, North Carolina, in 1999, she was a math and chemistry geek. She entered The University of North Carolina at Charlotte (UNCC) with a double major in math and chemistry. Stanley discovered a perfect combination of her two favorite subjects during a research rotation in a UNCC crystallography lab.

After completing a Bachelor of Arts in math and a Bachelor of Science in chemistry, she attended Yale University as a doctoral student, where she began doing her first crystallographic studies of the ribosome.

NIEHS Scientific Director Darryl Zeldin, M.D., said the institute was looking to expand its interest into the environmental influences of protein production, and was pleased that Stanley accepted the position. He said her expertise will help NIEHS answer basic questions about how environmental exposures impact human disease at the cellular level.

Running key to work-life balance

Stanley is married to a biochemist and is the mother of a 1-year-old. When asked how she balances being a wife, mother, and scientist, she said having a supportive spouse and participating in a fun activity have been crucial to her success. For her, running provides the outlet she needs. She especially looks forward to long distance runs. Stanley has completed seven marathons, three of them being the famed Boston Marathon.

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NIEHS fellows set record for Pathway to Independence Awards

By Staton Wade

Two more NIH Pathway to Independence Awards, or K99/R00 grants, given to NIEHS trainees, raise the number of successful applicants to six in 2014. Tracy Clement, Ph.D., and Anne Marie Jukic, Ph.D., recently learned of their awards, setting an NIEHS record for the number in a given year.

The award is a transition grant that ensures trainees the resources and mentoring needed to become successful independent researchers. After the training phase (K99), grantees who secure tenure-track positions can transition into R00 funding, to kick-start their independent careers.

Clement works in the Gamete Biology Group with Mitch Eddy, Ph.D., and Jukic is part of the Reproductive Epidemiology Group, working with Allen Wilcox, M.D., Ph.D. Both researchers study reproductive biology, and their grants were funded through the Eunice Kennedy Shriver National Institute of Child Health and Human Development.



Clement received a 2013 Fellows Award for Research Excellence for her work on ARP. (Photo courtesy of Steve McCaw)

Addressing mechanisms of male infertility

While at NIEHS, Clement has characterized the role of an actin-related protein (ARP) in spermatid development and male fertility. ARPs are important for basic cellular processes and responses to environmental stress, because they control cellular shape, organization, and movement. Clement's K99 funding will allow her to develop new ways of identifying the mechanisms of ARP action during the development of sperm.

“One of the aspects of this project that excites me the most is the development of a tissue culture system to view actin regulation and dynamics in the testis as spermatids develop,” said Clement. Spermatids are sperm precursors, and male infertility results from improper spermatid development. Nearly half of all cases of infertility are linked to the male, and nearly half of those are due to unknown causes. “This study will increase our understanding of how fertilization-competent sperm are produced,” said Clement.

Clement will receive mentoring support from NIEHS Laboratory of Reproductive and Developmental Toxicology (LRDT) scientists Eddy and Humphrey Yao, Ph.D., as well as Joseph Chalovich, Ph.D., in the Department of Biochemistry and Molecular Biology at East Carolina University.

Effects of vitamin D on reproduction

The Reproductive Epidemiology Group, led by Wilcox, developed epidemiological methods to study fertility and early development, for identifying environmental factors that contribute to infertility and poor reproductive outcomes in humans. Jukic has previously studied the effects of lifestyle and physical activity on fertility, and the normal variability of human reproductive factors, such as pregnancy length (see [story](#)).

With the help of NIEHS collaborators and mentors Wilcox, Donna Baird, Ph.D., and Clarice Weinberg, Ph.D., Jukic will turn to studying the effects of vitamin D on fertility and early development. “Small studies have reported detrimental effects of low vitamin D levels on reproduction, but large population-based human data are lacking,” said Jukic.

Applicants credit mentors and supportive colleagues

Both Clement and Jukic credited the support of their strong mentoring teams, previous grant recipients who provided writing advice, and NIEHS administration, including Tammy Collins, Ph.D., director of the Office of Fellows' Career Development (OFCD), and Deputy Scientific Director and Training Director Bill Schrader, Ph.D.

“My co-mentors helped me polish my specific aims, wrote letters of support, and humored my ideas in a way that fosters independent thinking, as is the intent of the grant,” Clement said.

For Jukic, in addition to her mentors' support and years of experience in fertility and pregnancy research, help also came from program officials in the NIEHS Division of Extramural Research and Training, who have expertise in the grant application process. “They were very helpful, even though I wasn't applying through NIEHS,” said Jukic.

(Staton Wade, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Chromatin and Gene Expression Group.)



Jukic was first author on a paper on variability of pregnancy length that was selected as a paper of the month and featured in the Environmental Factor. (Photo courtesy of Steve McCaw)

What is the award and how to apply

The NIH Pathway to Independence Award, or K99/R00 grant, allows fellows to showcase their ability to secure funding and financially jump-start their independent labs. The purpose of the K99/R00 is to support a new cohort of talented NIH-funded investigators and to ease their transition from the postdoctoral phase to stable, independently funded research careers.

In the K99 phase, fellows receive one to two years of support for mentored training that focuses on learning new techniques or establishing novel experimental systems that will allow them to competitively pursue their chosen research path. After transitioning into a tenure-track faculty position, awardees receive up to three years of additional independent funding in the R00 phase.

Applications for the Pathway to Independence Award are accepted in February, June, and October of each year. Applicants can apply anytime within four years of receiving their doctoral degree. Interested fellows should refer to the latest [Program Announcement](#) for more information.

Many NIH entities participate in the K99/R00 program. Applicants are strongly encouraged to contact the specific institute, center, or office through which their grant will be funded, prior to submission.

[More information](#) on K99/R00 funding can be found on the NIEHS website.

OFCD offers resources for grant-seeking fellows. A presentation on grantsmanship and K99/R00 grant applications will take place Oct. 22, including a panel discussion with recent recipients. Also, Schrader provides individual consultations to applicants in the months prior to grant submission.

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New study reviews needs for research on health effects of fracking

By Eddy Ball

A new paper by a working group of NIEHS grantees echoes prior recommendations for fracking research, but adds a novel twist with a call for community engagement, to frame the development of credible science as a foundation for evidence-based decision-making.

Led by [Trevor Penning, Ph.D.](#), of the University of Pennsylvania (UPenn), the Inter-Environmental Health Sciences Core Center Working Group on Unconventional Natural Gas Drilling Operations issued its recommendations for research on fracking in a commentary published July 18 in the journal *Environmental Health Perspectives*.

Weighing benefits with potentially adverse health effects

Natural gas is a much cleaner fossil fuel than oil or coal and can be extracted from tight shale formations through unconventional natural gas drilling operations (UNGDO), known as fracking. The review begins with a description of the many potential benefits of the operation. “[UNGDO] creates jobs, provides a potential route to energy independence, and may increase national security,” the authors wrote.

However, they also observe that some advocacy groups, such as Physicians for Social Responsibility, have serious environmental health concerns. The authors argue for a precautionary approach, with a moratorium on UNGDO until the potential health effects of fracking and related activities, such as transportation and silica mining, are better understood.

The authors identified 111 studies, only a handful of which were peer-reviewed environmental health studies. They also considered reports by government, health agencies, nonprofits, and the gas and oil industry.

Recommendations for research on fracking

According to the authors, their recommendations (see [text box](#)) are similar to those proposed by others, including the Union of Concerned Scientists in its 2013 [report](#), with one significant difference. The working group makes a strong case for emphasizing community-based participatory research to inform debate over the potential adverse health effects of fracking.

Referring to the Community First communication model (see [story](#)) developed for a team led by NIEHS grantee [Edward Emmett, M.D.](#), the authors argued, “Communities should be engaged in determining the most effective ways to disseminate research findings, and there should be timely and transparent dissemination and access to aggregated data.”



Penning heads the NIEHS-funded Center of Excellence in Environmental Toxicology at UPenn. EHSCCs conduct the kind of federally funded academic research the study singled out as one trusted model for future directions in studies of fracking. (Photo courtesy of the UPenn)

Variations on this communication model have become an important part of the NIEHS Partnerships for Environmental Public Health programs and clinical research involving human subjects. NIEHS currently funds a study designed along these lines, which is headed by working group member Erin Haynes, Dr.P.H., of the University of Cincinnati (see [story](#)).

In their conclusion, the authors also called for measures to harmonize study design, data collection, and analytical procedures, as well as reduce the possibility of conflict of interest. “Oversight by a single organization would avoid duplication of effort and unnecessary expenditure of resources,” they wrote.

Formation of the working group

NIEHS provides funding for scientific equipment, facilities, and other resources that are shared among researchers at [EHSCCs](#) affiliated with universities throughout the U.S. tackling related environmental health questions.

“The working group was convened following presentations on the potential of natural gas drilling to adversely affect public health at the 2012 annual Environmental Health Sciences Core Centers meeting at Harvard School of Public Health,” Penning said in a press release by Karen Kreeger of UPenn.

Sixteen of the twenty core centers funded by NIEHS joined the working group to review the literature on the potential public health impact of UNGDO and make recommendations for research. As a follow-up to the working group’s formation, Penning and colleagues also hosted a symposium on fracking in February of this year (see [story](#)).

Reinforcing earlier recommendations

The Inter-EHSCC Working Group looked at the state of the science in research on water contamination, air pollution studies, design of epidemiological studies, and integrating community perspectives.

As summarized in the UPenn press release, key recommendations include the following:

- Baseline ground water quality data should be taken before drilling begins, and be monitored over the lifetime and abandonment of the gas-producing well.
- Ambient and occupational air quality should be measured at active drilling sites, and be compared with baseline measurements in adjacent areas without drilling operations.
- An environmental epidemiological study should be performed to determine whether an association exists between health outcomes data and water quality in private drinking wells, in communities with and without hydraulic fracturing.
- An environmental epidemiological study should be performed to determine whether air pollution associated with UNGDO increases the incidence of respiratory illness and cardiovascular disease.
- Community-based participatory research principles should be embraced in designing and conducting studies on environmental and health impacts of UNGDO, so that a range of community perspectives is addressed. All stakeholders, including individuals, communities, industry, advocacy groups, and decision-makers, should be engaged early, to foster multidirectional communication and accountability.

Citation: Penning TM, Breysse PN, Gray K, Howarth M, Yan B. 2014. Environmental Health Research Recommendations from the Inter-Environmental Health Sciences Core Center Working Group on Unconventional Natural Gas Drilling Operations. Environ Health Perspect [doi.org/10.1289/ehp.1408207; online 18 July 2014]

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NIEHS-funded summer student wins President's award

By Joe Balintfy

May Wang, a 2013 NIEHS-funded Summer Research Experience Program (SREP) participant, received one of nine President's Environmental Youth Awards (PEYA) in an Aug. 12 White House ceremony. Wang's winning study, which was part of her NIEHS-funded research experience, tested how reusing activated charcoal can remove bisphenol A (BPA) from water.

"I was honored and inspired by the award ceremony," said Wang. "I was able to interact with the nation's leading environmental scientists and administrators, and my fellow awardees."

Since 1971, the President of the United States has joined with the U.S. Environmental Protection Agency (EPA) to recognize students from across the nation for contributions to environmental education and stewardship. Sixty students received PEYA awards, some individually, some as part of a group. Wang received the EPA Region 3 award. Region 3 includes Delaware, Maryland, Pennsylvania, Virginia, West Virginia, and Washington, D.C.

Filtering out BPA

Wang's paper, Remediation of bisphenol A contaminants in water by reusing an activated charcoal filter, expanded on research begun by students who preceded her in the summer program. The study demonstrated that activated charcoal, used as a filter, is effective for removal of BPA and is active for a number of times after initial use, making it a potentially effective and economical method to filter BPA from wastewater. Using this method would improve overall ecological health and significantly decrease risk of exposure to BPA.

"May developed an assay for BPA and showed that [BPA] can be cleared using an activated charcoal filter," said her advisor, [Jeffrey Field, Ph.D.](#), at the University of Pennsylvania Perelman School of Medicine. "Her study was simple, but had highly convincing data and was very well written."



Wang, center, is shown with Field, left, and EPA Administrator Gina McCarthy, who presented the award at the White House. (Photo by Eric Vance, courtesy of EPA)



Linked video:
[Watch a video of senior White House and Administration officials honoring recipients of the PEYA. May Wang appears 8 minutes in and is recognized by EPA Administrator Gina McCarthy at minute 29:00. \(41:10\)](#)

Download Media Player: Flash (Launches in new window)

Student scientist

A student at Council Rock High School South in Pennsylvania, Wang worked with Field as part of the Teen Research and Education in Environmental Science ([TREES](#)) program at Perelman, funded by the 2013 NIEHS SREP [grant](#).

“TREES offered me a unique hands-on learning experience in environmental science that has expanded my understanding of the environment and has prepared me well to continue pursuing my passion for science,” said Wang, who would like to collaborate with treatment facilities to implement her research findings.

“It’s important that we attract young students and encourage them to pursue careers in science,” added Mike Humble, Ph.D., the NIEHS health scientist administrator who oversees the program at NIEHS. “This is a great example of how a summertime opportunity can foster interest in research.”

(Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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According to Humble, SREP provides research experiences for high school and college students and for science teachers during the summer academic break. (Photo courtesy of Steve McCaw)

Arizona internship program marks ninth year

By Eddy Ball

With funding from NIEHS and other sources, this summer the University of Arizona (UA) gave 45 more high school interns an intensive 7-week enrichment experience in science.

The UA Keep Engaging Youth in Science (KEYS) program brought students together with a network of mentors — faculty members, postdoctoral students, and graduate students — as they worked 40 hours per week in various UA laboratories.

Reaching out to promising students in Arizona high schools

The goal of the full-time immersion program is to attract the best and brightest to careers in science, technology, engineering, and mathematics (STEM) education and to improve diversity in STEM-related fields by reaching out to students from groups that have been historically underrepresented.



KEYS intern Samantha Andrade, left, discussed her project with Lau. Andrade worked directly with UA researcher [Terrence Monks, Ph.D.](#), who shares a lab space and collaborates closely with Lau. (Photo courtesy of Jeb Zirato and Biomedical Communications)

“The top KEYS programmatic goal is to give students real-world experiences that spark scientific curiosity and discovery, which can play a huge role in helping them decide whether to pursue science careers,” said Serrine Lau, Ph.D., director of the NIEHS-funded [Southwest Environmental Health Sciences Center at UA](#).

Like the NIH Summer Internship Program at NIEHS, KEYS concludes each year in late July with a poster session highlighting work on student projects. At the KEYS Research Showcase, students present their work to members of their scientific communities, their families, and the general public.

In addition to letting students enjoy hands-on experiences in UA laboratories, the program gives graduate students and postdoctoral fellows opportunities to develop their skills as mentors.



From left, UA biomedical engineer [Ted Trouard, Ph.D.](#), looked over imaging results with lab mentor, Ph.D. student [Mike Valdez](#), and [Brian Liu](#), a KEYS intern. (Photo courtesy of [Mark Thaler](#) and [Biomedical Communications](#))

High-visibility, top-level support, and an enviable track record

The program began in 2005 as pilot program serving three students in a handful of UA laboratories, including Lau’s. Since then, KEYS has gained broad support across the UA scientific community and among UA leadership. It is currently co-directed by staff at [BIO5 Institute](#) and [Marti Lindsey, Ph.D.](#), Outreach Director of the Southwest Environmental Health Sciences Center at the UA College of Pharmacy.

The [photo essay](#) created by the UA Office of Communications to showcase the program links KEYS to the university’s “[Never Settle](#)” strategic plan that emerged out of a year-long planning process set in motion by UA President [Ann Hart, Ph.D.](#) The story includes statements of support by [Kimberly Espy, Ph.D.](#), UA senior vice president for research, and [Rick Myers](#), chair of the Arizona Board of Regents.



KEYS intern [Mateo Mahoney](#) dressed for success as he presented his research on medical devices during the program’s research showcase. (Photo courtesy of [Chad Westover](#) and [Biomedical Communications](#))



KEYS intern [Melissa Bohlman](#), center, discussed her research project during the poster session, which drew the UA scientific community to celebrate the accomplishments of the program’s young scientists.

The program's metrics are impressive. According to Lau, since the program began in 2007, more than 90 UA faculty members have mentored 233 interns, with more than half of the students from backgrounds underrepresented in science careers. Among all KEYS alumni, 78 are still high school students and 155 have gone on to pursue higher education.

Eighty-seven KEYS interns have chosen to attend UA, with 18 set to enter the university as freshmen this fall. Dozens of KEYS interns have earned recognition as well as competitive scholarships, including the Wildcat Excellence Award, National Merit Scholarships, and Flinn Scholarships.

In addition to NIEHS funding, the program relies on financial support from foundation, corporate, and UA sponsorships, as well as contributions from individual donors. Program leaders are currently working to build an endowment to enhance student support under the program.

(This story was adapted from the UA News photo-essay "UA training the next generation of STEM specialists.")

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ONES awardee honored by Oregon State University

By Eddy Ball

Oregon State University (OSU) has selected NIEHS grantee Stacey Harper, Ph.D., as the recipient of its 2014 Savery Outstanding Young Faculty Award, according to an Aug. 8 announcement by Harper's department head Craig Marcus, Ph.D.

An assistant professor of nanotoxicology in the Department of Environmental and Molecular Toxicology (DEMT) in the College of Agricultural Sciences, and the School of Chemical, Biological, and Environmental Engineering, Harper received an Outstanding New Environmental Scientist award in 2011.

Harper takes an integrative approach to studying the environmental, health, and safety impacts of nanotechnology. Her lab uses rapid assays to determine the toxic potential of nanomaterials, investigative tools to evaluate nanomaterial physiochemical properties, and informatics to identify the specific features of a nanomaterial that govern its environmental behavior and biological interactions.

The [Savery award](#) is presented each year to a faculty member of the OSU College of Agricultural Sciences, to recognize outstanding contributions through teaching, research, international, or extended education activities. Harper will receive the award, which includes a \$1,000 cash prize and a plaque, at an Oct. 8 faculty and staff luncheon.

Former winners include two other DEMT faculty members, NIEHS grantee Staci Simonich, Ph.D., in 2006 and chemist Jennifer Field, Ph.D., in 1999.



Prior to joining the faculty at OSU, Harper was a postdoctoral fellow in the university's Environmental Health Sciences Center, where she was mentored by NIEHS grantee Robert Tanguay, Ph.D. (Photo courtesy of Stacey Harper)

In addition to her most recent honor, Harper was the 2012 recipient of the L.L. Stewart Faculty Scholars award, which recognizes an outstanding faculty member at OSU with \$30,000 in additional research support. In 2011-2012, she served as president of the Pacific Northwest Chapter of the Society of Toxicology.

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Postdoctoral fellows use proximity to help land local academic positions

By Jacqueline Powell

Finding a local academic position is a challenge many postdoctoral research fellows take on. Two NIEHS fellows pulled off that feat this year, and their stories shed light on preparation that can pave the way for success in the academic job market.

Hazel Nichols, Ph.D., The University of North Carolina at Chapel Hill

In January, after just two years as a research fellow under the mentorship of Dale Sandler, Ph.D., head of the NIEHS Epidemiology Branch, Nichols became an assistant professor at The University of North Carolina at Chapel Hill (UNC) Gillings School of Global Public Health. In Sandler's lab, Nichols' research focused on breast cancer prevention and long-term survival, using sound epidemiologic evidence to inform personal and medical decision-making.

To prepare for a faculty position, Nichols began seeking funding opportunities soon after she arrived at NIEHS and received an award from the Avon Foundation. Although the opportunity at UNC presented itself earlier than expected, Nichols' mentor was very encouraging.

Although Nichols became aware of the position through a nationally posted announcement, the accessibility of UNC provided the advantage of networking opportunities. When she applied, Nichols was attending a cancer outcomes breakfast series at UNC and had also attended occasional seminars.

The proximity of UNC to NIEHS may be more of an asset now, because it facilitates collaboration on research she began as a fellow. "While being geographically close isn't required to collaborate, it's certainly much easier with face-to-face meetings," Nichols said.

Nichols received concrete support at NIEHS throughout the interview process, including critique of her interview seminar by Epidemiology Branch colleagues. An academic job seminar given by Sharon Milgram, Ph.D., director of the NIH Office of Intramural Training and Education, was also extremely valuable. "[Milgram] was available by email for follow-ups, and was very helpful when it was time to interview and negotiate the offer," Nichols said.



"Open communication with your mentor is extremely important. [Sandler] was very supportive about my application for the position, her main concern being whether or not it was a good fit for me," Nichols said. (Photo courtesy of Steve McCaw)

Her tradition of success continues. Since arriving at UNC, Nichols has secured a position on a National Institutes of Health National Center for Advancing Translational Sciences KL2 Mentored Clinical Research Scholar Award, as well as pilot funds from the UNC Lineberger Comprehensive Cancer Center and the National Cancer Institute Cancer Research Network.

Sabrina Robertson, Ph.D., North Carolina State University

Sabrina Robertson, Ph.D., began her new career in July as an assistant professor in the Department of Molecular Biomedical Sciences at the North Carolina State University (NCSU) College of Veterinary Medicine. Prior to that, she was a researcher under the mentorship of Patricia Jensen, Ph.D., head of the NIEHS Developmental Neurobiology Group.

During the third year of her fellowship, Robertson requested and received Jensen's support for teaching a course at NCSU, enabling Robertson to acquire valuable experience. While the responsibilities of leading the course required her to lecture multiple times a week at NCSU, Robertson managed simultaneously to uphold her teaching responsibilities, continue her research, and publish an article in a high-impact journal.

Teaching at NCSU also helped Robertson foster local professional connections. Winning an end-of-semester teaching award helped prove her teaching skills, and stretching herself to meet all these responsibilities was important in shaping Robertson's career path.

Although it was over a year before she saw an opening for a full-time teaching position at NCSU, Robertson's applications and interviews for other positions provided her with materials to work from. That proved invaluable, as she had only one week from the time she saw the listing to submit her application materials.

Robertson now coordinates a large core course in molecular biology, with three teaching postdoctoral fellows, six teaching assistants, and one lab manager. The course enrolls undergraduate and graduate students and involves weekly lectures and labs. Robertson is also responsible for designing new courses and will write grants and publish scholarly articles on student learning practices in the years to come.

In addition to her teaching experience and strong research background, Robertson's multiple leadership activities at NIEHS may have helped set her apart from other applicants. She actively volunteered for the NIEHS Trainees Assembly, organizing the distinguished lecture brown bag lunch series, and served on the career fair organizational committee.

(Former NIEHS postdoctoral fellow Jacqueline Powell, Ph.D., is a writer and analyst with Education and Training Systems International.)

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"Having experience teaching a course is absolutely necessary to be competitive for a teaching position," Robertson said. (Photo courtesy of Steve McCaw)

Teachers give NIEHS an A-plus rating

By Kelly Lenox

In late July, eleven teachers from North Carolina schools completed the NIEHS Science, Teachers, and Research Summer Institute (STaRS) program (see [story](#)). A few weeks later, the teachers' evaluations have been compiled, and NIEHS earned excellent marks.

“STaRS represents the future of science education,” said one educator.

Each of the program elements garnered high praise. “The lab activities, the lectures, and the facility tours helped me to understand the complexity of the research and all the parts that make a good study,” said another.

The participants also valued the close collaboration with colleagues from across the state who shared similar goals and challenges.

NIEHS offered the program in collaboration with North Carolina New Schools, a public-private partnership. Ondrea Austin, STEM field coordinator for the organization, echoed the teachers' enthusiasm.

“Kudos to you and your team on this outstanding program, and our deep thanks once again for your exemplary leadership and partnership,” wrote Austin. She noted that over half the respondents called the experience “the best professional development of their careers.”

Participants gave a resounding cheer for the value of the program to them and their students. They also praised the hard work and long hours put in by NIEHS scientists and staff. “They were very welcoming and bent over backwards to provide us with an experience that we can take back to our classrooms,” said another participant.

“We all are very pleased that this first year of STaRS serving a group of participants was such a success. We met our expectations, and more importantly, we met those of the teachers,” said Ericka Reid, Ph.D., director of the NIEHS Office of Science Education and Diversity ([OSED](#)).

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Huei-Chen Lao of OSED will continue her key role, visiting classrooms to support the teachers as they share lessons inspired by what they learned on their summer vacations. (Photo courtesy of Steve McCaw)

Clinical Feature

NIEHS receives human research accreditation, launches training programs

By Robin Arnette

The NIEHS Office of Human Research Compliance (OHRC) Human Research Protection Program (HRPP) has the important job of protecting human participants in clinical research studies. Following its March accreditation from the governing body that oversees such programs, OHRC has implemented a seminar series, workshops, and working groups to provide continuous training and education for NIEHS staff about human research protection issues in clinical research.

Joan Pakenham, Ph.D., [OHRC](#) director and vice chair of the NIEHS Clinical Research Program Institutional Review Board (IRB), said that every three years the National Institutes of Health HRPP must apply for reaccreditation from the Association for the Accreditation of Human Research Protection Programs Inc. ([AAHRPP](#)).

Pakenham explained why it is so important to receive and maintain accreditation. “Accreditation from AAHRPP means that the institute follows rigorous standards for ethics, quality, and protections for human research,” she said. “We want volunteers who participate in NIEHS-sponsored research studies to know that we are working hard to protect them.”



Pakenham and her staff will schedule additional OHRC training programs throughout the accreditation period. (Photo courtesy of Steve McCaw)

Seminar series and workshops

In one of several efforts to fulfill continuing requirements, OHRC initiated a seminar series, “Practical Applications and Regulatory Considerations in Human Research.” The inaugural lecture was presented July 28 by Stephanie Studenski, M.D., who spoke on “The Baltimore Longitudinal Study of Aging: America’s longest running scientific study on human aging” (see [text box](#)).

The seminar series continued Aug. 15 with “Certificates of Confidentiality: Protecting Human Subject Research Data in Law and Practice,” presented by Leslie Wolf, J.D., Professor of Law at Georgia State University College of Law. Wolf explained that Certificates of Confidentiality are an important tool in protecting the privacy of research study participants and clarified the specific situations in which they are employed. To find out more, please see the NIH Certificates of Confidentiality [kiosk](#).

The next lecture in the series Oct. 15 will feature Michele Evans, M.D., National Institute on Aging (NIA) deputy scientific director and chief of the Laboratory of Epidemiology and Population Sciences Health Disparities Research Section. Evans will discuss “Healthy Aging in Neighborhoods of Diversity Across the Life Span Protocol,” a method for involving community-engaged research in the inner city of Baltimore, Maryland.

OHRC will also sponsor an IRB training workshop Sept. 4 at Sigma Xi in Research Triangle Park, North Carolina. The workshop, “IRB Review of Public Health Emergency Research: An Introduction,” is open to IRB members, clinical researchers, and clinical staff. Advanced [registration](#) is required.

Research reveals keys to aging well

While growing older is a part of life, some may not look forward to the fragility and cognitive decline that often accompanies aging. However, the research performed by geriatrician and rheumatologist Studenski suggests it’s possible to lead active and productive lives regardless of age.

Studenski is chief of the NIA Longitudinal Studies Section, and director of the Baltimore Longitudinal Study of Aging ([BLSA](#)), America’s longest running scientific study on human aging.

She and NIA Scientific Director Luigi Ferrucci, M.D., Ph.D., believe that cognition and mobility are the major things people need to age well. In fact, some of her current work examines an emerging thought in the field — the brain has a processing speed that determines how fast it can do things. The phenomenon may impact conditions such as dementia and Parkinson’s disease.

“You can look at indicators of this processing speed in young adults and examine how they evolve over time,” Studenski said. “I think processing speed impacts a lot of things, not just cognition, but movement and mood.”

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Science Notebook

NTP symposium examines indoor air pollution from biomass fuels

By Audrey Pinto and Eddy Ball

An interdisciplinary team of speakers surveyed the state of the science, policy, and future directions of research on adverse health effects of indoor solid fuel combustion, during a symposium Aug. 18 at NIEHS, moderated by NTP toxicologist [Cynthia Rider, Ph.D.](#)

Organized and hosted by NTP, the meeting attracted NIEHS grantees and scientists from the U.S. Environmental Protection Agency (EPA) and RTI International, as well as researchers funded by nonprofits and other agencies. Attendees are dedicated to improving the health of the estimated 3 billion people worldwide who burn biomass, such as wood, dried dung, peat, and other organic solids, in indoor cookstoves and fire pits, to cook their traditional food and heat their homes (see [fact sheet](#)).

As NIEHS and NTP Director Linda Birnbaum, Ph.D., said in her welcome and introduction, some 4 million people die prematurely each year from cancer and other diseases directly caused or worsened by exposure to indoor air pollution from biomass combustion. She described a complex exposure, involving mixtures that are not completely understood, and improved cookstove interventions that are not always effective or adopted by the people who need them.

According to Birnbaum, the problem directly relates to priority themes and goals of the NIEHS strategic plan and crosses several disciplines with implications for human rights, gender inequities, community engagement, and health disparities. “I think it’s especially an issue for women and children,” she said.

A real commitment, but much more is needed

Birnbaum was followed by Claudia Thompson, Ph.D., who described the impressive NIEHS grants portfolio on cookstoves and the NIEHS-WHO Collaborating Centre for Environmental Health Sciences emphasis on translation and capacity building in developing countries.

Elaborating on themes introduced by Birnbaum and Thompson, keynote speaker [Sumi Mehta, Ph.D.](#), director of programs for the 1,000-partner Global Alliance for Clean Cookstoves (GACC), described the group’s goal of supplying 100 million households with improved cookstoves by 2020 through what she called an integrated market approach.



Rider is project leader on the NTP PAC mixtures assessment study. Along with moderating the meeting and introducing speakers, she also reported on her group’s research. (Photo courtesy of Steve McCaw)



“Some of the [indoor] exposures make Beijing look clean,” Birnbaum said as she described the conditions in homes using firepits and makeshift stoves. (Photo courtesy of Steve McCaw)

Mehta pointed to some of the gaps in knowledge and performance that must be addressed, including the discrepancy between lab performance and field performance of new technology, as well as the importance of demonstrating that adoption of improved cookstoves can actually save lives. There remain important co-exposures, such as kerosene lighting and second-hand smoke, that need to be better understood.



Just as Birnbaum had in her remarks, Thompson pointed to the major funding provided by NIEHS to advance the NIH cookstove initiative. Her slide underscored the importance of global health in the NIEHS mission and strategic plan. (Photo courtesy of Steve McCaw)



Linked video:

[Watch a video of Mehta's comments about on the efforts of GACC to address the health effects of indoor air pollution. \(03:09\)](#)

(Launches in new window)

Download Media Player: Flash [↗](#)

Analyzing exposures

Work on better understanding exposures is well underway at EPA and NTP. [David DeMarini, Ph.D.](#), a genetic toxicologist with EPA, addressed “Mutagenicity Emission Factors of Cookstoves: Health Effects Implications Relative to Other Combustion Emissions,” as part of the morning session’s four EPA cookstove research presentations.

Regarding test data from natural draft (ND) and forced draft (FD) cookstoves with analysis of fine particulate matter (PM 2.5) for 32 polycyclic aromatic hydrocarbons, DeMarini said, “It does reinforce how bad all of the stoves are compared to propane.” He found that even FD, the safest and most efficient of the biomass stoves, is far from safe. “FD has a mutagen factor based on fuel energy similar to that of diesel, a known carcinogen,” he said.

“Even the best stoves are not safe without adequate ventilation,” DeMarini cautioned. He said the ND, or rocket, stove is no better than the three-stone fire pit in use in many households, noting that vastly less pollution is produced by liquid and gas stoves, which perform as much as 100 times better than stoves burning solid fuels.

In her afternoon talk, Rider explained that the NTP polycyclic aromatic compound (PAC) mixtures assessment [program](#) is contributing data toward developing a methodology for risk assessment of whole mixtures of PACs. “We want to assess emission samples from cookstoves and woodstoves collected by field researchers,” she said. “This unique approach creates an unprecedented opportunity for multidisciplinary cooperation to better understand and inform communities of potential health risks of PAC exposure.”

Lessons from the field

[Tony Ward, Ph.D.](#), an environmental health scientist at the University of Montana, discussed a successful [outreach project](#) in Libby, Montana. “[People] were breathing in high levels of



According to Mehta, the key to success is a multifaceted, market-based approach that addresses the challenges associated with traditional cookstoves, encourages innovation, and establishes a global market. (Photo courtesy of Steve McCaw)

particulate matter outdoors and inside their homes during the winter months,” explained Ward. A unique community-based partnership provided Libby residents with EPA-certified wood-burning stoves, significantly reducing pollution levels.

[Marc Jeuland, Ph.D.](#), an environmental economist at Duke University, and [Pam Jagger, Ph.D.](#), an applied political economist at The University of North Carolina at Chapel Hill, working in India and Malawi, respectively, explained the challenges of getting rural villagers to adopt improved cookstoves (see [text box](#)). Both researchers suggested that continuous community involvement and marketing campaigns might boost improved cookstove use.



Early in the meeting, North Carolina State University engineering professor Andrew Grieshop, Ph.D., described the poor results of an intervention study in India. “It didn’t work for people, so they didn’t use it,” he said. “This was not meeting their family’s needs.” (Photo courtesy of Steve McCaw)



As part of the four-member EPA contingent, research engineer Jim Jetter, center, described his group’s work in the agency’s state-of-the-art cookstove testing facility in Research Triangle Park, North Carolina. (Photo courtesy of Steve McCaw)



Following the meeting’s 15 presentations was a panel discussion on moving environmental research forward that included, from left, Jeuland, Mehta, Grieshop, Jetter, and EPA research biologist Janice Dye, D.V.M., Ph.D. (Photo courtesy of Steve McCaw)



NIEHS Health Science Administrator Kimberly Gray, Ph.D., served as moderator for the panel discussion and helped the panelists as they articulated the meeting’s take-home messages. (Photo courtesy of Steve McCaw)

Next generation of researchers

The final speakers, [Eleanne van Vliet](#), a Dr.P.H. student at Columbia University, and Lucia Pruneda-Alvarez, a Ph.D. student at the Universidad Autonoma de San Luis Potosi, shared preliminary findings on the health effects of biomass fuels and PACs among Ghanian and Mexican women and children.

In concluding the meeting, a common theme emerged — there are tremendous challenges ahead that will require multidisciplinary, innovative approaches to improve the health of affected populations.

(Audrey Pinto, Ph.D., is technical editor for the journal *Environmental Health Perspectives*.)

Challenges and barriers

The complexity of human nature is never more apparent than when public health attention turns to behavior change, particularly age-old behaviors centered around food and cooking.

In the afternoon sessions, the scientists discussed some of the barriers to successful adoption of improved technologies among many low-income and rural communities.

- Perception — people in rural communities are not aware of the health benefits of reducing indoor and outdoor air pollution. As Jagger observed, “The doctors in Malawi have no idea that air pollution is a major cause of disease in their country.”
- Infrastructure — supply and demand depends on whether rural communities have access to stoves and a reliable source of electricity.
- Socioeconomic status — many people in rural communities are very poor, so the cost of improved cookstoves is prohibitive, especially if it involves structural changes to houses to provide effective chimneys.

Take-home messages

Improved cookstove adoption is positively related to perceptions of health and time savings.

Peer pressure and social norms as perceived through the actions of neighbors may be important.

Continuous involvement of heads of households must be maintained.

A combination of supply-chain improvements and carefully designed social marketing and promotion campaigns, and possibly incentives, to reduce the up-front cost of stoves may improve adoption and use of improved cookstoves in some areas.

As Jeuland concluded, “The key to real results and health benefits is reducing exposures. We must expand our scope to address what the communities want to do. In the end, we may be expecting a lot from a little stove.”

NAS agrees with NTP Report on Carcinogen listing decisions

By Robin Mackar

New reports from the National Academy of Sciences (NAS) find that the National Toxicology Program (NTP) listings of styrene and formaldehyde, in the 12th Report on Carcinogens (RoC) published in 2011, are accurate and appropriate.

The separate reports were developed after Congress directed the U.S. Department of Health and Human Services (HHS) to arrange for NAS to independently review the 12th RoC substance profiles of styrene and formaldehyde. NAS began work in September 2012.

The RoC is a science-based document that identifies cancer hazards. It is a cumulative report, prepared by NTP on behalf of the HHS Secretary.

“We appreciate the efforts of these two committees, convened by the NAS, and are very pleased with these supportive outcomes,” said NIEHS and NTP Director Linda Birnbaum, Ph.D.

Styrene

The NAS committee that reviewed the styrene assessment in the 12th RoC released its final [report](#) July 28.

After conducting both a peer review and an independent assessment of the styrene literature, the committee found that the overall conclusion reached by NTP in 2011, that styrene is reasonably anticipated to be a human carcinogen, is appropriate.

Styrene is an industrial chemical used to reinforce plastic and rubber products. The listing of styrene in the RoC was based on levels of styrene that workers are exposed to in an industrial setting.

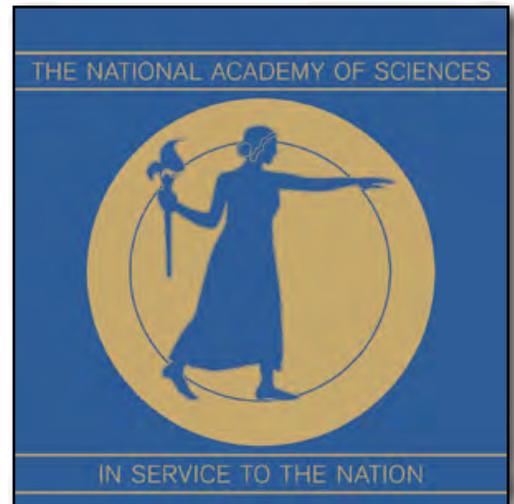
Formaldehyde

A separate NAS committee focused on formaldehyde. Their final [report](#), released Aug. 8, upheld the 12th RoC listing of formaldehyde.

The committee agreed with the NTP determination that evidence from studies in humans for nasopharyngeal cancer, sinonasal cancer, and myeloid leukemia was sufficient to support listing formaldehyde as a known human carcinogen.

As with the styrene report, the committee conducted both a peer review of the NTP formaldehyde assessment and an independent assessment of the literature.

Formaldehyde is a major industrial chemical used in building materials, chemical manufacturing, and other industries.



Ruth Lunn, Dr.P.H., director of the NTP Office of the Report on Carcinogens, along with her staff and NTP leadership, ensures a rigorous scientific review process for all NTP evaluations. (Photo courtesy of Steve McCaw)

Well-placed public trust

“The Report on Carcinogens has always had a high level of public trust,” said NTP associate director John Bucher, Ph.D. “These two reports from the National Academy of Sciences confirm that public trust and confidence in NTP’s rigorous scientific review process is well-placed.”

Several of the recommendations made by the committee have already been put in place, as NTP continues reviewing candidate substances for possible listing in the RoC.

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

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Symposium features talks on NIH core support and metabolomic profiling

By Eddy Ball

NIEHS health scientist administrator Daniel Shaughnessy, Ph.D., led a lineup of eight speakers at the Aug. 22 Metabolomics Symposium with a keynote address on “Metabolomics Studies and Environmental Health: Programs at NIEHS.” Shaughnessy discussed capacity building support through the NIH Common Fund [Metabolomics program](#), which has awarded grants to six regional cores across the U.S.

The event was held at RTI International in Research Triangle Park, North Carolina. It was co-sponsored by the NIH Eastern Regional Comprehensive Metabolomics Resource Core ([RCMRC](#)) at RTI, headed by Susan Sumner, Ph.D., and the Waters Corporation, which offers analytical system solutions, software, and services for scientists.

The symposium’s second keynote speaker, Robert Plumb, Ph.D., director of metabolomics profiling at Waters Corporation and visiting professor of analytical chemistry the Imperial College London faculty of medicine, explored “Metabolomics and Translational Medicine,” with a focus on the Medical Research Council (MRC)-National Institute for Health Research (NIHR) [National Phenome Center](#) in the U.K.

The symposium’s afternoon session featured talks by six scientists who are collaborating with the core at RTI to conduct ongoing metabolomic profiling studies.



Sumner spoke with characteristic enthusiasm about the success of the RTI core pilot projects. Hers was one of three cores funded by NIH in the first round of applications for fiscal year 2012. An additional three cores were funded for fiscal year 2013. (Photo courtesy of Steve McCaw)



Linked video:
[Watch a video of the launch of the National Phenome Centre in June 2013 \(06:53\)](#)

(Launches in new window)

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Advancing preventive and personalized medicine

In her opening remarks, [Sumner](#) outlined the potential of what she described as the metatype — the individual metabolic profile of an organism’s functional state or phenotype. Metatype is based on the results of advanced metabolomic assays of the low molecular weight complements of cells, tissues, and biological fluids.

“Metabotype can correlate with gender, race, age, ethnicity, drug use, chemical exposures, stress, weight status, health status, blood pressure, disease state, and nutritional intake,” Sumner said. With quality metabolomic data, this profiling offers the potential for diagnosing disease in its preclinical stages, monitoring personalized treatment to achieve optimal outcomes, identifying environmental exposures, and streamlined drug discovery and clinical trials.

NIH support

As [Shaughnessy](#) told the audience, next-generation metabolomics technologies, such as chromatography-mass spectrometry and nuclear magnetic resonance spectroscopy, have identified more than 20,000 known metabolites, to date. As technology advances, researchers may have the potential to double the number of unique chemical entities, including exogenous metabolites from environmental chemicals, toxins, dietary factors, and drugs.

Because of its tremendous potential across the spectrum of biomedical research, metabolomics has become a high priority for trans-NIH support. The program is dedicated to increasing national capacity for metabolomics studies nationwide with regional metabolomic core programs, training the next generation of researchers, synthesizing reference standards, promoting technology development, and enabling data sharing and international collaborations.

The program goal, Shaughnessy said, is to develop technologies to enable, better, faster, and cheaper approaches for identifying metabolites for public health research.

Applications in biomedical research and translation

[Plumb](#), whose role in the Department of Surgery and Cancer at Imperial says much about his dedication to translational medicine, dazzled symposium attendees with his vision of the future of personalized medicine, based on metabolomic profiling and phenome analysis. He began with the 100-100 concept — the goal of achieving 100 years of longevity at 100 percent of optimal health — and offered glimpses into how it can become a reality.

Among many technical developments to come, Plumb pointed to the potential for high-throughput imaging of drug and metabolite distribution in tissues, to monitor individual patient response to treatment. He described an operating theater of the future, where surgeons can access real-time tissue profiling as they perform operations and screen the metabolomic environment for more effective diagnosis than was ever possible with needle biopsy.

The afternoon presentations demonstrated the promise of metabolomics in a number of disease and therapeutic areas, showing how support from the NIH Common Fund Metabolomics program is advancing biomedical research, with implications for prevention, early-stage interventions, and treatment of cancer and other noncommunicable diseases (see [text box](#)).



As Shaughnessy reviewed the history of the NIH Metabolomics program, he said he was impressed by how much progress has been made. “Now we’re seeing a lot more data-based research,” he said. (Photo courtesy of Steve McCaw)



Plumb described new technology that promises to revolutionize clinical medicine, including the intelligent knife (iKnife) rapid evaporative ionization mass spectrometry for tissue profiling; desorption electrospray ionization mass spectrometry for imaging drug distribution; and augmented reality solutions for complex data visualization. (Photo courtesy of Steve McCaw)



Along with his accomplishments as a computational biologist and visionary, Plumb proved an accomplished stand-up comedian, who flavored his talk generously with witty remarks, keeping the capacity audience engaged and, as often as not, laughing. (Photo courtesy of Steve McCaw)



NIEHS and NTP Director Linda Birnbaum, Ph.D., was one of several institute representatives attending the symposium. (Photo courtesy of Steve McCaw)



Former NIEHS senior fellow Belinsky, center in glasses, took advantage of RTI core pilot funding to expand research funded by the National Cancer Institute using metabolomic profiling. (Photo courtesy of Steve McCaw)

Advancing translational research using metabolomics approaches

For free, and on a fee-for-service basis, researchers can access a range of metabolomic resources at RTI and the other five cores at the University of Michigan, University of Kentucky, University of Florida, Mayo Clinic, and University of California, Davis.

Like its sister cores, the RTI RCMRC also offers [supplementary grants](#) for one-year pilot projects to enhance metabolomics research and translation. The program targets investigators new to the metabolomics field, the development of new teams and partnerships, and high-risk and high-impact research. Recipients included six presenters at the symposium:

- Melinda Beck, Ph.D., The University of North Carolina at Chapel Hill (UNC) — “Metabolomic Profiling of Influenza A: 2009 Pandemic H1N1 in Lean and Obese Mice”
- Delisha Stewart, Ph.D., RTI International — “Metabolomics in Cancer Research”
- Steven Belinsky, Ph.D., Lovelace Respiratory Research Institute — “Metabolomics and Factors for Epigenetic Silencing of Lung Cancer Genes”
- Laura Cox, Ph.D., New York University Langone Medical Center — “Systemic Metabolic Effects of Early-life Microbiota Disruption”
- Snezana Petrovic, M.D., Ph.D., Wake Forest School of Medicine — “Correlation of Urine Metabolomics Profiles with eGFR, ACR, and Dietary Acid Load in Diabetic Patients From the African-American Diabetes Heart Study”
- David Collier, M.D., Ph.D., East Carolina University Brody School of Medicine — “Immersion Treatment for Adolescents With Morbid Obesity: What Does Metabolomics Tell Us About Treatment Failure?”

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A new approach to determine cancer risk of chemicals

By Sara Mishamandani

A new study by NIEHS-funded researchers at Boston University (BU) and the NIEHS National Toxicology Program (NTP) has shown that computational models of short-term exposure to a chemical can predict long-term cancer risk. The [study](#), led by computational biologist Stefano Monti, Ph.D., an associate professor at BU, is a step toward simpler and cheaper tests to screen chemicals for cancer risk.

The current gold standard for testing chemicals for cancer risk is a 2-year rodent bioassay, which can cost \$2 million to \$4 million per chemical to complete. As a result, less than 2 percent of the approximately 84,000 chemicals in commercial use have gone through standard carcinogenicity testing.

“Not enough attention is given to understanding chemicals before they are used by industry and released into the environment,” said [Monti](#). “This work has confirmed that it is possible to predict the long-term cancer risk by measuring the short-term effects.”

Understanding response to chemicals in the body

According to the authors, high-throughput genomic approaches have been applied to understand how cancer is initiated and progresses, to identify therapeutic targets and to discover biological markers of cancer. However, using these methods to study environmental causes of cancer has not received as much attention.

Researchers at BU teamed up with NTP molecular toxicologist [Scott Auerbach, Ph.D.](#), to build on current genomic analysis technologies, and develop affordable approaches to predict carcinogenicity and toxicity of thousands of environmental chemicals and mixtures. As part of this effort, BU Superfund Research Program (SRP) Center Director [David Sherr, Ph.D.](#), and Monti are developing a platform for predicting chemical toxicity and carcinogenicity.

Using a data set from the NTP [DrugMatrix](#) database, researchers compared gene expression responses to known carcinogens and noncarcinogens. From the data, they developed a predictive model to discriminate between the two. They also identified differentially expressed genes associated with cancer-causing chemicals and were able to zoom in on the potential mechanisms driving the initiation of cancer.

Moving forward

In the study, the researchers validated the model to predict carcinogenicity, using two large, rat-based gene datasets. They found that carcinogenicity predictions depend on the tissue exposed to the chemical of interest and confirmed and expanded on several previous studies implicating DNA damage, the aryl hydrocarbon receptor, and other pathways in the response to carcinogen exposure.

To their knowledge, the data collection they assembled represents the largest toxicogenomics resource analyzed to date. The collection allows the scientists to continue to evaluate issues related to variability in studies, differences due to tissue, exposure dose and length, sample size, and other factors, to achieve the maximum predictive accuracy using the model.

According to the authors, despite an overall decrease in incidence of and mortality from cancer, about 40 percent of Americans will be diagnosed with the disease in their lifetime, and around 20 percent will die of it. By further developing this platform for use, researchers will be able to better predict carcinogenicity and understand the biological process and pathways affected by exposure to different chemicals.



In September 2013, Monti visited NIEHS and described his latest work to develop a model for predicting toxicity and carcinogenicity. From left, NIEHS SRP Director Bill Suk, Ph.D.; NIEHS SRP Program Administrator Heather Henry, Ph.D.; Monti; and NTP Biomolecular Screening Branch (BSB) head Raymond Tice, Ph.D., discussed the implications of the findings for advancing predictive toxicology. (Photo courtesy of Heather Henry)



Auerbach is a member of the NIEHS Molecular Toxicology and Informatics Group within BSB. He is responsible for oversight of the NTP DrugMatrix database and ToxFX toxicogenomics analysis tool. (Photo courtesy of Steve McCaw)

Citation: [Gusenleitner D, Auerbach SS, Melia T, Gomez HF, Sherr DH, Monti S.](#) 2014. Genomic models of short-term exposure accurately predict long-term chemical carcinogenicity and identify putative mechanisms of action. *PLoS One* 9(7):e102579.

(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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Special seminar highlights global impact of air pollution

By Shannon Whirledge

A special seminar Aug. 1 at NIEHS featured Jinming Gao, M.D., Ph.D., professor of medicine and chief physician at Peking Union Medical College Hospital in Beijing. His talk, “Adverse Effect of Air Pollution on Asthma in China,” focused on airway health and disease, using the poor conditions in China as a model for the impact of environmental exposures on pollution-related respiratory disease.

The seminar was co-hosted by Acting Director of the NIEHS Clinical Research Program [Stavros Garantziotis, M.D.](#), and [Roy Pleasants, Pharm.D.](#), clinical pharmacist with the Pulmonary, Allergy, and Critical Care Medicine Division at Duke University. Grantziotis took advantage of Gao’s visit to North Carolina, as a featured speaker at the 2014 Carolina’s COPD (chronic obstructive pulmonary disease) [Symposium](#), to invite him to talk at NIEHS.

In his introduction, Garantziotis emphasized the relevance of Gao’s seminar for efforts to reduce air pollution as a strategy for disease prevention. “This presentation highlights the global effects of pollution on human health,” he said.

Lessons learned in China

Gao discussed a series of studies connecting air quality and pollution to lung health. He opened his seminar with several startling facts about air quality in China. According to a 2007 World Bank study, China is home to 16 of the 20 worst air-polluted cities. Also, more than 300,000 deaths due to pulmonary conditions and 20 million cases of respiratory disease are reported each year, costing more than 3 percent of China’s annual gross domestic product.

Likely contributing to the poor air quality is the nation’s reliance on coal. Coal supplies 70-75 percent of the energy needs of China, where 1.9 billion tons of coal are used each year.



Garantziotis, left, and Pleasants, right, were eager to co-sponsor a special seminar by Gao on such a relevant topic. Air pollution is one of the major environmental causes of disease. (Photo courtesy of Steve McCaw)

Because rates of asthma are on the rise, many research groups are striving to determine the mechanisms of asthma. As Gao explained, contributing factors include oxidative stress and damage; airway remodeling; inflammatory pathways and response; and genetic and environmental interactions. Risk modifiers, such as dietary factors, obesity, and secondhand smoke exposure, complicate the understanding of asthma risk, but also point to complementary interventions.

Beijing Olympics offered a unique research opportunity

Interestingly, the 2008 Summer Olympics in Beijing provided an opportunity to study the effects of intervention on lung health, by creating a window of improved air quality as a control. In the months leading up to and through the Olympics, the Chinese government implemented several air pollution reduction programs, including restrictions on automobile use, closing factories, and seeding clouds to induce rain fall.

These air quality improvement measures were associated with an attenuation of the systemic proinflammatory response and a reduction in the levels of circulating macroparticles. An NIEHS-funded study found that decreased air pollutant concentrations during the Olympics were associated with improved biological measurements related to inflammation and cardiovascular physiology in healthy young adults (see [story](#)).

There are now strategies being put in place in China to combat respiratory illness. In response to awareness efforts by scientists and the China Asthma Alliance, the Chinese government has spent more than \$10 billion to relocate dirty factories, assist the switch from coal to gas, and work to tighten rules on emissions. Patients with asthma have been advised to live at least 300 meters away from roadways to avoid exposure. The public receives a daily air quality forecast, as part of the weather report in Beijing. Furthermore, China now prohibits smoking in public places, and is working to inform the public of the harmful effects of smoking through outreach programs.

“We can learn valuable lessons about environmental health effects from other nations’ experiences,” Garantziotis stated. Gao highlighted a number of studies that provide compelling support for reducing air pollution, as a means to help prevent the development and worsening of respiratory illness.

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

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Gao's seminar generated considerable interest among researchers at NIEHS. From 1990 to 2000, asthma rates rose 64 percent in children in China. Understanding the contributing factors concerns scientists globally. (Photo courtesy of Steve McCaw)



Much of Gao's referenced work stemmed from studies in China. He indicated that the air quality in urban areas of China makes it "miserable for lung health." (Photo courtesy of Steve McCaw)

Putting data on the map – data science seminar highlights synthetic populations

By Gabriel Knudsen

Bill Wheaton, director of the Geospatial Science and Technology Program at [RTI International](#), presented a July 30 NIEHS Data Science Seminar Series lecture, discussing “Synthetic Populations: Concepts, Implementation, and Applications in Environmental Health Sciences.” The talk was hosted by Allen Dearry, Ph.D., director of the NIEHS Office of Scientific Information Management.

Wheaton uses computerized representations of households or individuals, known as synthetic populations, to build realistic models portraying population statistics, geography, and behavior. These models can support public health decisions, such as those necessary to control outbreaks of infectious diseases or mount response to natural disasters.

At RTI, Wheaton oversees the [Synthetic Microdata Household Viewer](#), developed in conjunction with the Models of Infectious Disease Agent Study at the National Institute of General Medical Sciences.

“In order to protect privacy, the interactive map doesn’t show actual households in their exact locations like Google Earth. Nonetheless, the data represent real households in reasonably accurate detail, enabling the map to show complex population distributions,” he said.

Computer models employing synthetic populations can be used to provide realistic information for public health decision-makers, by forecasting conditions, such as the aging of a population, in combination with an element of interest, such as obesity or heart disease.

Building models is difficult work even when laboratory data are available. Building models based on field data is doubly so. Disease modeling has often applied a measured value, such as infections in prior years, to current population data. Wheaton explained how using synthetic populations allows for more precise health forecasts. For example, information such as age, household size, school location, and other statistics were combined with geographical data to test the efficacy of closing schools for various numbers of days, in an exercise to model the spread of a virus.



As Dearry explained, “This is the first in a new series of data science seminars, that will introduce researchers to the challenge and advantages of sharing and reanalyzing datasets and moving along the continuum of data, to information, to knowledge.” (Photo courtesy of Michael Garske)



According to Wheaton, synthetic populations can help emergency managers planning evacuation routes, such as from the coast during a hurricane, or from the vicinity of a nuclear power plant, because they can map traffic loads, as well as the likely number of households without personal transportation. (Photo courtesy of Michael Garske)



Linked video:
[Stats in Action,” a U.S. Census Bureau video in which Wheaton discusses the use of American Community Survey data in synthetic population generation. \(04:39\)](#)
(Launches in new window)

Download Media Player:  Flash [⌵](#)

Finding the right data

Wheaton works with microdata, data that are not aggregated, but are read on an individual household level with identifying information removed. In contrast, most users of census data analyze aggregated values, typically in the form of a given number of households with a given characteristic, such as income and household size, within a given geographic area.

These microdata can then be used to model an entity or behavior. Most household and personal microdata that RTI uses come from the American Community Survey and the 2010 U.S. census.

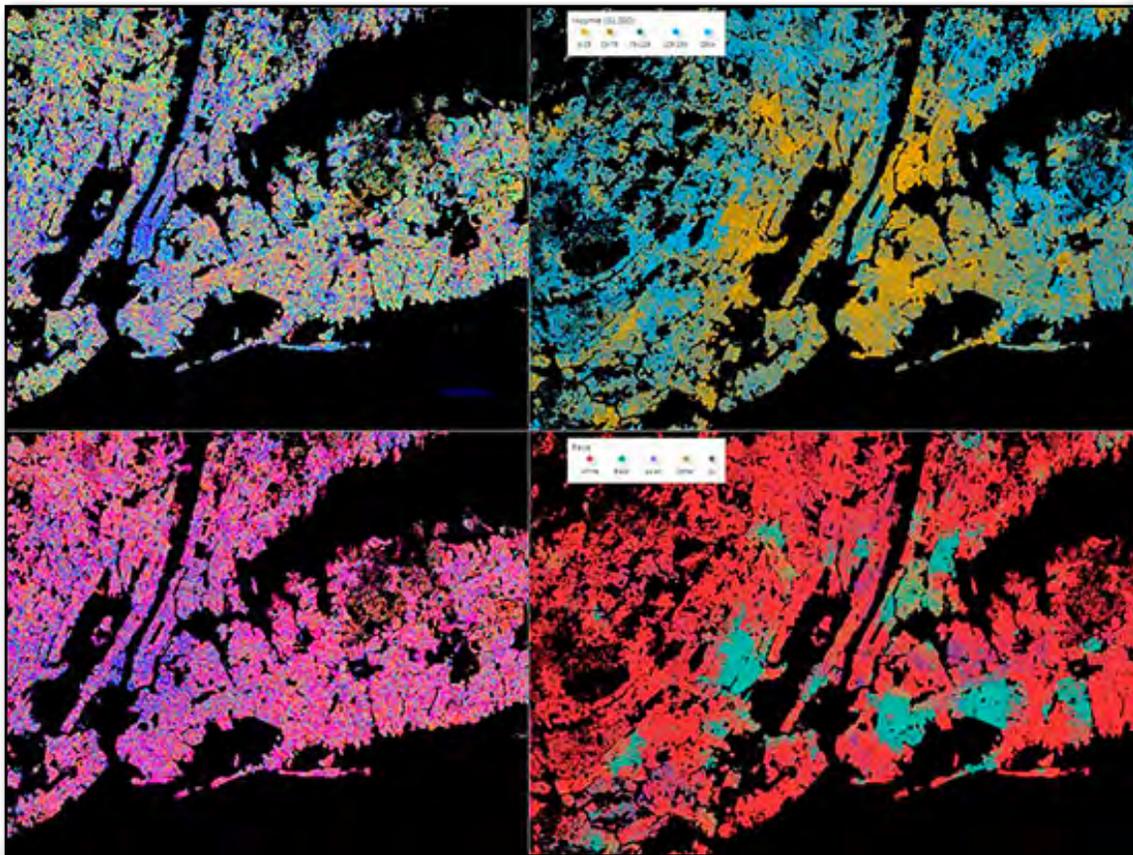
Mapping data on food insecurity

Another method for generating the microdata uses probabilities to interpolate individual data points from marginal data. National Health and Nutrition Examination Survey (NHANES) data are being used in this way to map food insecurity, by combining data on gender, race and ethnicity, income, and education levels, and mapping probabilities of food insecurity for different members of the synthetic population. Food insecurity means that people do not always know where they will get their next meal.

(Gabriel Knudsen, Ph.D., is an Intramural Research Training Award fellow in the National Cancer Institute Center for Cancer Research Laboratory of Toxicology and Toxicokinetics.)



Wheaton demonstrated the synthetic population viewer modeling the hypothetical spread of influenza. (Photo courtesy of Michael Garske)



“By representing each and every household as a point on the map, a wealth of complex patterns becomes apparent,” Wheaton said, describing the synthetic population viewer. (Image courtesy of RTI International, Inc.)

Webinars highlight European advances in exposome research

By Annah Wyss and Kelly Lenox

This summer, the NIEHS Exposome Webinar Series highlighted two groundbreaking European research efforts into the combined health effects of increasingly complex environmental exposures.

Denis Sarigiannis, Ph.D., of Aristotle University of Thessaloniki, Greece, presented on the Health and Environment-wide Associations Based on Large Population Surveys (HEALS) project July 14, and Martine Vrijheid, Ph.D., with the Centre for Research in Environmental Epidemiology in Barcelona, Spain, discussed the Human Early-Life Exposome (HELIX) project July 23. The projects explore the challenges and innovative solutions associated with leading-edge exposome research.



“The series will help in defining the concept of the exposome and determining the challenges we face in studying it,” said David Balshaw, Ph.D., lead of the NIEHS [Exposure Biology and the Exposome](#) program and host of the series.

HEALS: beyond the state of the art

The multifaceted [HEALS](#) project integrates genome-wide association studies with exposome-wide association studies, combining existing cohort data with a new longitudinal and nested case-control study, including twins and singletons, and their mothers and fathers. Detailed exposure data, gathered from exposure sensors, biomonitoring, and ambient monitoring, will be key to refining exposure models.

Another component of HEALS involves studying a full array of molecular pathways, with a focus on DNA methylation. By analyzing biomonitoring information and other biomolecular data obtained from samples provided by participants, the researchers aim to model lifetime exposures, from preconception through later life.

“The power of the project lies in large cohort data, brought together with a full array of analytical modeling and bioinformatics,” Sarigiannis said.

One goal of the project, according to Sarigiannis, is to move the state of the art forward. “It is important to be practical and focus on what can be of use to public health protection,” he said.

HELIX: early life exposures and childhood health

Like the HEALS project, [HELIX](#) aims to assess the associations between environmental hazards and health outcomes, with the added distinction of a focus on early life exposures and childhood health. “Pregnancy and childhood are vulnerable periods of rapid development,” Vrijheid said.

Using a network of cohorts from across Europe, the HELIX consortium pooled exposure and outcome data for nearly 32,000 mother-child pairs. And among a subcohort of 1,200 pairs, researchers collected and harmonized data on exposures, biomarkers, and phenotypes.

Finally, for a panel of 150 children and another panel of 150 pregnant women, HELIX collects long-term measurements, through use of repeated assays, exposure sensors, and diaries. “Participants carried exposure sensors in backpacks and smartphones on their waists,” said Vrijheid, describing some of the novel, individual-level exposure assessments scientists used.

The efficiencies of this tiered approach enable HELIX researchers to collect detailed information on numerous exposures, such as pesticides, phthalates, metals, water disinfection byproducts, and indoor air. Using data from geographic information systems, researchers integrate measures of air pollution, UV radiation, temperature, and the built environment into their research.

Vrijheid and colleagues hope that HELIX data will be used in future exposome research, while helping to build a more comprehensive approach to children’s environmental health.

(Annah Wyss, Ph.D., is an Intramural Research Training Award fellow with the NIEHS Genetics, Environment, and Respiratory Disease Group.)

The challenges of exposure biology research

By Joe Balintfy

The infographic below illustrates the complex challenges researchers face when studying how combined environmental influences affect health. It depicts environmental factors, such as pesticides, pollution, and tobacco, which play a role in adverse health outcomes such as allergies, obesity, and heart disease, which are on the rise worldwide. The silhouette of a woman running conveys that exercise can change some health outcomes. The runner is wearing a personal sensor — one of the many technologies being developed to measure a person’s exposure to environmental pollutants.

“Measuring all those exposures and health outcomes is an enormous task,” said Balshaw. “A big part of this field is developing technology that can capture and measure the influencers and results.” In an effort to encourage development of personal air pollution and health sensors, the My Air, My Health Challenge was announced in 2012. The challenge led to the development of innovative products, including a wearable personal air pollution sensor (see related [story](#)).

The infographic, which supports the NIEHS [2012-2017 Strategic Plan](#) goal of advancing understanding of the exposome, has been shared via social media, reaching more than 700 people on Facebook, and roughly 2,500 on Twitter. Produced in partnership with the NIEHS Office of Communications and Public Liaison, the graphic has been posted on the NIEHS website and is currently part of a National Institutes of Health (NIH) exhibit in Building 1 on the NIH campus in Bethesda, Maryland.

(Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

Exposure Biology Research is challenged with detecting and measuring combined environmental exposures and figuring out how the human body responds.

Environmental Exposures include what we breathe, eat and drink, or absorb through our skin. Each person experiences these combinations of exposures every day and can have different reactions. For example, environmental exposures can lead to changes in DNA, adversely affect health, or cause diseases.



 A key part of **Exposure Biology Research** is developing technology — such as cell and smart phones, monitors, sensors, cameras, computers, and software — to measure exposures and biological responses.

My Air My Health

The **My Air, My Health Challenge** was one example where researchers created a personal, portable, and wearable air pollution sensor.

To learn more about **Exposure Biology Research** and NIEHS-funded programs, go to <http://www.niehs.nih.gov/exposurebiology>

Peer reviewers support NTP listing recommendation for TCE

By Robin Mackar

A panel of experts spent Aug. 12 peer reviewing an NTP draft monograph on trichloroethylene (TCE), a chemical once prominently used as a degreaser for metal parts. The ten-member panel agreed with the NTP's preliminary decision to list TCE as a known human carcinogen in the [Report on Carcinogens](#) (RoC), based on sufficient evidence of carcinogenicity from studies in humans.

The vote came after presentations and discussions by NTP and the reviewers focusing on evidence for cancer at three sites — kidney, liver, and non-Hodgkin lymphoma. An NTP-sponsored public [webinar](#) earlier in the year also helped provide information about TCE that was used in the evaluation of the human cancer studies.

An overview of the 30 major human studies used in the TCE evaluation was presented by Jennifer Ratcliffe, Ph.D., of ILS, a contractor supporting NTP. Ratcliffe went over the study selection and quality evaluation. Stanley Atwood, Ph.D., also of ILS, presented information about the metabolism and genetic effects of TCE.

Kidney cancer

Ruth Lunn, Dr.P.H., director of the [Office](#) of the Report on Carcinogens, talked the panel through the human studies used by NTP when evaluating kidney cancer outcomes and TCE. She said the studies provide credible evidence of a causal association between increased cancer risk and exposure to TCE.

“The findings are consistent across the studies,” Lunn said. “The highest risk for kidney cancer was found in studies where workers were exposed to higher levels of TCE.”

Overall, the lead reviewers for the kidney cancer section of the draft had favorable comments.

David Richardson, Ph.D., an epidemiologist from the University of North Carolina at Chapel Hill, and others called for more descriptive language to better characterize kidney and other cancers.

The mechanistic studies for kidney cancer were also presented. Reviewer George Douglas, Ph.D., scientist emeritus at Health Canada, did not feel there was strong evidence to show a clear mechanism of action of mutagenicity. “I’d call the evidence presumptive and supporting, but not strong.”



At the head table, from right, are Lunn; panel chair David Eastmond; Mary Wolfe, Ph.D., NTP deputy division director for policy; and NIEHS and NTP Director Linda Birnbaum, Ph.D. (Photo courtesy of Steve McCaw)



Panel members Douglas, left, and Marie-Elise Parent, Ph.D., provide valuable input on the TCE monograph. (Photo courtesy of Steve McCaw)

John Bucher, Ph.D., NTP associate director reminded reviewers that epidemiological studies alone are enough to provide sufficient evidence of human carcinogenicity. He said identification of a mechanism is not required.

Non-Hodgkin lymphoma (NHL)

Ratcliffe presented human epidemiological studies on NHL, which is cancer that affects the body's white blood cells. The mechanistic studies were also presented. The panel agreed with NTP's assessment that there is limited evidence of a causal association between exposure to TCE and NHL from studies in humans.

Panel member Sarah Blossom, Ph.D., of Arkansas Children's Hospital Research Institute, commented on the studies focusing on immune effects of TCE that may be related to a mode of action for NHL. "We know it's immunotoxic, but we can't be sure it causes immune suppression."

The panel agreed with the preliminary evidence presented showing limited indication for a causal relationship between exposure to TCE and NHL from studies in humans.

Liver cancer

The human cancer and mechanistic studies were presented by Sanford Garner, Ph.D., also of ILS. Garner started out by saying that liver cancer is a relatively rare cancer and has a low survival rate.

"The data out there are basically inadequate to evaluate the relationship between liver cancer and exposure to TCE," Garner said. He pointed out that TCE-induced liver cancer is likely caused by complex mechanisms involving multiple pathways, including oxidative stress, genotoxicity, and more.

The panel agreed with NTP's preliminary conclusion that there is inadequate evidence of a causal relationship between exposure to TCE and liver cancer.

Overall listing recommendation and next steps

To wrap up the day, chair David Eastmond, Ph.D., of the University of California, Riverside, held a final vote on the preliminary listing decision for TCE.



Peer reviewer Blossom, provided expertise on the immunological aspects of TCE. (Photo courtesy of Steve McCaw)



Reviewer Lawrence Lash, Ph.D., left, and David Richardson, Ph.D., listened carefully to presentations, and offered comments throughout the meeting. (Photo courtesy of Steve McCaw)



In the audience was Edward Murray, Ph.D., acting director of the Division of Toxicology and Human Health Services at the Centers for Disease Control and Prevention Agency for Toxic Substances and Disease Registry. (Photo courtesy of Steve McCaw)

The panel agreed with NTP that TCE is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans. They went on to say that there are human epidemiological studies showing sufficient evidence for kidney cancer, as well as supporting evidence from toxicokinetic, toxicological, and mechanistic studies. They also agreed that there is limited evidence for TCE from studies of NHL in humans. Supporting evidence for the listing of TCE as a known human carcinogen is also found in animal studies.

NTP will carefully consider all comments made by the panel and the public, in revising the draft TCE monograph.

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

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This month in EHP

Environmental Health Perspectives (EHP) is pleased to announce its new impact factor of 7.03, and its inclusion, for the first time, in the category of toxicology. EHP is now the third-ranked journal in public, environmental, and occupational health, the fourth-ranked journal in toxicology, and the fifth-ranked journal in environmental sciences. The journal's all-time high impact factor was 7.26.

The September issue of EHP examines environmental influences on aging brains and scientists' questions about the health impacts of e-cigarettes, which are growing in popularity.

Time after Time: Environmental Influences on the Aging Brain

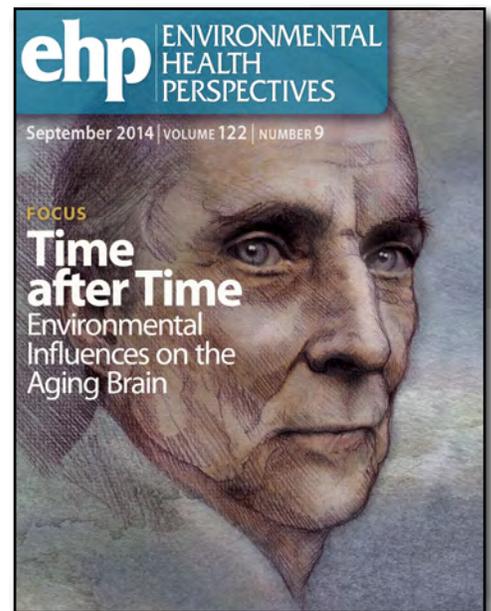
The population of Americans, aged 65 and older, is expected to double between 2010 and 2050, and by midcentury, the proportion of people over age 80 is projected to have quadrupled since 2000. So factors that affect this aging population are of increasing importance, particularly neurological diseases and disorders typically associated with advanced age. Investigators are studying the effects of present-day exposures and environmental influences, such as physical and mental exercise, as well as exposures that occurred much earlier in life, whose effects may only become apparent in old age.

Vaping and Health: What Do We Know About E-Cigarettes?

Are electronic cigarettes safer than conventional cigarettes, and should I switch? Physicians all over the country are encountering questions such as this from their patients, and they have no readily available answers. Out of nowhere, it seems, e-cigarettes — or electronic nicotine delivery systems, as they are formally known — are appearing at gas stations, convenience stores, and anywhere else cigarettes are sold. Advertisements boast that e-cigarettes offer health benefits by helping smokers quit, claiming that e-cigarette users only inhale harmless water vapor. The e-cigarette, it would seem, takes all the risk out of smoking. But many environmental health scientists aren't so sure.



<http://twitter.com/ehponline>



Featured research and related news articles this month include:

Early Postnatal Exposure to Ultrafine Particulate Matter Air Pollution: Persistent Ventriculomegaly, Neurochemical Disruption, and Glial Activation Preferentially in Male Mice — Echoes of Autism? Inhaled Ultrafine Particles and Brain Changes in Mice

Association of Global DNA Methylation and Global DNA Hydroxymethylation With Metals and Other Exposures in Human Blood DNA Samples — Hydroxymethylation and Metals: A Potential Epigenetic Marker for Effects of Toxic Exposures

Outdoor Particulate Matter Exposure and Lung Cancer: A Systematic Review and Meta-Analysis — Assessing the Health Threat of Outdoor Air: Lung Cancer Risk of Particulate Matter Exposure

Priorities for Breast Cancer Research: Taking Stock of Chemicals, Biomarkers, and Exposure Assessment Tools — Tools for Measuring Biomarkers: Taking Stock for the Next Phase of Breast Cancer Research

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Phillip Beachy to present upcoming distinguished lecture

By Raj Gosavi

Philip Beachy, Ph.D., a leader in the fields of adult stem cell biology and regenerative medicine, will present the next NIEHS Distinguished Lecture Series seminar Sept. 26. [Traci Hall, Ph.D.](#), acting head of the NIEHS Structural Biology Laboratory, will host his talk, “Hedgehog Signaling in Organ Homeostasis and Malignancy.”

[Beachy](#), a Howard Hughes Medical Institute Investigator, is an Ernest and Amelia Gallo Professor in the Stanford University School of Medicine, and a member of the Institute of Stem Cell Biology and Regenerative Medicine, also at Stanford. His research focuses on studying the role of Hedgehog family proteins in morphogenesis, or pattern formation, and in injury repair and regeneration, or pattern maintenance.

Beachy’s lab has discovered several important functions of Hedgehog proteins. His studies have furthered the understanding of prostate cancer, by showing how activation of Hedgehog can help distinguish metastatic prostate cancers from those that remain benign. In addition, recent studies have made critical insights into Hedgehog’s function in Down syndrome, as well as bladder repair in adult mammals.

“Dr. Beachy’s examination of the Hedgehog signaling pathway ranges from the identification of fruit fly and vertebrate hedgehog genes, to biochemical illumination of their functions in embryonic development and, recently, the revelation of mechanisms by which the Hedgehog pathway may induce or restrain cancer progression,” Hall said.



“Dr. Beachy’s work on Hedgehog proteins exemplifies a basic science-to-clinical study,” noted Hall. (Photo courtesy of Stanford University)

Work from his group has generated over 100 peer-reviewed publications, including several featured articles. Beachy was named a member of the National Academy of Sciences in 2002, and was selected as an American Academy of Arts and Sciences fellow in 2003. In 2011, he received the Keio Medical Science Prize for his work on Hedgehog as a key molecule in development. Beachy is also one of the founders of Fate Therapeutics, a biotech startup that uses stem cells for the development of innovative therapeutics.

(Raj Gosavi, Ph.D., is a research fellow in the NIEHS Structure and Function Research Group.)

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Extramural papers of the month

By Nancy Lamontagne

- [Perinatal DDT exposure linked to later risk of metabolic syndrome](#)
- [DDT alternative linked to transgenerational inheritance of disease](#)
- [Marine bacteria produce polybrominated diphenyl ethers](#)
- [Combined action of Srs2 and Exo1 enzymes helps maintain DNA](#)

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

Perinatal DDT exposure linked to later risk of metabolic syndrome

An NIEHS grantee and colleagues report that female offspring of pregnant mice exposed to the pesticide dichlorodiphenyltrichloroethane (DDT) have increased risk for obesity, diabetes, high cholesterol, and related conditions later in life. The study is one of the first to link DDT exposure with higher risk of developing metabolic syndrome as an adult.

Even though DDT was banned in the U.S. more than 40 years ago, it persists in the environment and is still used to control malaria in other parts of the world. People exposed to elevated levels of DDT and its metabolite dichlorodiphenyldichloroethylene (DDE) are more likely to have diabetes and insulin resistance. To find out if DDT impairs metabolism and energy expenditure, the researchers exposed mice from gestational day 11.5 to postnatal day 5 to doses of DDT comparable to exposures of people living in malaria-infested regions, and of pregnant mothers of U.S. adults who are now in their mid-50s.

The female offspring with DDT exposure showed reduced core body temperature, impaired cold tolerance, decreased energy expenditure, and a temporary early-life increase in body fat. In males, DDT exposure did not affect obesity or cholesterol levels and caused only a minor increase in glucose levels. The researchers gave the DDT-exposed offspring a high-fat diet for 12 weeks during adulthood. The female mice developed glucose intolerance; excess insulin levels and abnormal amounts of lipids circulating in the blood; and altered bile acid metabolism. The female mice fed the high-fat diet also showed further reductions in core temperature.

Based on their findings, the researchers say perinatal DDT exposure is likely a risk factor for reduced energy expenditure in people, even decades after DDT use has stopped.

Citation: [La Merrill M, Karey E, Moshier E, Lindtner C, La Frano MR, Newman JW, Buettner C. 2014. Perinatal exposure of mice to the pesticide DDT impairs energy expenditure and metabolism in adult female offspring. PLoS One 9\(7\):e103337.](#)

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DDT alternative linked to transgenerational inheritance of disease

A study supported in part by NIEHS showed that ancestral exposure to the pesticide methoxychlor may lead to greater susceptibility of future generations to adult onset kidney disease, ovarian disease, and obesity. The research indicates that exposure to methoxychlor, which was widely used in the 1970s as a DDT replacement, can promote epigenetic transgenerational inheritance of disease, in both males and females. Epigenetic transgenerational inheritance is a nongenetic form of inheritance in which epigenetic changes are passed down to generations that had no direct environmental exposure.

Methoxychlor was banned in the U.S. in 2003 because of its toxicity and ability to disrupt the endocrine system, but it is still used in many countries. The scientists exposed pregnant rats to methoxychlor, at a range typical of high environmental exposures. Their offspring showed increases in the incidence of kidney disease, ovary disease, and obesity spanning three generations. Analysis of the third-generation sperm epigenome of the methoxychlor lineage males identified differentially DNA methylated regions, termed epimutations. Additional experiments showed that transgenerational disease transmission occurred primarily through the maternal germline.

These new findings add to the researchers' earlier studies showing a variety of epigenetic effects for contaminants including DDT, plastics, pesticides, fungicides, dioxins, hydrocarbons, and bisphenol A.

Citation: [Manikkam M, Haque MM, Guerrero-Bosagna C, Nilsson EE, Skinner MK](#). 2014. Pesticide methoxychlor promotes the epigenetic transgenerational inheritance of adult-onset disease through the female germline. *PLoS One* 9(7):e102091.

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Marine bacteria produce polybrominated diphenyl ethers

Researchers discovered a widely distributed group of marine bacteria that produce polybrominated diphenyl ethers (PBDEs) nearly identical to toxic man-made fire retardants. The study is the first to isolate and identify bacteria that produce these endocrine-disrupting compounds, and the findings may help explain the PBDEs observed to bioaccumulate in the marine food chain.

PBDEs were widely used as flame retardants in furniture and other consumer products, until most were removed voluntarily from the market a decade ago. For some time, scientists have observed bioaccumulation of PBDEs in the fatty tissues of marine animals but believed the compounds came from man-made sources. More recently, mounting evidence pointed to microbial sources of marine PBDEs, but scientists did not know which organisms were producing the compounds.

In this study, researchers identified and isolated bacteria that produce PBDEs and discovered 10 genes involved in the synthesis of more than 15 bromine-containing polyaromatic compounds, including some PBDEs. They have since conducted DNA sequencing analyses that will let them probe the ocean for other biological sources of these chemicals and begin to assemble a complete picture of their human health risk.

Citation: [Agarwal V, El Gamal AA, Yamanaka K, Poth D, Kersten RD, Schorn M, Allen EE, Moore BS](#). 2014. Biosynthesis of polybrominated aromatic organic compounds by marine bacteria. *Nat Chem Biol* 10(8):640-647.

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Combined action of Srs2 and Exo1 enzymes helps maintain DNA

NIEHS grantees found that Srs2 and Exo1 enzymes act together to prevent and repair mistakes made during DNA replication in yeast cells. Many essential cellular functions are similar between yeast and people, so it is likely that similar DNA repair processes operate. These results have implications for understanding Aicardi-Goutieres syndrome, a rare disorder that affects the brain, immune system, and skin.

During DNA replication, ribonucleoside monophosphates, which are the building blocks of RNA, are inserted into DNA. During this process misinsertions can lead to lethal structural alterations. Among the study's key findings was that Srs2 helps open the DNA structure so that Exo1 can cleave out any misplaced ribonucleoside monophosphates. Both enzymes were previously known to play a role in DNA replication and repair, but the scientists say this is the first evidence of their role in preventing and correcting mutations derived from ribonucleoside monophosphates.

The research team also found that the Srs2-Exo1 cell repair mechanism prevents mutations from accelerating in yeast already deficient in the enzyme RNase H2. The enzyme serves as the primary removal mechanism for ribonucleoside monophosphate during cell growth. Yeast deficient in both RNase H2 and Srs2 had a tenfold increase in the number of mutations, chromosome losses, and chromosome breakages. These results may help scientists better understand Aicardi-Goutieres syndrome, which stems from inactivation of the human RNase H2 enzyme complex.

Citation: Potenski CJ, Niu H, Sung P, Klein HL. 2014. Avoidance of ribonucleotide-induced mutations by RNase H2 and Srs2-Exo1 mechanisms. Nature 511(7508):251-254.

(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 Monica Frazier, John House, Kelly Lenox, Mallikarjuna Metukuri, Jordan St. Charles

- [NTP research finds low doses of inorganic arsenic cause lung tumors in male mice](#)
- [Maternal smoking linked to altered DNA in newborns](#)
- [Control of histone expression by phosphorylation of an mRNA processing protein](#)
- [Retinoic acid-related orphan receptors involved in novel signaling pathway](#)
- [Crystal structure of an important inositol phosphate kinase](#)

NTP research finds low doses of inorganic arsenic cause lung tumors in male mice

Researchers at NIEHS found that exposure to low doses of inorganic arsenic caused lung tumors in male mice. While arsenic exposures in the parts-per-million range were known to be carcinogenic, this research is the first evidence of such effect in the parts-per-billion (ppb) range. This concentration is cause for concern, because it mimics the level of arsenic millions of people are exposed to in their drinking water.

Using a whole-life mouse model, the researchers exposed mice to inorganic arsenic in their drinking water beginning three weeks before breeding, continuing through pregnancy and lactation, up through two years of age. Arsenic concentrations were 50 ppb, 500 ppb, and 5,000 ppb. More than half of the male offspring in the study developed significant increases in benign and malignant lung tumors at the two lower doses. The researchers noted that the lowest dose, 50 ppb, is only five times the maximum contaminant level set by the U.S. Environmental Protection Agency for drinking water.

These findings provide further support for earlier studies that note differing responses to arsenic in male versus female mice. The authors call for further work to assess the carcinogenic potential of inorganic arsenic in mice at human relevant doses. **(KL)**

Citation: [Waalkes MP, Qu W, Tokar EJ, Kissling GE, Dixon D.](#) 2014. Lung tumors in mice induced by “whole-life” inorganic arsenic exposure at human-relevant doses. *Arch Toxicol* 88(8):1619-1629. [[Story](#)]

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Maternal smoking linked to altered DNA in newborns

New research demonstrates that mothers who choose to smoke during pregnancy may actually alter their offspring’s epigenetic DNA profile. In one of the largest studies of its kind, to date, researchers from NIEHS and Norway have identified specific modified regions in the genomes of children from mothers who smoked during pregnancy compared with children of nonsmokers.

Investigators interrogated DNA methylation marks in blood collected from 889 newborns, with 287 newborns from mothers with self-reported smoking during the first trimester, and discovered altered methylation patterns in or near 110 genes. Strikingly, some of these genes are related to the ability to quit smoking, nicotine addiction, and fetal development.

This work adds to the growing body of evidence that maternal exposure and behavior can modify DNA during fetal development. Additional research is needed to understand both the persistence of these DNA alterations, as children mature, and if these DNA alterations are related to established adverse outcomes in children born to maternal smokers, or are simply markers of exposure. It also establishes the critical importance of additional research needed to understand how maternal exposures during pregnancy affect the developing child. **(JH)**

Citation: [Markunas CA, Xu Z, Harlid S, Wade PA, Lie RT, Taylor JA, Wilcox AJ.](#) 2014. Identification of DNA methylation changes in newborns related to maternal smoking during pregnancy. *Environ Health Perspect*; doi:10.1289/ehp.1307892 [Online 6 June 2014].

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Control of histone expression by phosphorylation of an mRNA processing protein

By examining phosphorylation of the stem-loop-binding protein (SLBP), which has a role in processing histone mRNA, NIEHS scientists and their collaborators have detailed a new method of histone expression regulation. This research is important, because levels of histones, proteins that package DNA within the nucleus, have to be controlled carefully throughout the cell cycle. While DNA is replicating, histone levels must increase to package the new DNA, and following DNA replication, the presence of extra histones can be toxic to the cell.

Initially using biochemical assays, the scientists found that phosphorylation of SLBP at two different regions, increases the ability of the protein to bind to RNA. Interestingly, phosphorylation at the C-terminal tail of the protein increases RNA binding without actually coming into contact with the RNA. Further crystallography and nuclear magnetic resonance experiments showed that phosphorylation of this region caused a conformational change that increases RNA-binding abilities of the whole protein. The authors suggest this change occurs because phosphorylation increases the negative charges at the C-terminal tail that interact with and attract positive charges elsewhere in the protein. The process results in a more compact form that has a higher affinity for RNA. **(JS)**

Citation: Zhang J, Tan D, DeRose EF, Perera L, Dominski Z, Marzluff WF, Tong L, Hall TM. 2014. Molecular mechanisms for the regulation of histone mRNA stem-loop-binding protein by phosphorylation. Proc Natl Acad Sci U S A 111(29):E2937-E2946.

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Retinoic acid-related orphan receptors involved in novel signaling pathway

Scientists at NIEHS and their colleagues at several institutions revealed that two vitamin D derivatives function as antagonists of retinoic acid-related orphan receptor (ROR)alpha and RORgamma-mediated transactivation. This novel finding, along with the discovery that RORalpha and RORgamma are expressed in a wide range of immune and skin cells, sheds light on the complex regulation of the body's largest organ, the skin.

RORalpha and RORgamma are members of a larger family of nuclear receptors, which regulate many physiological processes, by binding to ligands that produce a transcriptional response. The main ligands for these receptors include cholesterol and its derivatives, making the ROR receptors attractive targets for therapeutics.

Prior to this work, researchers were unaware that secosteroids, such as the vitamin D derivatives 20(OH)D3 and 20,23(OH)2D3, could act as endogenous antagonists of RORalpha and RORgamma. Using functional assays and molecular modeling techniques, the authors found that both molecules act as antagonists of ROR-mediated activation of transcriptional responses.

In addition, they determined that both RORalpha and RORgamma is expressed in a variety of skin cells, including, but not limited to, sweat glands, hair follicles, sebaceous glands, and melanoma skin cell lines. Furthermore, these vitamin D3 derivatives act on immune cells expressing RORalpha or RORgamma. By acting as antagonists of RORalpha and RORgamma, these derivatives open new possibilities to modulate local (skin) or systemic (immune system) bioregulatory activities and the development of therapeutic strategies. **(MF)**

Citation: Slominski AT, Kim TK, Takeda Y, Janjetovic Z, Brozyna AA, Skobowiat C, Wang J, Postlethwaite A, Li W, Tuckey RC, Jetten AM. 2014. RORalpha and RORgamma are expressed in human skin and serve as receptors for endogenously produced noncalcemic 20-hydroxy- and 20,23-dihydroxyvitamin D. FASEB J 28(7):2775-2789.

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Crystal structure of an important inositol phosphate kinase

Researchers from NIEHS have identified the crystal structure of a bifunctional inositol phosphate kinase (IPK), IP6K/IP3K, from *E. histolytica* (*EhIP6KA*), and extrapolated the findings to human IP6K. The IP6Ks play pivotal roles in metabolic homeostasis and regulate interferon transcription in response to viral infection.

The present study, published in Nature Communications, described the crystal structure of the *EhIP6KA*. The authors also used site-directed mutagenesis of the human IP6K2 to describe two structural elements, an alpha-helical pair and a rare two-turn helix, that together form a substrate-binding pocket with an open clamshell geometry. InsP6 has substantial contacts with both structural elements whereas InsP3 rotates 55 degrees closer to the alpha-helices, thus providing insight into the molecular determinants of both IP3Ks and IP6Ks.

The discovery of IP6K structure illuminates the molecular basis for its kinase activities and offers a description of how separate IP3 and IP6Ks evolved from a bi-functional ancestor. The study provides important information for the rational design of inhibitors that might selectively target PDKG catalytic motif containing kinases, both for research tools and therapeutic applications. **(MM)**

Citation: [Wang H](#), [DeRose EF](#), [London RE](#), [Shears SB](#). 2014. IP6K structure and the molecular determinants of catalytic specificity in an inositol phosphate kinase family. Nat Commun 5:4178.

(Monica Frazier, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Mechanisms of Mutation Group. John House, Ph.D., is an IRTA fellow in the NIEHS Genetic Epidemiology Group. Mallikarjuna Metukuri, Ph.D., is a research fellow in the NIEHS Metabolism, Genes, and Environment Group. Jordan St. Charles, Ph.D., is a fellow in the NIEHS DNA Replication Fidelity Group.)

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Inside the Institute

Birnbaum visits First Environments Early Learning Center

By Allison Ashley

NIEHS and NTP Director Linda Birnbaum, Ph.D., toured the First Environments Early Learning Center July 30. Executive director Beth Lake, science teacher Jane Allen, and parents Erin Hines and Sania Tong Argao led Birnbaum around the cheerful building and grounds, discussing the sustainable operations and creative use of resources. NIEHS and the daycare share a commitment to [children's health and wellbeing](#) and [environmental sustainability](#).

Located on the U.S. Environmental Protection Agency (EPA) campus in Research Triangle Park, North Carolina, the nonprofit serves the families of federal employees and contractors at NIEHS and EPA.

Nature as teacher

Learning Center administrators believe that nature is an important teacher and they ensure students get plenty of instruction within the natural environment. Sustainability, outdoor safety, and stewardship of the soil, air, plants, and animals are just some the lessons children learn at the Center. "This is phenomenal. I didn't realize the [garden] space was so big," Birnbaum said.

The Seed to Table program imparts its lessons through a responsible hands-on-learning experience. The older children help plant the gardens and weed the beds, and the younger children water the plants using watering cans. Crops grown by the children are incorporated into school time meals. By exposing children to fresh tastes during the early developmental years, the center hopes to increase the chances that children will make healthier food choices as adults.

In an effort to further increase students' connection with nature, the outdoor environment is brought inside the classrooms in numerous ways, including large windows for natural lighting, small plants, and bug containers.



From left, Lake, Hines, Allen, and Birnbaum greet one another on Birnbaum's arrival. (Photo courtesy of Michael Garske)



Birnbaum, left, listens intently, as science teacher Allen discusses creatures of the garden. (Photo courtesy of Michael Garske)



Fresh vegetables grown at the center made for a delicious lunch. (Photo courtesy of Michael Garske)

After touring the center, Birnbaum read students a short story, “Knuffle Bunny: A Cautionary Tale,” written by Mo Willems. The adventurous tale is a 2005 Caldecott Honor book.

Birnbaum’s visit ended with the children singing songs, followed by a healthy lunch fresh from the garden planted, cared for, and harvested by the children and staff.

The center enjoys a five-star rating and a full enrollment largely due to its ability to keep highly-skilled staff long term, its emphasis on parent involvement, and its environmentally-conscious curriculum.

(Allison Ashley is a program specialist in the NIEHS Office of Communications and Public Liaison.)



Meeting with teachers and children was a rare opportunity for Birnbaum, pictured left with middle teacher and program director, Marsha Daniels. (Photo courtesy of Michael Garske)



Beth Lake noted the hard work of the center’s staff. (Photo courtesy of Michael Garske)



This cistern, decorated with the children’s artwork, collects rain water for reuse in the gardens. (Photo courtesy of Michael Garske)



With organic food growing near play areas, children can acquire a taste for healthy snacks, such as these banana peppers. (Photo courtesy of Michael Garske)



Birnbaum called herself a mystery grandma, as she read out loud to the children during story time. (Photo courtesy of Michael Garske)



The children sang some of their favorite songs for Birnbaum, right, and parent Hines. (Photo courtesy of Michael Garske)



Music and puppetry teacher Pamela Alberda, standing, led the children in a musical chorus, while Birnbaum, center, and Hines listened in. (Photo courtesy of Michael Garske)



Students learn how the garden feeds people and wildlife, and how the greenery provides safe haven for a variety of critters. (Photo courtesy of Michael Garske)

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2014 Feds Feed Families campaign helps knock out local hunger

By Ian Thomas

NIEHS employees concluded the 2014 Feds Feed Families campaign with its third and final collection Aug. 27, bringing in more than one ton — 2,534 pounds, to be exact — of nonperishable food and personal hygiene items. This marked the fifth year of NIEHS involvement in the program, in partnership with the Durham Rescue Mission and Food Bank of Central and Eastern North Carolina, who received the donations.

“This year’s theme was knock out hunger, and I’m really proud of the way our institute has stepped up to the plate, as it does every year, to honor that mission,” said Monya Brace, member of the NIEHS Office of Management and 2014 campaign co-coordinator.

Other co-coordinators included Bill Jirles, president of the American Federation of Government Employees Local 2923, and Sheila Withers, a representative of the Raleigh-Durham Area Chapter of Blacks In Government.

A national effort with roots at home

Since [Feds Feed Families](#) began in 2009, federal workers have donated and collected more than 24.1 million pounds of food and other nonperishable items to support families across the country. Food donated includes canned meats, meals, fruits, and vegetables, as well as cereal, peanut butter, juice, rice, pasta, and dried beans. NIEHS employees also brought in diapers, wipes, cleaning supplies, and hygiene products.

Still, despite the reach of the campaign throughout the nation, organizers insist that part of the program’s appeal is its emphasis on keeping donations at home.

“NIEHS is a leader in public health and gives so much to the U.S. research enterprise, but a lot of those efforts aren’t local,” said Jirles, a program analyst with the institute’s Office of Policy, Planning, and Evaluation. “That’s why it is such a special program, because when we donate thousands of pounds of food to the campaign, that equates to thousands of meals for families right here in the Triangle who might have otherwise gone hungry.”

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

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Pinkney Wilder III, left, and William Boyd, load the last of the NIEHS donations, as the 2014 campaign comes to a close. (Photo courtesy of Steve McCaw)



As she received a donation from Toni Ward, NIEHS and NTP Director Linda Birnbaum, Ph.D., center, enjoyed the gorgeous weather during the final curbside drop-off of 2014. (Photo courtesy of Steve McCaw)



National Institute of
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