

February 2015

NIEHS Spotlight



[White House announces climate change guide and toolkit](#)

Released Dec. 16, the materials will help health care providers, public health professionals, and policymakers understand and address climate issues.



[Big picture talk offers behind-the-scenes look at NTP in action](#)

The National Toxicology Program took center stage Jan. 20 as the latest seminar of the popular Big Picture, Small Talk series focused on the Elk River, West Virginia chemical spill.



[NTP provides lab and training to N.C. A&T University](#)

A student and a lab manager from N.C. A&T travel weekly to NIEHS to enhance their research using state-of-the-art facilities.



[Two tenure-track researchers join NIEHS](#)

In January, NIEHS officially welcomed two tenure-track scientists to lead new in-house laboratory research groups.



[Postdoc puts experience to work as medical affairs scientist](#)

In December 2014, Mallik Metukuri, Ph.D., became one of the latest NIEHS trainees to join the growing Ph.D. scientific workforce employed in the field of clinical trials.

Clinical Feature



[NIEHS will host IOM workshop on exposures and obesity March 2-3](#)

The meeting and webcast of the Institute of Medicine Roundtable will explore links between environmental exposures and obesity.

Science Notebook



[Exposome workshop uncovers the devil in the details](#)

Two days of breakout workgroups and animated discussion Jan. 14-15 highlighted the philosophical, practical, technical, and financial challenges that lie ahead.



[Distinguished lecture examines prenatal exposures in child development](#)

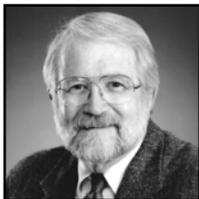
Frederica Perera, Ph.D., Dr.P.H., discussed her efforts to identify environmental risk factors and prevent adverse health impacts in children.



[NIEHS researchers determine new function for DNA repair protein](#)

In a Jan. 12 Nature Structural and Molecular Biology paper, Scott Williams, Ph.D., and his team unveil the first molecular structures and new functions for the Ctp1 protein.

NIEHS Spotlight



[Friends and colleagues remember former NIEHS geneticist de Serres](#)

The field of environmental mutagenesis lost one of its leading figures with the death Dec. 21, 2014 of Frederick de Serres, Ph.D., at age 85 in Chapel Hill, North Carolina.



[Former NTP scientific counselor Carney dies unexpectedly](#)

Friends and colleagues at NIEHS and NTP were shocked and saddened to learn of the sudden death Jan. 12 of toxicologist Edward Carney, Ph.D., at age 55.

Inside the Institute



[NIEHS tops \\$100,000 in donations for 2014 CFC](#)

NIEHS employees raised more than \$100,000 for charities both local and worldwide, through activities, sales, and payroll deductions.

Science Notebook



[Reproducibility advanced by new NTP systematic review handbook](#)

NTP released a handbook so anyone can adopt its systematic review process, helping advance reproducibility in environmental health sciences.



[NIEHS Superfund research training spurs collaboration with EPA](#)

The Penn SRP training featured research updates, new strategies for community engagement, and demonstration of mobile gas analyzer van.



[Behl gives Duke seminar on NTP flame retardant toxicity screening](#)

Mamta Behl, Ph.D., discussed NTP toxicity screening tests that compare new flame retardants to the compounds they are replacing.



[This month in EHP](#)

An eye-catching cover highlights the February Environmental Health Perspectives focus story on potential effects of marine plastic pollution.

Calendar of Upcoming Events

- **Feb. 2**, in Keystone 1003AB, 2:00 – 3:00 p.m. — Keystone Science Lecture Seminar Series presentation on “Identifying Cumulative Exposures to Chemicals in Pregnant Women: Nontargeted Screening of Environmental Chemicals,” by Tracey Woodruff, Ph.D.
- **Feb. 3**, in Rodbell Auditorium, 9:00 – 10:00 a.m. — Office of the Director seminar featuring Joel Tickner, Sc.D., discussing “Building a Research Agenda and Scientific Community of Practice for Chemical Alternatives Assessment”
- **Feb. 5**, in Rodbell Auditorium, 1:00 – 3:00 p.m. — NIEHS Cross-divisional Inflammation Faculty seminar and [webcast](#) on “Emerging Biomarkers of Inflammation”
- **Feb. 10**, in Rodbell Auditorium, 11:00 a.m. – noon — Distinguished Lecture Seminar Series featuring Myles Brown, M.D., on “Genetics and Epigenetics of Hormone Dependent Cancer”
- **Feb. 10 (offsite event)**, at North Carolina State University Centennial Campus, Toxicology Building, Room 2104, 4:00 – 5:00 p.m. — Environmental and Molecular Toxicology Program Seminar by Richard Kwok, Ph.D., discussing “The NIEHS GuLF STUDY: Investigating the Potential Human Health Effects of the BP/Deepwater Horizon Oil Spill”
- **Feb. 11**, webinar, 1:00 – 2:30 p.m. — NIEHS/EPA Children’s Center 2015 Webinar Series on “The Role of Environmental Exposure in Childhood Obesity, Metabolic Syndrome, and Neurobehavioral Abnormalities,” [register](#)
- **Feb. 13 (offsite event)**, at Duke University, Environment Hall Field Auditorium, noon – 1:30 p.m. — Integrated Toxicology and Environmental Health Program Spring 2015 Seminar Series featuring Jerry Yakel, Ph.D., on the “Role of Nicotinic ACh Receptors in Hippocampal Excitability and Plasticity”
- **Feb. 16-19 (offsite event)**, in Houston, Texas — 2015 Gulf of Mexico Oil Spill and Ecosystem Science Conference, [register](#) by Feb. 6
- **Feb. 18-19**, in Rodbell Auditorium, 8:30 a.m. – 5:00 p.m. — National Advisory Environmental Health Sciences Council meeting, [webcast](#)
- **Feb. 20**, in Rodbell BC, 1:00 – 2:00 p.m. — Keystone Science Lecture Seminar Series with Jack Gilbert, Ph.D., addressing “Adventures in our Microbial World”
- **Feb. 25 (offsite event)**, at Duke University, 103 Bryan Research Building, noon – 1:00 p.m. — Regulatory Networks in Health and Disease Seminar Series with John Cidlowski, Ph.D., presenting “The heartbreak of studying glucocorticoid receptors at the NIH”
- **Mar 2-3**, in Rodbell Auditorium, 8:30 a.m. – 6:00 p.m. — Institute of Medicine Roundtable on “The Interplay Between Environmental Exposures and Obesity,” [register](#) to attend in person or via webcast
- View More Events: [NIEHS Public Calendar](#)

Extramural Research

[Extramural papers of the month](#)

- [Causes of hospitalization during heat waves](#)
- [Phthalate exposure linked to lower IQ](#)
- [Cadmium exposure linked to shorter telomeres](#)
- [U.S.-wide study links autism with prenatal exposure to fine particulate air pollution](#)

Intramural Research

[Intramural papers of the month](#)

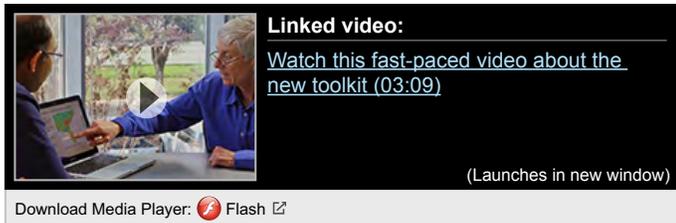
- [NTP uses new tool for analysis of rodent mammary gland development](#)
- [Discontinuation of tamoxifen may blunt benefit of breast cancer prevention](#)
- [Estrogen directs uterine biology in cell-type manner](#)
- [New class of PUF protein family as revealed via its structure](#)
- [NIEHS researchers explore new mechanisms of arsenic toxicity](#)

NIEHS Spotlight

White House announces climate change guide and toolkit

By Audrey Pinto

As part of the President's Climate Action Plan, the administration released Dec. 16 a voluntary guide, [Primary Protection: Enhancing Health Care Resilience for a Changing Climate](#).



Coauthored by NIEHS Senior Advisor for Public Health [John Balbus, M.D.](#), the guide offers health care system managers, health care providers, public health professionals, and policymakers a set of approaches to enhancing the resilience of health care systems to climate change impacts. The guide and an accompanying online toolkit comprise the core of the U.S. Department of Health and Human Services (HHS) Sustainable and Climate Resilient Health Care Facilities Initiative, which also involves a public-private partnership for the development and dissemination of the information.

“This guide and toolkit represent an important step forward in the [Climate Action Plan](#) and the administration's commitment to strengthening the resilience of the U.S. health care system, protecting vulnerable populations, and building a safer, healthier, and more prosperous nation,” Balbus said. “They outline best practices for mitigating the effects of extreme weather events on people and communities and ways to strengthen U.S. health care infrastructure and delivery settings, such as hospitals and emergency clinics.”

Building awareness and steps to resilience

In recent years, the number of weather-related events that adversely affect human populations and public health has been on the rise. Scientists warn that, in the future, communities will face more frequent and severe storms, causing costly damage and challenging an already fragile health care system to maintain continuity of care. Despite the warnings, most Americans are unaware of or confused by the [health risks associated with global warming](#).



Balbus is the lead on NIEHS and trans-National Institutes of Health initiatives in the area of climate change and human health. (Photo courtesy of Steve McCaw)



Health care system executives and public health leaders gathered with HHS Secretary Sylvia Burwell and other senior administration officials Dec. 16 in the Treaty Room of the Eisenhower Executive Office Building for a roundtable discussion of health care system sustainability and resilience. (Photo courtesy of John Balbus)

Using a five-element framework, the toolkit and guide are designed to help health care providers build a strong infrastructure to ensure continued quality of health care before, during, and after extreme weather events. Elements of the framework address identifying system and community vulnerabilities, understanding the relevant codes and regulations for buildings and infrastructure, enhancing the resilience of buildings and infrastructure, protecting critical assets including health care facility staff and their families, and using ecosystem services to buffer climate impacts.

As Balbus pointed out, “When health care systems invest in resilience and sustainability, they assure that their communities have uninterrupted access to quality health care services in the setting of weather and climate disasters and at the same time help reduce the costs and environmental impacts of their day-to-day operations.”

Balbus worked with coauthor [Robin Guenther](#) to create the new guide, which received substantial stakeholder input, including a workshop with environmental justice and public health representatives and formal peer review. Guenther is an architect honored for her work in designing sustainable health care facilities and a senior advisor to Health Care Without Harm, a collaborative campaign for environmentally responsible health care.

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

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Big picture talk offers behind-the-scenes look at NTP in action

By Eddy Ball

The National Toxicology Program (NTP) took center stage Jan. 20 with the latest seminar of the popular Big Picture, Small Talk series, which was designed as a forum for presenting scientific topics in a friendly way for a general audience.

A capacity audience of NIEHS employees turned out to hear NTP molecular toxicologist [Scott Auerbach, Ph.D.](#), discuss his group’s ongoing [research project](#) to characterize the chemicals involved in the Jan. 9, 2014 spill into the Elk River in Charleston, West Virginia.

The accidental discharge occurred at a Freedom Industries storage facility 1.5 miles upstream from the intake for the West Virginia American Water treatment plant that provides drinking water for some 300,000 people across nine counties.



Linked video:
[Watch the Jan. 10, 2014 PBS NewsHour report on the spill \(02:31\)](#)

(Launches in new window)

Download Media Player:  Flash [↗](#)

Big Picture, Small Talk – a winning combination

Understandably, many in the audience were Auerbach’s colleagues at NTP, but employees from other divisions at NIEHS who weren’t as familiar with the program also turned out for an informal, but informative look at how NTP relates to real-world concerns about chemical exposures. Among them were biologist Negin Martin, Ph.D., and librarian Erin Knight.

“I didn’t know that much about NTP,” Martin said, “so, it was nice to learn what kind of an event triggers an NTP study and what they do.”

“I love this series,” Knight added, “I think it brings together a great group of people who wouldn’t normally get together for a seminar. There’s always a good discussion of a topic that is very interesting.”

“This is sort of an everyone project,” Auerbach said of the motivation for featuring it as a Big Picture, Small Talk topic. He pointed to the number of people at NIEHS and NTP involved in some aspect of the study, including scientists, contract and acquisitions specialists, administrative support personnel, and communications staff. A [nomination](#) by the U.S. Centers for Disease Control and Prevention (CDC) prompted the study.

It was also a high-profile effort, of obvious interest to employees and the general public, and a natural fit for NTP with its mission of coordinating toxicological testing for the federal government. “NTP has fully transparent testing procedures and does not have a conflict of interest,” he added, pointing to the program’s reputation for objective and thorough toxicology testing, with regular reports for the public.

Mystery chemicals

One of the first questions to emerge as people learned of the 10,000-gallon spill of contaminated water, with its distinctive licorice smell, involved the little known chemical 4-methylcyclohexanemethanol (MCHM) that is used to wash coal. As Auerbach explained, the primary sources of information about MCHM were limited [studies](#) by the manufacturer, Eastman Chemical Company.

Auerbach outlined the logic behind a 6-step process that involved the coordination of 11 groups of scientists and support staff, as well as a [battery of screening and testing protocols](#). The study began with the CDC nomination in July 2014, as researchers set out to identify all of the chemicals involved in the spill. The team focused on addressing three major areas of uncertainties — development of unborn children, long-term effects, and reliability of safe level estimates.

Preliminary results from the toxicology studies suggest the chemical exposure that occurred due to the spill is unlikely to produce long-lasting health effects. Because MCHM has a noticeable odor at very low concentrations, Auerbach said the exposure was probably quite limited.

But although people may not have consumed or used much of the water, Auerbach added, local public health officials also didn’t think to save samples of treated water from the tap, to help researchers better calculate dose and more accurately conduct risk assessments. “If you have any trouble like this,” he urged the audience, “collect the water.”

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“Really, all of you have touched it at some level,” Auerbach said of the research project. “Thank you for contributing.” (Photo courtesy of Steve McCaw)



Auerbach’s presentation was so well attended that latecomers were hard pressed to find available seating. NTP toxicologist Cynthia Rider, Ph.D. filled in as host. (Photo courtesy of Steve McCaw)



Among attendees from outside NTP at the talk was Scott Redman, of the NIEHS Financial Management Branch in the Office of Management. (Photo courtesy of Steve McCaw)

NTP provides lab and training to N.C. A&T University

By Celso Furtado

The National Toxicology Program (NTP) [Pathology Support Group](#) is providing state-of-the-art laboratory facilities and training to student researchers from the North Carolina Agricultural and Technical State University (N.C. A&T). Participants are learning the latest techniques for collecting, processing, sectioning, and staining biological samples.

“They had been doing everything by hand and storing samples in the freezer, which reduced the quality of the samples for analysis,” said Natasha Clayton, supervisor of the laboratory and coordinator for the project.

Weekly trips to the NIEHS lab

Each Friday, Sherrell Pettiford, a senior majoring in laboratory animal science, and Dawn Conklin, lab manager at the university, travel from Greensboro to Research Triangle Park, where they work with Clayton to learn manual and automated pathology procedures, including histology, clinical chemistry, and hematology.

This training opportunity grew out of a project between Darlene Dixon, D.V.M., Ph.D., head of the NTP [Molecular Pathogenesis Group](#), and Jenora Waterman, Ph.D., associate professor of functional genomics in the N.C. A&T’s [Department of Animal Sciences](#).

The project requires histopathology tissue evaluation, and Clayton and Ronald Herbert, D.V.M., Ph.D., head of the NTP Pathology Support Group, quickly recognized the value of training Pettiford and Conklin in the preparation of samples using NIEHS laboratory processing equipment, which is not available at the university.

Pettiford’s study includes 20 pigs, half of which were housed indoors and half outdoors. She is researching the respiratory effects of the housing environment by examining samples of the trachea, which is the windpipe that connects the pharynx and larynx to the lungs.

A visible difference

“Friday after Friday, Ms. Pettiford and Ms. Conklin are able to compare the results of manual and automated processing as they go through each step and see the difference,” said Clayton. “At the same time, we train them to understand what they are doing and why they are doing it. We try to show the outcome, the end product, or the quality of the slide that is so important for diagnostic procedures.”



Pettiford’s project, “Swine Production Style Influences Histological Morphology, Proteomic Dynamics, and Superoxide Dismutase Expression of the Tracheal Epithelium,” was selected as one of three winners at the N.C. A&T Fall 2014 Undergraduate Research symposium. (Photo courtesy of Steve McCaw)



Conklin, who is a research technician at the university, will use her training on procedures and equipment to teach other students in the program. (Photo courtesy of Steve McCaw)

“I would like to thank NIEHS and NTP for all their time, because this is a time consuming process,” said Conklin. “This really is a high quality process that we can take to our labs, to show the techniques to other researchers. It’s not going to stay with just this lab.”

Supporting N.C. A&T is in-line with the NIEHS strategic plan goal of inspiring a diverse and well-trained cadre of scientists in the field of environmental health sciences.

(Celso Furtado is a special volunteer with the Office of Communications and Public Liaison)



Clayton, left, demonstrates analysis of slides using the multiple viewer microscope in the Pathology Support Group Core Laboratory. (Photo courtesy of Steve McCaw)

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Two tenure-track researchers join NIEHS

By Kelly Lenox

With January announcements, Scientific Director Darryl Zeldin, M.D., officially welcomed two tenure-track scientists to NIEHS to lead new in-house laboratory research groups.

Shanshan Zhao, Ph.D., who moved from the Fred Hutchinson Cancer Center in Seattle, is head of the Applied Statistics Group. Guohong Cui, M.D., Ph.D., a former fellow at the National Institute on Alcohol Abuse and Alcoholism, leads the In Vivo Neurobiology Group.

The other side of methylation

While at Fred Hutchinson, Zhao helped cancer epidemiologists answer research questions using statistical methods. For example, one study involved evaluating how methylation patterns differ in men who had recurrence of prostate cancer versus those who did not.

Although her first academic focus was mathematics, Zhao knew early on that pure mathematics would not be her field. “I wanted my work to be related to life, so I switched to statistics,” she explained. “Public health interested me, and it needs contributions from statisticians.”

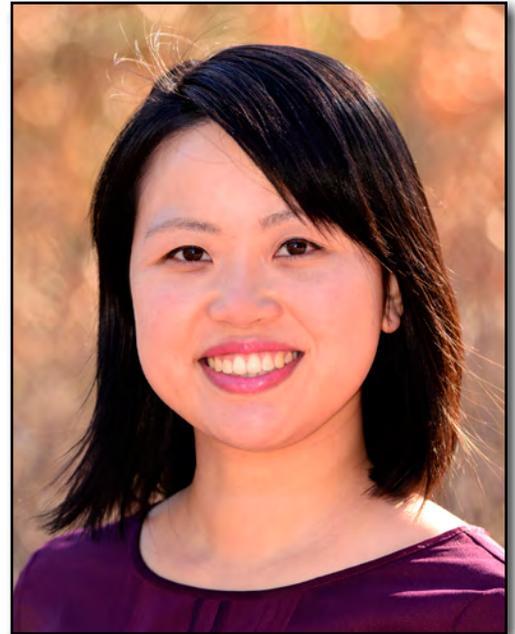
Both the collaborative environment she saw at NIEHS and the focus on environmental factors drew Zhao to the institute. “I had worked on methylation related to cancer, but here, scientists focus on the other side of methylation — studying how environmental factors connect to epigenetic methylation patterns.”

“I’m interested in causal pathway analysis,” Zhao said. “Methylation seems to be a mediator in this pathway, and there are rich data sets here that can help me to understand the pathway and develop statistical methods for this type of study.”

Focus on research

Cui’s research at NIEHS builds on his postgraduate work with brain circuits, specifically, studying the ways in which malfunctions in the brain’s basal ganglia lead to motor symptoms, such as those present in Parkinson’s disease. He was drawn to NIEHS both for its in-house research environment and the opportunity to continue exploring factors related to Parkinson’s.

Two questions in particular drive Cui’s research agenda at NIEHS. The first relates to how dopamine impacts the basal ganglia circuits to facilitate voluntary movement. “We have hypotheses, but so far, no direct evidence,” he said. The second is how the progressive loss of dopamine neurons might be slowed. “I have some ideas from my earlier research, and all the resources necessary to test them are available here at NIEHS.”



Zhao enjoys helping researchers convert their research concerns into mathematical questions. “I am like a bridge between the pure mathematics and the clinicians and biologists,” she said. (Photo courtesy of Steve McCaw)



Cui’s research aims include the study of the pathophysiology of Parkinson’s disease. (Photo courtesy of Steve McCaw)

Long before attending Beijing Medical University, Cui set his career sights on becoming a surgeon. While the course of his studies led him into research instead, his fundamental goal is unchanged. “I’m excited to be working for better treatments, and to help cure disease,” he said.

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Postdoc puts experience to work as medical affairs scientist

By Eddy Ball

In December 2014, Mallikarjuna Metukuri, Ph.D., became one of the latest NIEHS trainees to join the growing Ph.D. scientific workforce employed in the field of clinical trials.

Metukuri accepted a position away from the bench as a medical affairs scientist with the contract research organization (CRO) INC Research, which has more than 5,000 employees in 50 countries worldwide. His Raleigh, North Carolina-based employer is one of the leading companies in this rapidly growing field, which includes Triangle-based major players Quintiles, PRA Health Sciences, and PPD.

INC and other CROs support the Phase I, II, and III clinical trials with human subjects required by the U.S. Food and Drug Administration to ensure the safety and effectiveness of drugs developed by major pharmaceutical companies. Over the past decade, big pharma has been phasing out its in-house oversight of clinical trials, focusing its resources on drug discovery and development, and creating a profitable niche for CROs, which are experiencing double-digit growth each year.

“This is a great opportunity for me with a lot of growth potential,” Metukuri said of his move to INC. “I wanted to pursue my interest in translational research, and this position keeps me in touch with clinical trials going on all over the world involving drugs to treat disease across the spectrum, from psychological and neurological disorders to cancer, cardiovascular disease, and diabetes.”

From bench to desktop

During his postdoctoral training, Metukuri received extensive mentoring and instruction at the bench, honing his skills as a research scientist. After a 5-year stint at the University of Pittsburgh Medical Center, he joined the Metabolism, Genes, and Environment Group at NIEHS, headed by [Xiaoling Li, Ph.D.](#)

Careful attention to details and regulatory requirements

As a medical affairs scientist, Metukuri reviews and analyzes project-specific data and medical literature in a broad range of areas related to disease and drug development. He also manages committees related to the studies he oversees, data monitoring groups, data safety monitoring boards, and adjudication committees.

Because clinical trials are closely regulated by U.S. and foreign government agencies to protect the health and privacy of human subjects, it is important that research protocols are developed and approved prior to enrollment of subjects and followed carefully throughout the trials to endpoint adjudication. One of Metukuri’s regular duties involves identifying signs of potentially adverse events at any point in the clinical trial.

The medical affairs scientist is the primary interface for the trials under his or her oversight between the CRO and its pharmaceutical company clients, vendors, and other departments in the area of subject safety. He or she provides specialized knowledge for international guidance regarding the conduct of study-related committees.

From the beginning of his 3-year experience at NIEHS, Metukuri set his sights on developing the kind of diverse skill set that landed him the job at INC. He took advantage of career development workshops and other services coordinated and presented by NIEHS Office of Fellows' Career Development (OFCD) Director [Tammy Collins, Ph.D.](#)

In January 2012, he became a guest writer for the Environmental Factor newsletter, contributing papers-of-the-month summaries on the broad spectrum of outstanding research conducted by in-house labs at NIEHS and building an impressive portfolio of writing samples. He also worked as a special volunteer with the NIEHS Clinical Research Unit, where he got a close-up look at research involving human subjects.

“NIEHS offers exceptional opportunities for trainee career development,” Metukuri said. He credits encouragement and supportive mentoring from Li, Collins’ help with his resume and other aspects of career development, and extensive networking for the success of his job search.



Metukuri said his new job demands exceptional written and oral communication skills. “The OFCD’s career development activities organized by Tammy [Collins] and writing with the Efactor helped me a lot.” (Photo courtesy of Steve McCaw)



“When Mallik joined our group in 2011, he already knew where he wanted his career to go,” Li said. “He put in the extra effort necessary to conduct quality research and at the same time gain the other skills he needed to meet his career goals.” (Photo courtesy of Steve McCaw)



“Mallik started planning his career early on, and was able to strategically position himself to stand out to employers by developing the additional skills required of a medical affairs scientist,” said Collins. She is a former NIEHS trainee who knows from personal experience the importance of developing a diverse skill set. (Photo courtesy of Steve McCaw)

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Friends and colleagues remember former NIEHS geneticist de Serres

By Eddy Ball

The field of environmental mutagenesis lost one of its leading figures with the death Dec. 21, 2014 of Frederick de Serres, Ph.D., at age 85 in Chapel Hill, North Carolina. His death resulted from complications of the genetic condition alpha-1 anti-trypsin deficiency and a muscle-wasting disorder.

In the final phase of his life, de Serres combined the rigor of his intellect as a scientist with his personal health concerns, to become an expert on the disease that led to his death. He was a tireless advocate for the millions

of people worldwide, far too many of them never diagnosed, whose health is compromised by alpha-1 anti-trypsin deficiency (see [story](#)). The deficiency typically leads to severe chronic respiratory disease that is worsened by environmental exposures.

“Dr. de Serres was leaving NIEHS about the time I came here as a senior fellow,” said NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D. “But he was a pioneer in the field of environmental health science, and our paths crossed many times over the past 35 years. His death is clearly a real loss for the community.”

Among the many friends and colleagues who offered [online condolences](#) to the de Serres family were retired NTP toxicologists Jack Bishop, Ph.D., John (Jef) French, Ph.D., and Mike Shelby, Ph.D., commenting on de Serres’ important contributions to their careers and to the development of the field of environmental mutagenesis.

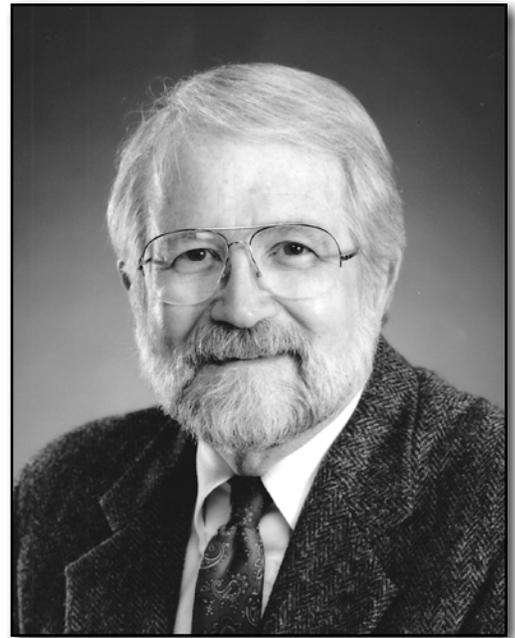
“For three decades Fred de Serres was the single biggest influence in my professional career,” wrote Shelby. “He hired me as technician in his laboratory, introduced me to scientific research, encouraged me to return to graduate school, served on my graduate committee, hired me at NIEHS, and involved me in multiple international scientific activities.”

A career devoted to studying gene-environment interactions

In several aspects, de Serres’ career paralleled the development of the field of environmental mutagenesis, beginning with positions as a biologist with the Oak Ridge National Laboratory, where he served as coordinator of the Environmental Mutagenesis Program 1969-1972, and the National Aeronautics and Space Administration 1964-1968.

de Serres was a resident of Chapel Hill and an adjunct professor at the University of North Carolina at Chapel Hill since 1972, when he accepted an appointment as the head of the NIEHS Laboratory of Environmental Mutagenesis. He served as NIEHS associate director for genetics for 10 years beginning in 1976. In addition to his genetics research, de Serres was the U.S. and NIEHS representative for a number of international projects related to mutagenesis and carcinogenesis.

In 1986, he joined Research Triangle Institute, predecessor of RTI International, as director of the Center for Life Sciences and Toxicology. Following his retirement in 1995, de Serres was a consultant before rejoining the institute as a guest researcher. A man of many interests, he was also president of a publishing company specializing in children’s literature (see [related story](#)), during his years of semi-retirement.



de Serres’ ties to the National Institutes of Health date back to 1952-1954, when he was a predoctoral fellow at the National Cancer Institute, prior to beginning his doctoral program at Yale. (Photo courtesy of Mark de Serres)

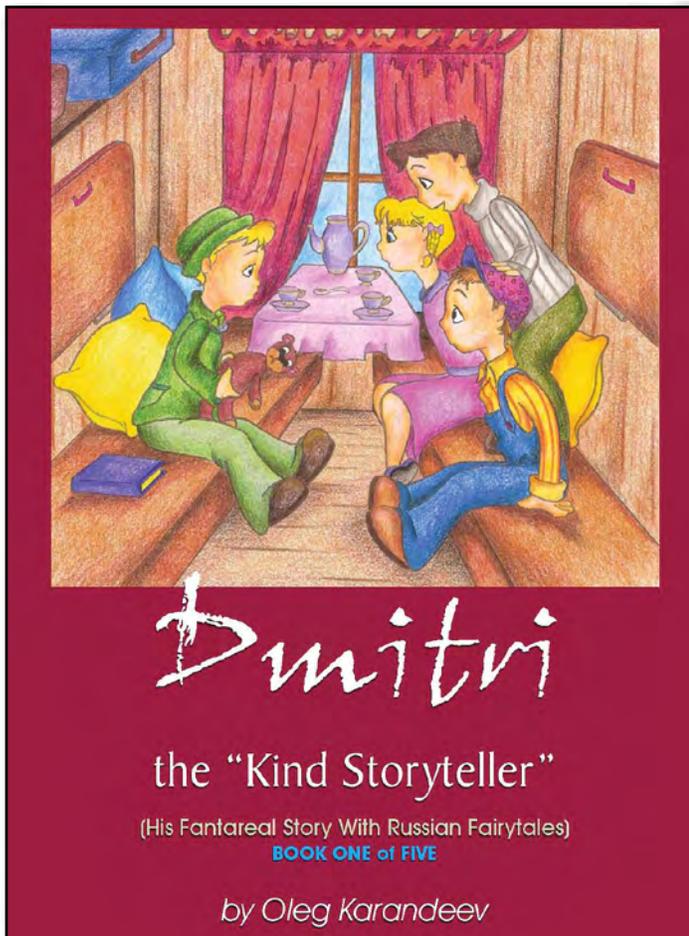


de Serres is shown in 1979 next to a poster of the US-USSR program he coordinated during the 1970s. By that time he was on the leadership team of then Director David Rall, M.D., Ph.D. (Archive photo courtesy of Steve McCaw and Image Associates)

The author of nearly 500 scientific publications, de Serres was a member of a long list of professional societies, editorial boards, committees, panels, and foundations. He received a number of honors during his career, beginning in 1955 with recognition from the Sigma Xi chapter at his alma mater, Yale University.

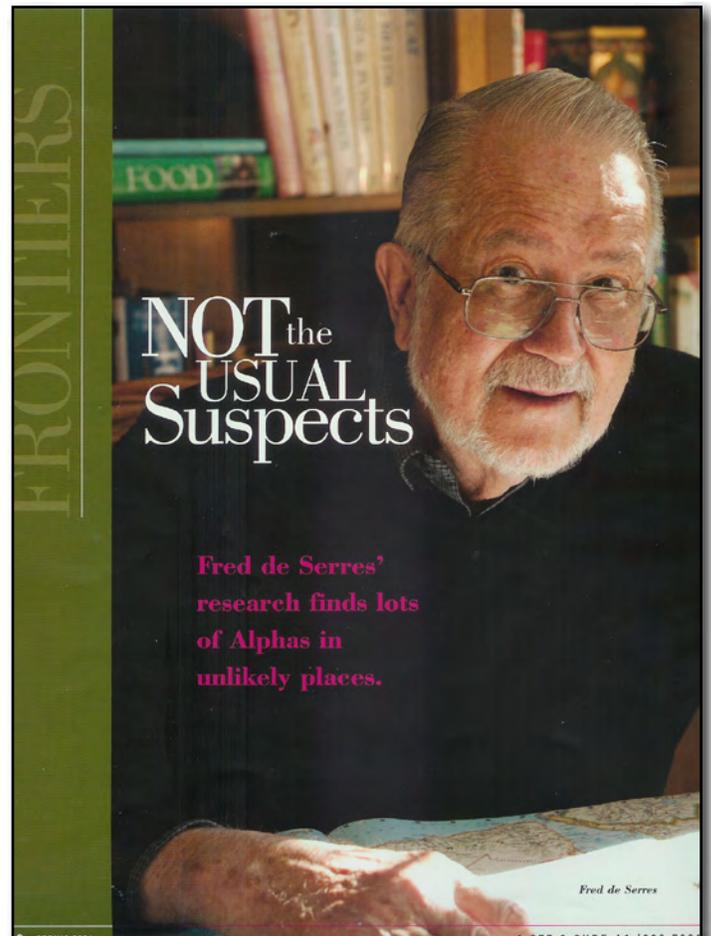
After becoming active in alpha-1 research and patient advocacy following his diagnosis in 1997, he was honored by the Alpha-1 Foundation and Alpha-1 Association. The title of his 2003 article in Environmental Health Perspectives summed up his attitude toward the disease, “Alpha-1 anti-trypsin deficiency is not a rare disease, but a disease that is rarely diagnosed.”

de Serres is survived by 4 children and their spouses, 9 grandchildren, and 4 great grandchildren. He was predeceased by his wife, Christine, and a son, Jonathan. He was buried Jan. 4 in a private ceremony. The family plans a memorial service later this spring.



de Serres' work as an editor and publisher displayed a different side of his varied interests and talents. As co-editor of "Dmitri," he combined his love of folklore and fairy tales with his practiced ear for conversational English to produce a far more readable version of these fairy tales by a Russian author. (Image courtesy of Frederick de Serres)

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de Serres was featured in the Spring 2004 issue of Frontiers, a publication of the Alpha 1 Foundation. From his population studies, he estimated that in the U.S there could be as many as one carrier or deficiency allele combination phenotype for every 11.3 individuals. The rate varies from country to country and is as high as one in 4.5 among people from the Iberian Peninsula, which includes Spain, Portugal, and some parts of France. (Image courtesy of Frederick de Serres)

Former NTP scientific counselor Carney dies unexpectedly

By Eddy Ball

Friends and colleagues at NIEHS and the National Toxicology Program (NTP) were shocked and saddened to learn of the sudden death Jan. 12 of toxicologist Edward Carney, Ph.D., at age 55. Carney, who served on the NTP Board of Scientific Counselors 2008-2011, collapsed on the Pere Marquette Trail near his home in Midland, Michigan, while enjoying one of his regular runs there.

Carney was technical leader of Developmental, Reproductive, and General Toxicology at Dow Chemical Company. He had worked in product safety and predictive toxicology for more than 22 years and was very active in the toxicology community. Carney held leadership positions in the Society of Toxicology and Teratology Society, where he formed lasting personal and professional relationships with NTP and NIEHS scientists.

Friends and colleagues reflect on a life well lived

“Ed will be missed by so many of the people he touched throughout his short life, including those in the toxicology community,” said NIEHS and NTP Director Linda Birnbaum, Ph.D. “In his work as an NTP scientific counselor, he brought a valuable perspective to our deliberations and a delightful sense of humor to our discussions.”

“I knew Ed quite well from his dedicated work as president of the Teratology Society and from our familiar circles at Cornell University,” said NIEHS health scientist administrator Thaddeus Schug, Ph.D. “Ed was a fun-loving person and an excellent scientist, and he was very beloved by all of us who knew him.”

“I had the opportunity to work closely with Ed,” added leader of the NTP Developmental and Reproductive Toxicology Group Barry McIntyre, Ph.D. “He was a fine scientist, with a kind heart and warm smile. I will truly miss his perspective and humor.”



Most attendees at NTP Board of Scientific Counselors meetings will remember Carney, left, as he appeared here in 2009 — boyishly handsome, friendly, and usually ready with a witty response. Seated with him is ad hoc member and North Carolina State University zoologist John Vandenberg, Ph.D. (Photo courtesy of Steve McCaw)



This informal photo of Carney as he prepared to board a plane appeared with the obituary posted by the Smith Minor Funeral Home in Midland. (Photo courtesy of Nancy Carney)

A long record of service to toxicology

In addition to his work with NTP, Carney held positions on the U.S. Environmental Protection Agency (EPA) Chartered Scientific Advisory Board, the European Centre for the Validation of Alternative Methods Science Advisory Board, the Hamner Institute's Board of Directors, and the U.S. Humane Society's Human Toxicology Project Consortium. He most recently took on assignments at the Joint Research Centre of the European Commission and EPA National Center for Computational Toxicology.

As busy as he was, Carney also found time to serve as an adjunct professor at the University of Michigan. Along with his passion for running and other outdoor activities, he was an accomplished musician and active supporter of musical education.

A memorial mass was held Jan. 17. A devoted husband and father, Carney is survived by his loving wife of 30 years, Nancy, and their three cherished sons, Alex, Kevin, and Philip. He is also survived by two brothers, and his father and stepmother.

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Clinical Feature

NIEHS will host IOM workshop on exposures and obesity March 2-3

By Kelly Lenox

The Institute of Medicine (IOM) [Roundtable on Environmental Health Sciences, Research, and Medicine](#) will hold its next workshop, The Interplay Between Environmental Exposures and Obesity, March 2-3 at NIEHS in Research Triangle Park, North Carolina. The event will be webcast for those unable to attend in person.



Scientific presentations will explore the role of chemical exposures in the development of obesity, through sessions focused on a life span view, possible biologic pathways and environmental influences, and effects of food additives and antibiotics. Research based on clinical studies as well as *in vitro*, animal models, and epidemiological approaches will be featured.

Speakers will discuss links between exposure to environmental chemicals and increased incidence of weight gain, glucose tolerance and insulin sensitivity, inflammation, and aspects of metabolic syndrome. Closing panel discussions will focus on opportunities for new research and possible policy actions.

The workshop is expected to have broad appeal, featuring presentations by scientists from NIEHS and the National Institute of Diabetes and Digestive and Kidney Diseases, current and former National Institutes of Health grantees, and international researchers.

To attend, either in person or via webcast, please [register](#) in advance.

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Science Notebook

Exposome workshop uncovers the devil in the details

By Eddy Ball

For many environmental health scientists, it is self-evident that the totality of internal and external exposures, the exposome, is more significant than any single exposure in the overall health of an organism. But, as the NIEHS Exposome Workshop Jan. 14-15 made abundantly clear, the process of putting the emerging exposome approach to work in scientific research is hardly straightforward.

The 2 days of breakout workgroups and animated discussions highlighted the philosophical, practical, technical, and financial challenges that lie ahead. David Balshaw, Ph.D., chief of the NIEHS Exposure, Response, and Technology Branch, emphasized that holistic approaches to exposure biology require global involvement.

“Although NIEHS has a significant role in implementing the exposome,” Balshaw told attendees, “it’s going to have to be an international EHS [environmental health science] community program.”

NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., pointed to the importance of crafting creative solutions, adopting new approaches in training, and reaching across the social, financial, and intellectual spectra. “We need partners,” she said. “I think one of the important things about the exposome is that it requires integrated methods.”

Linked audio:

Listen to an NIEHS podcast explaining the importance of studying the exposome. (6:31)

[Listen Now](#) (5MB)

[Read Transcript](#) (25KB)

(Launches in new window)

Download Media Player: [Quicktime](#)

A messy, but necessary process

The Exposome Workshop was necessarily short on data and long on discourse and analysis. Balshaw and his colleagues collected an impressive group of scientists from the U.S., Europe, and Asia, in fields ranging from clinical medicine, epidemiology, and toxicology, to exposure biology, pharmacology, and bioinformatics to review the state of the science in the emerging field of exposomics.

Although attendees were still divided on several issues — including some basic definitions — as the workshop came to an end, most were energized and ready to move forward with a clearer understanding of what needs to be done.

“We can’t let uncertainty prevent us from moving forward,” said [Susan Teitelbaum, Ph.D.](#), of Mount Sinai School of Medicine. Several attendees, such as Vermeulen, called for adapting the tools they have now to evaluate additional data, as scientists work toward the new tools and methodologies a global approach will require.



Balshaw encouraged attendees to repurpose what they already have, as they wait for new resources. “As you go home,” he said, “think about what you can do [right away].” (Photo courtesy of Steve McCaw)

One chemical – one set of outcomes no longer suffices

In planning their meeting, Balshaw and his colleagues across NIEHS underscored the role of work in the term workshop. Participants spent 5 months preparing for the workshop, hashing out the troublesome details behind the self-evident truth of the exposome. They discussed promotion strategies, including the development of exposome case studies, or use cases, as proof of principle. They also worked toward papers to submit to peer-reviewed journals.

A number of developments in [21st century environmental health science](#) parallel themes and goals in the NIEHS 2012-2017 [strategic plan](#).

Attendees engaged in virtual workgroups before meeting face-to-face at NIEHS to frame the following developments within the exposome concept:

- **Appreciating variation in host susceptibility and response** — Individuals experience a complex mixture of chemical, natural, and social exposures. A range of external and internal factors shapes how an organism responds as it struggles to maintain metabolic balance, or homeostasis.

[Gary Miller, Ph.D.](#), of Emory University and chair of the Biological Response Workgroup, introduced the concept of allostatic load as a way to discuss this variation. The term refers to the cumulative cost of correcting perturbations to homeostasis, and a way to frame resilience against further stress.

- **Understanding critical windows of development** — In a dynamic matrix, time is a key determinant in host response to internal and external exposures. Exposures vary in effect depending on when they occur during the lifetime. Exposures may also trigger changes in gene expression linked to the onset of disease later in an individual's life.

“We have to have life course information,” said Epidemiology Workgroup member [Roel Vermeulen, Ph.D.](#), of Utrecht University, Utrecht, The Netherlands.

- **Making fundamental changes in scientific method and promoting interdisciplinary approaches** — “The exposome is really about changing the way we do science, moving from a reductionist approach to an integrated complex exposure approach,” argued the chair of a breakout group on refining recommendations, [Dean Jones, Ph.D.](#), of Emory University.

Several researchers argued for the need to directly challenge disciplinary silos and reengineer training — and retraining — for the scientific workforce across the physical, medical, chemical, biological, and social sciences.



Teitelbaum, left, addressed questions about her report on epidemiology and the exposome from [Petros Koutrakis, Ph.D.](#), of Harvard University. (Photo courtesy of Steve McCaw)



[Shoji Nakayama, M.D., Ph.D.](#), left, shared insights from his work with the Japan Environment and Children's Study, a longitudinal birth cohort study involving 100,000 mothers and children. [Carolyn Mattingly, Ph.D.](#), of North Carolina State University, is lead researcher for the Comparative Toxicogenomics Database. (Photo courtesy of Steve McCaw)

- **Exploiting big data to survey the exposome** — Immediate goals include data mining and integration of existing epidemiological cohorts. Data Workgroup chair [Chirag Patel, Ph.D.](#), of Harvard University, floated the idea of establishing databases of databases and pursuing partnerships with private-sector information companies.

Exposome theorist [Martyn Smith, Ph.D.](#), of the University of California, Berkeley, proposed a global database of exposure, GHANES, modeled on the U.S. National Health and Nutrition Examination Survey (NHANES). Smith was a member of the response work group and chaired a breakout group on use cases.

These represent only a few of the many ideas attendees discussed during the workshop, but they are important components of what may one day become a cohesive theory of exposure biology.



When the discussion turned to the relative value of measuring internal and external exposures, NIEHS DERT Director Gwen Collman, Ph.D., called for integrated measurement. “My point is, it’s not one or the other,” she said. (Photo courtesy of Steve McCaw)



Like many attendees, Miller emphasized the biology of outliers, people who are especially resilient or especially susceptible to environmental exposures. (Photo courtesy of Steve McCaw)



Stephanie London, M.D., Dr.P.H., was one of several lead researchers in the NIEHS Epidemiology Branch at the workshop. (Photo courtesy of Steve McCaw)



Former NIEHS epidemiologist [Jane Hoppin, ScD.](#), of North Carolina State University, called for revisiting cohorts, data, and samples from earlier studies. “I’m really interested in how we can leverage what we already have in the freezer,” she said. (Photo courtesy of Steve McCaw)



Among attendees representing the three NIEHS research divisions were, from left, NTP toxicologist [Cynthia Rider, Ph.D.](#); Division of Extramural Research and Training (DERT) health scientist administrator [Danielle Carlin, Ph.D.](#); and Division of Intramural Research clinical researcher [Shepherd Schurman, M.D.](#) (Photo courtesy of Steve McCaw)

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Distinguished lecture examines prenatal exposures in child development

By [Robin Arnette](#)

A large body of research has presented compelling evidence that the environmental exposures a pregnant woman experiences adversely affect her unborn child. Work done by [Frederica Perera, Ph.D., Dr.P.H.](#), her colleagues at the Columbia Center for Children’s Environmental Health (CCCEH), and others suggest that those exposures may also negatively impact the child’s health into his or her adolescent years and beyond.

As a molecular epidemiologist and environmental health scientist at Columbia University in New York City, [Perera](#) focuses on preventing childhood neurodevelopmental impairment, asthma, obesity, and cancer through early identification of environmental risk factors. NIEHS and National Toxicology Program (NTP) Director [Linda Birnbaum, Ph.D.](#), invited Perera to the Distinguished Lecture Seminar Series, to talk about her research.

The CCCEH Birth Cohort Study

[Perera](#) and her team recruited 720 mother-child pairs during pregnancy from northern Manhattan and the south Bronx. Study details are given below.

Mothers

- Healthy, non-smoking
- Ages 18-35
- Provided urine and blood samples
- Wore prenatal personal air monitoring

Children

- Cord blood and placenta collected at birth
- Blood and urine sample collected from 2 years through adolescence
- Continued follow-up through adolescence

Most of the people in this area are low-income, African American and Dominican families. The study aims to identify the environmental risk factors associated with disease and prevent adverse health impacts.

Perera's Jan. 13 lecture, "The Fetal Window of Susceptibility: Using Molecular Epidemiology to Understand the Role of Prenatal Environmental Exposures on Child Health and Development," was based on data from the CCCEH Birth Cohort Study (see [sidebar](#)).



Linked video:
Watch as Perera describes research into how early exposures affect childhood development. (2:55)
(Launches in new window)

Download Media Player:  Flash [↗](#)

Environmental stress

Perera set the stage for her lecture by asking the audience to visualize the complex processes that take place simultaneously during human fetal brain development — this highly choreographed process is at the heart of fetal susceptibility. Perera said a high rate of cell proliferation puts DNA at risk of damage from chemicals and oxygen radicals. Moreover, because the fetus has immature defense mechanisms, it is less able to clear toxicants. While these strains weigh heavily on the fetus, the mother also has to deal with environmental pressures during pregnancy.

"We have to realize there is high vulnerability of the fetus to co-exposures to environmental toxicants and psychosocial stresses experienced by the mother," Perera said. "These stressors frequently occur in underserved populations."

Several previous studies from various scientists, such as former NIEHS Director Kenneth Olden, Ph.D., found that low-income communities are disproportionately exposed to toxic air pollutants. Perera corroborated this point by citing several sources of pollutants in New York City. For example, most of the Metropolitan Transit Association diesel bus depots and sewage waste transfer stations are located in northern Manhattan, namely Harlem, and the south Bronx. According to Perera, many of the buildings in these areas are under-maintained and are heavily treated with pesticides. As a consequence, their residents experience high rates of pesticide exposure, in addition to airborne pollutants.

Toxicants and neuronal development

Perera said that since burning fossil fuel was suspected of contributing to many of the health problems the community faces, the cohort study targeted a major class of pollutants from combustion of diesel, gasoline, coal, oil, and natural gas — the polycyclic aromatic hydrocarbons (PAHs).



"In a recent year, more pesticides were used in New York City to deal with cockroaches and other pests, than were used in agriculture for the entire state of New York," Perera said. "If you include all the other environmental exposures, material hardship, and psychosocial stress due to poverty, as well as less access to healthy food, the result is major health disparities." (Photo courtesy of Steve McCaw)



Birnbaum and Perera share a passion for environmental health. (Photo courtesy of Steve McCaw)

In addition to air pollution from combustion by-products, fossil fuel is the source of petrochemicals from which many billions of pounds of chemical products are derived. These include phthalates, pesticides, and materials treated with polybrominated diphenyl ether (PBDE) flame retardants. Petrochemicals are found in a number of consumer products, ranging from fragrances, plastics, and furniture to electronic equipment and shampoo.

Perera and her CCCEH colleagues conducted studies that focused on these toxicants. Their prenatal exposure findings suggest:

- Prenatal PAH exposure is associated with lower IQ scores and neurobehavioral problems, including ADHD, when children were assessed from early childhood through pre-adolescence.
- Children of mothers who had higher exposure to phthalates during pregnancy had significant IQ decreases when assessed at age 7.
- Newborns with high cord plasma levels of PBDEs showed a consistent pattern of having decreased IQ when assessed at ages 4 and 6.



NIEHS Scientific Director Darryl Zeldin, M.D., asked if the children's cohort had accompanying genetic data and whether future environmental exposure studies would include a genetic component. (Photo courtesy of Steve McCaw)

When science changes policy

Perera concluded her talk with the reforms in New York City that resulted, in part, from the Center's research. They include limits on idling trucks and buses, policies on traffic congestion, and legislation to restrict the use of toxic pesticides in public housing.

“These are beautiful examples of how environmental research can make the world better,” Birnbaum said.



Perera's talk brought current and former NIEHS scientists together. From left, Richard Paules, Ph.D., acting chief of the NTP Biomolecular Screening Branch; Jack Bishop, Ph.D., retired NTP geneticist; and Cindy Lawler, Ph.D., chief of the NIEHS Division of Extramural Research and Training (DERT) Genes, Environment, and Health Branch. (Photo courtesy of Steve McCaw)



Jerrold Heindel, Ph.D., a health scientist administrator in DERT, has administered many NIEHS grants focused on understanding the fetal window of susceptibility. (Photo courtesy of Steve McCaw)

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NIEHS researchers determine new function for DNA repair protein

By Robin Arnette

When NIEHS scientist Scott Williams, Ph.D., was a graduate student in 1998, he began studying a protein called Ctp1, also known as CtIP. He had no idea that nearly 17 years later, a visiting fellow in his own group would unveil the first molecular structures of Ctp1 and discover new functions for the protein.

The paper that touted the findings appeared online Jan. 12 in the journal *Nature Structural and Molecular Biology*. Reporting the only known crystal structure of the Ctp1 DNA binding region, the article is the first to describe the architecture of Ctp1 and suggest a new function — that of a DNA binding and bridging protein.

Previously published studies have determined that mutations in the human version of Ctp1 result in two rare developmental disorders known as Jawad syndrome and Seckel syndrome.

The NIEHS team found that mutations in fission yeast, corresponding to conserved amino acids that are absent in people with the two syndromes, interfered with the ability of Ctp1 to properly attach to broken DNA and facilitate DNA repair.

Ctp1 bridges the gap

[Williams](#), lead of the NIEHS Genome Integrity and Structural Biology Group, is interested in how cells recognize and repair DNA double-strand breaks caused by environmental exposures and normal cellular metabolism. He said DNA double-strand breaks are some of the most dangerous DNA lesions, because if left unrepaired, they can lead to genome rearrangements and contribute to carcinogenesis.

As a graduate student in biochemistry at the University of Alberta, Canada, Williams studied the protein interactions of the BRCA1 tumor suppressor. During that time, published studies revealed that the mammalian version of Ctp1 binds to BRCA1, which sparked Williams' curiosity about what roles Ctp1 plays in the cell.

While Williams worked his way through his doctoral program and postdoctoral training at the Scripps Research Institute in La Jolla, California, a large body of literature was accumulating on the role of Ctp1 in the repair of DNA double-strand breaks. The underlying molecular basis for the function, however, remained unknown.

Making Editor's Choice in Environmental and Molecular Mutagenesis

Another journal has taken notice of the work coming out of the Williams group. Andres was also lead author on a literature review picked for Editor's Choice by the [Environmental Mutagenesis and Genomics Society \(EMGS\)](#). According to Jeffrey Wickliffe, Ph.D., chair of the EMGS Public Relations and Communications Committee, selection of a review article as an Editor's Choice is rare. Most are important new observations.

“What sets this review apart is that the authors have condensed a large amount of information about a complex system into a concise, complete, and readable review,” Wickliffe said. “I have no doubt that this review will become part of cell and molecular biology graduate courses and serve as a starting point for investigations into cell responses to stress, evolutionary biology, neurology, aging, and oncology.”

The paper, which also received a cover highlight, reviews the biochemistry underlying the ways cells identify and repair spontaneous, radiation-induced and chemical-induced DNA damage that occurs at DNA ends.

Citation: [Andres SN](#), [Schellenberg MJ](#), [Wallace BD](#), [Tumbale P](#), [Williams RS](#). 2015. Recognition and repair of chemically heterogeneous structures at DNA ends. *Environ Mol Mutagen* 56(1):1-21.

Williams joined NIEHS in 2009 and combined structural methods with biophysical techniques and yeast genetics to find the answer. “We discovered that Ctp1 is made up of four flexible arms that can bind to the two broken DNA ends and act as a bridge,” Williams said.

“We think this function is important in coordinating both damaged DNA and proteins involved in DNA repair. In doing so, Ctp1 protects the integrity of the genome against environmental and natural insults,” he explained.

Proteins working in collaboration

Because the DNA molecule is a flexible structure, Williams said, it makes sense that the protein that grabs onto broken DNA ends should be flexible, too. He suggested imagining the entire genome as a bowl of spaghetti, in which one spaghetti strand breaks in two. “How do you ensure that the two ends don’t get lost in the bowl, because you need those same two pieces to become one again?” Williams asked. “A flexible Ctp1 that provides a bridging scaffold helps to solve the problem.”

Current research shows that Ctp1 doesn’t work alone. The protein acts in concert with the Mre11-Rad50-Nbs1 nuclease complex and influences its activity. Since Mre11, Rad50, and Nbs1 are also mutated in heritable, cancer predisposition syndromes, the team wants to know how Ctp1 collaborates with these complex members to recognize and repair DNA double-strand breaks. Future work should bring further clarity to Ctp1 functions.

Sara Andres, Ph.D., lead author and visiting fellow in the Williams group, said that although they have learned a lot, there’s still more to understand. “Like any biological system, knowing how DNA repair functions at the molecular level provides an instruction manual of sorts, with Ctp1 being chapter 1,” Andres said. “When DNA repair does go awry, causing diseases like Seckel syndrome or cancer, we have the knowledge to find a way to fix it.”

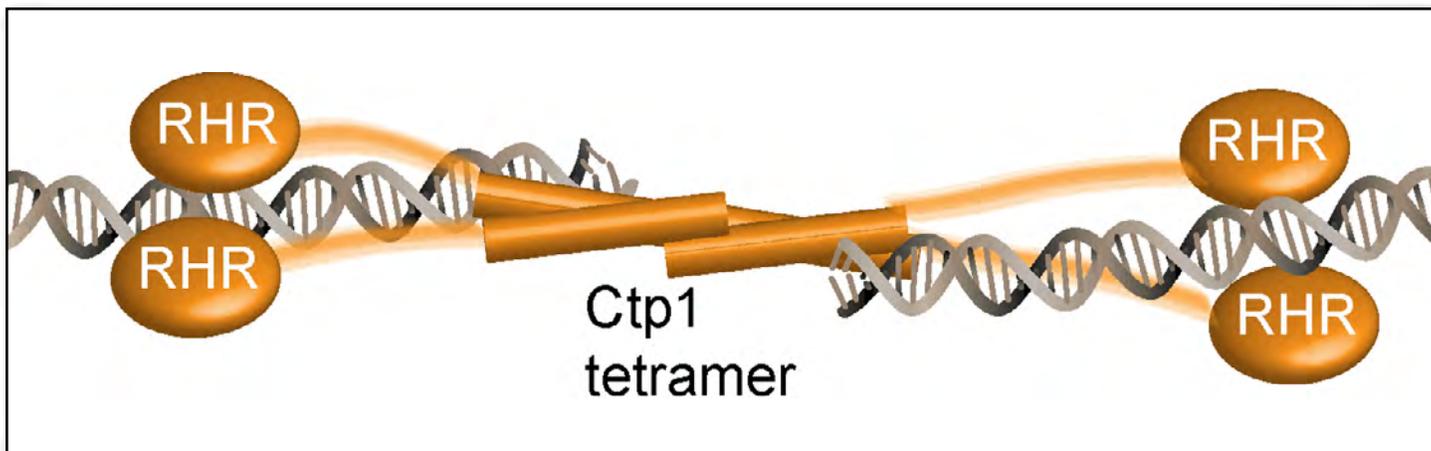
Citation: Andres SN, Appel CD, Westmoreland JW, Williams JS, Nguyen Y, Robertson PD, Resnick MA, Williams RS. 2015. Tetrameric Ctp1 coordinates DNA binding and DNA bridging in DNA double-strand-break repair. *Nat Struct Mol Biol*; doi:10.1038/nsmb.2945 [Online 12 January 2015].



DNA damaging agents, such as ionizing radiation (IR), shear both strands of DNA, creating damaged DNA. When the Williams group disrupted the Ctp1 tetrameric core in fission yeast and zapped the yeast with IR, the cells died, indicating that Ctp1 binding to DNA is vital for yeast survival. (Photo courtesy of Steve McCaw)



Andres is keen to continue her research on Ctp1. “Finding that Ctp1 is like a flexible bridge linking DNA is just the first step,” Andres said. “The real challenge now is to determine how that works in the context of the entire DNA repair complex.” (Photo courtesy of Steve McCaw)



Using biochemistry, structural biology, and genetic approaches in fission yeast, the Williams group generated a model that may explain how Ctp1 binds DNA. Williams said the Ctp1 tetramer interlocks at the center of the four-armed protein to bind and bridge broken DNA ends. RHR represents DNA binding domains, made up of the amino acids arginine (R), histidine (H), and arginine (R), that stabilize Ctp1 at the DNA break site. (Graphic courtesy of Scott Williams)

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Reproducibility advanced by new NTP systematic review handbook

By Kelly Lenox

The National Toxicology Program (NTP) released a handbook Jan. 12 detailing procedures for systematic review in literature-based health assessments. The NTP Office of Health Assessment and Translation (OHAT), which developed this methods guide for evaluating potential human health hazards, hopes use of the handbook will enhance reproducibility of environmental health sciences research, which is a growing concern across all fields of scientific research and is the subject of recent [National Institutes of Health initiatives](#).

As part of the systematic review process, the “[Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration](#)” features a tool for assessing the risk of bias in a study’s findings. The tool applies an approach to evaluating the risk of bias in human and animal studies that is similar to the methods used to critically assess clinical trials of new drugs.

“Establishing transparent and objective standards for systematic reviews in literature-based evaluations builds confidence in the subsequent public health decisions,” said Kristina Thayer, Ph.D., director of OHAT. “And as the methodology becomes adopted more widely, the reproducibility of environmental health studies will be enhanced.”



Thayer oversees NTP evaluations to assess the evidence that environmental substances cause adverse health effects. (Photo courtesy of Steve McCaw)

From clinical trials to broader application

“Interest has been growing in the fields of toxicology and pharmacology in extending systematic review methods beyond the traditional area of human clinical trials to consider other evidence streams,” said NTP leaders and staff in a [July 2014 editorial](#) in the journal *Environmental Health Perspectives*. Authors include NIEHS and NTP Director Linda Birnbaum, Ph.D., NTP Associate Director John Bucher, Ph.D., Thayer, and others.

“This handbook provides the methods for completing a literature-based evaluation for environmental health questions, and it addresses whether or not exposure to chemical X is associated with health effect Y,” said Andrew Rooney, Ph.D., OHAT deputy director.

“This document is intended to outline NTP methods, but it can also serve as a methods SOP [standard operating procedure] for external researchers,” he said, noting that this is the first handbook to cover systematic review methods for environmental health questions.



Rooney reviewed how his team used systematic review as part of a study of inflammation and atherosclerosis, in a Dec. 2014 inflammation seminar at NIEHS (see [story](#)). (Photo courtesy of Steve McCaw)

Risk of bias tool

Reproducibility of scientific studies increases when consistent means are used to assess internal validity, or risk of bias. Bias can lead to either underestimation or overestimation of an observed effect.

According to the editorial quoted above, there is a general consensus on methods used to assess outcomes of human clinical trials. However, environmental health sciences research uses studies of widely varying design — from epidemiology to mechanistic studies. “There is not currently a similar consensus on how to assess that the findings and conclusions of observational human, experimental animal, and *in vitro* studies are a true reflection of the outcome,” the editorial’s authors said.

To meet that need, OHAT developed a risk of bias tool, included in the handbook, for evaluating environmental health studies in humans or animals. Rooney pointed out that, as with the systematic review methodology, the tool outlines NTP methods and may also be used by external researchers to assess study quality.

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NIEHS Superfund research training spurs collaboration with EPA

By Sara Mishamandani

The University of Pennsylvania Superfund Research Program (Penn SRP) Center worked closely with the U.S. Environmental Protection Agency (EPA) to plan a day of training on mobile air monitoring technology, groundwater restoration, and community involvement for staff from the [EPA mid-Atlantic regional office](#). The Penn SRP Center and the EPA regional office both work to reduce the health effects of asbestos, which is a significant health concern in some areas of Pennsylvania. The event provided attendees an opportunity to exchange innovative environmental health research.

The Penn SRP Center was established last year with NIEHS funding to study asbestos exposure pathways that lead to diseases. The Center evolved out of the Penn [Center of Excellence in Environmental Toxicology](#) (CEET), which is funded through the NIEHS Environmental Health Core Centers program, because of concerns from the community living near the [BoRit Asbestos Superfund site](#) in Ambler, Pennsylvania.

The director of the Penn SRP Research Translation Core (RTC), Richard Pepino, arranged the training as part of the Core’s mission to solidify partnerships among EPA, CEET, and Penn SRP. The daylong event featured demonstration of a new EPA mobile air monitoring technology called the Trace Atmospheric Gas Analyzer Van, discussion of completed groundwater restoration actions, and the sharing of new strategies for community involvement. More than 80 EPA staff, in addition to SRP researchers and trainees, participated in the event.

Penn SRP Center asbestos research

Ian Blair, Ph.D., director of the Penn SRP Center, described ongoing research at the Center to address community concerns in Ambler. The Center is working to better understand how asbestos moves through the environment. Researchers also study how asbestos can be remediated, how to detect exposure, and how exposure and susceptibility affect health outcomes.

Blair discussed the use of novel high-resolution mass spectrometry-based methods to identify new biomarkers of mesothelioma, which is an aggressive cancer related to asbestos exposure. He recently discovered, in findings that are not yet published, three serum lipid biomarkers that are more sensitive and specific for detecting mesothelioma than protein biomarkers currently in use.

Blair also discussed how the Penn SRP RTC is informing stakeholders — in Ambler, as well as at local, state, and federal agencies — about research progress. Penn SRP has made significant progress in creating partnerships with EPA staff and reaching out to community members in Ambler.

Fostering collaboration

Trevor Penning, Ph.D., CEET director and Penn SRP Center deputy director, welcomed the participants and challenged them to form new partnerships. Penn researchers learned about EPA technologies and how they might facilitate CEET research. The session that demonstrated the capability of the EPA mobile air monitoring laboratory led to discussion on how this technology might be used in homes close to hydraulic fracturing sites in Pennsylvania, which is one focus of CEET.

“I find it critically important to strengthen ties with Region 3 EPA,” said Penning. “The region is faced with major environmental health issues, and by working together, we can find solutions to protect human health.”

(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.)



Training organizers Jessica Meeker, left, Penn SRP RTC coordinator, and Root, in front of the Trace Atmospheric Gas Analyzer Van. (Photo courtesy of Jessica Meeker)



From left, Blair; Cecil Rodriguez, director of the EPA Region 3 Hazardous Site Cleanup Division; Charlie Root, EPA Region 3 remedial project manager; Penning; and Pepino took advantage of the opportunity to form new collaborations. (Photo courtesy of Jessica Meeker)

Behl gives Duke seminar on NTP flame retardant toxicity screening

By Ernie Hood

Toxicologist [Mamta Behl, Ph.D.](#), of the National Toxicology Program (NTP), discussed the novel screening approach developed by NTP to assess the toxicity of classes of compounds in a Jan. 16 talk at Duke University. Her presentation, “Screening Compounds with Developmental and Neurotoxic Potential: Flame Retardants, a Case Example,” was part of the Integrated Toxicology and Environmental Health Program [seminar series](#) at the Nicholas School of the Environment. Early results indicate that some newer compounds may present just as much cause for concern as the older flame retardants they are meant to replace.

Before delving into the details of the screening battery, Behl addressed the need to efficiently characterize classes of compounds of environmental or occupational concern. “It’s important to be able to look at them in a timely manner,” she told her Duke audience. “If you’re looking at one chemical at a time, it takes years to get any sort of information, so this is an attempt to come up with a screening approach that allows us to get some information in a timely manner.”

Among flame retardants, the major brominated diphenyl ether (BDE), BDE-47, has been phased out of the marketplace. However, there are growing concerns about the effects of exposures to the new class of flame retardants, which are called aromatic phosphates and are now marketed as substitutes for some BDEs. Primary concerns include reproductive or developmental toxicity from long-term exposure, as well as neurological and systemic effects. As part of a larger flame-retardant effort, NTP is studying six of the aromatic phosphates, following their nomination by the Consumer Product Safety Commission.



Behl explained use of the novel screening battery to compare older phased-out flame retardants with newer substitutes. “We want to know the relative toxicity,” she said. (Photo courtesy of Steve McCaw)

Screening battery concept

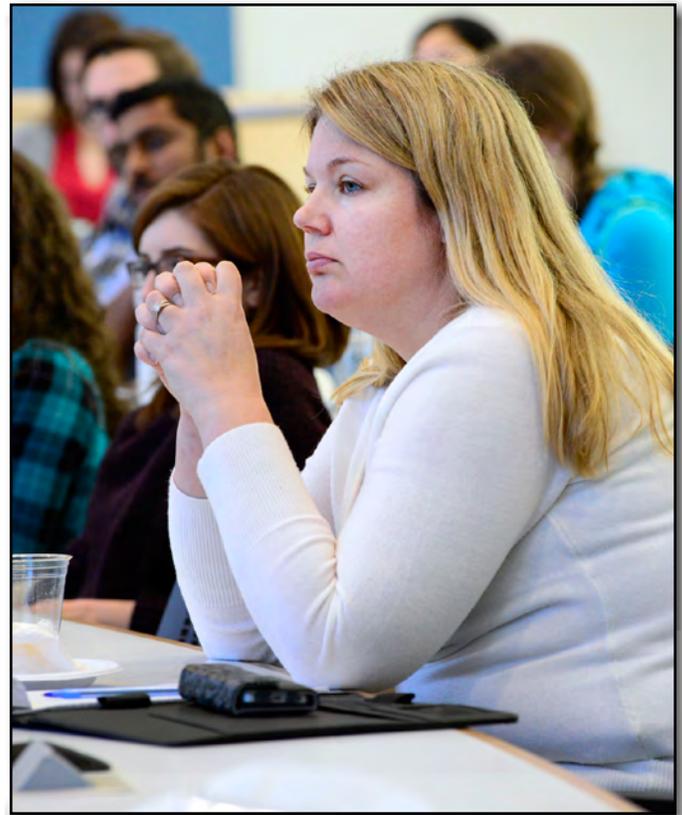
The screening battery is conducted in three phases, in increasing levels of biological complexity. The assays were designed to provide comparative toxicity information about four of the BDEs and six of the APs (see [text box](#)).

- **High-throughput screening using human cell lines** — Results showed a variety of toxicity levels among both classes. Mitochondrial toxicity appeared to be the most sensitive assay.
- **High content screens** — Neurotoxicological endpoints, such as neurite proliferation and outgrowth, neuronal firing, neuronal crest migration, genomics, and metabolomics, are measured. Again, results suggested that the substitute compounds might be as toxic to neural processes as the compounds they are intended to replace.
- **Screening in complementary animal models** — Exposure effects on feeding, growth, and reproduction were noted in the roundworm *Caenorhabditis elegans*. Studies in zebrafish are ongoing.

“The take-home message is that the alternative flame retardants may have cause for concern,” Behl said. “Their use as replacements for BDEs doesn’t necessarily mean they’re safe, so they should be tested in depth for further hazard characterization.”



Edward Levin, Ph.D., is a professor of psychiatry and behavioral sciences, organizer of the ITEHP seminar series, and a researcher with the NIEHS-funded Superfund Research Center at Duke. He introduced Behl and moderated the question and answer session. (Photo courtesy of Steve McCaw)



Nicholas School of the Environment faculty member Heather Stapleton, Ph.D., an NIEHS grantee who studies flame retardants, naturally had a keen interest in Behl's talk and asked several questions following the presentation. (Photo courtesy of Steve McCaw)



ITEHP seminars draw a large crowd to Field Auditorium, the high-tech classroom in Duke's Environment Hall. (Photo courtesy of Steve McCaw)

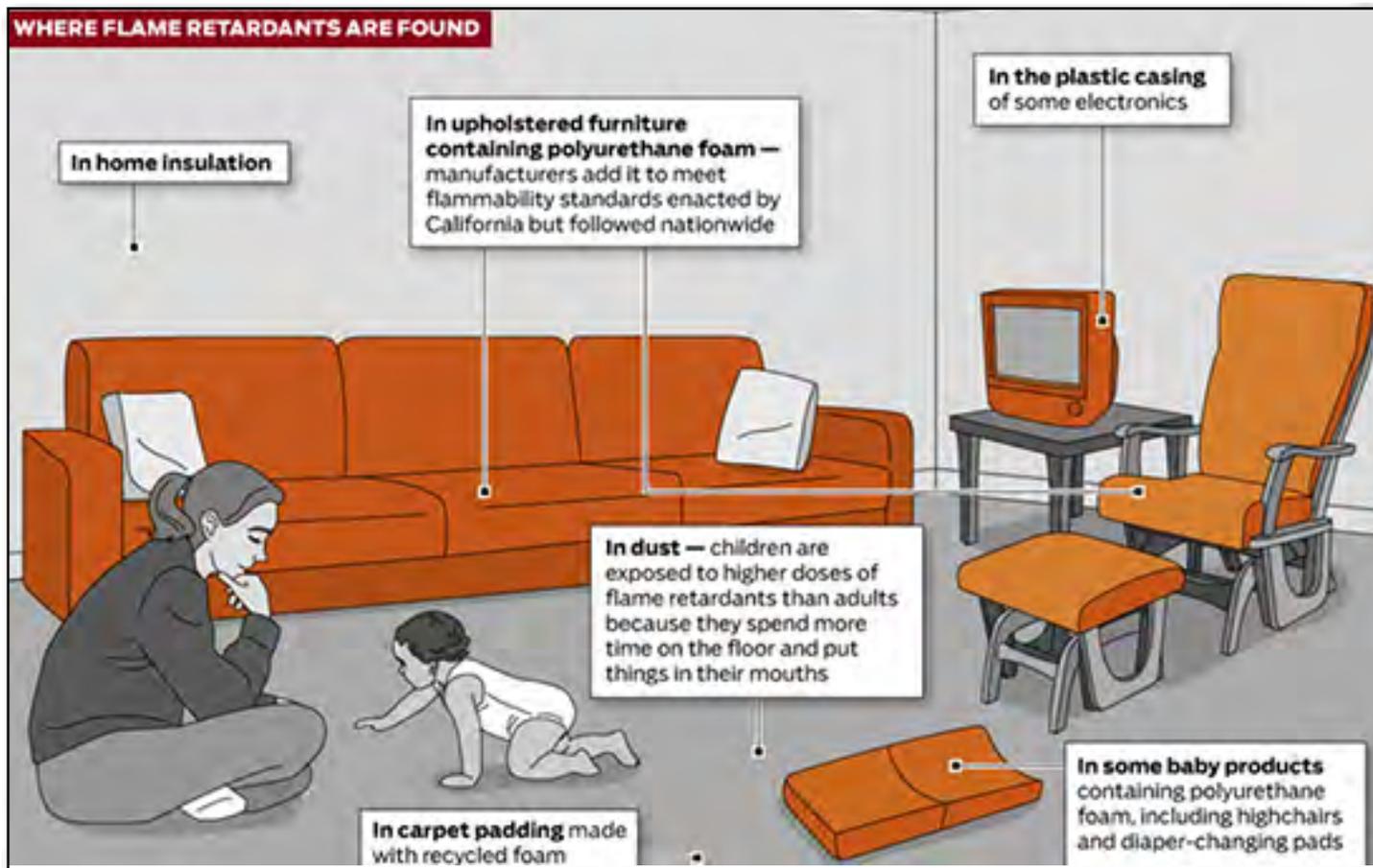
Tested flame retardants

BDEs and other aliphatics

- Polybrominated diphenyl ether (BDE-47) (phased out)
- Tris(2-chloroethyl) phosphate (TCEP)
- Tetrabromobisphenol A (TBBPA)
- Tri-*o*-cresyl phosphate (TOCP)

Replacements (aromatic phosphates)

- Triphenyl phosphate (TPP)
- Tert-butylphenyl diphenyl phosphate (BPDP)
- Tricresyl phosphate (TCP)
- 2-ethylhexyl diphenyl phosphate (EHDP)
- Isodecyl diphenyl phosphate (IDDP)
- Isopropylated phenyl phosphate (IPP)



With this slide, Behl set the stage for her discussion of the novel screening battery NTP is using to assess the relative neurotoxicity and developmental toxicity of flame retardants. (Graphic from EPA and *Chicago Tribune* reporting)

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

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This month in EHP

An eye-catching cover highlights the February Environmental Health Perspectives (EHP) focus story on potential effects of marine plastic pollution.

New Link in the Food Chain? Marine Plastic Pollution and Seafood Safety

Viewpoints on the human health risks of marine plastic pollution are nearly as complex as the underlying science. How much do plastics contribute to the chemical burden in seafood? What proportion of human exposure to plastic ingredients occurs through seafood? And, how concerned should we be about exposures to marine plastic pollution?



<http://twitter.com/ehponline>

Featured research and related news articles this month include:

Seeds of Toxicity? Erythrocytes and Lead-associated Kidney Damage — Researchers propose a hypothesis to explain lead-related toxicity in the kidney and present in vivo and in vitro data to support it.

The View From Afar: Satellite-derived Estimates of Global PM 2.5 — Using satellite data, scientists estimate trends over 15 years of global exposure to particulate matter less than 2.5 microns in diameter.

Tracking Alternative Flame Retardants: Hand-to-mouth Exposures in Adults — A new study assesses relationships between concentrations of two organophosphate flame retardants in house dust, hand wipes, and urine.

Shrimp Consumption After Deepwater Horizon: No Evidence of Excess Risks for Vietnamese Americans — A targeted health risk assessment of Vietnamese Americans in southeast Louisiana estimates no acute health effects or excess cancer risk for those who ate locally caught shrimp after the Deepwater Horizon oil spill.

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Extramural papers of the month

By *Nancy Lamontagne*

- [Causes of hospitalization during heat waves](#)
- [Phthalate exposure linked to lower IQ](#)
- [Cadmium exposure linked to shorter telomeres](#)
- [U.S.-wide study links autism with prenatal exposure to fine particulate air pollution](#)

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

Causes of hospitalization during heat waves

Researchers partially funded by NIEHS report that, among older adults, heat waves were associated with increased risk of hospitalization for fluid and electrolyte disorders, renal failure, urinary tract infection, sepsis, and heat stroke. Extreme heat is the most common cause of deaths tied to severe weather in the United States.

Most studies of heat-related health effects have looked at only a few predetermined health outcomes. For this study, the researchers considered all possible heat-related causes of hospitalizations from 1999 to 2010, by analyzing data in 214 disease groups from 23.7 Medicare enrollees per year (85 percent of Medicare enrollees), residing in 1,943 counties in the U.S.

The researchers found that older Americans were 2 1/2 times more likely to be hospitalized from heat stroke during heat wave periods than on non-heat wave days. Extreme heat also put the elderly at 18 percent greater risk of being hospitalized for fluid and electrolyte disorders; 14 percent greater risk for renal failure; 10 percent greater risk for urinary tract infections; and 6 percent greater risk for sepsis. The researchers said that sepsis had not been previously considered a possible outcome of extreme heat.

Longer and more extreme heat waves brought larger risks. Since risks remained elevated one to five days after a heat wave, prevention and treatment is critical not just during a heat wave, but also afterwards.

Citation: [Bobb JF](#), [Obermeyer Z](#), [Wang Y](#), [Dominici F](#). 2014. Cause-specific risk of hospital admission related to extreme heat in older adults. *JAMA* 312(24):2659-2667.

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Phthalate exposure linked to lower IQ

NIEHS-funded researchers found that children, aged 7, who experienced prenatal exposure to elevated levels of two phthalates had lower IQ scores than children exposed to lower levels. The new research adds to the group's earlier findings of associations between prenatal exposure to phthalates and problems with cognitive function and behavior at age 3.

The study included 328 New York City women and their children from the Columbia Center for Children's Environmental Health longitudinal birth cohort. During the third trimester of pregnancy, the researchers measured urinary metabolites of four phthalates — di-n-butyl phthalate (DnBP), di-isobutyl phthalate (DiBP), di-2-ethylhexyl phthalate, and diethyl phthalate.

At age 7, the children of the mothers with the highest concentrations of DnBP and DiBP metabolites had IQs 6.6 and 7.6 points lower, respectively, than children of mothers exposed to the lowest concentrations. They found no associations between the other two phthalates and child IQ. Other research has shown that a six- or seven-point decline in IQ can substantially affect academic achievement and occupational potential.

Although some phthalates are banned from use in children's products in the U.S., pregnant women are exposed to phthalates in consumer and personal care products.

Citation: [Factor-Litvak P](#), [Insel B](#), [Calafat AM](#), [Liu X](#), [Perera F](#), [Rauh VA](#), [Whyatt RM](#). 2014. Persistent associations between maternal prenatal exposure to phthalates on child IQ at age 7 years. *PLoS One* 9(12):e114003.

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Cadmium exposure linked to shorter telomeres

A study supported in part by NIEHS found an association between cadmium exposure and shorter leukocyte telomere length, a marker of cellular aging. Findings from the study also indicate that cadmium might be harmful at levels well below current safety standards set by environmental and occupational safety agencies.

Cell and animal studies have suggested that lead and cadmium induce a shortening of telomeres, which protect the ends of chromosomes. To study this type of cellular damage in people, the researchers examined leukocyte telomere length, as well as blood and urine samples, from more than 6,700 adults who participated in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2002. After adjusting for potential confounders, the highest (versus lowest) quartiles of blood and urine cadmium were associated with -5.54 percent (95 percent CI: -8.70, -2.37) and -4.50 percent (95 percent CI: -8.79, -0.20) shorter leukocyte telomere

lengths, respectively, with evidence of dose-response relationship (P for trend < 0.05). The difference between participants of the same chronological age with low and high cadmium exposure is equivalent to 11 years of calendar age. No association was found between lead levels and telomere length.

Since other studies have shown an association between shorter leukocyte telomere lengths and diseases of aging, including cardiovascular disease, type 2 diabetes, dementia, and cancer, the new findings provide insight into the biological mechanisms underlying cadmium exposure and chronic disease risks.

Citation: Zota AR, Needham BL, Blackburn EH, Lin J, Park SK, Rehkopf DH, Epel ES. 2015. Associations of cadmium and lead exposure with leukocyte telomere length: findings from National Health and Nutrition Examination Survey, 1999-2002. *Am J Epidemiol* 181(2):127-136.

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U.S.-wide study links autism with prenatal exposure to fine particulate air pollution

In one of the first U.S.-wide studies of air pollution and autism, NIEHS grantees report that women exposed to high levels of fine particulate matter during pregnancy — particularly in the third trimester — may have up to twice the risk of having a child with autism than mothers exposed to low levels of particulate matter.

The study examined the children of people living in all 50 states who were part of the Nurses' Health Study II, a cohort of more than 116,000 U.S. female nurses. From this group, the researchers identified 245 children with autism and a control group of 1,522 children without autism. They collected data on where participants lived during pregnancy and then predicted their exposure to airborne particulate matter, using previously validated spatiotemporal models based on data from the U.S. Environmental Protection Agency Air Quality System and various other sources.

The analysis showed that exposure during pregnancy to particulate matter with diameters less than or equal to 2.5 microns was significantly associated with an increased risk for autism. Exposure before or after pregnancy did not show such association. The association was stronger for exposure experienced during the third trimester, compared to the first and second trimesters. The scientists found little association between larger-sized particle air pollution and autism.

The researchers say that their findings suggest that air pollution is a modifiable risk factor for autism, and that reducing exposure during pregnancy could help lower the incidence of this neurodevelopmental disorder.

Citation: Raz R, Roberts AL, Lyall K, Hart JE, Just AC, Laden F, Weisskopf MG. 2014. Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case-control analysis within the Nurses' Health Study II cohort. *Environ Health Perspect*; doi:10.1289/ehp.1408133 [Online 18 December 2014].

(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 Deacquinita Diggs, Gabriel Knudsen, Deepa Singh, Shannon Whirledge, and Annah Wyss

- NTP uses new tool for analysis of rodent mammary gland development
- Discontinuation of tamoxifen may blunt benefit of breast cancer prevention
- Estrogen directs uterine biology in cell-type manner
- New class of PUF protein family as revealed via its structure
- NIEHS researchers explore new mechanisms of arsenic toxicity

NTP uses new tool for analysis of rodent mammary gland development

Scientists from the National Toxicology Program (NTP) Laboratory have successfully adapted the Sholl analysis as a method for assessing alterations in rodent mammary gland development following chemical exposure. The Sholl analysis is traditionally used to measure the complexity of branching neuronal dendrites, but this study demonstrates that it can also be used as an accurate, simple, quick, and cost-effective tool for examining changes in epithelial branching in the rodent breast.

Mammary gland whole mounts were obtained from a [previous study](#), in which timed pregnant rats were exposed to vehicle alone or ethinyl estradiol (EE), which is an endogenous estrogen used in birth control pills. Although histopathological analysis by the National Center for Toxicologic Research pathologists did not report any adverse effects in the rat mammary gland, the Sholl analysis revealed growth and developmental changes. The Sholl analysis indicated greater epithelial growth and enhanced branching density throughout the mammary epithelium of EE-treated rats compared with those of vehicle-exposed rats.

Because laboratories use a variety of techniques for measuring mammary gland development, the authors propose the use of the Sholl analysis as a reliable, standardized method for assessing changes in mammary gland development following chemical exposure. **(DD)**

Citation: [Stanko JP](#), [Easterling MR](#), [Fenton SE](#). 2014. Application of Sholl analysis to quantify changes in growth and development in rat mammary gland whole mounts. *Reprod Toxicol*; doi:10.1016/j.reprotox.2014.11.004 [Online 15 November 2014].

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Discontinuation of tamoxifen may blunt benefit of breast cancer prevention

For the majority of women using tamoxifen in the Sister Study, the benefit of breast cancer prevention appeared to outweigh the risks of not using the medication. However, a sizeable proportion of users lacked evidence that benefit exceeded risks, according to NIEHS epidemiologists. Tamoxifen has been approved by the Food and Drug Administration to both prevent and treat breast cancer.

The researchers identified 788 tamoxifen users among the 50,884 women in the Sister Study, which is a prospective cohort study of initially breast cancer-free women who have a sister with previously diagnosed breast cancer. Based on a risk-benefit index developed at the National Cancer Institute, these women were classified as having no, moderate, or strong evidence that the chemopreventive benefits of using tamoxifen outweighed the risk of side effects.

The majority, or 74 percent, of tamoxifen users had moderate or strong evidence that benefits exceeded risks, whereas 20 percent lacked such evidence. Women with an intact uterus, women older than 50 years of age, and African American women appeared to have less favorable risk-benefit indexes. Nearly half, or 46 percent of users, stopped taking tamoxifen before the recommended 5 years. Women with a sister diagnosed with breast cancer before tamoxifen initiation or who reported genetic testing appeared more likely to discontinue use.

Examination of tamoxifen use for breast cancer prevention in nonclinical trial settings, such as the Sister Study, provides important insight into risk-benefit profiles in the general population. Although many women who are at higher risk for breast cancer may benefit from taking tamoxifen, high levels of discontinuation can mitigate potential gains. (AW)

Citation: Nichols HB, DeRoo LA, Scharf DR, Sandler DP. 2014. Risk-benefit profiles of women using tamoxifen for chemoprevention. *J Natl Cancer Inst* 107(1):354.

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Estrogen directs uterine biology in cell-type manner

In an article published in *Biology of Reproduction*, NIEHS researchers used genetically modified mouse models to discover how the cell-type specific responses in the uterus govern the biological response to estrogen. This study demonstrated how estrogen signaling in neighboring cells of the uterus mediates distinct physiological responses in adjacent tissues. Uncovering the transcriptional profiles of specific uterine cell populations highlighted the complex signaling network that regulates female reproductive biology and implicated dysregulation of these networks in infertility.

Estrogen released from the ovary targets estrogen receptors in the uterus to regulate growth and proliferation during female reproductive events. The uterus is a heterogeneous tissue composed of cell types with specific functions following estrogen exposure. Building from previous [discoveries](#) in which conditionally ablating the estrogen receptor from the epithelial layer of the uterus resulted in infertility and impaired estrogen action, the researchers used whole genome transcriptional analysis to identify those genes that require an epithelial estrogen receptor compared with genes that signal through neighboring stromal cells.

These studies indicate that the cell-specific response to estrogen in the uterus occurs in a temporal manner, where stromal estrogen receptor signaling is required for the initial response to estrogen, but the epithelial estrogen receptor is required for the subsequent later-phase transcriptional response in the epithelium. An understanding of the precise mechanisms by which estrogens regulate uterine biology offers insight into the etiology of infertility and oncogenesis in women. (SW)

Citation: Winuthayanon W, Hewitt SC, Korach KS. 2014. Uterine epithelial cell estrogen receptor alpha-dependent and -independent genomic profiles that underlie estrogen responses in mice. *Biol Reprod* 91(5):110.

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New class of PUF protein family as revealed via its structure

NIEHS scientists and their collaborators have obtained the first crystal structure of the human Puf-A protein. The Puf-A protein exhibits an alternative fold for the PUF-family proteins, with 11 Pumilio (PUM) alpha-helical repeats that are arranged in an L-like shape. The structure is in contrast to the classical PUF proteins that only have eight PUM repeats, which are arranged in a crescent shape. The PUM repeats are important for binding of PUF proteins to RNA with high sequence specificity.

Based on a second crystal structure of the Puf-A and DNA complex, along with biochemical studies, the scientists demonstrated that Puf-A and its yeast homologue Puf6 can bind to both RNA and DNA without any sequence specificity. The researchers also demonstrated that a conserved basic surface of the yeast homologue, Puf6, is important for RNA binding, pre-rRNA processing, and mRNA localization.

Overall, the authors believe that, similar to the many alpha-helical repeat protein families, PUM repeats can also be assembled into folds that are different from that of the classical PUF proteins, thereby possibly facilitating binding to different structured nucleic acids. **(DS)**

Citation: Qiu C, McCann KL, Wine RN, Baserga SJ, Hall TM. 2014. A divergent Pumilio repeat protein family for pre-rRNA processing and mRNA localization. Proc. Natl Acad Sci U S A 111(52):18554-18559.

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NIEHS researchers explore new mechanisms of arsenic toxicity

NIEHS researchers recently explored a novel mechanism by which low-level arsenic exposures can lead to cellular toxicity. Inorganic arsenic salts are common environmental pollutants that may be encountered in water, food, drugs, dust, or smoke. Naturally high levels of inorganic arsenic in groundwater are a source of exposure to millions of people worldwide and present a significant public health problem. Long-term arsenic exposures are associated with a wide variety of deleterious health effects, including cancers, diabetes, cardiovascular disease, nervous disorders, and reproductive toxicities.

Human fibroblasts were used to assess genome-wide mRNA expression patterns following a short-term exposure of 24 hours to sodium arsenite, a water-soluble arsenic salt. Noncytotoxic concentrations of arsenite were used in an effort to avoid secondary effects on gene expression. Using a combination of microarray analyses and real-time polymerase chain reaction, the researchers found that exposure to environmentally relevant arsenic doses actually stabilized the mRNA coding for delta-aminolevulinic synthase 1 (ALAS1), which is the rate-limiting enzyme in heme biosynthesis. This stabilization is expected to lead to increased ALAS1 enzyme expression, which would then maintain intracellular heme levels despite the parallel induction of heme oxygenase 1 (HMOX1). It had been previously assumed that changes in gene transcription were the mechanism behind arsenic-induced changes in mRNA levels, but this new research suggests that a change in mRNA stability can be a factor in some cases. **(GK)**

Citation: Qiu LQ, Abey S, Harris S, Shah R, Gerrish KE, Blackshear PJ. 2014. Global analysis of posttranscriptional gene expression in response to sodium arsenite. Environ Health Perspect; doi:10.1289/ehp.1408626 [Online 21 November 2014].

(Deacquinta Diggs, Ph.D., is a National Health and Environmental Effects Laboratory fellow in the Environmental Protection Agency Developmental Toxicity Branch. 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. Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Mechanisms of Mutation Group. Shannon Whirledge, Ph.D., is a research fellow in the NIEHS Molecular Endocrinology Group. Annah Wyss, Ph.D., is a research fellow with the NIEHS Genetics, Environment, and Respiratory Disease Group.)

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Inside the Institute

NIEHS tops \$100K for 2014 CFC

By Ian Thomas

NIEHS employees united to donate more than \$100,000 towards the 2014 Combined Federal Campaign (CFC). Much of the money raised went to local charities like [Vets to Vets United](#) and [NC First Robotics](#). Combined, the contributions of NIEHS and other National Institutes of Health institutes and centers totaled more than \$2.36 million and went to more than 24,000 charities worldwide.

“All contributions to the CFC, no matter how big or small, make an incredible difference in the lives of those they go to support,” said Erik Tokar, Ph.D., NIEHS biologist with the National Toxicology Program (NTP). “2014 saw the addition of several new charities to our roster of recipients, and it’s great to see our institute embrace them with this level of giving.”

Tokar and NTP Health Scientist Administrator Lori White, Ph.D., co-chaired this year’s NIEHS campaign.

Myriad ways to give

Since 1961, the goal of the campaign has been to provide federal personnel with an opportunity to give back to their local communities through CFC donations directed to organizations they choose. The campaign team organized activities to encourage employee involvement, including a 5K Fun Run/Walk, Fall Fest, Discovery Lake Regatta, book sale, silent auction, and bake sale.

“As an avid runner, it probably won’t shock anyone that the Fun Run is always my favorite event,” joked Liam O’Fallon, a program analyst with the NIEHS Division of Extramural Research and Training.

A culture of giving

Unlike previous years, when NIEHS donations went exclusively to charities in North Carolina, 2014 marked the first time that federal employees could give to any listed charity in the world.

“I’m always so proud of the level of generosity our employees show through the CFC,” said NIEHS and NTP Director Linda Birnbaum, Ph.D. “They’re always willing to help those in need, particularly when a charity supports a cause that speaks to them, based on their personal experiences.”



Employees from across NIEHS raised money for various charities during the 5K Fun Run/Walk. (Photo courtesy of Steve McCaw)



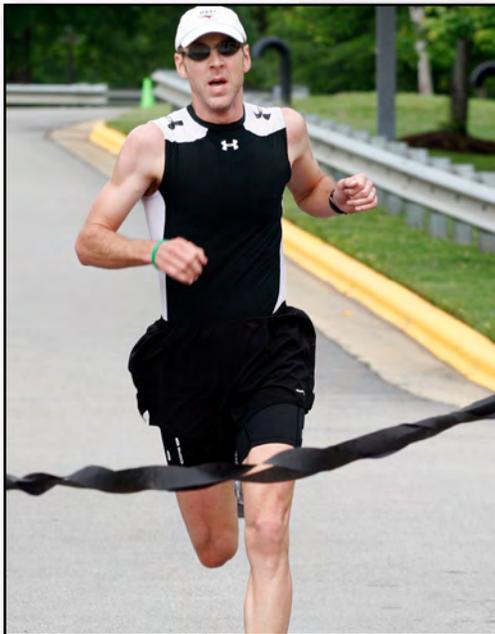
Birnbaum discussed the impact donations have on the lives of those they support, during a CFC event. (Photo courtesy of Steve McCaw)



Clyde Hasty, right, of the Health and Safety Branch took the opportunity to get to know some of the charities represented at the Fall Fest event. (Photo courtesy of Steve McCaw)



Charles Lipford and others took advantage of the book sale, to get in some early holiday shopping. (Photo courtesy of Steve McCaw)



“Anytime you get to enjoy your favorite pastime while helping those in need, you know it’s going to be a good day,” said O’Fallon, shown as he crossed the finish line of the 5K Fun Run. (Photo courtesy of Steve McCaw)



Tasty treats abounded at the bake sale. (Photo courtesy of Steve McCaw)

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

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