

March 2012

NIEHS Spotlight



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A webinar Feb. 8 highlighted research on pesticide exposure in children by scientists in the Centers for Children's Environmental Health and Disease Prevention.

Science Notebook



[Falk lecture features NYU epigenetics researcher](#)

The presentation, "Molecular Mechanisms of Epigenetic Inheritance," featured Danny Reinberg, Ph.D., a researcher who studies how epigenetics regulates gene expression.



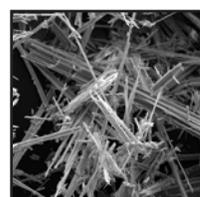
[Council talks highlight human studies of autoimmunity and immunotoxicity](#)

Members of the National Advisory Environmental Health Sciences Council heard two exciting scientific presentations at their meeting Feb. 16 at NIEHS.



[New grantee discovers treatment that may block Shiga toxin](#) ▶ Video

Somshuvra Mukhopadhyay, Ph.D., has found that manganese may prevent the potentially lethal effects of infection by a bacterial compound known as Shiga toxin.



[Interagency mineral fibers group meets at NIEHS](#)

The NIEHS commitment to mineral fibers research was front and center at the most recent meeting of the Interagency Asbestos Working Group Feb. 2-3, hosted by NIEHS.

NIEHS Spotlight



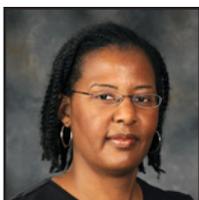
[Staff from NIEHS participates in UNC career development program](#)

The second annual Career Blitz featured 22 Ph.D.-trained scientists from a variety of traditional and non-traditional career paths.



[NIEHS grantees and research associates honored by AAAS](#)

Seven distinguished scientists with ties to NIEHS are among the 539 members of the American Association for the Advancement of Science elected as 2011 Fellows.



[Communications team recognized for intern program video](#)

NIEHS Communications staff took home a Pegasus Award of Distinction for one of its first video efforts, "Falling in love with research, students in the laboratory."



[NIEHS and NTP set to lead events at 51st SOT meeting](#)

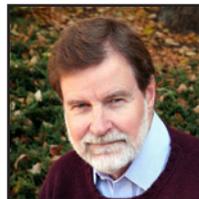
Staff from NIEHS and NTP, including Director Linda Birnbaum, Ph.D., will showcase new strategic directions, new opportunities for collaboration, and new technologies.



[Review calls for effective communication in evolutionary genomics studies](#)

NIEHS grantee Sarah Tishkoff, Ph.D., and co-authors underscore the importance of making sure that ethical evaluation keeps pace with advances in research strategies.

Science Notebook



[Researchers link oxidative stress and neurodegenerative disease](#)

Researchers from NIEHS and Florida International University offer an explanation for how degenerative nerve disorders, such as Huntington's disease, arise.



[Study finds traffic pollution leading to asthma has huge economic costs](#)

According to a new NIEHS-funded study, traditional risk assessment methods underestimate both the burden of disease and cost of asthma associated with air pollution.



[Children exposed to cadmium may be at higher risk for learning disabilities](#)

Children and teens with higher cadmium levels are more likely to have learning disabilities and be placed in special education, according to a new NIEHS-funded study.



[SRP researchers test less expensive method for tar remediation](#)

An NIEHS-funded study finds that alkaline and alkaline-polymer solutions might offer an effective and less expensive way to remove tars from gas plant sites.



[Studies find arsenic in food adds up](#)

Three studies published in the last two months with NIEHS and EPA support add to the growing body of evidence for proposals that arsenic levels in food require regulation.

NIEHS Spotlight



[Postdocs reach out to Durham middle schoolers](#) Video

NIEHS trainees launched the largest volunteer apprenticeship ever Feb. 9 in the Citizen Schools program at Lowes Grove Middle School in Durham, N.C.



[Nano consortium gathers at NIEHS](#)

The NIEHS nanotechnology consortium held its third biannual meeting Jan. 26-27 to hear research progress updates and convene a meeting of the steering committee.



[Grantee and two trainees named science communication fellows](#)

Three of the ten 2012 Science Communication Fellows announced Feb. 15 by Environmental Health Sciences are receiving training or research support from NIEHS.

Inside the Institute



[NIEHS honors African-American history with stories of runaway slaves](#)

NIEHS welcomed Freddy Parker, Ph.D., to Rodbell Auditorium for a one-hour seminar titled, "They Fled Too: Female Slave Runaways in North Carolina, 1775-1840."



[Award-winning anchor leads NIH salute to African-American history](#)

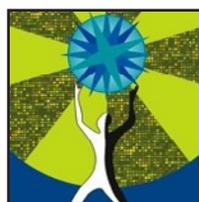
Scientists and staff gathered Feb. 16 on the NIH campus in Bethesda, Md., for the 2012 African-American History Month Observance Program featuring JC Hayward.

Science Notebook



[SRP researcher links contaminants in drinking water to mental illness](#)

Superfund researchers published findings that link early childhood exposure to PCE-contaminated water to increased risk of psychological disorders later in life.



[NIH pioneer discovers genes linked to high altitude tolerance](#) Video

A new NIEHS-funded study in Genome Biology is the latest manuscript to identify genetic adaptations prevalent in populations living in high altitudes.



[Panel peer reviews and approves seven NTP technical reports](#)

A panel of external scientific experts, convened by the National Toxicology Program, peer reviewed and approved the conclusions of seven draft technical reports.



[Webinar series addresses early-life exposures](#)

An NIEHS Superfund Research Program webinar Feb. 3 explored the potentially adverse effects of exposure to brominated fire retardants during critical windows of susceptibility.



[Federal agencies respond to test method recommendations](#)

U.S. federal agencies, including NIEHS, have agreed with recommendations for use of a method that requires fewer animals and enables pain-free product safety testing.

Calendar of Upcoming Events

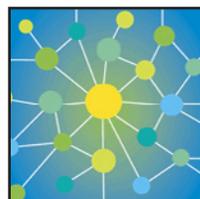
- **March 1**, in Keystone 1003, 1:00-2:00 p.m. — Keystone Lecture Seminar Series, with John Rawls, Ph.D., addressing “Microbial and developmental regulation of vertebrate energy balance”
- **March 3**, in Rodbell Auditorium, 8:30 a.m.-1:00 p.m. — 21st Annual Meeting of the Triangle Consortium for Reproductive Biology, “[Reproductive Tract Organogenesis](#)”
- **March 6-7 (offsite event)**, 8:00 a.m.-5:00 p.m., at NIH in Bethesda, Md. — Centers for Children’s Environmental Health and Disease Prevention Research Meeting
- **March 7-8 (offsite event)**, 8:00 a.m.-5:00 p.m., at NIH in Bethesda, Md. — Partnerships for Environmental Public Health Meeting
- **March 9**, in Keystone 1003, 2:00-3:00 p.m. — Keystone Lecture Seminar Series, “Assessing the Impact of Research,” by Kristi Holmes, Ph.D.
- **March 12 (offsite event)**, 1:30-2:30 p.m., in 3503 Thomas Hall, North Carolina State University — Department of Genetics Seminar, featuring Karen Adelman, Ph.D., topic TBA
- **March 21-22 (offsite event)**, 8:00 a.m.-5:00 p.m., at the Raleigh (N.C.) Convention Center — South Atlantic National Research Conference (SANRC), [registration](#)
- **March 23**, in Rodbell Auditorium, 8:30 a.m.-4:00 p.m. — Annual North Carolina Environmental Stewardship Initiative Meeting
- **March 26-29 (offsite event)**, 8:00 a.m.-5:00 p.m. — Environmental Health Sciences Core Centers Meeting
- **March 27 (offsite event)**, 12:00-1:00 p.m., at Sigma Xi in Research Triangle Park, N.C. — Sigma Xi lunchtime lecture series with Sri Nadadur, Ph.D., speaking on nanomaterials and health
- **March 27-29 (offsite event)**, 8:00 a.m.-5:00 p.m., at the Hyatt Regency Pier 66, Fort Lauderdale, Fla. — Worker Education and Training Program Awardee Meeting and National Trainers’ Exchange: “Training Today for a Safer Tomorrow”
- View More Events: [NIEHS Public Calendar](#)

Science Notebook



[This month in EHP](#) Audio

The lead story in this month’s issue examines the hypothesis that photosynthetic bacteria may be a major factor in neurodegenerative disease.



[Upcoming workshop on individual susceptibility](#)

An innovative interagency program opens its 2012 workshop series with an exploration of individual susceptibility to environmental stressors April 18-19 in Washington, D.C.

Extramural Research

[Extramural papers of the month](#)

- [Obesity and childhood phthalate exposure](#)
- [The cost of asthma from traffic-related air pollution](#)
- [Childhood exposure to tetrachloroethylene and later mental illness](#)
- [New zebrafish line for studying aryl hydrocarbon receptor](#)

Intramural Research

[Intramural papers of the month](#)

- [EET research may help in the fight against cancer](#)
- [Early-life soy exposure and gender-role play behavior in children](#)
- [Tet1 is essential for pluripotency in mouse embryonic stem cells](#)
- [The role of CD103\(+\) dendritic cells in allergic lung inflammation](#)

NIEHS Spotlight

Strategic planning shapes discussion at Council meeting

By Eddy Ball

Even though it was scheduled as a 45-minute presentation during the first session of the group's winter meeting Feb. 15-16, an update on [NIEHS strategic planning](#) struck a chord with members of the [National Advisory Environmental Health Sciences Council](#). The combination of a sobering report on budget prospects by NIEHS/NTP Director Linda Birnbaum, Ph.D., and the presentation of the preliminary NIEHS strategic plan by Deputy Director Rick Woychik, Ph.D., helped shape several of the discussions that followed.

Birnbaum opened the meeting with an [overview](#) of some of the exciting accomplishments by NIEHS employees and grantees since the last Council meeting in September 2011, including the final steps toward recruitment of her permanent leadership team. Early on in her report, Birnbaum showed her audience figures on the NIH, NIEHS, Superfund Research Program, and Worker Education and Training budgets that underscored the challenges that lie ahead for NIEHS and its grantees.

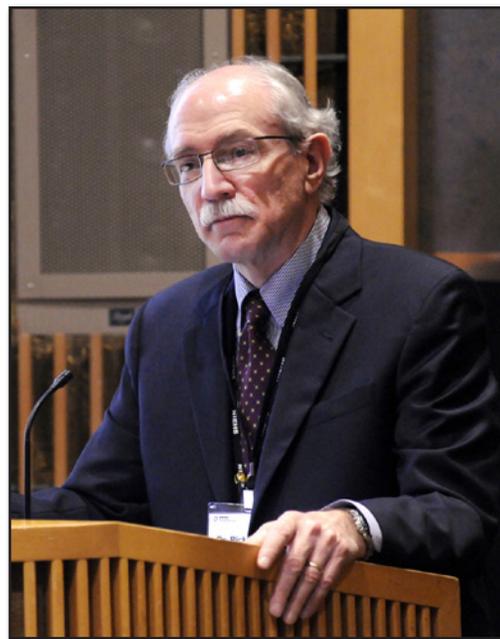
"Given the economy, NIH and NIEHS are doing pretty well," Birnbaum told the members. On several occasions during the two-day meeting, she also reminded her audience of the task facing the Institute. "Flat budgets really mean declining budgets.... In order to embark on new initiatives [such as those inspired by strategic planning], there are things that will have to come to an end."

Moving forward in a new budgetary landscape

Woychik's [presentation](#) sparked a discussion of the NIEHS mission, vision, structural pillars, and strategic goals that continued an hour beyond its scheduled time and generated some creative thinking about how to advance environmental science with limited resources. Birnbaum, who has spoken often of the one NIEHS concept, emphasized that part of the strategic planning process involves better coordination of the Institute's research divisions to maximize accessibility to resources.



Birnbaum listed a number of important studies published by NIEHS scientists and grantees since the last Council meeting in September 2011, along with high-profile meetings about autism, neurotoxicity, nanomaterials, and bioinformatics. (Photo courtesy of Steve McCaw)



Thanking members for their thoughtful input on the strategic plan, Woychik said, "The process of strategic planning is as important as the finished product." For many Council members, that process continued throughout their two-day meeting. (Photo courtesy of Steve McCaw)

NIEHS Scientific Director Darryl Zeldin, M.D., described efforts on the NIH level to similarly reduce duplication and make clinical research resources more available to extramural researchers. He cautioned, however, “It’s a two-way street.” For resource sharing to become most effective, he said, underutilized inpatient clinical resources at university hospitals should become more accessible for intramural scientists.

While some members wanted to wordsmith the mission and vision statements of the draft strategic plan, they seemed unanimous in their support of its call for much more collaboration and partnership to foster the kind of team science that is needed to impact complex public health issues. As Woychik explained, Council will revisit the strategic plan at its May meeting, when he is slated to present the latest draft for the group’s consideration.

Revisioning the way grants are managed

Returning to its original agenda, Council members heard a report on the [Draft NTP Monograph on Health Effects of Low-level Lead](#) and its peer review in November 2011 ([see story](#)), before moving into a presentation on the NIEHS grants portfolio and the grant award process by NIEHS Division of Extramural Research and Training Director Gwen Collman, Ph.D.

Along with showing pie charts indicating the percentages of grants according to mechanism and average size of various types of grants, Collman described options for fine-tuning NIEHS funding philosophies in the years ahead. “We’re always trying to make the most awards with the funds available,” she said. “But we [also] need to be seriously dealing with constraints in our budget.”

The options she presented to Council included setting caps to larger awards and making across-the-board cuts to grants, while also aligning funding with strategic planning goals and maintaining parity in success rates for young and senior investigators. “We want to be perceived as being fair,” Collman explained.

New initiatives and science talks

The second day of the meeting opened with a concept presentation on “[Microbiome/Environment Interactions](#)” by NIEHS Health Scientist Administrator Lisa Chadwick, Ph.D., which members approved. Other reports focused on the [U.S. Food and Drug Administration \(FDA\)/NIH Tobacco Initiative](#) ([see text box](#)) and efforts to enhance trainee outcome tracking.



Council members Grace LeMasters, Ph.D., left, and Stephen Lloyd, Ph.D., listened carefully to Woychik’s presentation. Lloyd said afterwards, “I think this is a really fantastic start,” but he also cautioned, “There may have to be as much of a paradigm shift in funding as how you identify the goals.” (Photo courtesy of Steve McCaw)

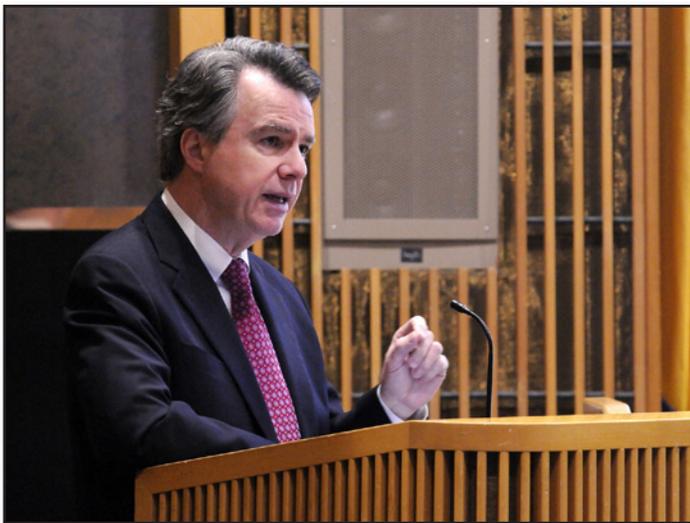


Member Palmer Taylor, Ph.D., sparked a discussion of ways to maximize resources. “Is there a way to coordinate these institutions and cores?” he asked. Seated with him are Julia Brody, Ph.D., left, and Andrea Hricko. (Photo courtesy of Steve McCaw)

The final two hours of the meeting were devoted to presentations on human research by NIEHS Acting Director of Clinical Research Fred Miller, M.D., Ph.D., and grantee Philippe Grandjean, M.D. ([see related story](#)).



Collman had obviously devoted a lot of thought to balancing strategic plan initiatives and budgetary constraints. She presented several options, but she was also eager to hear suggestions from Council members, several of whom are themselves grantees. (Photo courtesy of Steve McCaw)



Croyle described new funding opportunities to better understand how to prevent some of the 443,000 deaths each year in the U.S. from tobacco use and secondhand smoke. (Photo courtesy of Steve McCaw)

New funding for tobacco research

Along with reports on NIEHS activities, Council heard a report on new funding opportunities resulting from the [Family Smoking Prevention and Tobacco Control Act](#), by [Robert Croyle, Ph.D.](#), director of the Division of Cancer Control and Population Sciences at the National Cancer Institute (NCI). Signed into law June 22, 2009, the law empowers FDA to regulate the manufacture, marketing, and distribution of tobacco products to protect public health. The legislation authorizes the collection of user fees to fund regulatory activities. According to Croyle, about \$150 million of the \$500 million to be collected during fiscal year 2012 will be spent on regulatory-relevant scientific research.

Croyle made two important points about the program. The [research parameters](#) are very explicit, he said, restricting funding to science that can help FDA understand tobacco and its ingredients and constituents, tobacco addiction, tobacco marketing and labeling, and childhood tobacco use to inform regulatory efforts. Croyle pointed to smoking cessation studies as the kind of tobacco research that would not qualify under the program. FDA is currently preparing official guidelines for research that can be supported.

The second point Croyle emphasized was the program's independence. The tobacco industry, he noted, has absolutely no control over how the user fees are spent or the scope of FDA regulatory activities.

Participating NIH institutes are NCI; NIEHS; the National Heart, Lung, and Blood Institute; the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; the National Institute on Drug Abuse; and the National Institute of Mental Health.

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Workshop seeks to expand and improve data sharing

By Ernie Hood

Nearly 100 environmental health researchers, NIEHS program administrators, and other interested government officials gathered Feb. 6-7 in Research Triangle Park, N.C., to work together on the emerging practice known as data sharing.

Data sharing is well established in the genomics realm, with clear rules and guidelines in place for scientists to make their data broadly and quickly accessible to others. With environmental health science (EHS) data, however, the issues are more complex. That led NIEHS to issue a Request for Information (RFI) in June 2011, soliciting input and recommendations from the EHS research community, to use as the foundation for the Data Sharing Strategies for Environmental Health Science Research Workshop.

Why share environmental health science data?

In her opening remarks, NIEHS Division of Extramural Research and Training Director Gwen Collman, Ph.D., said there are solid reasons for NIEHS to work to expand EHS data sharing. “We at the Institute are quite interested in maximizing the NIH investments in the research we have funded over the years, to expand the opportunity for secondary analyses, for merging existing data resources, and for coordination between the various institutes’ missions, and, in general, to address some very common and challenging, complex disease/ environmental exposure relationships,” she noted.

The meeting’s first keynote presentation by Bruce Lanphear, M.D., also addressed that question. Lanphear, a professor of children’s environmental health at Simon Fraser University in Vancouver, British Columbia, and a pioneer in research on the adverse effects of environmental lead exposures, explained that roughly 80 percent of the scientists in the audience had at some point relied on data collected by someone else.

“That’s one of the main reasons we should share data,” Lanphear said. “If we want our data to matter, if we want it to be useful, we should expect it to be public. We should be willing to share it.”

Broad themes and unique considerations

In presentations from experts and in discussions, workshop attendees addressed each of the major themes that emerged from the responses to the RFI, including protection of privacy and confidentiality, Institutional Review Board issues, legal and regulatory issues, NIH programmatic and logistical considerations, and computational challenges. Attendees also explored the many unique aspects of EHS data sharing (see text box) that were part of the driving force for convening the meeting, with an eye toward eventually shaping best practices and guidelines.



In her presentation, Collman discussed the goals and purposes of the workshop, as well as next steps for broadening opportunities for EHS data sharing. (Photo courtesy of Steve McCaw)



Meeting co-organizer McAllister helped set the stage for the intimate two-day workshop. (Photo courtesy of Steve McCaw)

“We felt that there are particular issues with environmental health science data that are not there for gene-centric data,” said Kim McAllister, Ph.D., an NIEHS program administrator who co-organized the workshop. “So we want to make sure that any guidelines or recommendations we give our grantees would incorporate those unique considerations.”

One key concept that emerged during the workshop was the recognition that there is no single idea when it comes to data sharing. “It seems to me that we are talking about three different kinds of data sharing,” noted Howard Andrews, Ph.D., from the Columbia Center for Children’s Environmental Health.

“There’s data sharing that is voluntary and collaborative, there’s data sharing that is voluntary and non-collaborative,” Andrews said, “and, then there’s data sharing that is involuntary,” such as data sharing required by litigation or Freedom of Information Act requests. “There needs to be a framework that takes into account, in all three of those categories, a variety of aspects, such as adequacy of funding, adequacy of consent, conflict of interest issues, and more.”

McAllister said that the next step in the process is likely to be smaller follow-up workshops “to really flesh out some of these particular themes, just taking one of those areas and having some experts in that area in a think-tank sort of setting.” Ultimately, the goal is to delineate a broad NIEHS data-sharing strategy that will help overcome some of the current impediments to data sharing and foster collaborative, cross-disciplinary research.



In addition to strongly advocating data sharing, Lanphear called for the establishment of a mechanism for independent reanalysis of environmental health studies. (Photo courtesy of Steve McCaw)



Each of the workshop’s panel members related their own experiences with sharing of exposure data, including the biggest obstacles or hurdles they had encountered, and made recommendations for how to shape data-sharing plans. (Photo courtesy of Steve McCaw)

Unique considerations for the sharing of environmental health data

- The variation of environmental and biological measurements
- The potential to identify individuals based on the association of environmental exposures with geographical data
- The increased interest in return of individual or community-level environmental research results
- The regulatory implications of the use of environmental exposure and health data in developing U.S. national research policies
- The unique concerns of vulnerable populations who are disproportionately impacted by environmental exposures



Panel discussion participant Dale Sandler, Ph.D., right, chief of the NIEHS Epidemiology Branch, described some of the data-sharing considerations she has dealt with during the GuLF STUDY, the Agricultural Health Study, and the Sister Study. (Photo courtesy of Steve McCaw)



Panel member Howard McLeod, Pharm.D., director of the Institute for Pharmacogenomics and Individualized Therapy at the University of North Carolina at Chapel Hill, described his experiences with data sharing in the realms of pharmacogenomics and oncology. (Photo courtesy of Steve McCaw)

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

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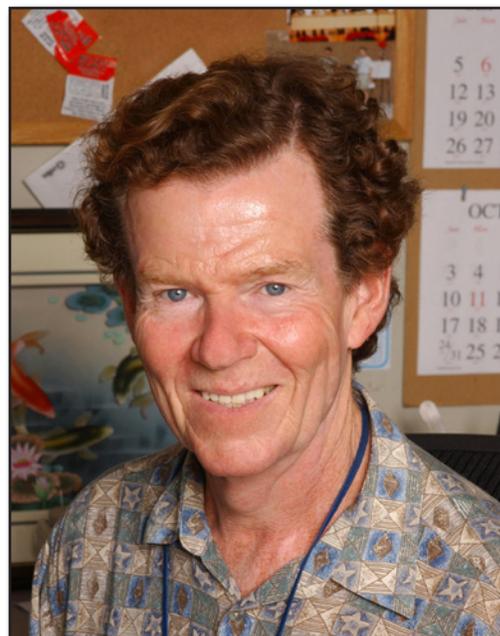
Rogan honored by the American Academy of Pediatrics

By Ian Thomas

NIEHS epidemiologist [Walter Rogan, M.D.](#), was named an honorary fellow by the [American Academy of Pediatrics](#) (AAP) for his exemplary service with the organization's Council on Environmental Health. Currently the head of the NIEHS Pediatric Epidemiology Group, Rogan has been a lead scientist and expert in the field of children's health for nearly four decades.

“My association with the Academy dates back quite a while now,” said Rogan, NIEHS liaison to AAP for 35 years. “In that time, we’ve made some remarkable strides toward increasing the public’s understanding of how the environment can impact children’s health. It’s been a privilege to have been a part of that endeavor, and I sincerely look forward to doing more in the future.”

Having worked extensively on several key pediatric issues, ranging from lead poisoning and well water safety to the effects of plant estrogens in soy-based products for infants, Rogan is widely recognized as one of the field’s leading minds with regard to environmental health and human growth and development. Over time, that expertise led him to author a number of AAP educational



Newly elected AAP honorary fellow Rogan
(Photo courtesy of Steve McCaw)

and policy materials, including several chapters in its Handbook of Pediatric Environmental Health, otherwise known as the Green Book.

“AAP is pleased to recognize Dr. Rogan for his incredible work in the field of children’s environmental health, as well as his longevity as a valued member of this committee,” said Jerome Paulson, M.D., the chairperson for AAP’s executive committee of the Council on Environmental Health and a professor of pediatrics and public health at George Washington University. “He’s been an outstanding link between the Academy and NIEHS, and his scientific input has been essential to maintaining the productivity and credibility of this committee’s work.”

Founded in 1930, the mission of AAP is to attain optimal physical, mental, and social health and well-being for all infants, children, adolescents, and young adults, by supporting the needs of its professional members. At present, the Academy has roughly 60,000 members in both primary care and subspecialty areas.

“All of us here at NIEHS want to congratulate Dr. Rogan on this terrific accomplishment,” said NIEHS/NTP Director Linda Birnbaum, Ph.D. “Walter has worn a lot of hats in his years with this Institute, and it’s that rich experience that makes him the perfect person to represent our mission with the Academy.”

Rogan received an M.D. from the University of California, San Francisco and an M.P.H. from the University of California, Berkeley, before arriving at NIEHS in 1976. Since that time, he has served as the Institute’s acting clinical director, as well as chief of the Epidemiology Branch and associate director of the Division of Biometry and Risk Assessment.

Rogan will officially be presented with an Honorary Fellow award at the May 21 AAP meeting in Washington, D.C.

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

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USGS support to advance erionite research

By Cindy Loose

A new award from the U.S. Geological Survey (USGS) will enable scientists from NIEHS and elsewhere to gather and explore the mysteries and hazards of a fibrous mineral thought to be many times more toxic than asbestos. The funding announced Feb. 8 will support working group retreats at the USGS [John Wesley Powell Center for Analysis and Synthesis](#) in Fort Collins, Colo.



A naturally occurring mineral listed as a carcinogen in the NTP [Report on Carcinogens](#), erionite is linked to increased risks of mesothelioma, lung cancer, and fibrogenic lung disease in Turkey. Deposits of the mineral have been identified in at least 12 U.S. states, according to USGS scientists ([see text box](#)).

Despite erionite’s potential threat to public health, most people have never heard of it and research is limited. There are no standards for mining or using rock containing erionite, and it has been used in at least one state to pave hundreds of miles of roads.

Raising awareness in the public health community

Last fall, NIEHS Senior Medical Advisor [Aubrey Miller, M.D.](#), organized and chaired an NIEHS-sponsored [workshop](#) that focused specifically on understanding the science, toxicology, and health implications of this mineral fiber. “We already know that erionite is a deadly substance. Based on what we have learned, we need to raise public awareness and, at the very least, prevent further exposure,” said NIEHS Senior Toxicologist [Chris Weis, Ph.D.](#), who also helped plan the workshop.

One of the immediate results of last fall’s workshop, attended by 30 scientists from a wide variety of disciplines, was a very rapid worker advisory issued by the [National Institute for Occupational Safety and Health \(NIOSH\)](#), warning of the dangers of erionite and listing protective measures to avoid exposure. The workshop also resulted in the development of the proposal to the Powell Center, which will cover travel and associated costs for meetings there over the next two years. The new award will enable researchers to continue their directed collaboration on erionite issues at state-of-the-art facilities designed for this purpose. The interdisciplinary erionite proposal, prepared by Miller and Gregory Meeker, a geologist with USGS, is one of five awarded by the Powell Center in 2012.

“The grant will act as a catalyst for new ideas,” said Miller. “Working collectively, people who bring different perspectives and areas of expertise can advance much more quickly on what is a complicated and important public health problem.”

One focus area cited by workshop participants is to update old maps showing locations of erionite deposits in the U.S. Such locations can then undergo further evaluation and, where indicated, the public and policymakers could be made aware of any potential dangers. Efforts will also be focused on standardizing mineral identification, sampling and analysis strategies, understanding exposures, and public health prevention.

The team of scientists who will coordinate research and share findings, thanks to the Powell Center support, include experts from NIEHS, NIOSH, the Agency for Toxic Substances and Disease Registry, and the universities of Cincinnati, Hawaii, Nevada, and North Dakota.



Miller is the NIEHS lead for asbestos and erionite research. (Photo courtesy of Steve McCaw)



Weis is the NIEHS Office of the Director lead on engineered nanomaterials (ENMs) research. He is interested in the similarities in physical characteristics among ENMs and mineral fibers. (Photo courtesy of Steve McCaw)

Erionite in the scientific literature

Erionite was originally a hot topic in the 1970's, after high rates of mesothelioma were identified in Turkey. Erionite, released when the rock is disturbed, has created cancer villages in parts of Turkey where rock containing erionite has been used for decades as a building material. In the worst hit villages in some years, almost half of all deaths have been from malignant mesothelioma, according to a [study](#) published in BMJ. Under normal circumstances mesothelioma is rare, affecting about one in a million people.

Interest in erionite in the U.S. spiked last year, after publication of a [study](#) led by Miller and [Michele Carbone, M.D., Ph.D.](#), director of the University of Hawaii Cancer Center. In this study, researchers took air samples from Dunn County, N.D., and from Turkish villages where high rates of mesothelioma were known to be associated with erionite exposure. The study found that airborne erionite concentrations measured in N.D. along roadsides, indoors, and inside vehicles, including school buses, equaled or exceeded concentrations in Boyali, a village in Turkey, where 6.24 percent of all deaths are caused by malignant mesothelioma.

Lack of awareness resulted in stone laced with erionite being ground into gravel and used to pave approximately 300 miles of road in Dunn County, according to the North Dakota Department of Health. The Centers for Disease Control and Prevention caution that disease caused by exposure may go unrecognized for decades, because of a latency period for mesothelioma of 30 years or more.

Citations:

[Baris YI, Sahin AA, Ozesmi M, Kerse I, Ozen E, Kolacan B, Altinörs M, Göktepe A.](#) 1978. An outbreak of pleural mesothelioma and chronic fibrosing pleurisy in the village of Karain/Urgüp in Anatolia. *Thorax* 1978 Apr;33(2):181-192.

[Carbone M, Baris YI, Bertino P, Brass B, Comertpay S, Dogan AU, Gaudino G, Jube S, Kanodia S, Partridge CR, Pass HI, Rivera ZS, Steele I, Tuncer M, Way S, Yang H, Miller A.](#) 2011. Erionite exposure in North Dakota and Turkish villages with mesothelioma. *Proc Natl Acad Sci U S A.* 108(33):13618-13623.

(Cindy Loose is a contract writer supporting staff at the NIEHS office in Bethesda, Md.)

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NIEHS and EPA launch 2012 webinar series

By Eddy Ball

With a focus on translation and disease prevention, a webinar Feb. 8 highlighted research on pesticide exposure in children by scientists in the [Centers for Children's Environmental Health and Disease Prevention](#), funded jointly by NIEHS and the U.S. Environmental Protection Agency (EPA).



The broadcast, which was the first in a Children's Centers [2012 Webinar Series](#), featured [Elaine Faustman, Ph.D.](#), of the University of Washington, and [Asa Bradman, Ph.D.](#), of the University of California, Berkeley. On the second Wednesday of each month, the series will offer presentations of findings on different aspects of children's environmental health, the research behind them, and their relationship to outreach and translation efforts by the centers toward protecting children from environmental threats for a lifetime ([see text box](#)).

NIEHS program director Kimberly Gray, Ph.D., who directs the Children's Centers program, said of the series, "This is a great way to build on our partnership with EPA and to broadly raise awareness of children's environmental health issues and the important contributions to public health by the science supported with in the Children's Environmental Health program."

Children are uniquely susceptible at home and in daycare

While both presenters focused on indoor environments, Faustman's research studied the homes of Yakima Valley, Wash., farm workers who bring organophosphate (OP) pesticides home from the fields on their clothing, while Bradman investigated exposures to indoor pesticides and other chemicals in California daycare facilities.

In both environments, children are exposed to contaminated dust, which they are likely to ingest because of their hand-to-mouth and crawling behaviors. As Bradman observed, children spend most of their time indoors, they have higher exposures than adults, and their developing bodies metabolize chemicals less efficiently than do the bodies of adults.

As the presenters pointed out, understanding and determining what exposures are harmful, and how to intervene and reduce exposures is essential. In her 2008 intervention study, Faustman wrote, "The social implications of such neurologic impairments can be far reaching," potentially reducing intelligence quotients and impacting special education programs.

Translating research into public health interventions

Intervention strategies by Faustman and Bradman were tailored to fit their different situations. Faustman's group launched a community-wide intervention, via a community randomized study, to reduce pesticide exposure among farm workers and their children. The two-year, comprehensive plan included activities at the community, organizational, small group, and individual levels. Intervention components were based on the existing literature and recommendations of the community advisory board formed at the initiation of the study.



Bradman underscored the importance of the childcare environment in health. He said 13 million children attend daycare nationwide. There are 50,000 licensed facilities in California alone. (Photo courtesy of Asa Bradman)



During the question and answer portion of the webcast, Faustman addressed emerging issues in children's environmental health. "If there's one area out there that's the giant in the room," she responded, "it's engineered nanomaterials — especially for children." (Photo courtesy of Steve McCaw)

The researchers tested a cohort of 571 households. They tested for metabolites of OP in samples collected from 202 adults and 204 children, and in house and vehicle dust from 203 and 177 households, respectively. One finding from the analysis was the seasonality of metabolite levels, which peaked during the spring when plants are thinned and sprayed to increase yield.

Bradman's intervention efforts arose from questionnaire information about chemicals and pesticide use in daycare facilities, which indicated that 69 percent of pest management was performed by pest control companies. Sample collection and analysis from 40 sites also sparked interest among daycare operators.

One especially effective intervention was outreach to educate pest control workers and center directors about the concept of [Integrated Pest Management \(IPM\)](#). IPM is a tiered approach that begins with household maintenance, such as cleaning and control of food and water sources. IPM reserves the use of pesticides for later stage control, rather than for prevention, and advocates use of closed pest control devices, instead of sprays that increase children's exposures.

"These are environments that should have better interventions," Bradman told webinar participants. Fortunately, he added, there is growing interest and awareness in California and nationwide.

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Staff from NIEHS participates in UNC career development program

By Robin Arnette

In the search for a satisfying career, students generally concentrate on doing well academically, but understanding what it takes to land that perfect job is just as important as acing exams. After all, if you could ask Bill Gates how he became an entrepreneur or pick Steven Spielberg's brain for movie-making advice, wouldn't you take advantage of the opportunity?

The University of North Carolina (UNC) School of Medicine attempted to give graduate students and postdoctoral fellows a similar opportunity by holding its second annual [Career Blitz](#) Jan. 25 in Chapel Hill. Sponsored by the UNC [Training Initiative in Biomedical and Biological Sciences \(TIBBS\)](#), the event featured 22 Ph.D.-trained scientists from a variety of traditional and non-traditional career paths. NIEHS was well represented, with nine current or former staff members serving on the panel ([see text box](#)). TIBBS Director Erin Hopper, Ph.D., and her supervisor Patrick Brandt, Ph.D., are also former NIEHS employees.

"The TIBBS program was started at UNC in 2007, to give graduate students opportunities to explore a variety of career options open to scientists and to develop the non-bench skills required for success in those careers,"

Sign up for the next Children's Center webinars

March 14:

- Biomarkers to predict and monitor asthma therapy, by Stanley Szeffler, M.D., of National Jewish Health
- Environmental triggers of asthma exacerbation, by Rachel Miller, M.D., of Columbia University

April 11:

- Developmental origins of male reproductive tract disorders, by Kim Boekelheide, M.D., Ph.D., of Brown University

The Feb. 8 webinar, like ones to follow, was recorded and will be archived online.

said Brandt, who is director of Science, Training, and Diversity. “Nearly 100 students and postdocs participated in our first Career Blitz event held in February 2011.”

Hopper joined the TIBBS team in November 2011, and the NIEHS ties that she and Brandt share meant that they had a ready-made pool of scientists to choose from. Hopper said she relied heavily on the scientific expertise at the Institute, inviting scientists from policy, grants administration, and basic research. Based on the students’ excitement, the planning paid off.

“This year’s event was a great success, with twice as many registrants as last year,” Hopper said.

Sheila Newton, Ph.D., director of the NIEHS Office of Policy, Planning, and Evaluation, was one of this year’s panelists. She believes that these kinds of programs are important and play a vital role in career development.

“There are so many ways in which scientific training can be an asset in the worlds of policy, science management, regulatory affairs, and journalism, to name a few, yet it’s often difficult for students to learn about these career options,” Newton said.

Making an impact

The scientists were grouped into eleven categories, with a pair from each career path stationed in adjacent rooms in UNC’s MacNider Hall. Students interested in a particular career could visit a room and hear a brief presentation and then ask a variety of questions, such as the scientist’s current job responsibilities, the route they took to their present position, and what happens during a typical work day. The sessions were staggered, so that the professionals could speak to students in large groups or have informal one-on-one discussions.

At the end of the program, students were asked to fill out evaluations, and they overwhelmingly gave the TIBBS Career Blitz high marks. Here are a few responses to the question, “What did you find most beneficial about the career blitz?”

- “The spectrum of careers was quite broad. Since I do not know what I want to do after graduating, it was helpful to see a broad range of jobs and narrow down my choices,” one wrote.
- “Getting to ask questions of the people who are out in the work force and actually getting real, honest answers,” noted another.



Newton, left, and Michael Humble, Ph.D., a health scientist administrator in the NIEHS Division of Extramural Research and Training, geared up for the afternoon. (Photo courtesy of Robin Arnette)



Bolick, left, and Harriet Kinyamu, Ph.D., a staff scientist for the NIEHS Laboratory of Molecular Carcinogenesis, reminisced about the Institute during a quick break. (Photo courtesy of Robin Arnette)

Although the students got a lot out of the sessions, the panel participants did as well. Sophie Bolick, Ph.D., a medical writer with [MedThink SciCom](#), is a former NIEHS postdoc and contributing writer to the Environmental Factor. Having been in the work force for a little over a year, she could empathize with the students.

“The UNC Career Blitz was a great experience from the other side of the table,” said Bolick. “Students and postdocs alike were very receptive to our suggestions and comments, and came prepared with great questions, which made the experience a lot of fun.”



Donna Baird, Ph.D., right in red, is a principal investigator in the NIEHS Epidemiology Branch. She and Kinyamu helped students prepare for a research career in a government lab. (Photo courtesy of Erin Hopper)



UNC representatives Ann Marie Bartholomew of the Office of Graduate Education, left, and Ashalla Freeman, Ph.D., director of Diversity Affairs, staffed the snack table in the refreshment room. (Photo courtesy of Robin Arnette)

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2012 TIBBS Career Blitz Panel

Following is a list of the career paths and science professionals at the Career Blitz. The names of current and former NIEHS staff are in **bold**.

Research in Big Pharma

- Richard Peterson, D.V.M., Ph.D.
- Jennifer McCafferty, Ph.D.

Research in Small Biotech

- **Kelly Mercier, Ph.D.**
- **Jimmy Smedley, Ph.D.**

Teaching-Intensive Careers

- Kassy Mies, Ph.D.
- Christopher Roy, Ph.D.

Research in Government Laboratories

- **Donna Baird, Ph.D.**
- **Harriet Kinyamu, Ph.D.**

Science Writing and Editing

- **Robin Arnette, Ph.D.**
- **Sophie Bolick, Ph.D.**

Science Administration and Outreach

- Joshua Hall, Ph.D.
- Amanda Marvelle, Ph.D.

Science Policy and Grants Management

- **Sheila Newton, Ph.D.**
- **Michael Humble, Ph.D.**

Intellectual Property

- Karthik Gopalakrishnan, Ph.D.
- Nathan Letts, J.D., Ph.D.

Business Development and Regulatory Affairs

- Brandy Salmon, Ph.D.
- Ayoola Aboyade-Cole, Ph.D.

Principal Investigator, Academic and Nonprofit Institutes

- Kathy Franz, Ph.D.
- Alison Harrill, Ph.D.

Research Roles in Academia

- **Allison Schorzman, Ph.D.**
- George Dubay, Ph.D.

NIEHS grantees and research associates honored by AAAS

By Eddy Ball

Seven distinguished scientists with ties to NIEHS are among the 539 members of the American Association for the Advancement of Science (AAAS) elected as 2011 Fellows. They were officially recognized for their contributions to science and technology at the Fellows Forum Feb. 18 at the annual meeting of AAAS in Vancouver, British Columbia, with a certificate and a blue and gold rosette as a symbol of their distinguished accomplishments.

NIEHS/NTP Director Linda Birnbaum, Ph.D., offered her congratulations to the new fellows. “This level of recognition by your peers is an important milestone in your scientific careers,” she said. “The NIEHS community is proud to have helped support your outstanding work.”

AAAS began electing fellows in 1874, an honor bestowed upon members by their peers. Fellow nominations may be made by the steering groups of the association’s 24 sections, by the chief executive officer, or by any three fellows who are current AAAS members, so long as two of the three sponsors are not affiliated with the nominee’s institution. Each nominee must receive the approval of a majority of the steering group members.



Analytical chemist Caruso is founding and editorial board member of the journal *Metalomics*. (Photo courtesy of Joe Caruso)

An honor roll of NIEHS grantees and research associates

- **Joseph Caruso, Ph.D.**, of the University of Cincinnati (UC) — Caruso is being honored for distinguished contributions to the fields of trace metal analysis, speciation, and metallomics, the study of metals and metal species in biological systems, and for past service as head of the chemistry department at UC and dean of the McMicken College of Arts and Sciences.
- **Andrew Feinberg, M.D.**, of Johns Hopkins University (JHU) — Feinberg was elected for seminal contributions to our understanding of epigenetics and the role it plays in cancer and other human disease. He is the Daniel Coit Gilman Scholar and Professor of Medicine, Molecular Biology and Genetics, Oncology, and Biostatistics, as well as director of the [Center for Epigenetics](#) in the Institute for Basic Biomedical Sciences at the JHU School of Medicine.
- **Stuart Lipton, M.D., Ph.D.**, of the Sanford Burnham Medical Research Institute — Lipton studies the molecular mechanisms of neurodegenerative diseases, including the role of excessive stimulation of ion channels and redox (S-nitrosylation-mediated) signaling pathways in nerve cells. His lab developed the first neuroprotective drug, memantine (Namenda®), approved for treatment of moderate to severe Alzheimer’s disease.
- **Jason Moore, Ph.D.**, of Dartmouth College — Moore’s work centers on improving the prediction, prevention, and treatment of common human diseases such as cancer, cardiovascular disease, and psychiatric disease, through the development, evaluation, and application of statistical and computational methods for genetic, genomic, and proteomic analysis.
- **Prakash Nagarkatti, Ph.D.**, of the University of South Carolina (USC) — Nagarkatti was elected for distinguished contributions in the field of immunology, specifically immune regulation, and for providing outstanding leadership as an associate dean to advance education and research. He has also made significant contributions in the field of immunotoxicology. In November 2011, he was appointed vice president for research at USC.

- **Fernando Pardo-Manuel de Villena, Ph.D.**, of the University of North Carolina at Chapel Hill — Pardo-Manuel de Villena was recognized for contributions in the fields of mouse genetics and genomics and the evolution of the mammalian karyotype. His laboratory studies nonrandom segregation of chromosomes during meiosis in mammals and is part of the Collaborative Cross project.
- **Cheryl Walker, Ph.D.**, of the Texas A&M Health Science Center — Walker is internationally recognized as a leader in developmental reprogramming and has been instrumental in defining this new field, which seeks to understand how environmental exposures early in life increase risk of disease in adulthood. She has shown that exposure to environmental estrogens during development reprograms the epigenome to increase expression of genes that promote tumor development in adulthood.



Oncologist Feinberg's lab has received a Centers of Excellence in Genome Sciences (CEGS) grant award from the NIH. (Photo courtesy of Johns Hopkins University)



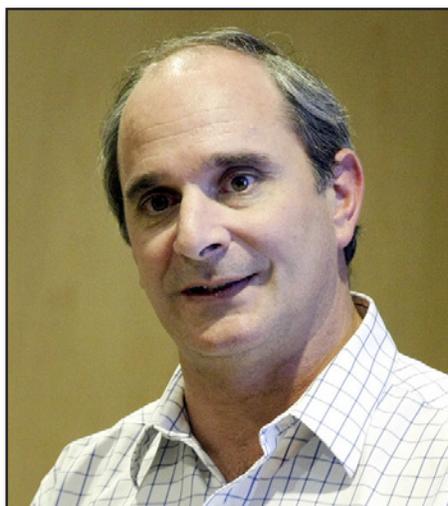
Neurologist Lipton also holds adjunct appointments at the University of California, San Diego, Salk Institute for Biological Studies, and The Scripps Research Institute. (Photo courtesy of the Sanford-Burnham Medical Research Institute)



Computational geneticist Moore is also associate director for bioinformatics at the Norris-Cotton Cancer Center. (Photo courtesy of Dartmouth College)



Immunologist Nagarkatti is also director of the NIH Center of Research Excellence in Inflammatory and Autoimmune Diseases. (Photo courtesy of the University of South Carolina)



Geneticist Pardo-Manuel de Villena was a pioneer in utilizing the results of the NIEHS Mouse Genome Resequencing and SNP Discovery Project. (Photo courtesy of Steve McCaw)



Developmental toxicologist Walker is a past president of the Society of Toxicology. (Photo courtesy of Cheryl Walker)

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Communications team recognized for intern program video

By Eddy Ball

The NIEHS Office of Communications and Public Liaison (OCPL) is taking home a [Pegasus Award of Distinction](#) for one of its first video efforts, “Falling in love with research, students in the laboratory.” The 3 1/2 minute video mixes still and motion photography with sound to highlight the four poster winners from the 2011 NIH Summer Internship Program at NIEHS.



Arnette joined OCPL in 2006. She writes and edits science stories in the Environmental Factor, provides content for the NIEHS Web pages, and prepares press releases on new scientific studies by NIEHS intramural researchers. (Photo courtesy of Steve McCaw)

Linked video:
[Watch as poster winners discuss their research and summer of discovery at NIEHS \(03:30\)](#)
(Launches in new window)

Download Media Player:  Flash [↗](#)

Written, produced, and directed by OCPL Science Writer/Editor Robin Arnette, Ph.D., the video features narration by OCPL Writer/Editor Ian Thomas. Contractor John Maruca of Image Associates handled filming, audio, and mixing for the video, which includes still photography by his colleague, Steve McCaw.

Not surprisingly, OCPL Director Christine Flowers was pleased by news of the award. “Winning a Pegasus says a lot about the creative talent of our team members who put together a terrific video at minimal cost,” she said.

The Pegasus Award is given to the top videos of the year in seven categories, recognizing exceptional work by non-broadcast professionals. Judged by broadcast and communications veterans, the award honors individuals, production companies, businesses, medical facilities, government agencies, educational institutions, and organizations from all over the United States.

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Thomas, who writes for the Environmental Factor, drew on his broadcast experience as narrator of the prize-winning video. (Photo courtesy of Jennifer Weinberg)

NIEHS and NTP set to lead events at 51st SOT meeting

By Ed Kang

2012 marks the [51st annual meeting](#) of the Society of Toxicology (SOT) and, this year, scientists and program managers from NIEHS and NTP, including Director Linda Birnbaum, Ph.D., will be on hand to showcase new strategic directions, new opportunities for collaboration, and new technologies. The SOT meeting is the largest gathering of its kind, drawing 7,500 toxicologists and other attendees from around the world.

In addition to 75 poster presentations and 30 scientific talks given by NIEHS and NTP staff throughout the five-day meeting, one of the much-anticipated events is an update from the NIEHS/NTP director on the state of federally funded science and emerging trends in toxicology research.



The 51st annual meeting of SOT takes place March 11–15, 2012, at the Moscone Convention Center in San Francisco. (Image courtesy of SOT)

This year, Birnbaum will use the venue to update the toxicology community on the soon to be final, five-year strategic plan for the Institute. The plan has been in development for about a year, with NIEHS leadership and staff working collaboratively with public stakeholders.

“We kicked off the planning process for our strategic plan at SOT a year ago, and I’m thrilled to now be giving a report on our nearly completed work,” said Birnbaum, who was president of the society in 2004 and continues to take an active leadership role. “Our new strategic plan will be a clear vision for how this Institute will continue to be a global leader in environmental health.”

In addition to new strategic directions, the staff of the NIEHS Division of Extramural Research and Training will be available to speak with current grantees and those interested in exploring new federal research funding opportunities. Program administrators from NIEHS will be answering questions about scientific review and grant opportunities.

In addition to one-on-one consultations, a luncheon seminar titled “Strategies for Submitting Successful Grants” will focus on first-time or previously unsuccessful grant submitters. Panelists will be on hand to talk about the ins and outs of what makes a successful grant submission; what to do before putting pen to paper; how to write the grant; what strategies are used to help make grant submissions stand out; and how the application progresses through the review process.

NTP is also using the SOT meeting as an opportunity to showcase powerful new technologies that enable toxicologists to increase the efficiency of toxicological assessments and reduce the time needed for data collection, analysis, and reporting.

The Chemical Effects in Biological Systems (CEBS) database integrates toxicology and toxicogenomics study information. Users can easily search and download data from more than 9,000 studies on different chemicals and drugs.

Don’t miss the following events at this year’s 51st meeting of the Society of Toxicology:

NIEHS, NTP, and EHP Exhibit

Monday, March 12 — 9:00 a.m.-4:30 p.m.
Tuesday-Wednesday, March 13-14 — 8:30 a.m.-4:30 p.m.

Booth 2037/2039/2137

Special Symposium: Meet the Director

Wednesday, March 14 — 9:00-11:45 a.m.
Room 302

Exhibitor Hosted Session: Introduction to the DrugMatrix and ToxFX Toxicogenomic Database and Analysis Tools

Monday, March 12 — 3:30-4:30 p.m.
Room 105

Breast Cancer as a Multifactorial Disease: Interaction of Genetics, Life Stage, and the Environment

Monday, March 12 — 2:00–4:45 p.m.
Room 103

Scientific, Regulatory, and Public Perspectives on the Credibility and Use of Alternative Toxicological Test Methods in a Legislative Framework

Wednesday, March 14 — 12:00-1:20 p.m.
Room 307

For a full list of the 100+ sessions, posters, and seminars by NIEHS and NTP staff, download the meeting [program](#).

DrugMatrix® is one of the world’s largest toxicogenomic reference resources ever assembled, and provides free access to profiles of 638 different compounds and drug signatures for more than 50 pathological endpoints. Users also have access to a reporting system called ToxFX®, which works with DrugMatrix to create fully annotated reports in minutes.

There will be live demonstrations of CEBS, DrugMatrix, and ToxFX at the meeting.

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

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Review calls for effective communication in evolutionary genomics studies

By Jeffrey Stumpf

A new review article co-authored by NIEHS [grantee](#) Sarah Tishkoff, Ph.D., underscores the importance of making sure that ethical evaluation keeps pace with advances in research strategies.

Writing in the journal *Trends in Genetics*, the team of scientists working in the fields of evolutionary genomics and bioethics — first author Joseph Vitti of Harvard University; Mildred Cho, Ph.D., of Stanford University; [Tishkoff](#); and lead researcher Pardis Sabeti, M.D., D.Phil., also of Harvard — argues that researchers need to think carefully about the social and political implications of their evolutionary and genetic findings. According to the authors, researchers have an obligation to communicate their research on natural selection to the public as precisely as possible and within a context that will discourage misinterpretation or misuse of their data.

Like her co-authors, Tishkoff, an NIH Pioneer Awardee, studies populations in Africa ([see related story](#)), the continent where human life first began, for insights into evolution, natural selection, and adaptations related to human health. As she uses genomic data to advance knowledge about human evolution, Tishkoff is mindful of the sensitivity of her field.

“Researchers investigating natural selection in the human genome need to be aware of the dark history surrounding these topics and of the acute social sensitivity that still exists,” Tishkoff and her colleagues wrote.

Prior mistakes foreshadow future controversies

Evolutionary genomics studies cover two potentially controversial topics — evolution and genetics. Tishkoff and co-authors warn that ignorance of the key concepts and intentional misrepresentation of results are at the root of the controversies. “Regrettably, advances in understanding of these topics have historically been misapplied to provide justification for unethical practices,” the authors argue. “Even today, scientific advancements are too easily warped to fit prejudicial agendas.”



Tishkoff is careful about how she communicates study findings to participants, as well as to colleagues and the general public. (Photo courtesy of the University of Pennsylvania)

Evolution is controversial because it is viewed as a purposeful process that causes a better result. The article notes that the phrase, survival of the fittest, implies the preservation of favored races in the struggle of life. Such interpretation has resulted in intolerable practices, such as eugenics, in the suppression of policies that aid the disadvantaged, and in the racially motivated charge that some populations are less evolved than others.

Genetic studies can justify fatalistic ideas that people cannot exceed the expectations of their genetic blueprint. The oversimplified importance given to genetics instead of environmental factors, the authors explain, led to dismantling of educational programs that serve low-income families, because of the mistaken idea that some people are hardwired to be unsuccessful.

Message to scientists: Be vigilant

The message from the researchers was clear — high impact research requires the highest self-assessment of the methodology and the conclusions. The authors note that the manner in which the discoveries are communicated is equally important. “Researchers should be vigilant in the dissemination of results, both through scholarly and lay media, and in their role steering public discourse about science.”

Communicating results to the lay media can put scientists in an uncomfortable position. While the scientific report may be written cautiously, journalists can change the tone and meaning of the discovery. The authors suggest the need to be proactive in working with journalists to maintain the integrity of high impact results.

In studies in evolutionary genomics, the authors warn that common biological terms, such as fitness, ancestry, and mutation, have been assigned values in the public vernacular. In her field of human evolution, Tishkoff explains how the theory that modern humans originated from Africa caused the racially charged belief that Africans are more closely tied to their ancestry, when in reality all human populations had the same time to adapt.

Much of the misplaced value on biological terminology is rooted in the lack of public understanding of evolution and genomics. Thus, Tishkoff and her colleagues remind scientists of their obligation to participate in science education and address misconceptions head on.

Citation: [Vitti JJ](#), [Cho MK](#), [Tishkoff SA](#), [Sabeti PC](#). 2012. Human evolutionary genomics: ethical and interpretive issues. *Trends Genet*; doi 10.1016/j.tig.2011.12.001 [Online 20 January 2012].

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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Postdocs reach out to Durham middle schoolers

By Eddy Ball

NIEHS trainees launched the largest volunteer apprenticeship ever Feb. 9 in the [Citizen Schools](#) program at Lowes Grove Middle School in Durham, N.C. The project is a volunteer effort benefitting from financial support by the NIEHS Office of Science Education and Diversity, as well as training and hands-on experience in workshops offered by the Environmental Health Perspectives (EHP) Science Education Program.



Linked video: [Learn more about citizen teachers by watching Citizen Schools 101 \(06:49\)](#)

(Launches in new window)

Download Media Player:  Flash 

Standing in for trainee [Nisha Cavanaugh, Ph.D.](#), who serves as project coordinator, NIEHS biologist [Mercedes Arana, Ph.D.](#), joined trainees [April Binder, Ph.D.](#), [Kristin Lichti-Kaiser, Ph.D.](#), [Darshini Trivedi, Ph.D.](#), and [Kirsten Verhein, Ph.D.](#), to offer groups of middle schoolers a preview of what they could look forward to in the NIEHS “Healthy Lungs, Happy Living” series, which began officially Feb. 16.

Young scientists on a mission

The team was the first contingent of a 15-member group of trainees who have been preparing since September 2011 to serve as citizen teachers in the low-income school. The group is dedicated to preparing what they are calling environmental ambassadors from participants in the ten-week afterschool apprenticeship program, raising awareness of the importance of environmental health through a curriculum of instruction and hands-on learning activities.

“The first four weeks is about the respiratory system, how air pollution affects lung function, and how lungs function in the body,” said Trivedi. “The next three weeks, we’ll build a mechanical lung and show them the effects of smoking on lung health and of asthma as a respiratory disease. The last three weeks, they’ll prepare for what we call the WOW! event — an evening when the student apprentices invite their friends and families to showcase what they’ve learned and talk about what the program has meant to them.”

Making a difference and rounding out skill sets

The NIEHS scientists are part of a nationwide program that has proven its worth by boosting participants’ success rates. According to Citizen Schools follow-up since 2002, young people who were part of the program are 20 percent more likely to graduate from high school, attend classes more often, outperform their peers in six measures of student success, and are 80 percent more likely to attend college.

Since its start by former college roommates Eric Schwartz and Ned Rimer in 1995, Citizen Schools has spread to 18 cities throughout the nation, providing hands-on learning taught by AmeriCorps educators and [volunteer experts](#) from all fields — from science to law to finance and community service. The program operates in 31 schools and has served 4,500 students through the efforts of 4,200 volunteers.

Along with all they’re giving to their students, NIEHS citizen teachers will also be receiving. They are bringing their passion about science to young minds and helping change the way America thinks about education. They are also building important careers skills in planning, teaching, and team building.



Arana, right, gave an introduction to the “Healthy Lungs, Happy Living” apprenticeship during the hook event at Lowe’s Grove Middle School. Beside her, left to right, are Trivedi, Verhein, and Lichti-Kaiser. (Photo courtesy of Steve McCaw)



Trivedi explained the basics of lung physiology to the students, using an anatomical model of the lung. (Photo courtesy of Steve McCaw)

Although they've benefited from advice from NIEHS outreach and education specialists Ericka Reid, Ph.D., Bono Sen, Ph.D., and John Schelp, this is a trainee-initiated, -built, and -operated program that will help the resumes and CVs of these young scientists stand out when it comes time to search for career opportunities.

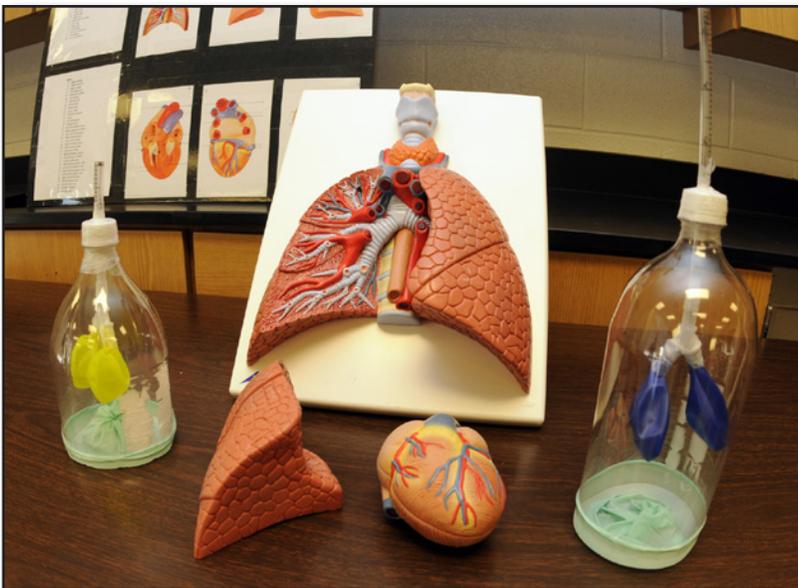
And, as a bonus, the NIEHS citizen teachers are also having a lot of plain old fun doing their thing and doing it well.



Lichti-Kaiser helped the students measure their lung capacity, using a simple prop. (Photo courtesy of Steve McCaw)



Students appeared to be having fun, as they exercised before measuring their lung capacity. (Photo courtesy of Steve McCaw)



An anatomical lung display and mechanical lung models, built by the fellows and students, will be important tools in the apprenticeship as the students learn about lung function. (Photo courtesy of Steve McCaw)



The NIEHS Office of Science Education and Diversity produced this simple, but informative poster about lung health and the environment. The NIEHS Citizen Schools team had the poster on hand for their recruitment presentation at Lowes Grove Middle School. (Photo courtesy of Donna Jeanne Corcoran)

The NIEHS team and its game plan

Each of the ten weekly modules is presented by a lead teacher (L) and volunteer(s).

- Feb. 16 — “Introduction to apprenticeship and knowledge assessment,” with Binder (L), trainee [Michelle Heacock, Ph.D.](#), trainee [Bret Freudenthal, Ph.D.](#), and Industrial Hygienist [Sharon Beard](#)
- Feb. 23 — “What the lungs do,” with staff scientist [Elena Braithwaite, Ph.D.](#) (L), trainee [Ashley Godfrey, Ph.D.](#), and trainee [Danielle Watt, Ph.D.](#)
- March 1 — “The importance of clear airways,” with Godfrey (L), Braithwaite, and [EHP Science Education and Outreach Program Manager Bono Sen, Ph.D.](#)
- March 8 — “How air pollution can affect lung function,” with Godfrey (L), and trainees [Timothy Gingerich](#) and [Gayle Hagler, Ph.D.](#), a volunteer from the U.S. Environmental Protection Agency
- March 15 — “Building a mechanical lung,” with trainee [Shay Covo, Ph.D.](#) (L), Gingerich, and Sen
- March 22 — “Understanding the effects of smoking,” with Trivedi (L) and Gingerich
- March 29 — “Asthma as a respiratory disease,” with trainee [Julie Lowe, Ph.D.](#) (L), Gingerich, and Trivedi
- April 5 — “WOW! Preparations,” with Arana (L), Lichti-Kaiser, and Verhein
- April 19 — “WOW! Preparations,” with Verhein (L), Arana, and Lichti-Kaiser
- April 26 — “WOW! Preparations,” with Lichti-Kaiser (L), Arana, and Verhein

Several of the trainee volunteers in the NIEHS Citizen Schools apprenticeship are veterans of EHP Science Education Program workshops, such as the one held Aug. 2-3, 2011 for science educators ([see story](#)), where they gained self-confidence and experience teaching. The NIEHS Office of Communication and Public Liaison, represented by Public Affairs Specialist Ed Kang, is working with the team to document the NIEHS Citizen Schools experience.

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Nano consortium gathers at NIEHS

By Thaddeus Schug

Despite their small size, engineered nanomaterials (ENMs) continue to generate a great deal of interest at NIEHS. A growing collaboration of researchers making up the NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) Consortium gathered for research updates Jan. 26-27 at NIEHS.

The NCNHIR Consortium is an interdisciplinary program consisting eight Cooperative Centers along with several other active grantees funded through the Nanotechnology Environmental Health and Safety program. The NIEHS also established contractual agreements with the Nanotechnology Characterization Laboratory for nanomaterial characterization and with the National Institute of Biomedical Imaging and Bioengineering to create an informational database.

The meeting was the third biannual meeting of this consortium and included presentations regarding individual project research progress by NCNHIR as well as updates on consortium-wide research efforts. The event also included a steering committee meeting in which consortium progress and future directions was discussed.

“It is very encouraging to see so much progress made by these investigators in such a short time period,” said Sri Nadadur, Ph.D., the meeting organizer, program director for the extramural Nanomaterials Environmental Health Safety research program, and the health scientist administrator at NIEHS who oversees much of the Institute’s research portfolio on nanomaterials in environmental health and safety. “I am particularly excited to welcome several new grantees to the consortium, and look forward to integration of their research into this collective effort,” added Nadadur.

The newest members of the consortium include Andrij Holian, Ph.D., director of the Center for Environmental Health Sciences at The University of Montana, Robert Tanguay, Ph.D., from Oregon State University, Som Mitra, Ph.D., from the New Jersey Institute of Technology, and Frank Witzmann, Ph.D., from Indiana University.



NIEHS Deputy Director Rick Woychik, Ph.D., welcomed consortium members to NIEHS and stayed to participate in discussions. (Photo courtesy of Steve McCaw)

NCNHIR center presentations

- Center for Nanobiology and Predictive Toxicology, Andre Nel, M.B.Ch.B., Ph.D., University of California, Los Angeles
- Linking the Physical and Chemical Characteristics of Quantum Dots to their Toxicity, Terrence Kavanagh, Ph.D., University of Washington
- Center for Estimating Human Health Risk from Exposure to Nanomaterials, Timothy Fennell, Ph.D., RTI International
- Pacific Northwest National Laboratory (PNNL) Center for Nanotoxicology, Joel Pounds, Ph.D., PNNL
- Respiratory Effects of Silver and Carbon Nanomaterials, Junfeng Zhang, Ph.D., University of Southern California
- Acute and Chronic Effects of Engineered Nanomaterial, Terry Gordon, Ph.D., New York University
- Biological Responses to Different Types of Carbon Nanotubes, Kent Pinkerton, Ph.D., University of California, Davis
- Interactions Between Ingested Silver Nanoparticles and the Varying Physicochemical or Microbial Environments of the Gastrointestinal Compartments, Martin Philbert, Ph.D., University of Michigan



Along with the presentations, attendees shared their work in a poster session. Judith Zelikauf, Ph.D., left, of New York University, discussed her group’s findings with Nadadur. (Photo courtesy of Steve McCaw)

Along with the research proposed to be carried out at their respective centers, these investigators as members of the consortium will work with a set of engineered nanomaterials, widely used in industrial applications with potential for human exposure, collectively nominated by the consortium — silver nanoparticles, cerium dioxide, and multiwall carbon nanotubes. These materials are of several shapes, sizes, and surface coating. All the members of the consortium will carry out investigations with this set of ENMs in their respective *in vitro* and *in vivo* models, and then share that data with the investigators developing computational models to predict potential health effects.

The group will meet again at the end of July in Portland, Ore.



Ingrid Bergin, V.M.D., left, discusses her experiments with NIEHS Senior Toxicologist Chris Weis, Ph.D., who is the nano lead in the NIEHS Office of the Director. (Photo courtesy of Steve McCaw)



NTP Deputy Division Director for Science Nigel Walker, Ph.D., was one several NIEHS/NTP scientists at the meeting. Walker is the NTP lead on ENM research. (Photo courtesy of Steve McCaw)



During their morning break, attendees gathered on the patio outside the Rall Building at NIEHS. (Photo courtesy of Steve McCaw)

(Thaddeus Schug, Ph.D., is a health scientist in the NIEHS Division of Extramural Research and Training and a regular contributor to the Environmental Factor.)

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Grantee and two trainees named science communication fellows

By Eddy Ball

Three of the ten 2012 Science Communication Fellows announced Feb. 15 by [Environmental Health Sciences \(EHS\)](http://www.EnvironmentalHealthNews.org) are receiving training or research support from NIEHS.



Like their predecessors, this year's fellows will spend the next year honing their communication skills and learning effective ways to inform journalists and the public about new research findings in environmental health and green chemistry. Their training begins with a conference March 8-10 in Washington, DC.

A number of NIEHS-supported scientists, including several Outstanding New Environmental Scientist awardees, have completed Science Communication Fellowships since EHS created the program in 2007. EHS and Advancing Green Chemistry (AGC) sponsor the fellowships. EHS publishes the online news sources, [Environmental Health News](http://www.EnvironmentalHealthNews.org) and [The Daily Climate](http://www.EnvironmentalHealthNews.org). AGC publishes chemistry updates [online](http://www.EnvironmentalHealthNews.org).

According to EHS, the yearlong part-time training is designed to polish science communication skills, and prepare researchers for talking to reporters and the public about scientific topics. The fellows work with editors and writing staff at EHS to produce original research reviews and commentaries on media coverage. The program is unique because it involves scientists who identify findings that shed light on links among the environment, human health, and chemistry.

The following 2012 Science Communication Fellows have ties to NIEHS:

- **Virginia Guidry, Ph.D.** — Guidry is a postdoctoral fellow in the Department of Epidemiology at the University of North Carolina (UNC) at Chapel Hill, who also received predoctoral support from an NIEHS training grant. A winner of a 2011 UNC Impact Award, Guidry studies the health impacts of air pollution from industrial livestock production while working with communities to conduct research and emphasize environmental justice. She is currently collaborating with science classes to examine asthma-related outcomes in children attending middle schools near industrial swine and poultry operations.
- **Cheryl Stein, Ph.D.** — Stein is an assistant professor in the Department of Preventive Medicine at Mount Sinai School of Medicine in New York City. She is an epidemiologist primarily researching the effects of exposure to environmental chemicals on pregnancy health and later child cognitive and behavioral development. She is the lead on two NIEHS researcher-initiated grants.



UNC postdoctoral fellow Virginia Guidry (Photo courtesy of UNC)



NYU Assistant Professor Cheryl Stein (Photo courtesy of Cheryl Stein)

- **Jennifer T. Wolstenholme, Ph.D.** — Wolstenholme is a postdoctoral fellow at the University of Virginia School of Medicine. Her research with mice investigates changes in social behavior and associated differences in gene expression in the brain following exposure to chemicals in plastics – specifically BPA. She examines the epigenetic modifications that may regulate these neurological changes to understand how some of these behaviors can be passed on to unexposed descendants. In addition, she plans to explore the individual differences that make some resilient to the exposures while others are susceptible.

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*UVA postdoctoral fellow Jennifer Wolstenholme
(Photo courtesy of Jennifer Wolstenholme)*

Science Notebook

Falk lecture features NYU epigenetics researcher

By Robin Arnette

The Hans L. Falk Memorial Lecture honors the memory of a scientist who was one of the founding members of NIEHS and an unwavering advocate for the study of how the environment influences disease. Fittingly, this lecture series features investigators who have made significant contributions to research related to environmental health sciences.

This year's lecture Feb. 14 featured [Danny Reinberg, Ph.D.](#), a researcher who studies how epigenetics regulates gene expression. Reinberg is a Howard Hughes Medical Institute investigator and professor of biochemistry at New York University School of Medicine. He presented a seminar titled, "Molecular Mechanisms of Epigenetic Inheritance." NIEHS Deputy Director [Rick Woychik, Ph.D.](#), served as host.

According to Reinberg, the field of epigenetics is the study of the heritable alterations to the genome that don't involve a change in the DNA sequence. Although epigenetics is still in its infancy, Reinberg said that the term was actually coined centuries ago by the Greek philosopher Aristotle. It wasn't until the mid-1940s that British biologist Conrad Waddington, Ph.D., offered an explanation for what it meant.

"He thought that within the development of an individual, phenotypic or outwardly-appearing changes happen without any modification of the genes," Reinberg said. "What we have to keep in mind is stem cells and differentiated cells have identical genomes. The only distinction is they have different profiles of gene expression."

Reinberg's lecture focused on his interest in how DNA wraps around histones, which are the structural proteins of chromosomes, and the distinct modifications that take place on histone tails. He explained that these histone modifications — acetylation, methylation, phosphorylation, ubiquitination, and others — can either allow or repress transcription. He also said that the proteins that make these changes may be targets for drug therapy.



Reinberg maintained, "If science continues to discover more about these epigenetic modifications, man will be able to cure some diseases." (Photo courtesy of Steve McCaw)



Rodbell Auditorium was at capacity during the Falk Lecture. Shown, left to right, are Karen Adelman, Ph.D., David Armstrong, Ph.D., Lutz Birnbaumer, Ph.D., Sheila Newton, Ph.D., and Jack Taylor, M.D., Ph.D. (Photo courtesy of Steve McCaw)

“The enzymes that do this are grouped into writers, readers, and erasers, and are mutated in many cancers,” he said. “Several companies have developed therapeutic strategies that attempt to circumvent their action on DNA.”

Unraveling the complexities of epigenetics

Some of Reinberg’s recent research suggests that certain methyl groups added to the histone proteins of a particular organism’s chromatin, which is DNA plus histones, also appear in the new cell when the original cell divides. This action ensures that the same pattern of gene expression is reproduced. Reinberg’s group determined that JARID2 is involved in the process and does its work in concert with several other proteins. JARID2, a human gene that encodes a protein required for proper development of an embryo, has a DNA binding domain and a domain that allows it to bind to and invigorate the multi-enzyme complex that performs the methylation that is also required for proper embryogenesis.

Reinberg will continue his studies on how epigenetic changes occur but, strangely enough, he didn’t start out in science interested in this topic. He said he began working with transcription but, as he dug deeper, the experiments kept pointing him to the histone modifications that were important for transcription.

“We wound up with gene products that were methylating here and there,” Reinberg added. “That’s where the science took me.”

Woychik summed up Reinberg’s work by saying it was truly on the cutting edge of understanding the molecular biology of epigenetic regulation of the mammalian genome.

“Epigenetics has changed our thinking on how the environment can influence human health and biology,” he said. “Reinberg’s research has had an enormous impact on the field of epigenetics research.”

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Woychik encouraged the audience to check out Reinberg’s website for more information about his other epigenetic projects. (Photo courtesy of Steve McCaw)



After the seminar, Falk family members posed with NIEHS/NTP Director Linda Birnbaum, Ph.D., in front of a photo of Hans Falk. Shown, left to right, are Raymond Falk, Ph.D., Irene Falk, Donald Falk, M.D., Gabrielle Falk, Birnbaum, and Stephen Falk, J.D. Falk’s widow has attended every one of the Falk lectures. (Photo courtesy of Steve McCaw)

Council talks highlight human studies of autoimmunity and immunotoxicity

By Anshul Pandya

Members of the National Advisory Environmental Health Sciences Council heard two exciting scientific presentations at their meeting Feb. 16 at NIEHS. The first, by Acting Director of the NIEHS Clinical Research Program [Fred Miller, M.D., Ph.D.](#), focused on environmental and genetic links to autoimmune disease. The second, by NIEHS grantee [Philippe Grandjean, M.D.](#), of the Harvard School of Public Health, discussed immunotoxicity in a population of children exposed to contaminants in a seafood-based diet.

Miller — autoimmune disease, when the body turns upon itself

Miller opened his talk by telling the audience, “Autoimmune diseases, like multiple sclerosis, lupus, scleroderma, myasthenia gravis, and myositis syndromes, have major public health implications.” Although, individually, most of these 80 diseases are rare, autoimmune diseases collectively affect some 22 million people in the U.S., with rates on the rise.

According to Miller, environmental factors implicated in autoimmune diseases include infectious agents such as bacteria and viruses, as well as non-infectious agents such as drugs, biologics, foods, ultraviolet radiation, and occupational exposures. He added that for some diseases the onset varies seasonally, as well as by geographic location, which also suggests an important role for environmental exposures.

Miller elaborated on the complex interplay between environmental factors and genes in the pathophysiology of various autoimmune diseases. “Defining the environmental and genetic associations for a specific autoimmune disease remains a challenge,” he explained. “While environmental factors can activate a gene or set of genes which may trigger an autoimmune disease, it is also possible that the activation of certain genes may also have a protective effect for some autoimmune diseases.”

Translating presentation into treatment

Miller specifically focused on a group of autoimmune disorders called the myositis syndromes, which are characterized by chronic inflammation of the muscles. His group uses epidemiological surveys, molecular genetic studies, and clinical evaluations to investigate the pathogenesis of the myositis syndromes, as well as to develop improved clinical tools for the assessment of innovative therapies for treating these life-threatening disorders.

Characterizing different forms of myositis, Miller explained, can yield important benefits for researchers, by allowing the better definition of the different environmental triggers, genes, and mechanisms at play in each phenotype. Patients and clinicians can be helped by this process, as well. “Once you understand these unique phenotypes, you can talk to a patient over the phone for about five to ten minutes and often get a feel for which group they’re going to fall into, and help them in terms of deciding what the next best treatments should be.”

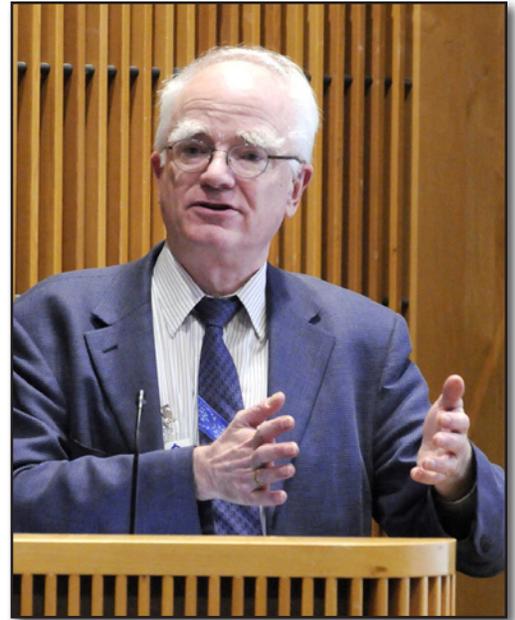


Describing autoimmune disease as “a rather neglected area ... that is very near and dear to my heart,” Miller argued that identifying mutually exclusive, stable phenotypes for individual diseases can help clinicians better identify, treat, and ultimately prevent them. (Photo courtesy of Steve McCaw)

Grandjean — connecting toxicants in diet to neurological and immunological effects

Grandjean discussed the neurotoxic and immunotoxic effects of environmental toxicants that bioaccumulate in marine food chains and end up in seafood, especially if the diet includes marine mammals, such as the pilot whale. Grandjean showed data from prospective epidemiological studies of birth cohorts in the Faroe Islands north of Scotland. In this fishing community, his team has conducted more than 8,000 extensive clinical evaluations of cohort members.

In the first part of his talk, Grandjean described his work with environmental toxicants, such as methylmercury and the organic pollutants polychlorinated biphenyls (PCBs) and perfluorinated compounds (PFCs), in terms of their effects on development. According to him, the effects clearly depend on the nature and dose of the toxicant. Grandjean also said that there seems to be a window of vulnerability where exposure to neurotoxicants could be most detrimental to a child's health. His group found changes in brain architecture and electrical signaling, as well as significant developmental deficits in motor function, attention, visuospatial function, language, and visual memory associated with increased methylmercury exposures.



Grandjean concluded by expressing his gratitude for NIEHS support for work on what he called a silent pandemic. “If we have made a small contribution to the science and perhaps to public policy, it’s to a great extent because you have supported us.” (Photo courtesy of Steve McCaw)

Immunotoxicants reduce the effectiveness of immunization in children

In the second part of his talk, Grandjean explored the interaction of immunotoxicants and vaccines. His team measured PFCs in the mother's serum during pregnancy, and later checked for the compounds in samples from the children at age five. Grandjean presented evidence to suggest that exposure to immunotoxicants is linked to a significant reduction in the effectiveness of tetanus and diphtheria immunization in triggering an antibody response, a reflection of how well the immune system is functioning.

“There are known problems with vaccine efficiency around the world,” Grandjean concluded. “We need to work together to ensure both at an individual level that we’re all protected from the diseases we’re vaccinated against and also at a population level that we keep immunity at a sufficiently high level to prevent epidemics from happening.”

(Anshul Pandya, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Neurobiology Ion Channel Physiology Group.)

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New grantee discovers treatment that may block Shiga toxin

By Ashley Godfrey

Carnegie Mellon postdoctoral researcher Somshuvra Mukhopadhyay, Ph.D., has found that manganese, an essential nutrient commonly found in nature, may prevent the potentially lethal effects of infection by a bacterial compound known as Shiga toxin. Mukhopadhyay's [results](#), published in the Jan. 20 issue of *Science*, show that manganese completely protects against Shiga toxicosis in animal models.

How Manganese Blocks Intracellular Trafficking of Shiga Toxin

Carnegie Mellon University
DEPARTMENT OF BIOLOGICAL SCIENCES

Linked video:

[Watch how manganese blocks cellular trafficking of Shiga toxin \(01:05\)](#)

(Launches in new window)

Download Media Player: Flash [↗](#)

The study was funded by the National Institute of General Medical Sciences and was carried out under the direction of Carnegie Mellon Professor [Adam Linstedt, Ph.D.](#) With new funding from NIEHS, Mukhopadhyay plans to advance his research on manganese and Shiga toxin, by building on these preliminary results using other animal models.

“I’m grateful to have the support of NIEHS to develop my independent work on manganese homeostasis and toxicity, and without the new funding, it would be extremely difficult for me to keep moving on the path to independence,” concluded Mukhopadhyay.

Neutralizing a major threat to global health

Infections with Shiga toxin-producing bacteria cause more than a million deaths each year. While these infections do occur worldwide, the majority of Shiga toxin infections arise in developing countries where they cause waterborne epidemics. “The possibility of having an inexpensive and widely available agent like manganese as a treatment for Shiga toxicosis is exciting,” explained Mukhopadhyay.

Shiga toxin is a protein produced by certain strains of *Shigella* and *E. coli* bacteria. When cells take up the toxin, it interferes with cellular functions and leads to cell death, which in turn can cause symptoms ranging from mild intestinal disease to kidney failure. Unfortunately, there is no cure for these infections, because antidotes for the toxin are not available and treating patients with antibiotics actually increases the amount of toxin released by the bacteria.

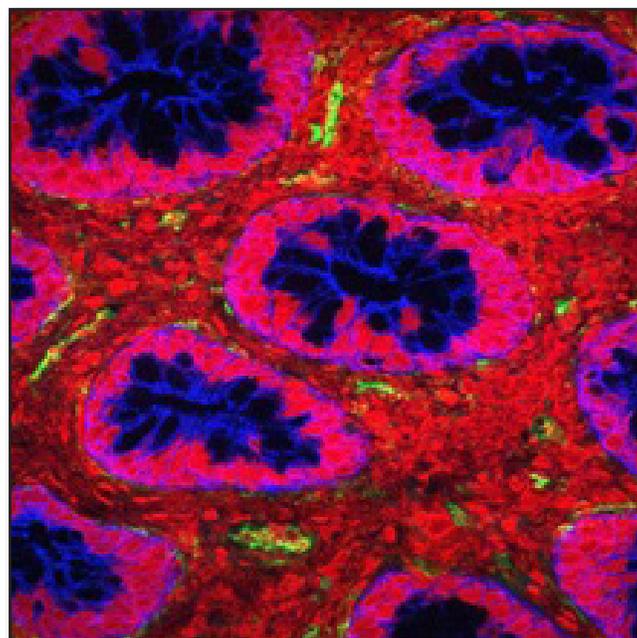
“The challenge is to neutralize the toxin that is released from the bacteria,” emphasized Mukhopadhyay.

He and Linstedt have potentially answered this challenge by focusing their research on the process that Shiga toxin takes advantage of to avoid being degraded by cells. While conducting basic biological research on how cellular components function, they discovered the protective effect manganese had on cells and mice exposed to lethal doses of the Shiga toxin.

Paving the road to independence

Mukhopadhyay is a recent recipient of an NIH Pathway to Independence Award (K99/R00). This competitive award is designed to facilitate the transition into independent research positions for promising young scientists. The initial K99 award provides one to two years of mentored, postdoctoral support and the second phase R00 component supports up to three years of independent research.

Mukhopadhyay applied to NIEHS for this award, due to the significant environmental health focus of his postdoctoral work. His research goals are to understand



*Above is a microscope image showing the Shiga toxin (green) in the intestine. In developed countries, Shiga toxicosis is most common during foodborne outbreaks, like the widespread *E. coli* outbreak this past summer in Germany and Western Europe, where more than 3,700 people were infected and 45 died. (Image by S. Schuller, Wellcome Images)*

how manganese homeostasis is regulated, and to learn more about the process by which manganese and other metal toxins can cause toxicity. While low levels of manganese are required for life, and non-toxic levels protect against Shiga toxicosis, manganese itself becomes toxic at high levels.

Manganese toxicity is a significant clinical problem, because environmental and occupational overexposure can lead to the onset of Parkinson's syndrome, a neurological syndrome distinct from Parkinson's disease, which currently has no treatment.

Mukhopadhyay's long-term goal is to continue to expand his work on the regulation of manganese homeostasis. In doing so, he hopes to gain a better understanding of the underlying biology behind manganese-induced Parkinsonism, which will hopefully lead to new therapies. This work will also directly aid in the development of manganese, at non-toxic levels, as an intervention for human Shiga toxicosis.

Citation: Mukhopadhyay S, Linstedt AD. 2012. Manganese blocks intracellular trafficking of Shiga toxin and protects against Shiga toxicosis. *Science* 335(6066):332-335.

(Ashley Godfrey, Ph.D. is a postdoctoral fellow in the Molecular and Genetic Epidemiology Group in the NIEHS Laboratory of Molecular Carcinogenesis.)

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Mukhopadhyay, left, and his mentor Linstedt are excited about the possible use of manganese as an inexpensive, accessible treatment for Shiga toxicosis. They plan to continue their research by using situations that more closely mimic Shiga toxin infection in humans. "We have also formed a collaboration to test the protective effect of manganese against Shiga toxicosis in non-human primates," said Mukhopadhyay. (Photo courtesy of Somshuvra Mukhopadhyay)

Interagency mineral fibers group meets at NIEHS

By Eddy Ball

The NIEHS commitment to mineral fibers research was front and center at the most recent meeting of the Interagency Asbestos Working Group Feb. 2-3, hosted by NIEHS. Speakers addressed developments in understanding and addressing public health consequences of exposures to asbestos and asbestos-like fibers ([see text box](#)).

The meeting was chaired by David Weissman, M.D., director of the Division of Respiratory Disease Studies at the National Institute for Occupational Safety and Health (NIOSH).

Welcoming members from nine federal agencies on day one was NIEHS/NTP Deputy Director Rick Woychik, Ph.D. The agenda prominently featured a review of NIEHS/NTP work by Senior Medical Officer Aubrey Miller, M.D.; Health Scientist Administrator Danielle Carlin, Ph.D., who updated attendees on the NIEHS asbestos grant portfolio; and NTP toxicologist Scott Masten, Ph.D. Masten also joined toxicologist Matt Stout, Ph.D., in the afternoon for a presentation on the NTP research program.

NIEHS/NTP Director Linda Birnbaum, Ph.D., attended most of the meeting and was on hand the second day, as the group heard presentations on erionite by Miller and on carbon nanotube issues relevant to asbestos by Toxicology Liaison Chris Weis, Ph.D.

Asbestos concerns rooted in NTP listing

As Woychik told the group, “NIEHS has longstanding involvement and concern regarding the health effects stemming from asbestos fibers. Our NTP program listed asbestos as a carcinogen in 1980 and did some of the early pioneering toxicology work.” Along with ongoing support for research, he noted, in 2009, NIEHS sponsored a state of the science workshop on asbestos and related fibers ([see story](#)).

In an update on NTP’s ongoing research on the health effects of fibers, Masten and Stout reported on the comprehensive NTP naturally occurring asbestos and related mineral fibers program, triggered by nominations from the U.S. Environmental Protection Agency (EPA) and the U.S. Centers for Disease Control and Prevention (CDC) in 2006. The agencies cited widespread community exposures, insufficient toxicity data, and a need to better understand the influence of mineralogy and morphology on toxicity.

Efforts are currently underway to identify and procure suitable natural mineral fiber samples of amosite, Libby amphibole, and possibly erionite, as well as complete detailed physical and chemical characterizations, to be used as the basis for proceeding to short-term in vivo toxicity and biopersistence studies, and chronic toxicity and carcinogenicity studies. According to Stout, one of the first important questions to answer involves the dose-response characterization for the fibers, both inside the respiratory tract and in other organs.

Erionite — another mineral fiber of concern

Concerns about erionite, Miller explained, date back to epidemiological studies in the Cappadocian Region of Turkey that inspired animal toxicity studies and in vitro experiments leading to findings by the World Health Organization and the NTP branding the mineral a known human carcinogen. With the discovery of erionite in the cap rock of the Killdeer Mountains in North Dakota in the mid-2000s, concern among U.S. scientists has increased exponentially ([see related story](#)).

Miller reported on investigations of erionite in Turkish villages with high rates of mesothelioma compared to N.D. This work showed similarity of the physical and chemical properties of the erionite at both locations and ongoing exposures of concern in N.D. (see [story](#) and [study](#)). He pointed to the identification of additional erionite deposits



Mineral fibers such as anthophyllite, one of the five amphibole forms of asbestos, are a public health concern because of their toxicity and widespread presence in the environment. (Photo courtesy of USGS)



“We thought we were busy enough with Libby,” Miller told the audience. “Now we had erionite, too.” (Photo courtesy of Steve McCaw)

in the western U.S., the emergence of cases of erionite-related mesothelioma in North America, and the possibility that other mineral fibers in the zeolite group may also be a public health concern.

Nano — manmade fibers that may act like asbestos

Following a report by NIOSH industrial hygienist Ralph Zumwalde, Weis reported on NIEHS activities in the area of nanotechnology environmental health and safety. As he explained, the initiatives have four primary goals:

- Understand engineered nanomaterials (ENM) biological actions
- Identify methods to quantify exposure in diverse matrices
- Develop predictive models for health effects assessment
- Guide development of second generation ENMs with minimal adverse biological and health effects

“There are so many parallels here with particle and fiber toxicology,” Weis said about the urgency of research on ENMs, which is being conducted by the three research divisions of NIEHS/NTP.



“Nanomaterials are a little out of topic for this asbestos conference,” Weis conceded, “but we have an opportunity at this stage, right now, to avoid many, many mistakes that we’re still trying to overcome with respect to mineral fiber environmental health and safety.”
(Photo courtesy of Steve McCaw)

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Additional interagency representatives presenting at the meeting included:

- CDC Agency for Toxic Substances and Disease Registry — Vik Kapil, D.O., and Vinicius Antao, M.D., Ph.D.
- CDC NIOSH — Martin Harper, Ph.D., and Patricia Sullivan, Sc.D.
- U.S. Consumer Product Safety Commission — Kris Hatlelid, Ph.D.
- Mine Safety and Health Administration — Chris Findlay
- Occupational Safety and Health Administration — Dan Crane
- EPA —Helen Dawson, Ph.D., Philip Cook, Ph.D., Stephen Gavett, Ph.D., David Berry, Ph.D., Danielle DeVoney, Ph.D., Ann Strickland, J.D., and Phillip King
- U.S. Food and Drug Administration (FDA) — Steven Wolfgang, Ph.D.
- U.S. Geological Survey (USGS) — Greg Meeker
- April 26 — “WOW! Preparations,” with Lichti-Kaiser (L), Arana, and Verhein

In addition to NTP research programs, ongoing topics of discussion included: 1) standardization of terminology; 2) activities concerning Libby, Mont., and other EPA Superfund sites; 3) availability of research materials; 4) EPA clarification that the Alternative Asbestos Control Method is not approved; 5) fiber mesothelioma potency related to fiber surface area; 6) fluidized bed method for asbestos contaminated soils; and 7) concern of the widespread use of Libby-derived vermiculite in U.S. and Canadian schools and homes.

Along with erionite and nanomaterials, new topics for discussion included FDA concerns about asbestos-contaminated talc and clinical issues in asbestos-related disease, including lung cancer screening with CT scans, use of digital imaging versus plain films for B-reading, and recent changes in diagnostic criteria for asbestosis by the College of American Pathologists that are not consistent with previous guidelines nor scientifically supported or justified.

Researchers link oxidative stress and neurodegenerative disease

By Robin Arnette

Scientists have known for decades that certain kinds of DNA damage may cause neurodegenerative illnesses in humans, but the exact mechanism for how it worked remained elusive. Now, researchers from NIEHS and Florida International University (FIU) in Miami offer an explanation for how degenerative nerve disorders such as Huntington's disease arise.

Research from other groups determined that a three nucleotide segment of DNA called trinucleotide repeats (TNRs) are expanded or appear in multiple copies in Huntington's disease patients, but NIEHS Laboratory of Structural Biology investigator [Samuel Wilson, M.D.](#), and former colleague [Yuan Liu, Ph.D.](#), went a step further. They demonstrated that expansions in TNRs are linked to cellular oxidative stress or highly reactive oxygen atoms that damage DNA. A summary of the findings was published online in a [review article](#) on Jan. 27 in Trends in Biochemical Sciences. The report advanced a hypothesis that Wilson, Liu, and their collaborators introduced in two earlier papers (see [Liu et al., 2009](#) and [Kovtun et al., 2007](#)).

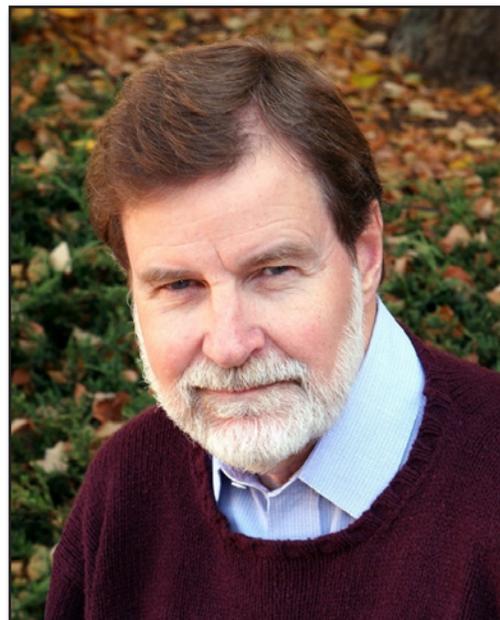
"We felt that the molecular mechanism for triplet repeat expansion was not spelled out enough in the original articles," Wilson said. "The review will be more widely read and clarifies how base excision repair could be connected to triplet repeat expansion."

The birth of TNRs

Wilson explained how the pieces of the puzzle fit together, by providing background on how he believes expansions of TNRs originate. He said cells maintain an environment of positive- and negative-charged ions. When that balance is disturbed, normal cellular processes produce peroxides and free radicals that harm all components of the cell, especially the DNA, by creating small lesions that attach to nucleotides. If the damage isn't fixed, it could lead to mutations or breaks when the DNA makes copies of itself during replication.

Base excision repair (BER), according to Wilson, corrects the problem by removing this oxidized DNA but, in the process, it creates a strand break that allows the DNA to snap into a hairpin structure. The resulting gap is filled in with extra nucleotides and sealed. During the next round of replication, the additional nucleotides will result in a slightly longer DNA thread. Each subsequent round of copying will lead to multiple copies of the first additional nucleotides, collectively known as TNRs.

Wilson said, "In the pathobiology of DNA expansion, we suggest that this mechanism is one of the early events that initiate a shorter expansion. Longer expansions associated with Huntington's disease might occur through a different mechanism."



Wilson said that he and Liu started this work because they were interested in the diseases that occur as a result of oxidative stress. At first, they assumed that those diseases were primarily cancer, but their data also provide a linkage to neurological disease. (Photo courtesy of Steve McCaw)



Liu is an assistant professor in the department of chemistry and biochemistry at FIU. Her lab specializes in studying oxidative damage and the resulting genomic instability that it brings. (Photo courtesy of Yuan Liu)

TNRs are part of disease etiology

In the DNA of a person with [Huntington's disease](#), according to the Nature Publishing Group website [Scitable](#), the sequence CAG is repeated anywhere from 37 to 121 times, but there are many other neurodegenerative diseases that are associated with triplet repeat expansion. For example, in [Jacobsen syndrome](#), CGG is repeated 100-1000 times, and in [myotonic dystrophy](#), CTG may appear up to 3000 times.

Wilson said, in addition to the development of TNRs via oxidative stress, children may inherit the propensity to have triplet repeat expansion from their parents. However, these individuals may have a bright future. Wilson and Liu's work in mouse models demonstrated when the BER enzyme that removes oxidative lesions is eliminated, TNRs fail to occur.

Liu said, "Our study on understanding these mechanisms will help to identify base excision repair as a new target for prevention, diagnosis, and treatment of oxidative stress-induced human neurodegenerative diseases."

Citation: [Liu Y, Wilson SH. 2012.](#) DNA base excision repair: a mechanism of trinucleotide repeat expansion. *Trends Biochem Sci*; doi:10.1016/j.tibs.2011.12.002 [Online 27 January 2012].

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Study finds traffic pollution leading to asthma has huge economic costs

By Brant Hamel

The impact of asthma on health and quality of life is severe, and a new [study](#) by NIEHS-funded researchers emphasizes that the economic costs attributed to childhood asthma, induced or exacerbated by traffic-related pollution, are equally troubling. Their findings appeared online Jan. 26 in the *European Respiratory Journal*.

Using new methodology that includes estimates of asthma cases directly caused by traffic pollution, researchers estimated an economic burden of more than \$18 million annually for the communities of Long Beach and Riverside in Southern California. "The fact that together these two communities account for only 2 percent of the population of California suggests that the statewide costs are truly substantial," the researchers wrote, noting that the total cost nationwide is a significant economic burden that disproportionately falls on those living near high traffic corridors.

[Sylvia Brandt, Ph.D.](#), an associate professor of resource economics at the University of Massachusetts Amherst, was first author on the study. The lead researcher was NIEHS grantee [Rob McConnell, M.D.](#), a professor of preventive medicine and the deputy director of the NIEHS/U.S. Environmental Protection Agency-supported Children's Environmental Health Center at the University of Southern California (USC).



Brandt's research focuses on two areas where traditional economic theories have failed to solve difficult problems in the allocation of public goods — fisheries management and chronic illness. (Photo courtesy of the University of Massachusetts Amherst)

The work relied heavily on previous work by McConnell's group that derived the extent of childhood asthma care in Long Beach and Riverside attributable to traffic-related pollution, along with estimates of the economic cost of this care gathered from a variety of sources.

A sharper lens for viewing risk assessment

Typically, risk assessment analyses of the economic impact of air pollution have considered only how it leads to an increase in symptoms and the direct costs for medical treatment of existing asthma cases. "Traditional risk assessment methods underestimate both the burden of disease and cost of asthma associated with air pollution," the authors argued.

The unique methodology in this study also allowed an estimate of asthma cases that were directly caused by traffic pollution and the indirect costs of caring for a child with asthma. The authors found that including this data almost doubled the estimated economic cost for these two communities alone. They propose that the novel approach used in the study is widely applicable for studying other urban areas with concentrations of housing close to major roadways.

Brandt found that the average annual cost of asthma care was approximately \$4,000 per case, with the loss of income due to the need to care for an affected child as the largest single component of cost. The authors said they used conservative cost estimates and did not account for the decrease in quality of life due to the disease. This cost value represents 7 to 8 percent of the median household income in this area, a level the authors consider as unsustainable for the average family.

Brandt noted that costs of asthma care could be decreased by policies to improve air quality, including tighter emission limits, more use of public transportation, and limitations on housing developments in close proximity to major roads. As cost of asthma care is equal to more than 20 percent of the annual budget for the Long Beach Department of Health and Human Services, there could be a significant return on investments in improving air quality.

Citation: [Brandt SJ, Perez L, Künzli N, Lurmann F, and McConnell R](#). 2012. Costs of childhood asthma due to traffic-related pollution in two California communities. *Eur Respir J*; doi 10.1183/09031936.00157811 [Online 26 January 2012]. [Summary](#)

(Brant Hamel, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Signal Transduction Molecular Endocrinology Group.)

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McConnell is the lead researcher for a large prospective cohort study within the Children's USC Health Study investigating environmental factors involved in the development and exacerbation of asthma. (Photo courtesy of USC)

Children exposed to cadmium may be at higher risk for learning disabilities

By Carol Kelly

Children and teens with higher cadmium levels are more likely to have learning disabilities and be placed in special education, according to a new NIEHS-funded [study](#) published by a team of researchers led by [Robert Wright, M.D.](#), from Harvard University. Research Fellow Timothy Ciesielski, M.D., Sc.D., also from Harvard, was first author on the study.

While the study also investigated a potential linkage with attention deficit hyperactivity disorder (ADHD), no statistically significant association was found. This finding may or may not be indicative of a distinction between neurocognitive and neurobehavioral dysfunction from cadmium exposure. As the authors point out, special education placement tends to be a catch-all that may include ADHD in some places.

The link between cadmium and learning disabilities may be occurring at typical exposure levels, an inference drawn from the use of a nationally representative sample of students 6-15 years old. “If these associations are replicated in other populations, then neurodevelopmental toxicity may be a sensitive endpoint to consider in future cadmium risk assessments,” the researchers wrote.

The study used data from the National Health and Nutrition Examination Survey ([NHANES](#)), a unique study with both interviews and physical examinations, sponsored by the Centers for Disease Control and Prevention. According to the researchers, the NHANES research design has widely recognized strengths in terms of statistical power and generalizability. Additionally, because cadmium accumulates in the kidneys for extended periods, the urinary cadmium concentration data obtained from NHANES indicates long-term exposure of children.

A research focus on neurodevelopmental toxicology and children

Wright, a physician who leads the [Harvard School of Public Health Superfund Research Program](#), conducts extensive research in neurodevelopmental toxicology, particularly genetic and environmental factor interactions that may influence brain development and function. Wright specializes in evaluating children with learning and behavioral disabilities suspected to have been exposed to environmental toxicants.

According to Wright, human movement, awareness, sensations, language, thought, and memory — the essence of humanity — are all controlled by the brain and central nervous system. Because this system is so vital, understanding how chemicals impact neurodevelopment, even at low exposure levels, is a high priority in environmental health. By focusing on real human exposures to known toxicants like cadmium, Wright’s team hopes its research will ultimately help inform public health guidelines to protect child neurodevelopment.



*Wright is especially interested in the synergistic effects from exposure to psychosocial stress and one or more environmental toxicants.
(Photo courtesy of Robert Wright)*

What and where is cadmium?

As the authors explain, cadmium, a heavy metal, occurs naturally in lead, copper, zinc, and other ores. Water sources near existing and former cadmium-emitting industries have shown a marked elevation of cadmium in sediments and aquatic organisms. Except in the vicinity of cadmium-emitting industries or incinerators, the intake of cadmium from drinking water or ambient air is of minor significance for children. The U.S. Environmental Protection Agency requires water suppliers to limit the cadmium concentration in water to a level of less than five micrograms per liter.

Cadmium can be released into the atmosphere through metal production activities, fossil fuel combustion, and waste incineration. Cadmium emissions travel through the atmosphere resulting in long-range deposition, causing varying concentrations of this metal in soil and water.

Crops grown in contaminated water or soil are the main source of cadmium exposure for the general population. Among crops, tobacco leaves naturally accumulate large amounts of cadmium. The greatest potential for above-average exposure to cadmium is from smoking, which may double the cadmium exposure of a typical individual.

Although researchers generally know where cadmium is geologically located, exposure sources are varied and can be difficult to isolate. More research is needed on the particular origins of cadmium exposures, to better understand the health risks.

Citation: Ciesielski T, Weuve J, Bellinger DC, Schwartz J, Lanphear B, Wright RO. 2012. Cadmium Exposure and Neurodevelopmental Outcomes in U.S. Children. *Environ Health Perspect*; doi: 10.1289/ehp.1104152 [Online 27 January 2012].

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

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SRP researchers test less expensive method for tar remediation

By Nancy Lamontagne

Superfund Research Program (SRP) researchers from the University of North Carolina (UNC) at Chapel Hill have published an NIEHS-funded [study](#) showing that alkaline and alkaline-polymer solutions might offer an effective and less expensive way to remove tars from former manufactured gas plant sites. Manufactured gas plants made flammable gas for heating and lighting in the United States and Europe until the 1950s.

According to the study, there are an estimated 36,000 to 55,000 former manufactured gas plants and related facilities in the U.S. Most of these plants produced waste tars that contain many known or suspected carcinogens and are challenging to remove. Cleanup for one site typically costs millions of dollars, according to the U.S. Environmental Protection Agency.

“Our work demonstrates a physicochemical method that is relatively inexpensive to apply, and that effectively and efficiently mobilized tars that were trapped under capillary forces,” said [Cass Miller, Ph.D.](#), the Daniel A. Okun Distinguished Professor of environmental sciences and engineering at the UNC Gillings School of Global Public Health. “Because of the large number of tar-contaminated sites that exist and the economical nature of this proposed method, abundant opportunities exist for field-scale applications of the method.”

Challenges of remediation

As the researchers explain, remediation methods must take into account the complex characteristics of manufactured gas plant tars, which contain thousands of compounds and vary in composition from site to site. The tars don't mix with water and, because they are also denser than water, they can move down through the water table until reaching a confining layer such as silt or clay. The tars can also become trapped in porous materials via capillary forces and can be non-Newtonian fluids, meaning they don't behave like water or other similar fluids. "In short, tars contain virtually every complication that one could conceive of in a subsurface and contaminant," Miller said.

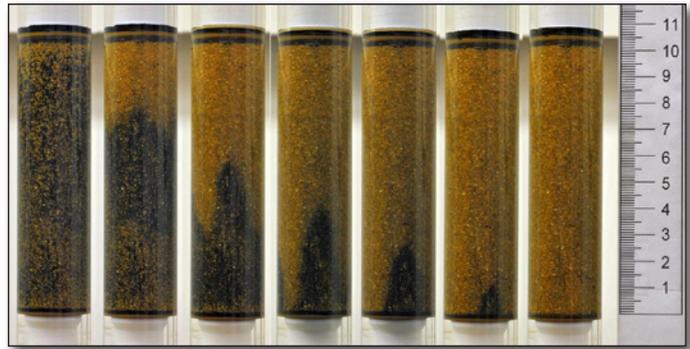
The researchers investigated mobilizing pore-trapped tars with alkaline agents, because these chemicals are readily available, inexpensive, and exhibit properties beneficial for contaminant mobilization. To test this method, they injected tar into sand-filled glass columns, which replicated natural mineralogy. Flushing the columns with alkaline solutions of sodium hydroxide (NaOH) removed up to 44 percent of the tar, and adding the polymer xanthan gum to the NaOH solution boosted the tar removal up to 93 percent. Other experiments showed that solutions of NaOH significantly reduced the forces that trap the tar in porous material.

The researchers say that the tar removal likely occurs because of reduced interfacial tension between the tar and water, due to stable displacement of the tar, and because the trapped tar formed a more connected phase. The team is continuing to evaluate the chemical mechanisms involved in the mobilization technique and is performing additional experiments in heterogeneous three-dimensional systems typically found in subsurface environments. They are also investigating ways to remove the small amount of residual contamination that remains after mobilization.

Citation: Hauswirth SC, Birak PS, Rylander SC, Miller CT. 2012. Mobilization of manufactured gas plant tar with alkaline flushing solutions. *Environ Sci Technol* 46(1):426-433.

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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A solution of NaOH and xanthan gum is flowed downward through a column of tar-contaminated sand and imaged every 90 minutes. From left to right, the tar saturation is 32 percent in the first photo and 3.7 percent in the last, corresponding to a removal of 88 percent of the tar. The ruler is marked in centimeters. (Photo courtesy of Cass Miller)



Miller tested a new way to remove tars from sites of former manufactured gas plants. He says that these tars contain virtually every complication that one could conceive of in a subsurface and contaminant. (Photo courtesy of UNC)

Studies find arsenic in food adds up

By Angela Spivey

Three studies published in the last two months by grantees of the NIEHS Superfund Research Program (SRP) and NIEHS/EPA Centers for Children’s Environmental Health and Disease Prevention Research add to the growing body of evidence for proposals that arsenic levels in food require regulation.

The studies show that, in some cases, the amount of total arsenic being consumed in certain common foods is as much or more than the acceptable limits set for drinking water by the U.S. Environmental Protection Agency (EPA). In all three studies, the authors conclude that the results point to a need to set regulatory limits for arsenic in food.

“It’s possible that for a large number of individuals, their main exposure route to arsenic is food, not water. But we don’t have guidelines on what the acceptable levels are for arsenic in food,” said [Brian Jackson, Ph.D.](#), director of the Trace Element Analysis Core Facility at Dartmouth College, a member of the SRP, and the lead author of two of the studies.

Popular foods may be sources of arsenic

The research findings, published in December 2011 and January and February 2012, show that in addition to plain rice, foods that may be sources of arsenic exposure include toddler formula, baby foods, cereal bars, and energy gels used by athletes.

“From all these food products, the exposure is cumulative,” Jackson said. One food alone would not be cause for concern, but eating a diet made up exclusively of rice-based foods may expose people to arsenic levels comparable to the current drinking water limits. “Groups at potentially greatest risk are toddlers who are fed a rice syrup-based toddler formula, and potentially people who are following a gluten-free diet,” Jackson explained. Many gluten-free products substitute rice for wheat.

The most recent of the three studies, published Feb. 16 in *Environmental Health Perspectives*, found that organic brown rice syrup, which is used in organic food products as an alternative to high fructose corn syrup, can contain significant concentrations of inorganic arsenic, the form classified as a human carcinogen. Toddler formula, cereal bars, and energy foods aimed at athletes that contained organic brown rice syrup had higher total arsenic concentrations than similar products that didn’t contain the syrup. One toddler formula that listed organic brown rice syrup as the main ingredient had inorganic arsenic concentrations that were up to 2.5 times the EPA safe drinking water limit.



Jackson discovered arsenic where many people would never expect to find it — in baby formula and organic rice products. (Photo courtesy of Dartmouth College)



Karagas identified rice as the source of elevated arsenic levels in a cohort of U.S. women. (Photo courtesy of Dartmouth College)

Infants of special concern

Jackson's January 2012 study, published in *Pure and Applied Chemistry*, showed that infant formula and jarred baby foods are a significant source of arsenic exposure. Though many of the formulas and foods tested had relatively low levels of arsenic, 1-23 nanograms per gram of food, the levels were of concern because the arsenic was mostly of the toxic inorganic form and because infants are so small.

"Especially for some of the second- and third-stage foods, infants could be getting a high rate of exposure to arsenic based on their body weight," Jackson said. These exposures do not include any additional exposure from water or from rice-based cereals. "However, comparing levels in food to safe drinking water limits is not ideal. Drinking water limits are based on lifetime exposure and can't be translated to any single food item. This further highlights the need for guidelines or regulations specifically for food," cautions Kathryn Cottingham, Ph.D., who leads the Children's Center study investigating dietary sources of arsenic among infants.

An earlier study showed that in pregnant women, rice consumption was associated with increased urinary levels of arsenic. Women who had eaten rice in the previous two days had urinary arsenic concentrations of 5.27 micrograms per liter, compared to 3.38 micrograms per liter for those who hadn't eaten rice, a statistically significant difference. The study was published December 2011 in the *Proceedings of the National Academy of Sciences*. [Margaret Karagas, Ph.D.](#), was the senior author of this study and principal investigator of the cohort.

Citations:

[Gilbert-Diamond D, Cottingham KL, Gruber JF, Punshon T, Sayarath V, Gandolfi AJ, Baker ER, Jackson BP, Folt CL, Karagas MR.](#) 2011. Rice consumption contributes to arsenic exposure in U.S. women. *Proc Natl Acad Sci U S A.* 108(51):20656-20660.

[Jackson BP, Taylor VF, Punshon T, Cottingham KL.](#) 2012. Arsenic concentration and speciation in infant formulas and first foods. *Pure Appl Chem* 84(2): 215-223

[Jackson BP, Taylor VF, Karagas MR, Punshon T, Cottingham KL.](#) 2012. Arsenic, Organic Foods, and Brown Rice Syrup. *Environ Health Perspect*; doi: 10.1289/ehp.1104619 [Online 16 February 2012].

(Angela Spivey is a contract science writer for the NIEHS Superfund Research Program.)

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SRP researcher links contaminants in drinking water to mental illness

By Rebecca Wilson

The solvent tetrachloroethylene (PCE) is known to cause mood and anxiety disorders in adults, but a new study from the Boston University Superfund Research Program (SRP) shows that childhood exposure may also lead to mental health problems in adulthood. [Ann Aschengrau, Sc.D.](#), published findings that link early childhood exposure to PCE-contaminated water to increased risk of psychological disorders later in life. The NIEHS-funded study appeared Jan. 20 in the journal *Environmental Health*.

Aschengrau conducted a retrospective epidemiological study of 1,500 exposed and unexposed individuals, and found that those with prenatal and early childhood exposure to PCE were nearly twice as likely to be diagnosed with bipolar disorder or post-traumatic stress disorder compared to the unexposed group.

Findings with a Cape Cod cohort

Study participants lived in and around Cape Cod, Mass., between 1968 and the 1980s. Subjects in the exposed group lived in homes where water was supplied by vinyl-lined municipal pipes that were found to be leaking PCE into the drinking water supply. Pipes were flushed in the 1980s to correct the problem. Participants in the unexposed group lived in the area at the same time, but their water was not supplied by the contaminated lines.

Aschengrau said of the exposures, “While it is impossible to calculate exactly the amount of PCE people were exposed to, some recorded levels were as high as 1,550 times the currently recommended safe limit.” She found that while the incidence of bipolar disorder and post-traumatic stress disorder increased with any level of exposure, the highest rates of incidence were among those who had the highest estimated exposures.

Participants completed questionnaires, reporting on whether or not they had experienced symptoms of depression, schizophrenia, bipolar disorder, or manic-depressive disorder. They were also asked whether or not a health care provider had ever said they had the illness and, if so, when that diagnosis occurred.

According to the study, many adults are exposed to PCE in the dry cleaning and textile industries. The solvent is also used as a metal degreaser and can be found in the automotive industry. It is a neurotoxin known to cause mood changes, anxiety, and depressive disorders in people who are exposed through their occupations. Interestingly, Aschengrau reported that she found no association between PCE exposure and depression.

Citation: [Aschengrau A, Weinberg JM, Janulewicz PA, Romano ME, Gallagher LG, Winter MR, Martin BR, Vieira VM, Webster TF, White RF, Ozonoff DM. 2012. Occurrence of mental illness following prenatal and early childhood exposure to tetrachloroethylene \(PCE\)-contaminated drinking water: a retrospective cohort study. Environ Health 11\(1\):2. \[Summary\]\(#\)](#)

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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NIH pioneer discovers genes linked to high altitude tolerance

By Jeffrey Stumpf

With the wide range of ecosystems that humans populate, it is possible that populations in extreme climates may have adapted to harsh conditions through evolution.

A new study in *Genome Biology* is the latest manuscript to identify genetic adaptations prevalent in populations living in high altitudes. Led by a recipient of a 2009 NIH [Pioneer Award](#) funded by NIEHS, [Sarah Tishkoff, Ph.D.](#), the research team describes mutations in genes involved in adaptation to low oxygen levels, including *CBARA1*, *VAV3*, *ARNT2*, and *THRB*, three of which have not been previously implicated in genome-wide high altitude studies.



An earlier study by Aschengrau ([see story](#)) linked PCE exposure and birth defects. (Photo courtesy of Boston University)

Tishkoff, a professor at the University of Pennsylvania, and her colleagues teamed up with professors in the department of biology of Addis Ababa University to conduct genome-wide association studies (GWAS) comparing populations that live in contrasting regions in Ethiopia.



Linked video:
Learn more about Tishkoff's work by [viewing her Penn Engaging Minds series lecture, 'Human Origins in Africa' \(42:03\)](#)

(Launches in new window)

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Living with less oxygen

Tolerance to high altitude conditions had previously been researched using populations living in Tibet and the Andes. These mountain-dwelling people contained mutations in genes that are associated with hemoglobin levels, the proteins that bind oxygen in the blood. Increases in hemoglobin would be favorable for living in hypoxic, or low oxygen, conditions.

In some people, especially pregnant women, hypoxia can cause sickness and sometimes death. Like the Tibetans and Andeans, the Amhara people living in the Ethiopian highlands experience fewer complications due to the altitude. Tishkoff's group discovered genes in the Amharas that were different from the genes found in the Tibetans and Andeans, but still involved in tolerance to hypoxic conditions. Thus, populations may have adapted to the same conditions through independent mutations — a process called convergent evolution.

A search for candidate genes

Evolutionary biologists, such as Tishkoff, are taking advantage of the recently available opportunity to cost-effectively sequence multiple human genomes. However, knowing entire DNA sequences from different populations does not tell the entire story. Because of variability among people, Tishkoff noted that finding important mutations that change evolutionary processes requires drastic differences to measure.

“The easiest way for us to [find genetic variants that play a role in functional adaptation] is to look at situations where there's been very strong selective pressure — a disease with a really high mortality rate or here at high altitude where there are hypoxic conditions,” Tishkoff was quoted as saying in a University of Pennsylvania press release about the study. “This kind of situation makes a dramatic difference in terms of who passes on their genes, so it gives us more power to find the genetic signatures left behind.”



Tishkoff spoke at NIEHS during a meeting of the [National Advisory Environmental Health Sciences Council](#). She is a Penn Integrates Knowledge professor with appointments in the Perelman School of Medicine and the biology department at the University of Pennsylvania. (Photo courtesy of Steve McCaw)

Choosing the road less traveled

The concept of extracting blood samples from populations in the Ethiopian highlands seems relatively straightforward. However, the lack of infrastructure, limited resources, and even impassable roads made conducting science in these remote locations a major challenge.

“What we planned as a two-month trip turned into a five-month trip,” Tishkoff recalled during a talk at NIEHS this past September ([see story](#)). “There are a lot of challenges to doing this kind of research in Africa.”

With members of her lab, Tishkoff travelled with all the necessary supplies in a mobile lab. The lack of electricity in some villages required that they power their centrifuge using a generator or car battery.

To maintain high ethical standards, the studies required multiple rounds of ethical reviews, institutional review board consent at the university level, and consent from the communities and individuals ([see related story](#)).

Despite the difficulties, Tishkoff maintains that studies in Africa are especially powerful resources, not only to learn medically important genetic information about the understudied African populations, but also to understand human evolution.

“Because of the high levels of genetic, cultural, and climatic diversity in Africa, there has likely been local adaptation within populations from different regions practicing diverse lifestyles,” Tishkoff said in an interview published in *Human Biology*. “Therefore, the possibility of geographically restricted rare, as well as common, functional variants requires the inclusion of a broad range of geographically and ethnically diverse African populations in human genetic studies.”

Citations:

[Scheinfeldt LB, Soi S, Thompson S, Ranciaro A, Meskel DW, Beggs W, Lambert C, Jarvis JP, Abate D, Belay G, Tishkoff SA](#). 2012. Genetic adaptation to high altitude in the Ethiopian highlands. *Genome Biol* 13(1):R1 [Online 20 January 2012].

[Tishkoff S](#). 2011. Interview with Sarah Tishkoff: perspectives for genetic research in African populations. Interview by Giovanni Destro-Bisol. *Hum Biol* 83(5):637-644.

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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Panel peer reviews and approves seven NTP technical reports

By Robin Mackar

A panel of external scientific experts convened by the National Toxicology Program (NTP) peer reviewed and approved the conclusions of seven draft technical reports. The two-year studies outlined in the NTP technical reports covered a broad spectrum of substances ranging from a popular herbal supplement and industrial solvents to HIV treatment approaches. The meeting Feb. 8-9 was webcast and included presentations and comments from the public.



NTP's Hooth reminded the panel members of their charge at the onset of the NTP Technical Reports Peer Review meeting. (Photo courtesy of Steve McCaw)

After brief welcoming remarks by NIEHS/NTP Director Linda Birnbaum, Ph.D., and NTP Associate Director John Bucher, Ph.D., and accolades to NTP's Michelle Hooth, Ph.D., and David Malarkey, D.V.M., Ph.D., for overseeing the reports, the meeting began with a short presentation by Hooth outlining the panel's charge.

Hooth discussed how NTP technical reports describe the methods, results, and NTP conclusions. She said NTP conclusions are presented as levels of evidence under the specific conditions of each study, and that both the clear and some-evidence conclusions indicate positive responses for carcinogenic activity in the rodent studies. It was the panel's role to determine whether the study's experimental design, conduct, and findings support the NTP's conclusions.

Presentations on Ginkgo and DMPT

June Dunnick, Ph.D., of NTP kicked off the first studies to be reviewed, which were on N,N-Dimethyl-p-toluidine (DMPT), a high-production chemical used in dental materials and bone cements. Dunnick presented data showing that both rats and mice developed tumors after being given DMPT for up to two years. The NTP also found anemia-like symptoms in rats and mice. All three primary reviewers, as well as the panel, concurred with the clear -evidence call made by the NTP.

The second report on *Ginkgo biloba* extract was presented by NTP's Cynthia Rider, Ph.D. Ginkgo is among the top five herbal supplements on the market, with an estimated 7.7 million Americans taking it in 2002. Ginkgo extract was given orally to mice and rats for up to 105 weeks. The NTP found an increase in liver cancer in male and female mice, and in cancer of the thyroid gland in male and female rats and male mice.

Written and oral comments from the American Herbal Products Association and from Intertek Cantox were presented to the panel. The comments largely focused on the Ginkgo biloba extract used in the NTP studies, claiming that it was not representative of ginkgo products in the U.S.



Rider smiled as she completed her presentation on the NTP ginkgo studies. (Photo courtesy of Steve McCaw)



Dunnick of NTP responded to comments made by panel members on the DMPT technical report. (Photo courtesy of Steve McCaw)



Chair Stephen Roberts, Ph.D., center, of the University of Florida, kept the meeting and the discussion moving along nicely. He was flanked by NTP's Danica Andrews, right, the designated federal official and Malarkey. (Photo courtesy of Steve McCaw)

With citations in hand, Rider said, “The range of constituents in the ginkgo extract used in our NTP studies is within the ranges found in the U.S. market.” After a brief discussion around this topic, Birnbaum commented on the importance of putting human-use doses into context for people, so they can better understand, appreciate, and use the NTP findings.

NTP pathologist Mark Hoenerhoff, D.V.M., Ph.D., also added to the discussion by presenting molecular work conducted by NTP on ginkgo, which begins to unravel the underlying mechanisms for the tumors in the rodent studies. “We really applaud this extra effort by the NTP. It is very helpful in interpreting the data,” said Paul Howard, Ph.D., of the National Center for Toxicological Research (NCTR) at the U.S. Food and Drug Administration. Hoenerhoff’s findings are being submitted to a peer-reviewed journal.

Remaining technical reports approved

After hearing the study overview and conclusions put forward by NTP study scientist Michael Wyde, Ph.D., on beta-picoline, a solvent used to make pharmaceuticals, resins, dyes, rubber accelerators, and insecticides, the panel voted to accept the NTP conclusions as written.

The reviewers also heard presentations on two dermal studies that were conducted by NTP. The panel approved of the studies and conclusions presented by NTP’s Minerva Mercado-Feliciano, Ph.D., on pyrogallol, a byproduct of plant tannins used to make consumer products, such as some hair dyes and photography developers. After hearing the discussion on trimethylolpropane triacrylate from NTP’s In Ok Surh, Ph.D., and a few public comments, the panel recommended minor revisions to the NTP conclusions on this industrial compound. The NTP will consider the input from the panel in finalizing the technical reports.

On the second day of the meeting, the panel also approved the two final reports on AIDS therapeutics. After a brief introduction from Howard, Julian Leakey, Ph.D., also of NCTR, thoughtfully walked the panel through the details



Howard not only provided insightful comments on many of the reports, but was also one of several staff scientists from the NCTR facility in Arkansas who presented at the meeting. (Photo courtesy of Steve McCaw)



Hoenerhoff’s presentation on the molecular studies on Ginkgo biloba extract was one of the highlights of the meeting. The panel seemed to enjoy hearing about these additional studies. (Photo courtesy of Steve McCaw)



Panel member Michael Elwell, D.V.M., Ph.D., of Covance Laboratories is shown voting on one of the seven technical reports the members reviewed. (Photo courtesy of Steve McCaw)

of the two reports on 3'-azido-3'-deoxythymidine (AZT) and its combined mixtures with lamivudine or nevirapine. AZT is widely used worldwide, as part of combination drug therapy, to stop mother-to-child transmission of HIV. However, the long-term or lifetime consequences of perinatal exposure to these therapies are unknown. The studies were conducted in genetically modified mice.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison.)

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Webinar series addresses early-life exposures

By Emily Zhou

An NIEHS Superfund Research Program (SRP) [webinar](#) Feb. 3 explored the potentially adverse effects of exposure to brominated fire retardants (BFRs) during critical windows of susceptibility. Hosted by SRP Director Bill Suk, Ph.D., the Risk eLearning Web Seminar was the first in a continuing series on the long-term health consequences of early-life environmental exposures.

According to the presenters, BFRs are present everywhere in the environment, and exposures to these chemicals at an early age can lead to a range of detrimental health effects later in life, either by increasing susceptibility to disease or by initiating disease processes.

Fire retardant chemicals in the environment

The first speaker in the webinar was NIEHS/NTP Director Linda Birnbaum, Ph.D., a leader in research on polybrominated diphenyl ethers (PBDEs), a group of chemicals widely used as fire retardants. “BFRs do not bind chemically to polymers in textiles and plastics,” Birnbaum said. “They leach out or evaporate from flame retarded products,” spreading widely in dust, water, and air.



Linked video:

[Watch interviews with Birnbaum and Stapleton \(02:39\)](#)

(Launches in new window)

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Birnbaum presented data indicating that levels of PBDEs in humans and animals increased dramatically from 1970 to 2005. Levels are much higher in the U.S. than in Europe. (Photo courtesy of Steve McCaw)

From consumer products, furnishings, and building materials, PBDEs enter air and dust in indoor environments, while landfills and waste treatment facilities carry the chemicals into the food chain, affecting wildlife, plants, and water. Birnbaum pointed to a number of animal and recent human studies that have found correlations between PBDEs and impaired reproductive function, altered neurological development, obesity, and diabetes.

The European Union has banned use of all PBDEs, and the U.S. is soon to follow with a voluntary phase out, but they are persistent chemicals and many PBDE-treated products are still in use. A rapid increase in BFR use in Asian markets has contributed to global concern about ongoing exposures, as have studies showing elevated levels of PBDE in people working in electronics waste disposal sites in China and Nicaragua.

High exposure of toddlers to chemicals that mimic thyroid hormone

“PBDEs are present in much higher quantities in [household] dust than in soils,” said the second speaker, Heather Stapleton, Ph.D. Stapleton is an SRP grantee, an NIEHS Outstanding New Environmental Scientist awardee, and an assistant professor at the Duke University Nicholas School of the Environment. Because children are spending more time indoors and have a greater number of hand-to-mouth contacts with household dust and treated products, toddlers are the most highly exposed age group for PBDE exposure, which is associated with altered thyroid regulation that may be playing a role in deficits in neurological development.

Taking blood samples, as well as samples from hand wipes and house dust, Stapleton’s laboratory conducted studies of birth outcomes in pregnant women and of toddlers. Study results showed the presence of PBDEs in all serum samples and a strong association between PBDEs in serum and PBDE residues on hand wipes. Exposure patterns change with age, Stapleton said, from mother’s milk for infants, to dust for toddlers, and to diet for older children and adults, but dust is a key route of exposure for all age groups. Observing an association between socioeconomic status and PBDE level, Stapleton speculated that PBDE’s might also be an environmental justice issue.



Stapleton said the greatest exposure to flame retardants occurs in indoor environments. “Even some materials in our cars are treated with flame retardants.” (Photo courtesy of Duke University)

PBDEs as a neurotoxicant and possible carcinogen

Although Birnbaum and Stapleton had also raised the question of whether PBDEs, because of their structural similarity to polychlorinated biphenyl (PCBs), could be neurotoxic and even carcinogenic, the final speaker of the seminar, Prasada Kodavanti, Ph.D., addressed the issue in greater detail from the perspective of neurotoxicology. Kodavanti is a senior researcher in the Neurotoxicology Branch at the U.S. Environmental Protection Agency.

As Kodavanti explained, PBDEs have chemical structures that are very similar to known cancer-causing and neurotoxic compounds, such as PCBs, dioxins, and other persistent organic pollutants, and that levels of PBDEs are doubling every two to five years, quickly approaching the levels of PCBs in humans. The mechanisms of action are similar to those proposed for PCBs, with depression of serum T4, effects on intracellular signaling, and effects on neurotransmitters.

Kodavanti pointed to changes in the expression of proteins that related to energy metabolism, calcium signaling, and growth of the nervous system. He cautioned that PCBs and PBDEs might have synergistic effects on reproductive and neurological development.

(Emily Zhou, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)



“One approach [to understanding risk of adverse health effects],” Kodavanti said, “could be to compare current levels of PBDEs in humans with those of PCBs that are known to produce adverse human health effects, including developmental neurotoxicity.” (Photo courtesy of Prasada Kodavanti)

Green chemical considerations for new flame retardants

Birnbaum closed her talk with a few caveats for developing safer flame retardants, with the following factors in mind:

- Alternative chemicals other than BFRs or other classes of fire retardants
- Minimized potential for hazard and exposure
- Low persistence and bioaccumulation for breakdown products, as well as parent chemicals
- Low toxicity, less potential for harm when exposure occurs
- Low exposure, less potential for release

Market considerations for flame retardant alternatives

Birnbaum also acknowledged alternatives need to be cost-effective and functional by addressing the following issues:

- Aesthetics and performance — appearance, durability, fire safety
- Process equipment cost
- Alternative technologies, barriers, surface treatments, graphite impregnated foams

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Federal agencies respond to test method recommendations

By Debbie McCarley and Cathy Sprankle

U.S. federal agencies, including NIEHS, have agreed with recommendations for use of a method that requires fewer animals and enables pain-free testing to categorize chemicals and products that are likely to cause allergic contact dermatitis in humans as strong skin sensitizers.

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) evaluated the scientific validity of the proposed method, the murine local lymph node assay (LLNA), and recommended how it could be used for regulatory testing and safety decisions. Regulatory agencies, including the U.S. Food and Drug Administration, U.S. Environmental Protection Agency, Consumer Products Safety Commission (CPSC), and Occupational Safety and Health Administration, have indicated that they will take actions in response to the ICCVAM recommendations to encourage use of the LLNA for this purpose where appropriate.

“Based on the ICCVAM evaluation, the LLNA can be used to identify those chemicals likely to pose the greatest hazard of allergic skin reactions for consumers and workers,” noted William Stokes, D.V.M., director of the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological



Methods (NICEATM), which administers ICCVAM. “The LLNA will also provide important animal welfare benefits compared to historical testing methods by eliminating animal discomfort during testing and using 40 to 50 percent fewer animals.

Protecting consumers and workers from allergic contact dermatitis

Allergic contact dermatitis (ACD) is a skin reaction characterized by localized redness, swelling, blistering, or itching after direct contact with a skin allergen. Poison ivy is a well-known cause of ACD, but the condition also develops in people exposed to skin-sensitizing chemicals and products in the home or workplace. These substances include chemicals such as formaldehyde, formulations such as pesticides, and metals such as nickel. Occupational skin diseases, including ACD, are the most common type of occupational disease, with government estimates of the annual costs exceeding \$1 billion.

To protect workers and consumers, U.S. regulatory agencies require the testing of chemicals and products to determine their potential to cause ACD. For over 10 years, the LLNA has been accepted worldwide as a valid alternative to traditionally used guinea pig test methods for assessing ACD hazard potential for most testing applications. Compared to guinea pig tests, the LLNA uses fewer animals, requires less time to perform, provides dose-response information, and eliminates the pain and distress produced by positive reactions.

Identifying strong skin sensitizers

However, past use of the LLNA has been limited to a “yes/no” determination of whether or not a substance has the potential to cause ACD in humans. The CPSC, under the Federal Hazardous Substances Act, currently requires hazard labeling of only those products that are considered to be strong skin sensitizers. Based on requests from the CPSC, ICCVAM and NICEATM evaluated the extent that the LLNA could be used to correctly predict strong versus other than strong human skin sensitizers.

ICCVAM recommended a specific potency criterion that will allow results from the LLNA to be used to categorize chemicals and products as strong skin sensitizers. However, since this criterion identified only about half of the known strong human skin sensitizers tested, the potency criterion should be used only in a screening approach. Chemicals that meet the criterion could be categorized as strong skin sensitizers but chemicals that do not meet the criterion would require additional testing or information to determine that they are not strong skin sensitizers.

Setting the stage for adoption of the LLNA by federal agencies

The ICCVAM recommendations were communicated last summer to the ICCVAM member agencies ([see story](#)). ICCVAM member agencies are Federal regulatory and research agencies that require, use, generate, or distribute toxicological and safety testing information for chemicals, products, and other substances.

Details on the ICCVAM evaluation of the use of the LLNA to categorize skin sensitizers, including a recommended protocol for the LLNA, more information on the ICCVAM recommendations, and the agency responses, can be found on the [NICEATM-ICCVAM website](#).

The [U.S. Public Health Service Policy on Humane Care and Use of Laboratory Animals and Animal Welfare Act](#) regulations require consideration of alternative methods that may reduce, refine, or replace animal use prior to the approval of procedures involving animals, and their use when determined scientifically appropriate. Since the new testing methods reduce animal use and avoid pain and distress compared to traditional testing methods, they must now be considered and used for safety studies when appropriate.

NIEHS and NTP Director Linda Birnbaum, Ph.D., endorsed the ICCVAM recommendations shortly after they were issued. She noted that NIEHS scientists and the NIEHS Institutional Animal Care and Use Committee have been advised to consider the LLNA for studies evaluating ACD hazard potential, and to use the method when determined appropriate.

(Debbie McCarley is the special assistant to Rear Adm. William Stokes, D.V.M., director of NICEATM. Cathy Sprankle is a communications specialist with ILS, Inc., support contractor for NICEATM.)

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This month in EHP

By Eddy Ball

The lead story in this month's [Environmental Health Perspectives \(EHP\)](#) examines the hypothesis that cyanobacteria may be a major factor in neurodegenerative disease. Research has pointed to the cyanobacterial toxin BMAA (beta-methylamino-L-alanine) as the probable cause of amyotrophic lateral sclerosis–parkinsonism/dementia complex, which strikes the Chamorro people of Guam. Now some scientists speculate BMAA may be involved in other neurodegenerative conditions as well.

A second news story explores concerns over the number of medically unnecessary computerized tomography (CT) scans performed on patients each year. Mounting questions over cancer risks from ionizing radiation have medical professional organizations striving to improve CT imaging protocols so the technology prevents more problems than it causes.

This month's [Researcher's Perspective Podcast](#) features a discussion with Boston University research pharmacist Katherine Kelly on concerns over the use of phthalates as a timed-release coating on pharmaceuticals and dietary supplements.

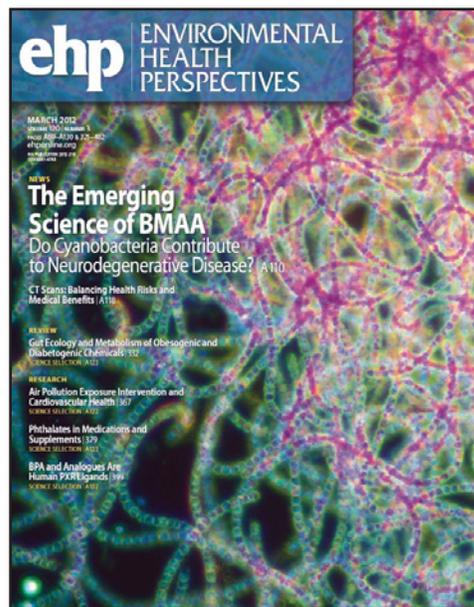
Research this month includes:

- Gut Ecology and Metabolism of Obesogenic and Diabetogenic Chemicals
- Air Pollution Exposure Intervention and Cardiovascular Health
- Phthalates in Medications and Supplements
- BPA and Analogues Are Human PXR Ligands

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<http://twitter.com/ehponline>



Upcoming workshop on individual susceptibility

By Eddy Ball

An innovative interagency program opens its 2012 workshop series with an exploration of “[Biological Factors that Underlie Individual Susceptibility to Environmental Stressors, and Their Implications for Decision-Making](#)” April 18-19 in Washington, D.C.



The workshop, which is part of the National Academies’ Emerging Science for Environmental Health Decisions series, is free and open to the public. Registrations are now being accepted for [attendees](#) and for the live [webcast](#).

Why individuals may respond differently to environmental exposure

The workshop will focus on the endogenous and biological factors that influence individual variability in response to environmental exposures, such as genetics and epigenetics, physiology, life stage, and other biological differences. Presenters will explore new and innovative approaches for characterizing individual variability, as well as approaches for and challenges to communicating the relationships among individual variability, disease susceptibility, and public health.

Sponsored by NIEHS, the program holds three workshops per year on the use of new discoveries, tools, and approaches for guiding environmental health decisions. The workshops provide a public venue for communication among government, industry, environmental groups, and the academic community.

The April workshop is the tenth in the [series](#), which began in July 2009 with a workshop on “Use of Emerging Science and Technologies to Explore Epigenetic Mechanisms Underlying the Developmental Basis for Disease.” Past presentations are archived online, and videos are available for several recent workshops.

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Extramural papers of the month

By Nancy Lamontagne

- [Obesity and childhood phthalate exposure](#)
- [The cost of asthma from traffic-related air pollution](#)
- [Childhood exposure to tetrachloroethylene and later mental illness](#)
- [New zebrafish line for studying aryl hydrocarbon receptor](#)



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

Obesity and childhood phthalate exposure

NIEHS grantees have published research that shows an association between obesity and childhood exposure to phthalates. These man-made endocrine disruptors are commonly used in plastic flooring and wall coverings, food processing materials, medical devices, and personal care products.

The researchers measured phthalate concentrations in the urine of 387 African-American and Hispanic children in New York City who were between 6 and 8 years old when enrolled in the study. One year later they measured the children's body size characteristics, including body mass index (BMI), height, and waist circumference. The urine test showed that more than 97 percent of study participants had been exposed to phthalates. The researchers found that increased body size in overweight children correlated with higher levels of exposure to monoethyl phthalate and to the sum of the low molecular-weight phthalates studied. More research is needed to definitively determine whether phthalate exposure causes increases in body size, but the work does provide evidence that phthalates could contribute to childhood obesity.

Citation: Teitelbaum SL, Mervish N, Moshier EL, Vangeepuram N, Galvez MP, Calafat AM, Silva MJ, Brenner BL, Wolff MS. 2012. Associations between phthalate metabolite urinary concentrations and body size measures in New York City children. *Environ Res* 112:186-193.

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The cost of asthma from traffic-related air pollution

NIEHS-funded researchers have estimated that childhood asthma associated with air pollution in Long Beach and Riverside, Calif., costs \$18 million each year. Asthma cases attributed to traffic-related pollution contributed to almost half of the cost, and the remaining cost came from asthma exacerbations triggered by traffic-related pollution in children with asthma not caused by air pollution.

According to the researchers, traditional methods for assessing risk from air pollution have underestimated the overall burden of asthma and the costs associated with air pollution. They estimated the annual costs of childhood asthma from traffic-related pollution using their previous estimates of the number of asthma cases attributable to pollution, cost estimates for asthma exacerbations that occur because of regional air pollutants, and information on health care visits by children with asthma. They included a broad range of health care costs such as parents' missed work days, extra doctor visits, travel time, and prescriptions.

The researchers calculated the total annual cost for a typical asthma case to be \$3,819 in Long Beach and \$4,063 in Riverside. The largest portion of this cost came from asthma-related school absences, which often require that parents or caregivers miss work. The investigators say that their new method takes into account the full impact of traffic-related pollution and can be applied to other urban areas.

Citation: Brandt SJ, Perez L, Künzli N, Lurmann F, McConnell R. 2012. Costs of childhood asthma due to traffic-related pollution in two California communities. *Eur Respir J*; doi: 10.1183/09031936.00157811 [Online 26 Jan 2012]. [Story](#)

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Childhood exposure to tetrachloroethylene and later mental illness

NIEHS grantees have published a study linking early childhood exposure to the solvent tetrachloroethylene with mental health problems later in life. Tetrachloroethylene is used in dry cleaning and other industries.

Tetrachloroethylene has been shown to increase anxiety and depression, but little is known about how prenatal and early childhood exposure to the solvent affects risk for mental illness. The vinyl liner of water distribution pipes installed in Cape Cod, Mass., from the 1960s to early 1981 led to tetrachloroethylene contamination in drinking water at concentrations from 1.5 to 7,750 parts per billion. The researchers studied people who were born in Cape Cod between 1969 and 1983, including 831 people who experienced prenatal and early childhood tetrachloroethylene exposure, and 547 people who were unexposed. They used questionnaires to gather information on mental illnesses, demographic and medical characteristics, other sources of solvent exposure, and places of residence from birth through 1990.

The study showed that subjects with prenatal and early childhood exposure had an increased risk of bipolar disorder and post-traumatic stress disorder, but not an increased risk for depression. Although the tetrachloroethylene in Cape Cod has been addressed by periodic pipe flushing, people are still exposed to the contaminant in the dry cleaning and textile industries.

Citation: [Aschengrau A, Weinberg JM, Janulewicz PA, Romano ME, Gallagher LG, Winter MR, Martin BR, Vieira VM, Webster TF, White RF, Ozonoff DM](#). 2012. Occurrence of mental illness following prenatal and early childhood exposure to tetrachloroethylene (PCE)-contaminated drinking water: a retrospective cohort study. *Environ Health* 11(1):2. [Story](#)

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New zebrafish line for studying aryl hydrocarbon receptor

NIEHS-supported researchers have developed a new zebrafish line that expresses a non-functioning aryl hydrocarbon receptor (AHR)2. AHR2 mediates the toxic effects of dioxin, and a functional knockout line for this receptor could help reveal more about its role in toxicological response and other biological processes.

Zebrafish offer a useful model for studying the effects of exposures on development. They have AHR2, AHR1A, and AHR1B versions of the receptor. The researchers used a method called targeting induced local lesions in genomes (TILLING) to create a mutation in the *ahr2* gene (*ahr2*(hu3335)) and then confirmed the absence of AHR2 activity in the resulting mutant line. With the new zebrafish line, investigators can study AHR2 function throughout the organism's lifespans or examine the function of AHR1A and AHR1B, which has been difficult to do.

Citation: [Goodale BC, La Du JK, Bisson WH, Janszen DB, Waters KM, Tanguay RL](#). 2012. AHR2 mutant reveals functional diversity of aryl hydrocarbon receptors in zebrafish. *PLoS One* 7(1):e29346.

(Nancy D. Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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Intramural papers of the month

By Sonika Patial and Ian Thomas

- [EET research may help in the fight against cancer](#)
- [Early-life soy exposure and gender-role play behavior in children](#)
- [Tet1 is essential for pluripotency in mouse embryonic stem cells](#)
- [The role of CD103\(+\) dendritic cells in allergic lung inflammation](#)

EET research may help in the fight against cancer

Researchers have found that the removal of small molecules produced in the body called epoxyeicosatrienoic acids (EETs) may prevent the formation of blood vessels that feed tumor cells. A collaborative team, made up of scientists from NIEHS and other institutions, made the discovery and published the findings in the *Journal of Clinical Investigation*. Their paper was also the first to demonstrate that EETs work with a protein known to induce blood vessel growth, called vascular endothelial growth factor (VEGF), to promote metastasis or the spread of cancer.

High levels of EETs are beneficial in patients with diseases, such as hypertension, heart attack, and stroke, because the molecules cause blood vessels to dilate. This action reduces the pressure in the vascular system, and protects against cell death. However, lots of EETs in the body also make tumor cells grow faster. To determine the role EETs played in cancer, the team developed four strains of mice, three with high levels of EETs and one with low levels of EETs.

The team determined that EETs in the healthy tissue surrounding the tumors activate blood vessel formation which feed the tumors. The mice with higher EETs also produced more metastatic tumors than the mice with lower EETs. These results have important implications for the development of new cancer therapies.

Citation: Panigrahy D, Edin ML, Lee CR, Huang S, Bielenberg DR, Butterfield CE, Barnes CM, Mammoto A, Mammoto T, Luria A, Benny O, Chaponis DM, Dudley AC, Greene ER, Vergilio JA, Pietramaggiori G, Scherer-Pietramaggiori SS, Short SM, Seth M, Lih FB, Tomer KB, Yang J, Schwendener RA, Hammock BD, Falck JR, Manthati VL, Ingber DE, Kaipainen A, D'Amore PA, Kieran MW, Zeldin DC. 2012. Epoxyeicosanoids stimulate multiorgan metastasis and tumor dormancy escape in mice. *J Clin Invest* 122(1):178-191. [Story](#)

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Early-life soy exposure and gender-role play behavior in children

According to scientists from NIEHS and the University of North Carolina Gillings School of Global Public Health, early-life soy exposure is associated with play behavior that is less typically female in girls at 42 months of age. The team did not observe similar changes in boys. The work represents an important issue in children's health, because soy-based infant formula contains isoflavones, estrogen-like compounds that can induce changes in gender-typical behavior in experimental animals if they are exposed to high doses at a young age.

In this study, scientists examined parents' reports of gender-typical play behavior in 3,664 boys and 3,412 girls at 30, 42 and 57 months of age, in relation to their exposure to soy-based and non-soy-based infant feeding methods, categorized as primarily breast-fed, early formula-fed, early soy-fed, and late soy-fed.

While less feminine behavior was found in early soy-fed girls, defined as those introduced to soy at or before 4 months of age, the researchers emphasize that these girls were not outside the normal range for typical female behavior. Additionally, this finding was not observed at 30 and 57 months, suggesting that the influence of an environmental factor, such as soy, may become more or less important over time.

Citation: [Adgent MA, Daniels JL, Edwards LJ, Siega-Riz AM, Rogan WJ](#). 2011. Early-life soy exposure and gender-role play behavior in children. *Environ Health Perspect* 119(12):1811-1816.

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Tet1 is essential for pluripotency in mouse embryonic stem cells

In a new study, researchers at NIEHS and the University of New York School of Medicine found that acute short term depletion of Tet1 results in the loss of mouse embryonic stem cell (mESC) identity. The finding is in contrast to genetic deletion of Tet1, which has been previously shown to have no effect on the maintenance of embryonic stem cells in an undifferentiated state. The conclusions help scientists better understand how embryonic stem cells sustain their pluripotency or the ability to differentiate into specialized cells in the body.

Tet1 is an enzyme that catalyzes the oxidation of 5-methylcytosine to 5-hydroxymethylcytosine (5hmC) and promotes DNA demethylation. Investigators used RNA interference to deplete the levels of Tet1 in mESCs and measured the expression levels of genes involved in the maintenance of an undifferentiated state, genes involved in differentiation, and levels of 5hmC. The results showed that depletion of Tet1 in mESCs led to a reduction in 5hmC and the expression levels of genes involved in maintaining the pluripotent state with a simultaneous increase in the expression of genes known to induce differentiation. The study also goes on to show dependence of LIF/Stat3 signaling on Tet1.

The data support the hypothesis that an acute short-term depletion of Tet1 induces reduction in 5hmC, and uncovers a molecular mechanism by which Tet1 regulates the pluripotency state.

Citation: [Freudenberg JM, Ghosh S, Lackford BL, Yellaboina S, Zheng X, Li R, Cuddapah S, Wade PA, Hu G, Jothi R](#). 2011. Acute depletion of Tet1-dependent 5-hydroxymethylcytosine levels impairs LIF/Stat3 signaling and results in loss of embryonic stem cell identity. *Nucleic Acids Res*; doi:10.1093/nar/gkr1253 [Online 30 December 2011].

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The role of CD103(+) dendritic cells in allergic lung inflammation

NIEHS researchers determined that a specific subset of dendritic cells (DC) expressing the integrin CD103, induces T helper type 2 (Th2) responses to inhaled allergens, such as cockroach antigen and allergens present in house dust extracts. This novel finding could lead to improved therapies for preventing allergic sensitization to common indoor allergens.

The researchers prepared DCs from lungs of allergen-treated mice and separated the cells into subsets based on their expression of specific cell surface markers. These purified DC subsets were then cultured with naïve, allergen-specific CD4(+) T cells. The results showed that CD103(+) cells primed Th2 differentiation, whereas a different DC subset, expressing CD11b, primed Th1 differentiation. Mice lacking CD103(+) dendritic cells showed substantially reduced allergic responses to inhaled allergens.

The results of this study demonstrate that CD103(+) dendritic cells play an essential role in inducing Th2 type immune response to inhaled allergens. The paper not only provides insight into the roles of the two subsets of resident lung dendritic cells in allergic inflammation, but it might also reveal novel opportunities to reduce the severity of allergic inflammation.

Citation: [Nakano H, Free ME, Whitehead GS, Maruoka S, Wilson RH, Nakano K, Cook DN. 2012. Pulmonary CD103\(+\) dendritic cells prime Th2 responses to inhaled allergens. Mucosal Immunol 5\(1\):53-65.](#)

(Sonika Patial, D.V.M., Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction. Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

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Inside the Institute

NIEHS honors African-American history with stories of runaway slaves

By Ian Thomas

As part of its 2012 celebration of African-American History Month, NIEHS welcomed [Freddie Parker, Ph.D.](#), to Rodbell Auditorium for a one-hour seminar titled “They Fled Too: Female Slave Runaways in North Carolina, 1775-1840.” Based on this year’s theme of recognizing the achievements of women in black history, Parker’s lecture provided those in attendance with an historical account of life as a female slave on the run.

“A lot of studies have been done on runaway slaves since the inception of Negro History Day in 1926,” said Parker, currently a professor of history at North Carolina Central University (NCCU) in Durham, N.C. “However, in all that time, not one book or scholarly article has been devoted solely to female runaway slaves.”

Untold stories

According to Parker, the vast majority of previous research on runaway slaves has dealt almost exclusively with men, in large part because reported cases of runaway males far outnumbered those of females. While there are a wide range of reasons for this, Parker surmised that the presence of children played a pivotal role in a woman’s decision to flee.

“Since so much of the South was agrarian in nature at that time, females were encouraged, and often times demanded, to have multiple children at a very early age,” he explained. “Because of this, many women were far more reluctant to leave their plantations, or subject their families to a dangerous life on the run in the swamps and wilderness, where they’d be forced to take refuge.”

Further complicating matters were the staggering mortality rates of newborns at the time.

“If a woman in the eighteenth century was pregnant twenty times during her life, only half of those children were actually born, because of the enormous health disparities and diseases which were prevalent at the time,” Parker noted. “Out of those ten kids, only six survived past age 5.”



Parker is helping give voices to men and women traditionally overlooked by conventional historians. (Photo courtesy of Steve McCaw)



NIEHS Deputy Associate Director for Management Chris Long, front, joined colleagues from the Office of Management in the stirring African-American anthem “Lift Every Voice and Sing.” (Photo courtesy of Steve McCaw)

Right at home

A native of Hillsborough, N.C., Parker earned both his bachelor's and master's degrees from NCCU before moving on to the University of North Carolina at Chapel Hill, where he earned his doctorate in American history. The author of such books as "Running for Freedom: Slave Runaways in North Carolina, 1775-1840" and "Stealing a Little Freedom: Advertisements for Slave Runaways in North Carolina, 1791-1840," Parker is a long-time member of both the North Carolina Historical Commission and the state's African-American Heritage Commission.

"It's always such a pleasure to have Dr. Parker speak at our events," said [Veronica Robinson](#), secretary of the local chapter of [Blacks in Government](#), which co-sponsored Parker's talk along with the NIEHS Diversity Council. "As a researcher, he has a real passion for the field of African-American history though, as a North Carolinian, he also brings a unique perspective on our state's place in that history."

Currently, Parker serves as chairman of the board of the African-American History Project Advisory Board at Tryon Palace in New Bern, N.C., and as president of the Historical Society of North Carolina.

Setting the record straight

"I've spent the bulk of my entire research career studying those men, women, and children who were slaves right here in North Carolina," Parker concluded. "These are people who haven't really had a voice in our state's history, with the exception of how they were portrayed by their owners. That's why it's so important that we, as historians, endeavor to tell those stories as accurately as we can, so that future generations know who they were and how they lived."

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

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Robinson was visibly moved and engaged as Parker described the lives of female slaves in North Carolina. Seated beside her is Diversity Council chair Brad Collins. (Photo courtesy of Steve McCaw)



The program attracted a cross section of people at NIEHS, including Jenn Evans, left, of Employee Services, and Otis Lyght, a contractor with the NTP Pathology Support Group. (Photo courtesy of Steve McCaw)

Award-winning anchor leads NIH salute to African-American history

By Ian Thomas

Scientists and personnel from across the federal government and the field of public health gathered Feb. 16 on the NIH campus in Bethesda, Md. to celebrate the latest chapter in the agency's 2012 African-American History Month Observance Program. In honor of this year's theme, recognizing the achievements and contributions of black women to American history and culture, NIH proudly welcomed award-winning journalist, [J.C. Hayward](#) as the event's keynote speaker.

"Throughout the course of our nation's history, we've seen some amazing women do amazing things," said Hayward, vice president of media outreach for Washington D.C. television station, WUSA 9, who then led the crowd in an a cappella rendition of "Joy Today is Mine." "These heroes have been an inspiration to generations of black women. Although as our nation continues to grow in diversity, it's vital that we remember how their achievements shaped the future for not only African Americans, but all Americans."

A remarkable journey

As Washington D.C.'s first female anchor, Hayward has been a member of WUSA9 for forty years, serving in a wide range of roles, both in and out of the newsroom. In addition to her accolades as an anchor, Hayward has also received several awards for documentaries including "Sahel: The Border of Hell" and "Somalia: The Silent Tragedy," all of which culminated with her recent induction into the [National Association of Black Journalists Hall of Fame](#).

"We came here today to honor the roles of women in African-American history and nowhere is that more personified than with someone like J.C. Hayward," added Janine Clayton, M.D., deputy director of the [NIH Office of Research on Women's Health](#). "For years, she's inspired us with stories which, time after time, continue to lend a voice to those who would not otherwise be heard."

On the topic of inspiration, however, Hayward added that she didn't have to look very far for hers.

"My mother instilled in me a sense of pride, a sense of confidence and definitely the ability to dream big," said Hayward, who was named a 1982 Washingtonian of the Year by Washingtonian Magazine. "You won't find her in any history books, but when you're looking at me, you're looking at her."



Hayward paid tribute to the famous, and not so famous, African-American women of the 20th and 21st centuries. (Photo courtesy of NIH)



Brown sang, as Marshall provided keyboard accompaniment during the entertainment portion of the celebration. (Photo courtesy of NIH)

Honoring heroes of past, present, and future

Throughout the ceremony, Hayward and her peers credited a number of female pioneers, such as Rosa Parks, Dorothy Brown, and Shirley Chisholm, all of whom helped pave the way for the modern day civil rights movement. Still, the group also recognized the need for future generations to further the cause.

“We’ve been fortunate here at NIH to have had some wonderful role models in our midst, but it’s important for all of us to continually look to the future by supporting the next generation who will take us there,” said NIH Director Francis Collins, M.D., Ph.D. “For this reason, our institutes and centers continually strive to support the careers of new scientists by recognizing and recruiting candidates from those same minority and underrepresented areas of our society.”



Shown, left to right, Hayward joined Collins, Rodgers, and Clayton as musicians entertained the audience. (Photo courtesy of NIH)

Others in attendance included Griffin P. Rodgers, M.D., director of the [National Institute of Diabetes and Digestive and Kidney Diseases](#), Jeff Ortiz of the NIH chapter of [Blacks in Government](#), as well as jazz musicians DeCasto Brown and Terry Marshall who performed a cultural medley of songs.

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

Notable women in African-American History

- Vivian Pinn, M.D. (1941-present) As the first African-American woman to chair an academic pathology department in the United States, at Howard University College of Medicine, Pinn was appointed the first full-time director of NIH’s Office of Research on Women’s Health in 1991.
- Maria Stewart (1803-1879) One of the first women in American history to lecture publicly on women’s rights, Stewart was a regular contributor to the *Liberator* newspaper, an early 19th century publication dedicated to the abolitionist movement.
- Shirley Chisholm (1924-2005) The first black woman to be elected to Congress, Chisholm represented the state of New York for seven terms, spending her entire political career fighting for social justice and educational opportunities for minorities. In 1972, she also became the first black woman in history to run for the Democratic presidential nomination.
- Dorothy Brown, M.D. (1919-2003) In addition to being the first female surgeon of African-American descent in southeastern U.S. history, Brown became the first black woman in Tennessee history to be elected to the state’s legislature in 1966.
- Ida Wells-Barnett (1862-1931) A newspaper editor and journalist, Wells went on to lead the American anti-lynching crusade of the 1890s. From 1898 to 1902, she also served as secretary of the National Afro-American Council and eventually founded the Negro Fellowship League to aid migrants from the South.



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