

March 2011

NIEHS Spotlight



[Birnbaum testifies on drinking water quality](#)

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[Council moves ahead with strategic planning and concept clearances](#)

Although uncertain budget prospects cast a bit of a pall over the proceedings, the NIEHS Council accomplished a great deal in its two-day meeting Feb. 16-17.



[Woychik talks about NIEHS and the 2012-2016 Strategic Plan](#)

NIEHS Deputy Director Richard Woychik, Ph.D. responded to questions about his presentation Feb. 16 on the NIEHS 2012-2016 Strategic Plan.



[NIEHS reaches out in New Orleans](#)

NIEHS/NTP Director Linda Birnbaum, Ph.D., and other representatives from the Institute engaged the New Orleans community during a visit to the city Feb. 23-24.

Science Notebook



[Astrocytes give humans an intellectual edge](#)

Neuroscientist Maiken Nedergaard, M.D., gave the NIEHS Distinguished Lecture Feb. 8 on brain cells known as astrocytes, which are important in learning and memory.



[Combined effects of lead exposure and stress on cognitive deficits](#)

NIEHS grantee Deborah Cory-Slechta Ph.D. addressed a capacity audience from NIEHS and EPA Feb. 3 on the combined effects of lead and stress on cognitive function.



[NIH study finds two pesticides associated with Parkinson's disease](#)

New research finds people who used the pesticide rotenone or paraquat developed Parkinson's disease approximately 2.5 times more often than non-users.



[Deciphering a core process in Parkinson's disease](#)

Two new NIEHS studies offer insights into mechanisms of the chronic neuroinflammation that drives progressive neurodegeneration in Parkinson's.

NIEHS Spotlight



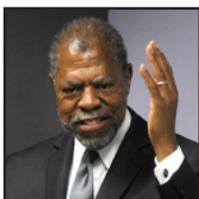
[DISCOVER grantees consider the value of center funding](#)

NIEHS DISCOVER program grantees shared successes and talked about translation of their research when they got together for a meeting and series of presentations Feb. 1.



[Workshop examines the role of air pollution on neural health](#)

On February 2-3, investigators with expertise on air pollution and neurobiology gathered at EPA to assess the state of the science in the field of air pollution and brain health.



[Olden speaks on urban and global environmental public health](#)

NIEHS Director Emeritus Ken Olden, Ph.D., discussed urban environmental public health at a monthly breakfast meeting of the Triangle Global Health Consortium Jan. 28.



[Superfund researcher honored for best paper of 2010](#)

Superfund Research Program grantee and LSU chemist Barry Dellinger, Ph.D., was recognized for his progress with environmentally persistent free radicals.



[New Science Communications Fellows have ties to NIEHS](#)

Six of the ten 2011 Science Communication Fellows announced Feb. 7 by Environmental Health Sciences have received NIEHS training or research support.

Science Notebook



[Chromatin meeting highlights genomic rearrangements and small molecule inhibitors](#)

NIEHS principal investigators and trainees attended the latest meeting of the Atlantic Coast Chromatin Club at the N.C. Biotechnology Center Jan. 31.



[Peer review panel deliberates NTP Technical Reports](#)

The National Toxicology Program (NTP) convened a peer review of draft NTP Technical Reports by an external scientific panel at a meeting Jan. 26 at NIEHS.



[Dudek explores synaptic plasticity during Council presentation](#)

On Feb. 17 Council members heard about new findings on synaptic plasticity during a presentation by NIEHS Principal Investigator Serena Dudek, Ph.D.



[New insights into fitness versus fatness and diabetes risk](#)

A new exercise program for employees at the NIH in Bethesda, Md., has the added advantage of helping researchers learn more about diabetes and obesity.



[Kensler discusses bench to tea-time research on Nrf2](#)

During his guest lecture at NIEHS Feb. 7, toxicologist Thomas Kensler, Ph.D., provided a new twist to the age-old axiom about eating your vegetables.

NIEHS Spotlight



[Ron Mason honored by international scientific development group](#)

NIEHS Principal Investigator Ron Mason, Ph.D., has been honored once again for his outstanding contributions to the field of electron spin resonance.



[Yao wins award from professional scientific society](#)

NIEHS Principal Investigator Humphrey Hung-Chang Yao, Ph.D., will receive the 2011 Young Andrologist Award at the American Society of Andrology annual meeting.



[Trainees honored by SOT Carcinogenesis Specialty Section](#)

Two of the first of this year's SOT awards to NIEHS/NTP trainees and scientists are going to Visiting Fellow Zhengyu Yin, Ph.D., and doctoral student Jessica Graham.



[NIEHS-supported trainee to attend Nobel-Lindau meeting](#)

Brown University graduate research fellow Catherine Volle has been selected to attend the 61st Lindau Nobel Laureate Meeting June 26-July 1 in Lindau, Germany.



[Aubrey Miller to speak on Gulf oil spill response](#)

NIEHS Senior Medical Advisor Aubrey Miller, M.D., will address the NIH role in the aftermath of the Gulf oil spill at an Environmental Information Association meeting.

Science Notebook



[Paper described as “tour de force” featured in microbiology journal](#)

A new NIEHS paper describes for the first time a key transcriptional mechanism for regulation of drug and lipid metabolism in the human liver.



[This month in EHP](#)

The feature article of the March issue of EHP explores nanomaterial safety with “Engineered Nanoparticles in Consumer Products: Understanding a New Ingredient.”



[NIEHS extends deadline for scientific director applications](#)

NIEHS has extended the application deadline for the position of director of the Division of Intramural Research (scientific director) to March 31, 2011.



[Alternative testing panel to meet in Bethesda](#)

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) is convening an international peer review panel March 29-30.

Inside the Institute



[Revisiting an almost forgotten chapter of local black history](#) Video

As part of the NIEHS Black History Month celebration Feb. 2, employees found themselves right in the middle of the making of a new documentary.



[Green leader featured at Black History Month event](#) Video

In its celebration of Black History Month, NIEHS neighbor EPA hosted a talk by sustainability specialist George Benjamin Brooks, Ph.D., Feb. 15.



[Chinese delegation visits NIEHS](#)

NIEHS welcomed a delegation from China to help celebrate the Chinese New Year and foster good will between China and the U.S., during a tour and reception held Feb. 16.

Extramural Research

[Extramural papers of the month](#)

- [Rapid evolution in Hudson River tomcod](#)
- [Elevated plasma cytokines in children with autism spectrum disorder](#)
- [Glutathione variant linked to lung function growth](#)
- [Interactions of lifetime lead exposure and stress](#)

Intramural Research

[Intramural papers of the month](#)

- [Uncontrolled neuroinflammation drives progressive neurodegenerative disorders](#)
- [Interleukin-10 protects against ozone-induced lung inflammation](#)
- [Mutations resulting from subtle chemical “trickery”](#)
- [Categorizing heterogeneous myositis syndromes by phenotype](#)

Calendar of Upcoming Events

- **March 4 (off-site event)** in room A247 in the Levine Science Research Center at Duke University, 12:00-1:30 p.m. — Integrated Toxicology and Environmental Health Seminar Series, featuring Jean Harry, PhD, speaking on “Neuronal/Glial Interactions and Inflammation: Possible Targets for Neurotoxicity, Neuroprotection, and Therapeutic Opportunities”
- **March 7** in Rodbell Auditorium C, 11:00 a.m.-12:00 p.m. — Epidemiology Branch Seminar Series presentation on “The PhenX Toolkit - Consensus Measures for Phenotypes and Exposures,” by Carol Hamilton, Ph.D.
- **March 10** in Rodbell Auditorium A, 6:00-8:30 p.m. — Graduate Women in Science meeting
- **March 11** in Rodbell Auditorium, 8:30 a.m.-3:15 p.m. — North Carolina Environmental Stewardship meeting
- **March 14** in Rall F-193, 10:00-11:00 a.m. — Laboratory of Signal Transduction Seminar Series, featuring Binks Wattenberg, Ph.D., speaking on “The Multiple Personalities of Sphingosine Kinase: Signaling Enzyme and Keystone of Sphingolipid Metabolism”
- **March 14-15** in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — Gulf Long-term Follow-up Study (GuLF STUDY) Scientific Advisory Board Meeting
- **March 16** in Keystone 2164/66, 8:00 a.m.-2:00 p.m. — GuLF STUDY Exposure Assessment Meeting
- **March 23** in Rall F-193, 11:00 a.m.-12:00 p.m. — Laboratory of Neurobiology Seminar Series featuring Herbert Covington, Ph.D., topic TBA
- **March 30** in Rall F-193, 11:00 a.m.-12:00 p.m. — Laboratory of Neurobiology Seminar Series featuring a presentation on “The Concept of ‘Efficacy’ in Pharmacology and Drug Discovery,” by Terry Kenakin, Ph.D.
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Birnbaum testifies on drinking water quality

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., was back on Capitol Hill Feb. 2, testifying at a U.S. Senate “Oversight Hearing on Public Health and Drinking Water Issues.” Along with U.S. Environmental Protection Agency (EPA) Administrator Lisa Jackson, Birnbaum testified as an expert witness in the first part of the full Committee on Environment and Public Works [hearing](#) chaired by Sen. Barbara Boxer, D-Calif.



Linked video:
[Watch Birnbaum's testimony from minute 59:55 to 67:13](#)
(Launches in new window)

Download Media Player:  Flash [↗](#)



During her testimony, Birnbaum referred twice to the Congressionally mandated Report on Carcinogens, prepared by the NTP for the secretary of the U.S. Department of Health and Human Services. She noted that CrVI has been listed as a known human carcinogen since 1980 and that TCE was listed in 2005 as reasonably anticipated to be a carcinogen. (Photo courtesy of Steve McCaw)

Jackson, the lead speaker at the hearing, opened with an explanation of the rationale and painstaking process behind the EPA decision to begin regulating perchlorate, a component of rocket fuel, and 16 other volatile organic compounds that can cause cancer at high enough doses. During questioning by the committee, Jackson defended her agency’s plans to step up protection for the estimated 5 million to 17 million Americans exposed to perchlorate in their drinking water, which marks a reversal of Bush administration drinking water policies.

Birnbaum presented her [testimony](#) following Jackson’s comments. Along with discussing perchlorate, she addressed health issues posed by hexavalent chromium, or Chromium VI (CrVI), and trichloroethylene (TCE), with several references to NIEHS-supported research on the chemicals’ potential health effects and the development of novel techniques for testing and remediating them in drinking water. Birnbaum also responded to questions about study design and the rationale for the high doses of chemicals used in animal studies.

In her testimony on perchlorate, Birnbaum explained, “We’re concerned about perchlorate, because it can affect thyroid function by inhibiting the transport of iodide into the thyroid. Iodide uptake is necessary for the normal production of thyroid hormones, which are essential in fetal and post-natal neurodevelopment.”

Windows of susceptibility and the fetal basis of disease played into Birnbaum’s testimony, as she articulated concerns about the chemical. “A series of papers from the CDC [the Centers for Disease Control and Prevention] and NIEHS between 2009 and 2011 confirmed that perchlorate levels in fetuses and infants compare with perchlorate levels in their moms,” she continued. “At this point, we’re not sure if low doses of perchlorate in drinking water result in harm to human development, but it’s an important question.”

After their testimony, Birnbaum and Jackson fielded questions from committee members. Most of the questions for Birnbaum were scientific, but in response to a question from Sen. Frank Lautenberg, D-N.J., she crossed into the public policy arena with a statement about right to know. “I certainly as a citizen, like everyone else in this room, would like to know what I’m drinking,” she said.

As the committee moved into the second part of the hearing, Boxer, a long time advocate of protecting drinking water, thanked Birnbaum and Jackson as she observed, “I think that we’ll be seeing a lot more of you both as we move forward in this Congress.”

The hearing continued with testimony from Environmental Working Group President Ken Cook, representatives of municipal water systems serving Milwaukee, Wis., Norman, Okla., and Fairfax, Va., and Johns Hopkins Bloomberg School of Public Health Associate Dean Thomas Burke, Ph.D.

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In her [testimony](#), Jackson maintained, “Strong science and the law will continue to be the foundation of our decision making at EPA. EPA takes its obligation to ensure the safety of the water supply very seriously and will continue to do all that we can, using sound science and the law, to protect people’s health.” (Photo courtesy of EPA)

Council moves ahead with strategic planning and concept clearances

By Ernie Hood

Although uncertain budget prospects cast a bit of a pall over the proceedings, the [National Advisory Environmental Health Sciences \(NAEHS\) Council](#) accomplished a great deal in its two-day meeting Feb. 16-17.

One highlight was the first appearance before Council by new NIEHS Deputy Director [Richard Woychik, Ph.D.](#) He briefed the Council members on his initial major project—the 15-month, highly inclusive process of formulating a new Strategic Plan for the Institute. The plan, which will include the composition of new NIEHS mission and vision statements, will guide Institute activities and priorities from 2012-2016 ([see related story](#)).

Along with discussing the upcoming Strategic Plan and speculating about how NIEHS could best weather a flat or reduced budget, Council also voted to approve seven innovative new Concept Clearances ([see text box](#)).



For the first time in several years, every Council member was in attendance for the Feb. 16-17 meeting. (Photo courtesy of Steve McCaw)

Updates on DERT, NTP, and neuroscience research at NIEHS

NIEHS Division of Extramural Research and Training (DERT) Director [Gwen Collman, Ph.D.](#), updated Council on extramural grant-making activities, including an in-depth discussion of the philosophies underlying NIEHS DERT practices and the many challenges facing the division in the coming years. NTP Associate Director [John Bucher, Ph.D.](#), reported to Council about the major, three-day NTP workshop held in January in Raleigh, NC by the NTP—“[Role of Environmental Chemicals in the Development of Diabetes and Obesity.](#)” The workshop was organized by Kristina Thayer, Ph.D., director of the [NTP Center for the Evaluation of Risks to Human Reproduction](#).

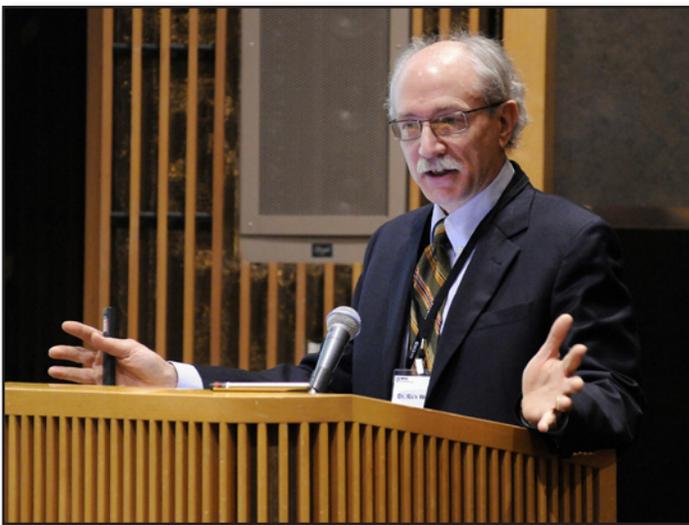
As part of the update by NIEHS Acting Scientific Director David Miller, Ph.D., Council was also treated to a fascinating scientific lecture by [Serena Dudek, Ph.D.](#), the principal investigator of the Synaptic and Developmental Plasticity Group in the NIEHS Laboratory of Neurobiology ([see related story](#)).

The NAEHS Council will meet again May 18-20.

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



Along with an update about the budgetary situation, NIEHS/NTP Director Linda Birnbaum, Ph.D., briefed Council on staff changes, recent activities, and honors for the Institute. (Photo courtesy of Steve McCaw)



In his first appearance before Council, Woychik described the 15-month process of composing a new Strategic Plan for the Institute for 2012-2016. The process is designed to ensure maximum engagement of all NIEHS personnel and all external stakeholder groups. (Photo courtesy of Steve McCaw)



Council member Kenneth Ramos, Ph.D., of the University of Louisville, makes a point about the Strategic Planning process during one of the Council's discussion periods. (Photo courtesy of Steve McCaw)



Jerry Heindel, Ph.D., acting chief of the DERT Cellular, Organs and Systems Pathobiology Branch made the first of several Concept Clearances that Council considered. (Photo courtesy of Steve McCaw)



Despite the looming budgetary issues, Collman was still able to enjoy a light-hearted moment during Council proceedings. (Photo courtesy of Steve McCaw)

Concept clearances

DERT program administrators and health scientist administrators presented concepts for new programs, funding mechanism changes, and new partnerships for advancing research and training in the environmental health sciences (EHS). They also proposed the new programs using several different grant mechanisms (see NIH list of [Activity Codes](#)):

- A Program Announcement (PA) on the role of environmental chemical exposures in the development of obesity, diabetes and metabolic syndrome, comprised of R01 and R21 grant opportunities
- A Request for Applications (RFA) on environmental influences on stem cells in development, health, and disease
- A DERT-NTP collaboration on transgenerational inheritance in mammals after exposure (TIME)
- A proposal for an NIEHS Translational Research Program reviving the P01 grant mechanism, which has been under a moratorium since 2007
- A proposal to enhance research resources in the environmental health sciences through R24 and P41 grant mechanisms — neither of which NIEHS has offered previously — that would provide the EHS community access to unique capacity, technology, and tools
- A proposal to enhance undergraduate EHS training opportunities by participating in the NIH Summer Research Experience Program (R25), supplementing the National Institute of General Medical Sciences (NIGMS) Minority Access to Research Careers (MARC) Undergraduate Student Training in Academic Research (U-STAR) awards (T34), and continuing to provide administrative supplements to support research experiences for high school students and college undergraduates

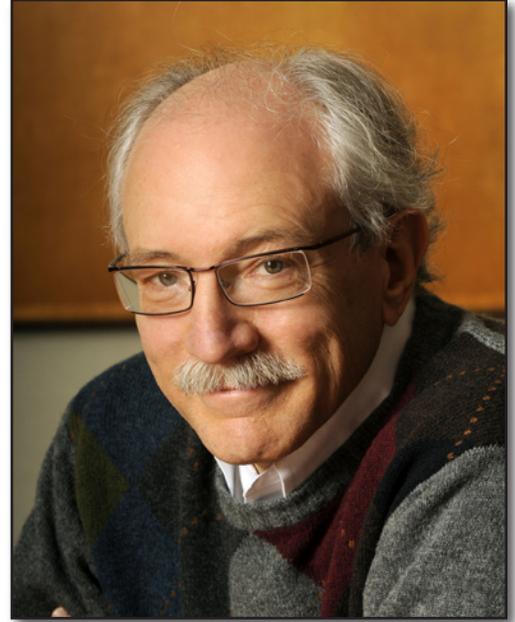
Woychik talks about NIEHS and the 2012-2016 Strategic Plan

By Ernie Hood

NIEHS Deputy Director Richard Woychik, Ph.D. responded to questions from the Environmental Factor about his presentation Feb. 16 on the [NIEHS 2012-2016 Strategic Plan](#) and his first two weeks at the Institute working closely with NIEHS/NTP Director Linda Birnbaum, Ph.D.

FACTOR: Why is it so important for the Institute to formulate a new strategic plan?

WOYCHIK: A strategic plan gives everyone associated with the Institute — internal, external, the environmental health sciences community — a sense of where we are going. As part of the process, you do an evaluation of your strengths and weaknesses. What are the real opportunities and the threats that are out there in the biomedical environment? So, it gives you a chance every five years to really look at how the world community has changed, and then to evaluate what we have done, at what parts of the previous strategic plan are still applicable or unfinished business and are important to help guide the future directions of the Institute — and the new opportunities and new areas we want to be moving in over the course of the next five years.



During his first days on the job, Woychik made it clear to all that he plans to be a deputy director who is accessible to employees and stakeholders and involved in all aspects of the Institute's operations. (Photo courtesy of Steve McCaw)

First impressions

FACTOR: You've only been here at NIEHS a couple of weeks now, but you certainly seem to have hit the ground running. What are your first impressions?

WOYCHIK: My first impressions are very positive. First of all, starting with an institute that has a focus that is so much in alignment with my own personal passions is something I am very excited about, and the first two weeks on the job confirm that all of my due diligence about the interests of the Institute was in fact spot on. So it's great to be amongst groups of people [like this], certainly Linda, with her passions and interests; I'm clearly in the right place relative to scientific focus.

The other thing I've been struck by is the quality of the people here. It's a place where I'm amazed at how much you can get done in a relatively short period of time. Plus, as I've been getting to know people throughout the organization, I've been exceedingly impressed with the quality of the work that we've done, and I'm very encouraged by the quality of the work and the impact that we can have over the next five to ten years.

Positive responses from Council

FACTOR: Following your briefing to Council ([see related story](#)) about the process and timelines for the Strategic Plan, you seemed very pleased with the members' comments.

WOYCHIK: First of all, I'm encouraged that they were so supportive of the process, and supportive of us doing this now. There really weren't any negatives about what we're proposing to do and the timeframe in which we're doing it. What didn't get captured in the public discussion were the many very positive statements that many Council members made to me personally at the coffee break.

So I think there's a real sense of interest, that the timing is right to take a look at mission and vision, and to develop the strategic goals for the next five years. I was also very encouraged just by the engagement. It's clear that there's a lot of passion out there around issues in environmental health science.

FACTOR: Another large theme that emerged in the Council meeting was the current budget atmosphere, and the uncertainties that are being faced over the near term. Will that have any effect on the strategic planning process?

WOYCHIK: I think that when you have budgetary challenges, it's all the more reason to be doing a strategic plan, because the plan will also lay out your priorities as you move forward. So, if there are budgetary shortfalls, then one knows exactly, based on the grassroots input, where the interests are, and where the funds should be placed, as the highest priorities, and the second-highest priorities. Another thing that I was very encouraged with was the idea several members articulated of making sure that NIEHS is partnering and collaborating with other institutes and other agencies.

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

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NIEHS reaches out in New Orleans

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., and other representatives from the Institute engaged the New Orleans community during a visit to the city Feb. 23-24. The visit involved several meetings focused on local environmental health concerns and the NIEHS programs that address them including the Institute's [multi-faceted response](#) to the Gulf oil spill (GOS).

The visit began with a luncheon dialogue hosted by the Bayou Interfaith Shared Community Organizing followed by a tour of the lower Ninth Ward in New Orleans, hosted by NIEHS grantees at Tulane University School of Public Health and Tropical Medicine. The NIEHS delegation also drove out to Terrebonne Parish where they listened to residents in the coastal town of Montegut.

Strategic planning process emphasizes transparency and inclusion

Asked about the Strategic Planning process, Woychik pointed to the combination of [Web-based tools](#) and stakeholder meetings designed to promote participation in the development of the final product.

Linda and I feel very strongly that we want to structure the process in such a way that all stakeholders understand — we want to hear from you. So we've developed both a Web-based system and an in-person, large group meeting that is scheduled far enough in advance so that anyone and everyone who is interested in having input into this process will have an opportunity to contribute. We're going to be publishing the process, when the time periods are when you'll have a chance to give us input, and in what format the input will be provided. So pay attention to those things, and then follow the progress, and anyone in the community will have a chance to comment on the progress that we make. I hope that at the end of this process, fifteen months later, the entire environmental health sciences community will feel that we have a plan that really provides a roadmap and guidance on what we can be doing to impact the quality of human health and human suffering.

Later, the NIEHS delegation attended an evening community forum Feb. 23, hosted by Mary Queen of Vietnam Community Development Corporation at Ba Mien Restaurant in New Orleans East. Birnbaum addressed more than 100 attendees as part of a panel of local, state and federal agency representatives.

Birnbaum described NIEHS programs launched in response to Hurricane Katrina and the GOS, Birnbaum noted that NIEHS grants in New Orleans totaled \$4.6 million last year. She also praised collaboration among Gulf region scientists, community groups, and NIEHS, encouraging partners to offer NIEHS their input and share their grass-roots knowledge of their city and region.

“We want to hear what’s going on,” she explained. “See where we can build on the partnerships we have on the ground. That’s what keeps us going. That’s what helps drive our work in the community.”

Birnbaum made a point of highlighting outstanding grantees, including Tulane University’s Maureen Lichtveld, M.D. and Barry Dellinger, Ph.D., director of the Superfund Research Program at Louisiana State University (LSU).

As she did at each of the venues during the visit, Birnbaum emphasized interdisciplinary scientific research, interagency collaboration, and community engagement. “NIEHS hosted a series of community forums, stakeholder visits, webinars, and instructional meetings throughout the five-state Gulf region,” she told her listeners, “in order to promote awareness, participation, and coordination for all of these programs among local residents, state and local health departments, regional universities and researchers, and federal agency partners.”

During the evening forum, one attendee praised the NIEHS approach in the Gulf. “Thank you for the scientific focus of this study; it’s critical,” said Karen DeSalvo of the City of New Orleans Health Department.

The following day, Birnbaum joined NIEHS leads on the GOS response for an update and roundtable at the Deep South Center at Dillard University, where the Institute funds the Minority Worker Training Program directed by Beverly Wright, Ph.D. On hand at the meeting were NIEHS GOS leads, Chief Medical Officer Aubrey Miller, M.D., Epidemiology Branch Chief Dale Sandler, Ph.D., Worker Education and Training Program Director Chip Hughes, Acting Chief of the Susceptibility and Public Health Branch Claudia Thompson, Ph.D., and Director of Communications Christine Flowers.



Birnbaum, second from right, joined panelists at the evening reception to hear concerns and questions voiced by members of the community impacted by Hurricane Katrina and the GOS. (Photo courtesy of John Schelp)



The audience took Birnbaum and fellow panelists at their word as they passed around a microphone so anyone who wanted to give input had an opportunity to be heard. (Photo courtesy of John Schelp)

The NIEHS delegation made an additional stop later that afternoon at the LSU Health Science Center School of Public Health for a meeting with Superfund site investigators and oil spill grant investigators to discuss ongoing work and future plans.

The visit to New Orleans was part of a series of [community forums](#) Birnbaum began in 2009 when she began as director of NIEHS.



The audience at Dillard University included NIEHS staff and several grantees. (Photo courtesy of Jim Remington)



The panel at Dillard University included, right to left, Wright, Birnbaum, Sandler, and, only partially visible, Hughes. (Photo courtesy of Jim Remington)



Today the city of New Orleans still has many reminders of the force of Hurricane Katrina and the frustrations of rebuilding the city. (Photo courtesy of John Schelp)



But there are also signs of the city's resilience, as people prepare their new and revitalized dwellings to face future threats from flooding. (Photo courtesy of John Schelp)

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DISCOVER grantees consider the value of center funding

By Matt Goad

NIEHS Disease Investigation Through Specialized Clinically-Oriented Ventures in Environmental Research (DISCOVER) program grantees shared successes and talked about translation of their research (see text box), when they got together for a meeting and series of presentations Feb. 1 in the NIEHS Rodbell Auditorium.

To open the meeting, representatives from the three DISCOVER centers presented summaries of the research they have conducted with their NIEHS grants.

A panel discussion with the grantees and NIEHS representatives followed. One of the most stimulating exchanges of their daylong meeting took place as they explored what makes the center grant design for integrating basic and clinical research with multi-faceted translation initiatives, so innovative and productive.

The challenge

George Leikauf, Ph.D., an NIEHS grantee from the University of Pittsburgh Graduate School of Public Health, kicked off the discussion about funding mechanisms with a challenge to the grantees to articulate just why what they accomplished with the centers grants could not have been achieved as well with the typical individual researcher-initiated grant (R01).

“Maybe we’re in the mid-stage of this,” Leikauf admitted. “Maybe we’re in the middle of the pregnancy, and we don’t necessarily want to judge whether an Einstein’s going to be born, but I think it’s something that needs to be addressed.”

Gary Miller, Ph.D., an NIEHS grantee from the Rollins School of Public Health at Emory University, took the Einstein reference a step further to emphasize the need to take an even longer term perspective on the topic. “Einstein was kind of a goof until he was about 20,” Miller said. “We need to go way past birth to see the outcome from him.”

A dynasty of researchers

Miller pointed to the example of the trainees included in the center model, as a benefit above and beyond what an R01 grant can provide. **Marsha Wills-Karp, Ph.D.**, of the Cincinnati Children’s Hospital Medical Center, also spoke about the dynasty of researchers and clinicians that go into making a center successful by fostering interdisciplinary collaborations.



Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, opened the meeting last month with a charge to attendees. “What we want to get out of today is your thoughts about how NIEHS can develop a better, more robust translational research program that better fits all the needs of the environmental health sciences community,” Collman said. (Photo courtesy of Steve McCaw)



Leikauf, sparked a lively discussion at the DISCOVER meeting when he asked how center grants promote quality research and effective translation. (Photo courtesy of Steve McCaw)

[Patrick Breyse, Ph.D.](#), director of the Center for Childhood Asthma in the Urban Environment at Johns Hopkins Bloomberg School of Public Health, offered a more specific example. Breakthroughs on the connection between disruption of the Nrf2 gene pathway and asthma, Breyse explained, wouldn't have been possible without access to human tissue that the center grant made possible by increasing collaboration between departments at Johns Hopkins.

In addition to the Johns Hopkins center, the other DISCOVER centers are The Role of Airborne PAHs (polycyclic aromatic hydrocarbons) and DEP (diesel exhaust particles) in the Pathogenesis of Childhood Asthma center at Columbia University's Mailman School of Public Health, and the Cardiovascular Disease and Traffic-Related Air Pollution center at the University of Washington School of Public Health, directed by [Joel Kaufman, M.D.](#)

NIEHS Health Scientist Administrator Kimberly Gray, Ph.D., pointed to the notable success of bringing non-environmental scientists into the centers. The Hopkins and Columbia centers worked within their department's existing cadre of scientists to expand exploration, and the Washington center developed a new team of scientists, including a cardiologist/stem cell scientist and a vascular physiologist from the urology department, to investigate other potential mechanisms of diesel's effect on cardiovascular disease risk.

During her presentation in the morning session, [Frederica Perera, Dr.P.H.](#), director of the Columbia center, spoke of the benefits of having a physician scientist, Rachel Miller, M.D., as part of the team's leadership. Miller's clinical knowledge helps to balance Perera's public health and environmental health science background, Perera noted.

"It's very helpful to have the clinician's point of view," Perera added, and Miller made outreach to clinicians more effective.

Also making a presentation at the daylong meeting was [Steven Kleeberger, Ph.D.](#), principal investigator in the Environmental Genetics Group, who spoke about the Intramural Director's Challenge study focused on mechanisms of oxidative stress-induced disease.

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



Although the Columbia team left early to beat a snowstorm approaching New York and missed the afternoon's panel discussion, Perera and her group outlined their programs in basic and clinical research, treatment, and prevention during a morning presentation. (Photo courtesy of Steve McCaw)



Attending one of his first meetings since joining the top leadership of NIEHS, Deputy Director Rick Woychik, Ph.D., center right, said he knew collaborative research could be done with an R01 grant, but added, "I also know that there are limitations." Seated to his right is Kim McAllister, Ph.D., an NIEHS health science administrator and co-chair of the panel discussion. McAllister's colleague, Program Administrator David Balshaw, Ph.D., left, sits at the end of the row. (Photo courtesy of Steve McCaw)



Kleeberger discussed his research with a cohort of children in Argentina on the influence of gender and breastfeeding on susceptibility to severe acute lung disease among intensively monitored infants at high risk. (Photo courtesy of Steve McCaw)



The panel at the meeting included DISCOVER grantees, grantees from other types of center programs, and NIEHS scientists. Shown above, NIEHS Principal Investigator Fred Miller, M.D., Ph.D., above, brought his perspective as a clinical researcher to bear on the discussions. Miller heads the NIEHS Environmental Autoimmunity Group on the NIH campus in Bethesda, Md. (Photo courtesy of Steve McCaw)

Translation on several levels

Translational research was built in as a major component of the DISCOVER grants. The “bench to bedside” and “bench to public health” concepts of developing practical applications of basic research – and how to measure that translation – were major topics of discussion at the meeting.

One of the advantages of the DISCOVER centers, researchers agreed, is that their collaborative nature lends itself to combining animal and human studies, which helps the transition from the basic and clinical research into education of patients, parents, and practitioners; community engagement; treatment; prevention; and change in public health policy.

The challenge, though, comes from knowing how to measure the practical applications of the research beyond the high-impact research studies generated.

Christie Drew, Ph.D., chief of the [NIEHS Program Analysis Branch \(PAB\)](#), spoke about the issues her branch has with deciding how to track research outcomes, whether it be legislative testimony, public policy change, or impact in the community. Specific reporting guidelines can be helpful, Drew said, but she also worried that they can be constrictive.

Drew also mentioned the draft of the new [metrics manual](#) that PAB is working on to help grantees to become aware of how their activities further the goal of translation and suggest new metrics for measuring their impact.

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Workshop examines the role of air pollution on neural health

By Thaddeus Schug

Investigators with expertise on air pollution and neurobiology gathered Feb. 2-3 at the US Environmental Protection Agency (EPA) to assess the state of the science in the field of air pollution and brain health effects, and to promote opportunities for research in this evolving research area. The workshop on “Air Pollution and Brain Health” was sponsored by the NIEHS Division of Extramural Research and Training (DERT) and attended by NIEHS grantees and other researchers, as well as NIEHS and EPA grant administrators.

In her welcoming remarks, DERT Director Gwen Collman, Ph.D., said, “The time is right to look at the neural components caused by air pollution across the full range of human development. We need to put all available data and resources on the table, and assess where we are with respect to indoor, outdoor, *in vitro*, *in vivo*, and human studies,” she added. “Once we have identified the information gaps, we can move forward to develop new initiatives and resources to guide regulatory agencies,” said Collman.

EPA National Program Director for Air Research Dan Costa, Sc.D., followed Collman with a keynote lecture covering what is known about the current standards and systems involving air pollution health effects. Costa reviewed the mounting evidence linking air pollution to neural dysfunctions, including a study that tied diesel exhaust to increases in cardiac arrhythmias in humans. “The nervous system plays a significant role as an arbitrator of systemic response, and environmental stressors such as particulate matter appear to have both direct and indirect influences on neuronal function.”

The remainder of the agenda was divided into three sessions, in which groups moved sequentially from an overview of current understanding through a series of questions designed to probe the state of the science of air pollution for future research needs and implementation. Each of the sessions was facilitated by DERT Health Scientist Administrators with related research and administrative interests.

Workshop organizer Annette Kirshner, Ph.D., led the first group, which explored the most likely components of air pollution responsible for causing adverse effects on the nervous system and what is known physiologically about how these components access the brain. Several pollutants, including polycyclic hydrocarbons, black carbon, heavy metals, ozone, and roadside exhaust, were mentioned as potential airborne neural hazards.



In her opening remarks, Collman mentioned that air pollution studies are an integral to both NIEHS and EPA and that she encourages collaborations between the agencies. (Photo courtesy of Steve McCaw)



Kirshner, right, looked on as Costa answered questions from panelists following his keynote lecture. (Photo courtesy of Steve McCaw)

The second group, led by Cindy Lawler, Ph.D., and Kimberly Gray, Ph.D., set out to determine the effects of air pollution on neural development during the critical windows of susceptibility. Much of the discussion centered on determining what mechanisms confer vulnerability — genetics, epigenetics, or the presence of multiple diseases.

The final group, led by Sri Nadadur, Ph.D., discussed the potential cellular and molecular mechanisms implicated in compromised brain function resulting from air pollutant exposure. Panelists engaged in a lengthy debate over the utility of current *in vitro* and *in vivo* modeling systems and human studies, and how they could be used to develop a better understanding of the mechanisms associated with air pollution-induced brain disease.

During the final summary session, discussion turned to ways NIEHS could advance the science of air pollution and brain health as well encourage optimal collaboration of researchers from different disciplines. Kirshner concluded, “I believe we have a much better understanding of the research gaps and the tools and resources needed to formulate a path forward.” She added, “It is also clear that there is a real need to foster collaboration among all of you and to think about better integration and interdisciplinary research in the field.”



Epidemiologist, Beate Ritz, M.D., Ph.D., discussed how air pollution influences the development and progression of Parkinson’s disease. (Photo courtesy of Steve McCaw)



NIEHS grantee Joel Kaufman, M.D., left, and Nadadur shared a laugh during panel discussions. Kaufman is a physician-epidemiologist and principal investigator on an NIEHS-funded Specialized Center for Research on Cardiovascular Disease and Traffic-Related Air Pollution at the University of Washington. (Photo courtesy of Steve McCaw)



NIEHS Acting Scientific Director David Miller, Ph.D., was a panelist on the group exploring the mechanisms of air pollution-induced neural disease. Miller’s research focuses on the transport systems that shuttle xenobiotics across the blood-brain barrier. (Photo courtesy of Steve McCaw)

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction and a regular contributor to the Environmental Factor. He is currently on detail as a program analyst in the NIEHS Division of Extramural Research and Training.)

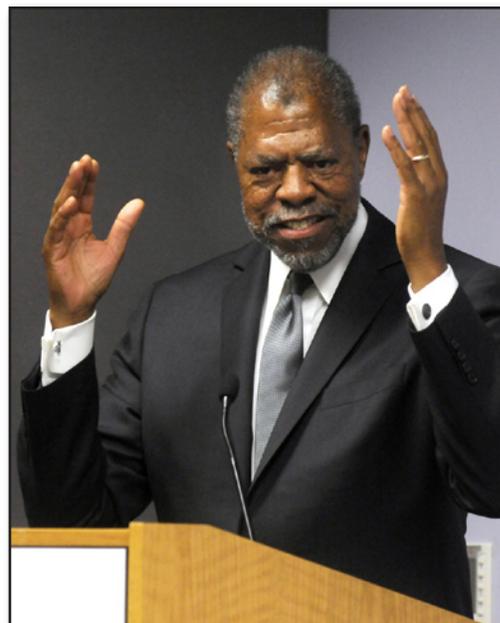
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Olden speaks on urban and global environmental public health

By Eddy Ball

As NIEHS Director Emeritus Ken Olden, Ph.D., gets ready to complete the latest chapter in his outstanding career, he took time out of his busy schedule to discuss his vision of urban environmental public health. Olden gave the keynote presentation at a monthly breakfast meeting of the [Triangle Global Health Consortium \(TGHC\)](#) Jan. 28 at the North Carolina Biotechnology Center (NCBC) in Research Triangle Park, N.C.

[Olden](#) is founding dean of the new school of urban public health at the City University of New York, a position he accepted in 2008 when he left his lab at NIEHS. He served as [NIEHS director](#) from 1991 to 2005.



Olden emphasized the shared concerns of urban and global health. “What we learn [about public health] in New York is global,” he said, describing New York as a “microcosm of the world.” (Photo courtesy of Steve McCaw)

Linked video:
Watch as Olden talks about how changing an individual's environment can help prevent disease and increase quality of life. (09:43)
(Launches in new window)

Download Media Player: Flash [↗](#)

Focus on global and urban public health issues

Facilitated by Consortium Executive Director Nicole Fouché, Ph.D., the meeting also featured opening comments by Congressman Brad Miller, D-N.C. Like Olden, Miller spoke on the topic of urban and global environmental public health. Miller related his experiences visiting Nairobi, Kenya, where two million people live in the second largest slum in Africa. Miller said of the impact of the urban population boom and growth of the aging population worldwide, “It’s not pretty... and our future is tied up with all that.”

As Olden began his presentation, he used a sports analogy to impress upon the audience how important it is to recognize emerging public health issues before they become too great to overcome. He reminded his listeners of hockey great Wayne Gretsky’s secret for success — “I skate to where the puck is going to be, not where it has been.”

Like Gretsky, Olden explained, public health professionals need to look ahead, to focus on emerging issues of urban public health and the impact of a population with a life expectancy that has increased dramatically over the last century. Although public health made great strides in the 20th century and was responsible for most of the 35-year increase in life expectancy since 1900, Olden said, “Public health [currently] has fallen behind in terms of public understanding and resources.”



In his opening remarks, Miller, the politician, was also a diplomat, as he turned the podium over to Olden. Miller described Olden as “someone who knows more about what I’m talking about than I do.” (Photo courtesy of Steve McCaw)

New ideas for a new century

According to Olden, public health advocates have failed to make a compelling argument to truly awaken the voters' genuine interest in public health. Part of the reason is, he said, "We're still focusing on 20th century problems," such as infectious diseases. While mainstream medicine emphasizes drugs and high-tech procedures to treat disease in individuals, public health advocates have not effectively engaged communities and informed people of the value of preventing disease in the first place.

Olden singled out four major issues that he said will dominate public health in the 21st century:

- Prevention of the chronic diseases, such as diabetes and chronic obstructive pulmonary disease (COPD), that are quickly becoming the major diseases worldwide
- Promotion of healthy cities, which are growing rapidly as people everywhere leave rural areas in search of opportunity, pushing the percentage of people living in cities to 50 percent worldwide and 80 percent in the U.S. and other developed countries
- Healthy aging, so people can remain disease free, active, and productive during what Olden called one of the "critical windows of development" beyond retirement, contributing to economic output and decreasing healthcare costs
- Elimination of health disparities, which will only increase in severity as minority populations increase

Olden's talk was well received and sparked a lively discussion about health issues and productive aging, with one member of the audience, TGHC board member and North Carolina State University associate professor and director of Global Health Initiatives Marian McCord, Ph.D., suggesting, "We should retire the word 'retire.'" Olden concluded with a vision for the future, "The best and brightest will be going into public health," helping people live longer, better lives while saving health care resources by preventing disease.

The audience at NCBC, like people elsewhere in the Triangle, can look forward to seeing and hearing more of Olden in the future. As he ushers the new school of urban public health through the accreditation process and looks back at his remarkable accomplishments in New York City, Olden is also considering the next phase in his career back on home turf, as CUNY begins its search for a permanent dean to head the vision Olden made into a reality.



As Olden spoke, former NIEHS molecular biologist [Ken Tindall, Ph.D.](#), seated, and Fouché listened to their guest. Tindall is currently NCBC senior vice president for science and business development, as well as vice chair of the TGHC board of directors. (Photo courtesy of Steve McCaw)



Former NIEHS Biologist Judd Spalding, right, and former NIEHS Principal Investigator Ray Tennant, Ph.D., were on hand to hear their former leader talk. Spalding and Tennant were instrumental in the National Center for Toxicogenomics, one of Olden's major initiatives as director. (Photo courtesy of Steve McCaw)



Among the diverse audience was North Carolina Department of Health and Human Services epidemiologist Winston Liao, who asked Olden if he could suggest some possible options for raising awareness of chronic lower respiratory diseases, especially those approaches that related to community involvement and public health strategies. (Photo courtesy of Steve McCaw)



Several members of the UNC Gillings School of Global Public Health turned out for Olden's talk, including Louise Winstanly, above, an adjunct assistant professor and bioethics consultant. (Photo courtesy of Steve McCaw)

Promoting world health by raising awareness locally

The Triangle Global Health Consortium describes its mission as establishing North Carolina as an international center for research, training, education, advocacy and business dedicated to improving the health of the world's communities. It seeks to engage academic, governmental, business, and nonprofit organizations in this collaborative effort.

The TGHC's board and steering committees reflect the broad range of input described in its mission statement. Board members range from leaders in the academic community, such as chair Margaret (Peggy) Bentley, Ph.D., associate dean of global health at the UNC Gillings School of Global Public Health, and non-profits, such as Pape Gaye, president and CEO of IntraHealth International, to business people, including Jack Bailey, senior vice president of the Private, Public, and Institutional Customers division at GlaxoSmithKline.

Steering committee members include NIEHS/NTP scientist Rear Admiral William Stokes, D.V.M., director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), who serves with several other practitioners of human, animal and environmental health on the TGHC One Health Collaborative Steering Committee. Organizational members range from Duke University and North Carolina Central University and non-profits FHI (Family Health International) and RTI (Research Triangle Institute) International to biotech companies Arbovax and SCYNEXIS.

In addition to its breakfast series, which takes place on the fourth Thursday of each month, the Consortium is an intellectual hub and clearinghouse for global health in the area, enhancing the awareness of and connections between North Carolina's experts and expertise. In this way, it enhances the efficacy of each organization dedicated to improving the health of the world's communities. Stay posted to the TGHC [Web site](#) for news, events, and opportunities.

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Superfund researcher honored for best paper of 2010

By Melissa Kerr

Superfund Research Program (SRP) grantee and Louisiana State University (LSU) chemist [Barry Dellinger, Ph.D.](#), was recognized for his progress with environmentally persistent free radicals (EPFRs). The journal [Environmental Science & Technology \(ES&T\)](#) selected Dellinger's paper, "[Potential for Misidentification of Environmentally Persistent Free Radicals as Molecular Pollutants in Particulate Matter](#)," for an Editor's Choice Award as one of ES&T's Best Papers of 2010.

Dellinger, an LSU professor of environmental chemistry, heads the LSU SRP Center focused on [Health Impacts of Toxic Combustion By-Products](#) and is the principal investigator on an SRP grant for [Development of a Demonstrable Model of Dioxin Formation](#).

"ES&T published nearly 1500 papers last year, and [Dellinger's] paper was chosen among 70 papers nominated by our editors as one of the very best in 2010," said ES&T Editor [Jerald Schnoor, Ph.D.](#) He also praised Dellinger for helping make ES&T one of the leading journals in its field.

"This is the paper I joked would never be published as [it was] too controversial," Dellinger noted afterwards. The results of his team's research suggest that EPFRs and molecular pollutants are virtually indistinguishable when analyzed under standard chemical analysis methods. Using that knowledge, Dellinger suggests, "The origin of the toxicity of PM [particulate matter] contaminated with toxic organic compounds should be considered for re-evaluation to include the possibility that EPFRs may be a significant contributor, and the impact of some molecular pollutants may have been overestimated."

Free radicals wreak havoc

Dellinger's previous research has shown that free radicals — electrically charged atoms or molecules — have the ability to bind to fine and ultrafine particulate matter (PM) causing a stabilization of the radical. That stabilization makes it resistant to reaction with molecular oxygen, in other words, environmentally persistent. EPFRs have been shown to cause DNA damage and could be the source of some of the health effects previously thought to have been caused by exposure to PM alone.

Using a variety of general-use chemical solvents, the team measured the variances of the extractability of the radical from the PM and observed the variances of chemical reactions with the solvents. They found that polar solvents, such as methyl alcohol, isopropyl alcohol, and dichloromethane, extracted the radicals. The non-polar solvents, such as toluene and tert-butylbenzene did not have the same ability to extract.

They also report, "Samples were prepared to contain only free radicals, yet molecular products were identified by standard solvent extraction procedures." Without accounting for the potential for these reactions to occur, the resulting data would be skewed.



Dellinger has received a number of awards for his research, including election as an American Association for the Advancement of Science Fellow in 2010 ([see story](#)) and the American Chemical Society's prestigious Astellas USA Foundation Award ([see story](#)) in 2008. (Photo courtesy of Barry Dellinger)

The findings from this research suggest that EPFRs have the potential to be a more potent contributor than PM to induced oxidative stress, and that the “chemical analysis of organics in PM may be subject to misinterpretation.” The ability for scientists to understand the contribution of EPFRs to the level of toxicity is fundamental for a clearer picture on the harmful impacts of PM.

Schnoor describes ES&T as a hybrid of a magazine and a research journal, publishing the latest in environmental science, technology, and policy. According to its website, ES&T strives for originality when deciding the types of papers it chooses to publish. The journal plans on publishing a news story about the honor and recognition Dellinger and his co-authors have received.



Linked video:
Watch an interview with ES&T Editor Jerald Schnoor, Ph.D., as he discusses the journal (12:05).
(Launches in new window)

Download Media Player:  Flash 

Citation: [Truong H, Lomnicki S, Dellinger B](#). 2010. Potential for Misidentification of Environmentally Persistent Free Radicals as Molecular Pollutants in Particulate Matter. *Environ Sci Technol* 44(6):1933–1939.

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

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New Science Communications Fellows have ties to NIEHS

By Eddy Ball

Five of the ten 2011 Science Communication Fellows announced Feb. 7 by [Environmental Health Sciences \(EHS\)](#) have received training or research support from NIEHS. Like their predecessors, this year’s fellows will spend the next year polishing their communication skills and learning effective ways to inform journalists and the public about new research findings in environmental health and green chemistry.

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. Among them was Laboratory of Neurobiology (LN) Biologist Negin Martin, Ph.D., who was selected to be a part of the program in 2009 when she was completing a fellowship with LN Chief David Armstrong, Ph.D.

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.

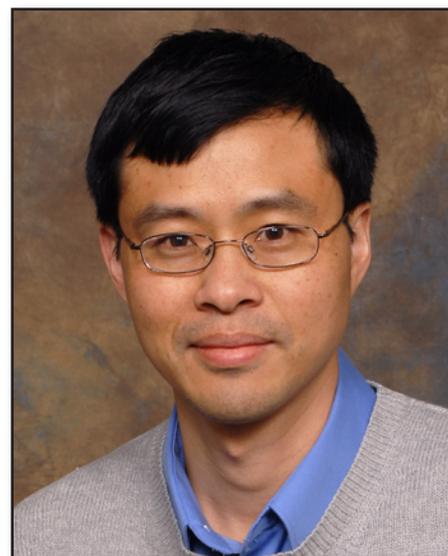


*Braun is working with [Russ Hauser, M.D., Sc.D.](#), and [Robert Wright, M.D.](#), through an NIEHS grant funding research on early life exposure to lead, bisphenol A, phthalates, and childhood neurodevelopmental outcomes. He is first author on a new review with Hauser, “[Bisphenol A and children’s health](#),” published online ahead of print in *Current Opinion in Pediatrics* Feb. 2. (Photo courtesy of Joe Braun)*

EHS and Advancing Green Chemistry (AGC) sponsor the fellowships. EHS publishes the online news sources, [Environmental Health News](#) and [The Daily Climate](#). AGC publishes chemistry updates [online](#).

The EHS announcement included the following awardees with ties to NIEHS:

- **Joe Braun, Ph.D.**, is a research fellow in the Department of Environmental Health at the Harvard School of Public Health. As an epidemiologist, he studies the role of endocrine disrupting compounds – such as bisphenol A and phthalates – in children’s development. His current research examines whether these compounds impact children’s traits that are sex linked, such as visual and spatial abilities, aggression, hyperactivity, anxiety, and depression.
- **Aimin Chen, M.D., Ph.D.**, is an assistant professor in the Department of Environmental Health in the University of Cincinnati College of Medicine. He conducts epidemiologic research of environmental toxicants and their effects on mothers’ and children’s health. His current research interests focus on children’s health outcomes from exposure to heavy metals, flame retardants, and electronic-waste recycling processes.
- **Roxanne Karimi, Ph.D.**, is a postdoctoral research associate in the School of Marine and Atmospheric Sciences at Stony Brook University. She studies the transfer of pollutants – such as mercury – through aquatic food webs and examines human exposure to these pollutants from fish consumption.
- **Brandon Moore, Ph.D.**, is an assistant professor at Louisiana Tech University. His research compares reproductive effects in wildlife – specifically reptiles and fish – from exposure to different levels of pollution in the environment. He investigates reproductive organs and cell processes to understand how pollutants can shape and alter sexual development and function in wildlife. Observed alterations in organ structures and associated genetic markers between unexposed and exposed animals shed light on potential reductions in reproductive fitness and fertility.
- **Tamara Tal, Ph.D.**, is an NIEHS postdoctoral fellow at Oregon State University. As a developmental toxicologist, she studies how changes in the way genes are read or processed during development lead to abnormal brain function later in life. Broadly, her current work seeks to understand adverse behavioral outcomes following developmental exposure to a wide range of environmentally prevalent chemicals. To do so, she uses zebrafish to investigate how early life exposures to neurotoxic chemicals alter the chemical or cell signals that promote normal brain development.
- **Heather Volk, Ph.D.**, is a research assistant professor in the Department of Preventive Medicine and the Zilkha Neurogenetic Institute in the Keck School of Medicine at the University of Southern California, as well as at the Saban Research Institute at Children’s Hospital Los Angeles. An epidemiologist, her research focuses on examining the interaction of environmental and genetic risk factors on neurodevelopment. She currently studies environmental exposures for autism and is focusing on the potential impact of traffic-related air pollution.



Chen’s NIEHS grant funded a study of developmental neurotoxicants in e-waste that was profiled in the Environmental Factor (see story) in January of this year. (Photo courtesy of the University of Cincinnati)



Karimi earned her doctorate with NIEHS Superfund Research Program (SRP) training support at Dartmouth College. In December 2007, she was awarded SRP’s Karen Wetterhahn Memorial Award (see story) as an outstanding scholar and citizen scientist. (Photo courtesy of Roxanne Karimi)



During his doctoral studies at the University of Florida, Moore received research support through an NIEHS [grant](#) to reproductive biologist Louis Guillette, Ph.D., for studying inhibins and environmental estrogens in ovarian disease. Moore was first author on five publications associated with that grant. (Photo courtesy of Brandon Moore)



Tal is a trainee in the laboratory headed by [Robert Tanguay, Ph.D.](#), a professor in the Oregon State University Department of Environmental and Molecular Toxicology and director of the [NIEHS Toxicology Training Grant](#) there. (Photo courtesy of Tamara Tal)



Volk is first author on a new study, partially funded by an NIEHS [grant](#), that found an association between residential proximity to a freeway and an increased risk of autism. She collaborated with NIEHS-supported scientists at the University of California, Davis Medical Investigation of Neurodevelopmental Disorders (MIND) Institute. (Photo courtesy of Heather Volk)

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Ron Mason honored by international scientific development group

By Eddy Ball

NIEHS Principal Investigator [Ron Mason, Ph.D.](#), has been honored once again for his outstanding contributions to the field of electron paramagnetic resonance (EPR), which is also known as electron spin resonance (ESR).

In his announcement of Mason's selection as 2011 Gold Medal winner Feb. 7, [International EPR \(ESR\) Society \(IES\)](#) President Jack Freed, Ph.D., noted Mason's "long career with interests spanning physical chemistry through to medicine" and singled out his "pioneering work in the use of spin traps *in vivo* and methods for ascertaining true radical formation." The Gold Medal is the society's highest award.

EPR/ESR is a sophisticated spectroscopic technique that detects free radicals in chemical and biological systems. Mason is a physical chemist who heads the Free Radical Metabolism Group in the NIEHS Laboratory of Toxicology and Pharmacology.

Mason's group uses EPR/ESR and the immuno-spin trapping technique developed by his group in 2006 to detect and identify



Mason is a productive investigator who has published more than 350 peer-reviewed articles. He joined NIEHS in 1978. (Photo courtesy of Steve McCaw)

free radical metabolism of toxic chemicals, drugs, and biochemicals to unravel the molecular mechanisms that lead to oxidative stress and development of disease. The group has also become interested in determining measurable, sensitive and specific biomarkers for oxidative damage in rodents and humans.

The Gold Medal is the latest in a long list of awards for Mason's work. He was honored in 2010 by the Electron Spin Resonance Spectroscopy Group of the Royal Society of Chemistry with the 25th Annual Bruker Prize for his "major contribution to the field of ESR spectroscopy" ([see story](#)). He received the 2007 Senior Investigator Lifetime Achievement Award from the Society for Free Radical Biology and Medicine. In 2006, Mason was selected as NIEHS Scientist of the Year and, in 2008, as Mentor of the Year.

According to its Web site, IES has been an internationally active group since its inception in 1989. The Society strives to stimulate scientific development of EPR/ESR, facilitate communication among researchers, and encourage the use of the techniques across a wide variety of research fields.

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Yao wins award from professional scientific society

By Robin Arnette

[Humphrey Hung-Chang Yao, Ph.D.](#), has been at NIEHS for only six months, but his exciting research on the fetal origins of adult diseases has led the [American Society of Andrology \(ASA\)](#) to grant him one of its highest accolades. Yao, a principal investigator in the Laboratory of Reproductive and Developmental Toxicology (LRDT), will receive the 2011 Young Andrologist Award during the upcoming ASA meeting April 2-5 in Montreal.

The award, sponsored by the Texas Institute for Reproductive Medicine and Endocrinology, P.A., is given to an active ASA member, 45 years old or younger, who has made significant contributions to the field of andrology — a branch of medicine that deals with male diseases and the male reproductive system.

"The awards committee solicits nominations from ASA members," Yao said. "It is an honor to receive recognition from my peers."

Going where the research leads

Yao came to NIEHS from the University of Illinois at Urbana-Champaign, where he still holds an appointment as an associate professor in the Department of Comparative Biosciences.

He originally trained as a physiologist and developmental biologist, but his research interests in testis development kept pointing him toward andrology and toxicology.

"I wanted to understand if genetic mishaps that occur during fetal development or *in utero* exposure to a certain chemical, could make a person more susceptible to reproductive problems," Yao explained. "There is an increasing trend of fertility problems in the U.S. and other developed countries, many of the cases with unknown causes. These problems could be a result of genetic defects, environmental exposure to harmful chemicals, or both."



Yao leads the Reproductive Developmental Biology Group within the LRDT. He joined NIEHS in August 2010. (Photo courtesy of Steve McCaw)

In his current research, Yao uses mouse models to figure out the fundamental process of testis development in embryos. By manipulating various genes in the fetal testis, his group identified several genetic factors that were critical for testis development during fetal life. The results of one of those mutation experiments led to the testicles of a newborn mouse being underdeveloped. When the mouse matured, it produced fewer sperm. Yao said that he's now following up those investigations with environmental exposure studies.

He added, "We're exposing normal pregnant mice to different endocrine disruptors to see if we can re-create the problems in the embryos that we saw in the genetic model. If we are able to generate similar results, the findings would suggest that genetic factors and environmental exposures could affect the same developmental pathway."

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The American Society of Andrology (ASA)

Comprised of more than 775 members from around the world, the ASA is a partnership of scientists and clinicians whose specialties include male reproduction, endocrinology, urology, anatomy, gynecology/obstetrics, biochemistry, animal science, molecular and cell biology, and reproductive technologies. Founded in 1975, the ASA encourages a multi-disciplinary approach to promote scientific interchange and knowledge about the male reproductive system.

Trainees honored by SOT Carcinogenesis Specialty Section

By Eddy Ball

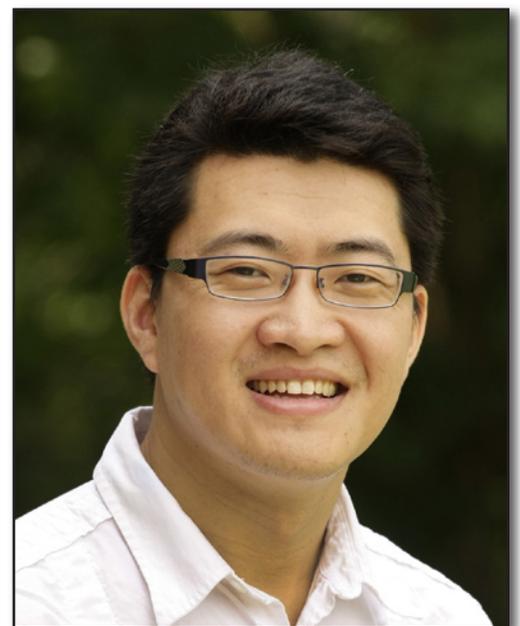
Two of the first of this year's Society of Toxicology (SOT) awards to NIEHS/NTP trainees and scientists are going to NIEHS Visiting Fellow Zhengyu Yin, Ph.D., and NIEHS-supported doctoral student Jessica Graham.

The Dharm V. Singh Carcinogenesis Endowment Graduate Student Awards and Postdoctoral Awards will be conferred at a reception March 6 by the SOT Carcinogenesis Specialty Section (CSS), recognizing the top abstracts submitted by a large pool of students and postdocs involved in carcinogenesis research.

NIEHS/NTP Director Linda Birnbaum, Ph.D., congratulated Yin and Graham on their performance and pointed to the importance of training. "Both the intramural and extramural programs understand the importance of cultivating the next generation of environmental health scientists," she said. "We look to these young investigators as our best resource for pursuing the goal of promoting public health through solid scientific research."

Zhengyu Yin

Yin, who graduated in 2009 from the [Toxicology Graduate Education Ph.D. Program](#) at the University of Rochester supported by an NIEHS center grant, is a member of the NIEHS [Cell Biology Group](#)



Yin maintains that better understanding the role of RAP80 could lead to the development of new and novel therapeutic approaches for radiotherapy and other anticancer procedures. (Photo courtesy of Steve McCaw)

headed by Principal Investigator and Chief of the Laboratory of Respiratory Biology [Anton Jetten, Ph.D.](#) As part of his first place award in the postdoctoral category, Yin will receive \$500.00 for his abstract, “RAP80 Plays a Critical Role in Maintaining Genomic Stability.” He will also receive an honorable mention from the Molecular Biology Special Section (MBSS) for the Postdoctoral Fellow Research Award competition.

Yin used experiments with RAP80 knockout mice to demonstrate that RAP80 is a tumor suppressor gene and that deficiency of RAP80 leads to genomic instability and predisposition to cancer. According to Yin, the gene encodes a UIM-containing protein playing a critical role in DNA repair.

Jessica Graham

Graham is a graduate student in the [Joint Graduate Program in Toxicology](#) of Rutgers University and the University of Medicine and Dentistry of New Jersey (UMDNJ) and is supported through an NIEHS [center grant](#). Her advisor is Principal Investigator and Professor [Helmut Zarbl, Ph.D.](#), who is director of the NIEHS-funded Center for Environmental Exposures and Disease at UMDNJ/Rutgers. For her first place win in the graduate student category with her abstract, “The *Fry* tumor suppressor encodes an inhibitor of epithelial mesenchymal transition,” Graham will also receive a plaque and \$500.

Graham’s analysis of approximately 4,500 human breast tumor mRNA profiles and studies using the human MDA-MB-231 mammary tumor cell line showed that decreased expression, function, or loss of mammalian *FRY* results in increased susceptibility to mammary carcinogenesis and progression of breast cancer.

Established in 1986, the CSS will celebrate its 25th year as an SOT specialty section at a reception in March. Along with recognizing student and postdoctoral trainee accomplishments, members of the CSS will also hear a brief tribute to long-time members of the section by NIEHS grantee James Swenberg, D.V.M., Kenan Distinguished Professor of Environmental Sciences and Engineering and former director of the Curriculum in Toxicology at the University of North Carolina at Chapel Hill Gillings School of Global Public Health.



Along with her NIEHS support, Graham is also funded by a predoctoral fellowship from the New Jersey Commission on Cancer Research. Graham anticipates these studies will enable the future development of novel approaches to breast cancer screening, diagnosis, prevention, and treatment. (Photo courtesy of Jessica Graham)



“Zhengyu is among the brightest young scientists I’ve worked with at NIEHS,” Jetton said of his protégé. “He’s thinking creatively about how to intervene in the progression of cancer in new ways that may lead to new treatment strategies available to oncologists.” (Photo courtesy of Steve McCaw)



“Jessica is the best graduate student I have mentored in 24 years. The fact that she received this Singh Award — her second award from SOT as a graduate student — speaks volumes about Jessica’s intellect, creativity, and fearless approach to cancer research. It also speaks about the quality of training at UMDNJ/Rutgers and the boost we get from NIEHS support.” (Photo courtesy of Helmut Zarbl)

NIEHS-supported trainee to attend Nobel-Lindau meeting

By Eddy Ball

Brown University graduate research fellow Catherine Volle has been selected to attend the 61st [Lindau Nobel Laureate Meeting](#) June 26-July 1 in Lindau, Germany, as part of a contingent of about 40 other NIH-supported students. Volle, who receives training support through an NIEHS grant, will join approximately 20 Nobel laureates in physiology or medicine and some 550 other outstanding students from throughout the world in a series of lectures, discussion sessions, and other activities designed to foster inter-generational scientific discourse.



Linked video:
[Watch the Nature video, 'The Spirit of Lindau'](#) (16:00)
(Launches in new window)

Download Media Player:  Flash 



Shown in her lab at Brown, Volle is an example of how NIEHS support is being used to encourage efforts to cross disciplinary boundaries. “I sometimes think of myself as a missionary bringing chemistry to the biologists and biology to the chemists,” she said of her studies. (Photo courtesy of Catherine Volle)

Volle is a member of the Brown University [laboratory](#) headed by NIEHS Outstanding New Environmental Scientist (ONES) awardee and chemist [Sarah Delaney, Ph.D.](#) ([see story](#)). In her research with the Delaney group, Volle seeks to define the mechanisms by which DNA damage, resulting from an inflammatory response or other environmental source of damage, contributes to dynamic DNA mutations ([see text box](#)).

Commenting on her upcoming trip this summer, Volle said, “I’m grateful to be presented with this opportunity. It’s not every day you get to meet some of the leading international scientists, both the Nobel laureates and the other young researchers, and have a dialogue with them, especially at such a formative point in a young scientific career.”

As one of what the Lindau organizers describe as “international Best Talents,” Volle will participate in an activity-filled week of social and intellectual interaction among laureates and students living, eating, and talking together in and around the historic island city of Lindau. Lindau sits on Lake Constance, the Bodensee, where the borders of Germany, Austria, and Switzerland meet.

The Lindau meetings began in 1951 as a sort of reunion for expatriate German scientists who left their country during the Nazi period. From the outset, organizers envisioned the meeting as a non-ideological gathering of inquiring minds dedicated to transferring knowledge between generations.



Delaney, who is Volle’s mentor at Brown and an NIEHS [grantee](#), said of her student, “Catherine’s enthusiasm in the lab carries over to her interest in and passion for all aspects of science and she will take full advantage of this terrific opportunity.” (Photo courtesy of Sarah Delaney)

This year, the American contingent of students, recruited and sponsored by NIH, the U.S. Department of Energy, and Oak Ridge Associated Universities, will be part of a group representing 70 nations. Participating universities were able to submit six nominees each, two to each of the sponsoring groups.

The National Institute of General Medical Sciences (NIGMS) is the NIH lead on the Lindau selection process. NIH, which provides support for its trainees attending the meeting, will also sponsor International Day at the meeting. The theme will be “Health and Health Research.”

Using chemical techniques to investigate biological systems

In her work in the Delaney lab, Volle studies the interplay between DNA structure and oxidative damage.

Volle investigates the structure adopted by trinucleotide repeats (TNR) in various contexts, particularly in the nucleosome core particle, the most basic unit of chromatin packing. TNRs are known to form non-canonical structures in the cell, leading to their expansion in the genome.

This expansion is the cause of several neurodegenerative diseases, such as Huntington’s disease. Volle is exploring whether those non-canonical structures can form in a nucleosome, and whether the presence of the oxidative lesion 8-oxoG or its repair can induce non-canonical structure formation in the nucleosome. She is also investigating the ability of 8-oxoG to modulate hairpin structure in CAG repeat oligonucleotides and duplex constructs.

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Aubrey Miller to speak on Gulf oil spill response

By Eddy Ball

NIEHS Senior Medical Advisor [Aubrey Miller, M.D.](#), will address the NIH role in the aftermath of the Gulf oil spill at a meeting of environmental, health, and safety professionals March 27-30 in Savannah, Ga. Miller will deliver his presentation, “Gulf Oil Spill: Health Concerns and the NIH Response,” as the featured keynote address at the 28th annual meeting of the [Environmental Information Association \(EIA\)](#).

Since the Deepwater Horizon incident on April 20, 2010, Miller has been involved in the Institute’s [multi-faceted response](#) to the Gulf oil spill (GOS). His activities in this area include founding and co-chairing, with the Centers for Disease Control and Prevention, the federal Interagency Oil Spill Health Monitoring and Research Workgroup comprised of over 50 agency representatives.

As one of the NIEHS leads in the Gulf, Miller has testified before U.S. Senate and House committees and partnered with NIEHS/NTP scientists and staff to develop an informational health and toxicology website to support the public health response. He is also an associate investigator for a new longitudinal cohort study (GuLF STUDY) to evaluate the health effects of over 50,000 workers involved in the GOS cleanup and is serving as the NIH spokesperson on the spill.

The Environmental Information Association

From its beginning as the National Asbestos Council, EIA has provided professionals in the environmental industry with information needed to remain knowledgeable, responsible, and competitive in the environmental health and safety industry. Conference session topics include indoor air quality, environmental sampling and analysis, lead-based paint abatement, asbestos management, regulatory compliance, auditing, environmental site assessments, and environmental management systems.

Each year the conference brings together representatives of federal regulatory agencies and professionals working in the areas of environmental health and safety to address developments in the field and engage current topics. EIA offers continuing education units for members of several organizations attending its annual conferences and conducts certification programs for several environmental health occupations.

Joining Miller as speakers at the conference will be [Martin Jones](#), a specialist in environmental law with Gust Rosenfield, P.L.C., and [Linda Reinstein](#), CEO and co-founder of the Asbestos Disease Awareness Organization as special plenary session presenters, as well as an outstanding line up of the industry's top experts on asbestos, lead, mold, and indoor air quality.



Miller also supervises the NIEHS office in Bethesda, Md., where he, Senior Advisor for Public Health John Balbus, M.D., Toxicology Liaison Chris Weis, Ph.D., and Legislative Liaison Mary Gant represent the Institute in Washington, D.C., and on Capitol Hill. (Photo courtesy of Steve McCaw)



In December 2010, NIEHS/NTP Director Linda Birnbaum, Ph.D., honored the Institute's Gulf oil spill response team. Shown, back row, from left to right. Ted Outwater; Vanessa Knight, Emily Starnes, Kathy Ahlmark, Sharon Beard, Joseph "Chip" Hughes, Steve Kleeberger; John Bucher; Gwen Collman, Scott Masten, Kent Stone, Darryl Zeldin, Paul Jung, and James Remington. Seated, from left to right, Cheryl Thompson, Christine Flowers, Dale Sandler; Laurie Johnson, Richard Kwok, and Carolyn Mason (Not pictured) Aaron Blair, Allen Dearry, Larry Engel, Lindsay Lloyd, Robin Mackar, Aubrey Miller; Connie Riley, Dudley Riner, Margarita Roque, Angie Sanders, William A. Suk, and Claudia Thompson. (Photo courtesy of Steve McCaw)

Science Notebook

Astrocytes give humans an intellectual edge

By Robin Arnette

Neuroscientist Maiken Nedergaard, M.D., gave the NIEHS Distinguished Lecture Feb. 8 and talked about brain cells known as astrocytes, which are important in learning and memory. Nedergaard has examined the differences between rodent and human brains, in regard to astrocyte form and function, and she relayed the remarkable findings during the seminar. Acting Scientific Director [David Miller, Ph.D.](#), hosted the event.

[Nedergaard](#) explained that an astrocyte is a glial cell, a star-shaped supporting cell with fine fibril processes radiating from the center, which transmit information. She said that glial cells and neurons are the two major cell types in the brain, and that proportionally, humans have more glia than neurons, compared to roundworms or rodents. Nedergaard believes that researchers should keep this fact in mind when planning their brain studies.

“If we’re thinking about brain disorders in people, it may be inappropriate to base our studies on animal models, because any human brain disease would be more of a glial disease than it would be in rats,” Nedergaard maintained. “However, it makes me wonder why we need more supportive cells in our brain.”

Of mice and men

Nedergaard said that evolutionary pressures steadily increased both the number and structural complexity of astrocytes in animal species. As a result of these changes, she speculates that human astrocytes contribute to the cognitive functions in humans, including language, reasoning, and problem solving.

To tease out exactly what makes human astrocytes special, Nancy Ann Oberheim, a medical student in Nedergaard’s lab, used immunohistochemistry to compare astrocytes in human and mouse brain. Nedergaard said that comparing both cell types under the microscope was the obvious place to start, but no one had looked at human astrocytes in detail since they were first described 150 years ago.

Oberheim found that human astrocytes were much larger than the rodent versions. In fact, the maximum



Nedergaard is co-director of the Center for Translational Neuromedicine and professor of neurosurgery at the University of Rochester School of Medicine and Dentistry. She hopes her work will help scientists understand how humans process sensory information, make decisions, and store memory. (Photo courtesy of Steve McCaw)



Miller called Nedergaard a pioneer in the field of electrophysiology and imaging. Many of the techniques she discussed in the seminar were developed in her lab. (Photo courtesy of Steve McCaw)

cellular diameter of a human astrocyte was almost three times that of a mouse astrocyte, corresponding to a 20-fold increase in volume. The human astrocyte also had 40-50 major glial fibrillary acidic protein (GFAP+) processes, compared to approximately 3-5 GFAP+ processes in the mouse. Nedergaard said these differences meant that an individual astrocyte in the human brain had more synapses — a junction that allows a neuron to transmit electrical or chemical signals to another cell — and that one human astrocyte could integrate more information.

Boosting brain power

Nedergaard then wanted to know if the presence of human astrocytes in a mouse brain would alter the animal's behavior. To find out, two of Nedergaard's colleagues at the University of Rochester School of Medicine and Dentistry, Assistant Professor Xiaoning Han, M.D., and Professor Steven Goldman, M.D., Ph.D., implanted human astrocytes into the brains of young, immunosuppressed mice and waited at least one year. Using an antibody specific for human cell nuclei, Nedergaard saw that the human astrocytes differentiated as they would in human brain, creating chimeric mice.

To determine if these mice were smarter than normal mice, her team evaluated memory recognition in the chimeric mice. In collaboration with Professor Alcino Silva, Ph.D., at UCLA, the Nedergaard lab utilized a fear conditioning behavioral test that used an auditory tone. After several weeks of instruction, Nedergaard placed a normal and a chimeric mouse in separate cages and prepared to test her pupils.

“At first, both mice started exploring their surroundings as mice generally do, but when we used the tone, both mice froze,” she said. “After a few seconds, the normal mouse started exploring again, while the chimeric mouse continued to stand still. This freeze can go on for several minutes.”

Nedergaard said that her studies suggest human astrocytes differ from the astrocytes of other animals, and that these attributes impart greater learning capacity to humans. Her findings not only have implications for improving memory, but they may also lead to better treatments for brain disease.

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Combined effects of lead exposure and stress on cognitive deficits

By Emily Zhou

NIEHS [grantee](#) Deborah Cory-Slechta Ph.D. addressed a capacity audience from NIEHS and the Environmental Protection Agency (EPA) Feb. 3 on the interaction of lead and stress and their combined effects on cognitive function. [Cory-Slechta](#) is a professor of Environmental Medicine in the Molecular Toxicology and Environmental Medicine Cluster at the University of Rochester School of Medicine and Dentistry.



The Nedergaard seminar drew numerous staff members with varying interests, including Toxicology Branch group leader [Rajendra Chhabra, Ph.D., D.A.B.T.](#) (foreground), Laboratory of Toxicology and Pharmacology (LTP) principal investigator [Jean Harry, Ph.D.](#), Division of Extramural Research and Training (DERT) Health Scientist Administrator [Annette Kirshner](#), and LTP principal investigator [Robert Langenbach, Ph.D.](#) (Photo courtesy of Steve McCaw)

Cory-Slechta and colleagues are examining the hypothesis that lead and stress interact by altering corticosterone, which then modulates mesocorticolimbic (MES) function and associated behavioral and neurochemical effects of lead. Their current results show that any lead exposure appears to permanently alter corticosterone levels.

“These changes are dynamic across time, and differ markedly by gender, prenatal stress, and offspring stress challenges,” said Cory-Slechta during the talk. Her presentation was hosted by NIEHS Health Scientist Administrator Annette Kirshner, Ph.D., as part of the NIEHS Division of Extramural Research and Training Keystone Lecture Series.

Learning deficits in a mouse model

Cory-Slechta’s rat and mouse model studies showed a strong association of elevated lead exposure with impulsivity, one of the three diagnostic components of attention deficit hyperactivity disorder. Female rats exhibited synergistic effects from exposure to lead and prenatal and offspring stresses. Continuous lead and prenatal stress synergistically increased impulsivity in male mice, with similar, but non-significant trends in females.

At the molecular level, it is very hard to pinpoint the mechanisms of lead and stress in causing learning impairments. Cory-Slechta and colleagues have found lead enhanced glucocorticoid receptor (GR) activation. Further studies are needed to confirm this result. Cory-Slechta has shown that lead causes hypothalamic-pituitary-adrenal (HPA) axis dysfunction, including elevated and blunted cortisol levels, altered glucocorticoid negative feedback regulation, and altered GR function. In addition, researchers also suspect catecholamines and serotonin are involved in MES pathways. They are looking further into lead and stress effects on trophic factors and cytokines.

An interesting observation Cory-Slechta made was that exposure to lead and stress causes learning deficits in female mice but leads to learning enhancement in male mice. This gender-influenced response to environmental toxicants has been observed for glucocorticoids. It has further illustrated that environmental toxics and stresses can influence very complicated systems that involve many neural signaling components and hormonal components. Cory-Slechta cautioned that future biochemical studies or therapeutic interventions should keep gender differences in mind.

What the findings mean for children

According to Cory-Slechta, the combined effects of lead and stress are translatable to humans. The Rochester cohort study with children at age 6 suggests that stress can enhance elevated blood lead-associated IQ reductions.

“Caveats exist in these studies,” Cory-Slechta pointed out. Brain hemisphere plays a role in differences in neurochemical outcome. Furthermore, study results differ between behaviorally tested subjects and untested subjects in responses to dopamine and norepinephrine.

As Cory-Slechta explained, lower socioeconomic status (SES) children in the U.S. are now the primary target of elevated lead exposure. Low SES is already a recognized risk factor for disease and behavioral dysfunctions, including learning disorders in children, an effect believed due to greater environmental stress in low SES



While Cory-Slechta is confident of the effects she’s seen in her experiments, she’s raised questions about the adequacy of mouse models to reflect the kinds of stress humans of lower socioeconomic status experience in their daily lives. (Photo courtesy of Steve McCaw)

populations and associated prolonged cortisol elevation. Lead and stress both affect brain MES systems and produce similar behavioral deficits.

Cory-Slechta receives additional [grant support](#) from NIEHS to investigate postnatal exposure to ultrafine particles in ambient air pollution. She was at NIEHS for a two-day NIEHS air pollution workshop held at EPA. Her research has focused largely on environmental neurotoxins as risk factors for behavioral disorders and neurodegenerative disease. She has also begun to examine mixtures of neurotoxic chemicals and risk modifiers to help explain the additive and synergistic effects of exposures to multiple stressors.

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

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NIH study finds two pesticides associated with Parkinson's disease

By Robin Arnette

New research shows a link between use of two pesticides, rotenone and paraquat, and Parkinson's disease. People who used either pesticide developed Parkinson's disease approximately 2.5 times more often than non-users.

The [study](#) was a collaborative effort conducted by researchers at NIEHS and the [Parkinson's Institute and Clinical Center](#) in Sunnyvale, Calif.

“Rotenone directly inhibits the function of the mitochondria, the structure responsible for making energy in the cell,” said [Freya Kamel, Ph.D.](#), a researcher in the intramural program at NIEHS and co-author of the paper appearing online in the journal *Environmental Health Perspectives*. “Paraquat increases production of certain oxygen derivatives that may harm cellular structures. People who used these pesticides, or others with a similar mechanism of action, were more likely to develop Parkinson's disease.”

The authors studied 110 people with Parkinson's disease and 358 matched controls from the [Farming and Movement Evaluation \(FAME\) Study](#) to investigate the relationship between Parkinson's disease and exposure to pesticides or other agents that are toxic to nervous tissue. FAME is a case-control study that is part of the larger [Agricultural Health Study](#), a study of farming and health in approximately 90,000 licensed pesticide applicators and their spouses. The investigators diagnosed Parkinson's disease by agreement of movement disorder specialists and assessed the lifelong use of pesticides using detailed interviews.

There are no home garden or residential uses for either paraquat or rotenone currently registered. Paraquat use has long been restricted to certified applicators, largely due to concerns based on studies of animal models of Parkinson's disease. Use of rotenone as a pesticide to kill invasive fish species is currently the only allowable use of this pesticide.



Kamel was honored as NIEHS Outstanding Staff Scientist ([see story](#)) at the Science Day awards ceremony in 2008. (Photo courtesy of Steve McCaw)

“These findings help us to understand the biologic changes underlying Parkinson’s disease. This may have important implications for the treatment and ultimately the prevention of Parkinson’s disease,” said [Caroline Tanner, M.D., Ph.D.](#), clinical research director of the Parkinson’s Institute and Clinical Center, and lead author of the article.

Citation: [Tanner CM, Kamel F, Ross GW, Hoppin JA, Goldman SM, Korell M, Marras C, Bhudhikanok GS, Kasten M, Chade AR, Comyns K, Richards MB, Meng C, Priestly B, Fernandez HH, Cambi F, Umbach DM, Blair A, Sandler DP, Langston JW. 2011. Rotenone, paraquat and Parkinson’s disease. Environ Health Perspect; doi:10.1289/ehp.1002839 \[Online 26 January 2011\].](#)

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Tanner combines her expertise in neurology, environmental toxicology, and epidemiology in the search for answers about environmental exposures in the development of Parkinson’s. (Photo courtesy of Caroline Tanner)

Deciphering a core process in Parkinson’s disease

By Eddy Ball

Two new studies from researchers at NIEHS offer insights into mechanisms of the chronic neuroinflammation that drives progressive neurodegeneration in Parkinson’s disease (PD). Gradual degeneration of dopamine neurons is a hallmark of PD, the second most common neurodegenerative disease, but what drives the process — and what molecular targets may offer promise for interventions — has remained elusive.

The authors are members of the NIEHS [Neuropharmacology Group](#) headed by Principal Investigator [Jau-Shyong Hong, Ph.D.](#) On both of the studies, Intramural Research Fellow Hui-Ming Gao, M.D., Ph.D., served as first and corresponding author. The team included Visiting Postdoctoral Fellow Hui Zhou, Ph.D., former Visiting Fellow Feng Zhang, Biologist Belinda Wilson, and Special Volunteer Wayneho Kam.

Findings from their experiments shed light on the processes that trigger the persistent neuroinflammation that is a precursor to PD and point to potential interventional targets for slowing or halting disease progression.

“We are very excited by these discoveries,” Hong said of the group’s work. “We hope they’ll lead to a better understanding of how to mitigate or prevent the tremendous burden of this tragic disease during the critical five- to seven-year preclinical period of PD progression.”

PD develops over decades before the cumulative degeneration of dopamine neurons in the substantia nigra of the brain results in a progressive worsening of motor dysfunction, characterized by tremor and impaired muscular coordination. PD, which currently is treated only symptomatically, affects more than one million people in the United States.



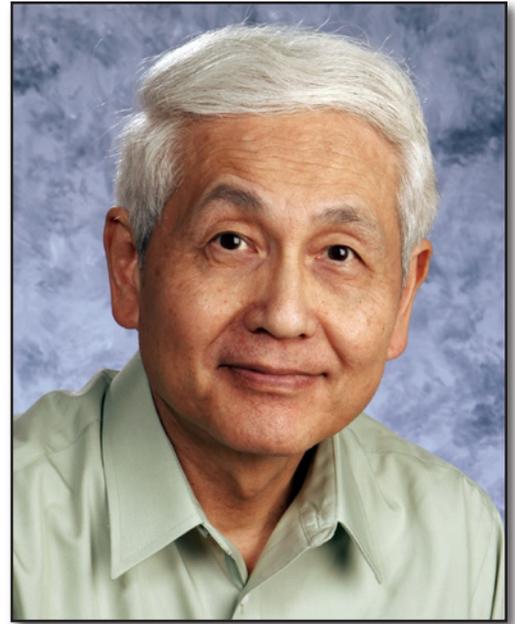
During her training in the Hong group, Gao has been an author on 17 studies — 10 of them as first author. (Photo courtesy of Steve McCaw)

Gene-environment interaction is key to triggering PD

In a [study](#) published online in *Environmental Health Perspectives*, the scientists demonstrated an important connection between neuroinflammation and a polymorphism in the gene expressing the protein alpha-synuclein in a mutant mouse model. They compared the outcomes of wildtype and transgenic mice following exposure to the endotoxin liposaccharide (LPS), which initiated systemic and brain inflammation in the mice.

Although both groups of mice exposed to LPS initially displayed acute neuroinflammation, only the transgenic mice overexpressing alpha-synuclein developed chronic progressive degeneration of the nigrostriatal dopamine pathway, buildup of aggregated, nitrated protein, and the Lewy body-like inclusions in nigral neurons characteristic of PD.

The team tested their hypothesis further by determining that inhibition of two inflammatory enzymes — inducible nitric oxide synthase and NADPH oxidase — with compounds known as DPI and 1400W resulted in attenuation of nigral alpha-synuclein and dopaminergic neurodegeneration. “Our two-hit progressive model underlines a central role of gene-environment interactions in the development of PD,” the researchers concluded.



Hong has published over 300 peer-reviewed articles in leading biomedical journals, as well as 50 book chapters. He was a senior staff fellow at the National Institute of Mental Health before joining NIEHS in 1980. (Photo courtesy of Steve McCaw)

Neutralizing the HMGB1 protein may offer an approach for treatment

In a second [study](#) published in the *Journal of Neuroscience*, the research team reports isolating the protein — high-mobility group box 1 (HMGB1) — that binds to brain immune cells, known as microglial macrophage antigen complex 1 (Mac1), to activate an inflammatory cascade involving nuclear factor kappa-beta and NADPH oxidase. The lethal combination, according to the scientists, drives the persistent neuroinflammation involved in the neurodegeneration of PD.

The team exposed reconstituted mixed glial and neuron-enriched glial cell cultures to three toxins often used to create PD models — 1-Methy-4-phenylpyridium (MPP+), LPS, and the pesticide rotenone — demonstrating, for the first time, that persistent neuroinflammation is essential for progressive degeneration of dopamine neurons in PD and that it occurred only in neuron-glia mixed cultures. With neutralization of HMGB1 and genetic ablation of Mac1, the researchers were able to block over-activation of microglia and the progressive neurodegeneration of PD.

The team concluded, “Mac1 might become a promising target for the development of therapeutic agents halting the vicious cycle between uncontrolled neuroinflammation and degenerating neurons, and thereby retarding the progression of PD.”

Citations:

[Gao HM, Zhang F, Zhou H, Kam W, Wilson B, Hong JS](#). 2011. Neuroinflammation and alpha-synuclein dysfunction potentiate each other driving chronic progression of neurodegeneration in a mouse model of Parkinson’s disease. *Environ Health Perspect*; doi:10.1289/ehp.1003013 [Online 18 January 2011].

[Gao HM, Zhou H, Zhang F, Wilson BC, Kam W, Hong JS](#). 2011. HMGB1 acts on microglia Mac1 to mediate chronic neuroinflammation that drives progressive neurodegeneration. *J Neurosci* 31(3):1081-1092.

Chromatin meeting highlights genomic rearrangements and small molecule inhibitors

By Archana Dhasarathy

NIEHS principal investigators and trainees attended the latest meeting of the Atlantic Coast Chromatin Club (ACCC) January 31. The ACCC is a special interest group that sponsors an ongoing series of talks by area scientists on the topic of chromatin, the complex of histone proteins and DNA that makes up our chromosomes, which is central to several important biological processes in the cell.

Held at the North Carolina Biotechnology Center, the meeting drew scientists from the NIEHS Laboratory of Molecular Carcinogenesis (LMC), Duke University, North Carolina State University, and the University of North Carolina at Chapel Hill (UNC-CH).

Genome rearrangements and structural abnormalities of chromosomes

[Beth Sullivan, Ph.D.](#), an assistant professor in the Department of Molecular Genetics and Microbiology at Duke University, presented her research on genome rearrangements and chromosomal abnormalities. Chromosomes, the hereditary structures in our cells, are maintained stably by specialized structures such as telomeres and centromeres. Defects in these structures cause numerical and structural abnormalities of chromosomes, leading to reproductive failure, genetic diseases, and cancer.

One such genome rearrangement is called a dicentric, an abnormal chromosome containing two centromeres. Sullivan said that dicentrics in humans are surprisingly very highly stable, especially if one of the centromeres is inactivated. Her laboratory is trying to address how dicentrics are formed, what happens after they form, and how and when inactivation of one of the centromeres occurs.

To answer these questions, Sullivan and her colleagues developed a system to create these dicentrics in the laboratory. “We needed to have a human system that would be more relevant to what we see in patients,” she said. To this end, they took advantage of a mutant dominant negative version of a protein called TRF2, which normally protects chromosome ends.

Using this elegant system, they noticed non-random dicentrics were formed by fusion of acrocentric chromosomes. Perhaps not coincidentally, acrocentric fusions are among the most prevalent naturally occurring



The Old North State Board Room at the North Carolina Biotechnology Center offers an intimate setting for the monthly meetings of the ACCC. The program includes pizza and drinks for attendees at the evening lectures. (Photo courtesy of Steve McCaw)



Sullivan explored the consequences of defects in telomeres, which protect chromosome ends from degradation, and centromeres, which ensure equal segregation of chromosomes during cell division. (Photo courtesy of Steve McCaw)

chromosome abnormalities in humans. Expression of the mutant TRF2 also adversely affected nuclear organization of DNA and proteins, and the stability of the nucleolus, a structure in the cell nucleus that transcribes and assembles ribosomal RNA. Sullivan's laboratory is currently investigating the molecular basis for their observations, which have enormous significance for human health.

Selective small molecule inhibitors

Following Sullivan's talk, Martin Herold, Ph.D., a postdoctoral associate in the laboratory of Stephen Frye, Ph.D., at the [UNC-CH Center for Integrative Chemical Biology and Drug Discovery](#), presented his research toward the development of potent and selective small molecule inhibitors targeting the malignant brain tumor (MBT) protein repeats. Access to the information encoded in chromatin by the cellular machinery is regulated via specific chemical modifications to DNA and histone proteins. Proteins in the cell control this process by "writing, reading, and erasing" this code. The MBT domains recognize methyl-lysine marks on histone tails, and their binding is involved in gene silencing, tumor suppression, and cellular differentiation.

Herold and his colleagues used a structure-based design to develop antagonists to the MBT repeat of a protein called L3MBTL1. Analyses of the crystal structure of L3MBTL1, and comparison to other domains, enabled them to identify features that were specific to the MBT repeat that could be used to improve potency and selectivity.

Using different kinds of assays, the researchers were able to pinpoint one of the compounds they screened, a nicotinamide compound called UNC669, which showed a 5-fold increased binding affinity and a 6-fold improved ligand efficiency compared to the canonical histone peptide alone. In collaboration with the Structural Genomics Consortium at the University of Toronto, UNC669 was the first small molecule to be co-crystallized with a methyl-lysine reader protein. Herold and his team are now using the compound in functional cell-based assays, to determine its effect on chromatin regulation in cells.

(Archana Dhasarathy, Ph.D., is a postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis.)



Herold, above, listened to Sullivan's talk, as he waited his turn as the second speaker on the program. (Photo courtesy of Steve McCaw)



Also in the audience were NIEHS Laboratory of Molecular Carcinogenesis postdoctoral fellows Sergei Nechaev, Ph.D., right, and Takashi Shimbo, Ph.D. (Photo courtesy of Steve McCaw)

A regional special interest group on chromatin structure and function

The ACCC meets in the evening on the last Monday of the month at the North Carolina Biotechnology Center. The group is supported in part by NIEHS, the UNC-CH School of Medicine, the North Carolina Biotechnology Center, Duke Medicine, and companies such as current corporate sponsor Active Motif, a developer of innovative cell biology-based research tools and biocomputing resources.

In addition to its monthly meetings, each fall for the past five years, usually in October, the ACCC has also held an all-day annual conference at the William and Ida Friday Center in Chapel Hill, N.C., with high profile speakers.

NIEHS Transcriptional Responses to the Environment Group Principal Investigator Karen Adelman, Ph.D., and Eukaryotic Transcriptional Regulation Group Principal Investigator Paul Wade, Ph.D., were organizers of the 2010 annual conference, along with colleagues from Duke University and UNC-CH. The meeting attracted more than 100 scientists from North Carolina and beyond.

For information about upcoming meetings, please contact Professor Laura Rusche, Ph.D., at Duke University (lrusche@duke.edu).

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Peer review panel deliberates NTP Technical Reports

By Ernie Hood

The National Toxicology Program (NTP) convened a peer review of draft NTP Technical Reports by an external scientific panel at a [meeting](#) Jan. 26 at NIEHS. Assessing the daylong consideration of technical report documents, NTP Deputy Program Director for Science Nigel Walker, Ph.D., said, “We were very pleased with the depth and breadth of the comments.”

The gold standard in observational toxicology

The Technical Reports describe the results of two-year bioassays of nominated substances in male and female mice and rats. They reflect considerable effort on the part of NTP scientists and contractors — often involving 50-70 people and many years worth of work. Draft reports are prepared by an internal team led by NTP pathologist David Malarkey, D.V.M., Ph.D., and NTP toxicologist Michelle Hooth, Ph.D., and are reviewed by NTP scientists before they are released to the public and presented to the external peer review panel.



This was the first meeting of the new NTP Special Emphasis Panel founded to peer review draft NTP Technical Reports. As shown above, the panel members had a considerable amount of material to consider as they came to their conclusions. (Photo courtesy of Steve McCaw)

The conclusions reported are seen by regulatory agencies as authoritative sources in their decision-making. “Part of the NTP mission is providing information on hazardous substances to the stakeholders in the community, and to me, the Technical Reports meetings are where the rubber meets the road for that part of our mission,” says Walker. “They exemplify everything NTP is about.”

Review panel outcomes

At the January meeting, the panel reviewed draft NTP Technical Reports on kava kava extract, a botanical product used widely as a dietary supplement; retinoic acid/retinyl palmitate, a formulation of vitamin A widely used in cosmetic products; methyl *trans*-styryl ketone, a compound used as a synthetic flavoring or fragrance agent; styrene-acrylonitrile (SAN) trimer, a chemical byproduct suspected to be associated with childhood cancers; and alpha, beta-thujone, a compound found in herbal medicines, food and beverage flavorings, cosmetic products, and repellants.

The panel accepted the draft conclusions as written for methyl *trans*-styryl ketone and alpha, beta-thujone, but recommended changes for the conclusions for the other compounds, including changing the draft conclusion for SAN trimer from “equivocal evidence of carcinogenic activity” in male F344/N rats to a finding of “no evidence.”

Due to time constraints, consideration of the draft Technical Report for senna, an herb used as a stimulant laxative, was postponed until the peer review panel in April.

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

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Panel member Diane Birt, Ph.D., director of the Center for Research on Botanical Dietary Supplements at Iowa State University, was a primary reviewer of the Technical Reports on kava kava extract and alpha beta-thujone. (Photo courtesy of Steve McCaw)



Panel member Russell Cattley, V.M.D., Ph.D., executive director of pathology at Amgen Inc., contributed many cogent comments over the course of the meeting. (Photo courtesy of Steve McCaw)



Shown right to left, NIEHS/NTP Director Linda Birnbaum, Ph.D., panel chair Raymond Novak, Ph.D., corporate director of research at Shriners Hospital for Children in Tampa, Fla., and Walker gave careful consideration to the Technical Report presentations. (Photo courtesy of Steve McCaw)

Dudek explores synaptic plasticity during Council presentation

By Eddy Ball

Continuing the tradition of scientific talks by outstanding researchers at their meetings, on Feb. 17 members of the [National Advisory Environmental Health Sciences Council \(NAEHSC\)](#) heard about new findings on synaptic plasticity by NIEHS Synaptic and Developmental Plasticity Group Principal Investigator [Serena Dudek, Ph.D.](#)

Following a brief report about the NIEHS Division of Intramural Research, Acting Scientific Director David Miller, Ph.D., introduced Dudek, who spoke on “New Insights into Regulating Synaptic Plasticity: Implications for Autism and Schizophrenia.”

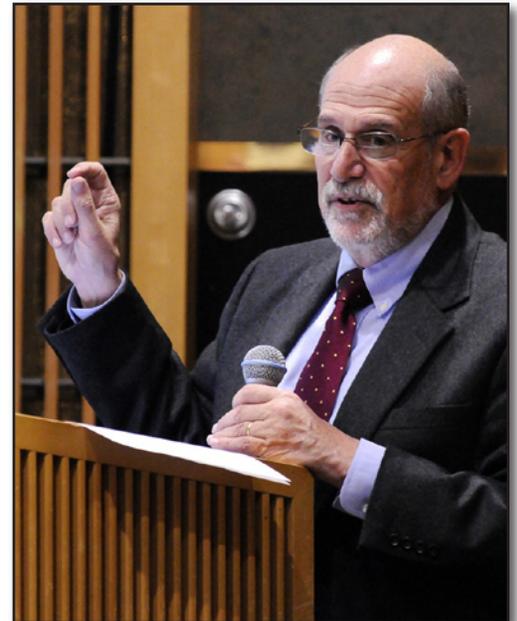
Dudek and her group study synaptic plasticity, the process by which the mammal brain adapts to changes in its internal and external environment, across brain regions and at different stages of development. “We think this is the process that underlies learning and memory in the young and in adults,” Dudek said at the beginning of her presentation.

The group’s most recent work involves investigating regulation of synaptic plasticity in the CA2 region of the hippocampus. Unlike the adjacent CA1 and CA3 regions, CA2 is a largely uncharted portion of the hippocampus, where Dudek suspects much more can be learned than previously thought about learning as well as the development of social interaction disorders. Growing evidence suggests that the CA2 is important for social behavior and is impaired in cases of bipolar disease and schizophrenia ([see text box](#)).

While the formation of the gross structure of the brain, its hardwiring, takes place largely before birth, refinement of the brain’s microscopic structure continues well beyond, especially during critical periods of postnatal development when synaptic plasticity is most robust. This refinement also occurs throughout life, as new learning takes place. Environmental exposures during these critical periods, though, have the potential to change the brain’s circuitry in potentially harmful ways.

Looking for answers in the CA2

Dudek turned to the CA2 region for her latest experiments, because, she explained, “There’s really something fundamentally different about this region.” CA2 neurons are highly resistant to most protocols for inducing long-term potentiation (LTP), making the CA2 a fertile ground for discovering molecules that can inhibit synaptic plasticity. For example, in regard to calcium, which is important for plasticity, Dudek found, “The CA2 neurons have almost four times as much of the buffering capacity as do CA1 neurons....”



Miller spent about ten minutes reviewing new tenure track appointments, awards to scientists and trainees, and high-profile publications, before introducing Dudek to members of Council. (Photo courtesy of Steve McCaw)



Dudek received the A.E. Bennett Research Award from the Society of Biological Psychiatry for research by a young investigator in 2009 and was granted tenure in October 2010. She was honored during the 2009 Science Awards Day as Mentor of the Year. (Photo courtesy of Steve McCaw)

Once we get the calcium up to a comparable level to what's seen in CA1, [however,] we see that the CA2 neurons can express LTP. The CA2 neurons have all the right machinery there.”

Dudek has continued to explore the ways calcium is limited in neurons by buffering and extrusion, another of the ways cells deal with calcium. Her group has established that proteins regulating calcium extrusion, such as Pep-19, which is highly enriched in the CA2, can inhibit LTP in CA1 neurons, which normally express robust LTP.

To further explore other molecular players, and to determine the role of CA2 in behavior and learning, Dudek and her collaborators studied mice with a knockout of a CA2-enriched gene, RGS-14. These mice actually had robust plasticity in CA2 and surprisingly, faster memory acquisition. Dudek is currently studying the effects of caffeine and social neuropeptides, which appear to induce LTP in CA2.

Dudek emphasizes, “These are still very new experiments, and we've got a lot of work to do to identify the specific molecular players” and how they function along a veritable labyrinth of pathways. Still, the group plans to continue this line of investigation, because “this is an area of research that could really turn out to be important in brain function,” Dudek said.

Dudek, who said she's been interested in the brain since she was in high school, is clearly excited about the possibility of uncovering the mechanisms responsible for regulating synaptic plasticity. She is also seeking to understand what kinds of environmental exposures, such as endocrine disrupting compounds, may impair the normal strengthening and weakening of synapses, and identifying potential targets and interventions for normalizing plasticity in people with autism, schizophrenia, and other psychiatric disorders.

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Refinement of the microscopic structure of the brain

In determining its neural circuitry, the mammalian brain undergoes two processes — strengthening synapses or long-term potentiation (LTP) and weakening of synapses known as long-term depression (LTD) and leading to pruning — that are both important in determining how effectively the organism adapts to its environment by shaping brain circuitry in response to experience. Dudek is especially interested in just how these processes are regulated in the brain, which may be especially relevant for understanding developmental brain disorders such as autism and schizophrenia.

“Any gene mutation or environmental toxicant that influences synaptic transmission at all would have the effect of modulating the likelihood of getting LTP or LTD during development,” Dudek explained. “We might envision a situation where what we might end up with is abnormal pruning of the brain's circuitry, [which] can have lifelong consequences in cognition.”

Referring to autopsy and imaging studies, Dudek noted that a thickening of the cerebral cortex has been observed in the brains of people with autism, possibly due to less than normal pruning of synapses, while a greater than normal pruning of synapses has been found in schizophrenics.

New insights into fitness versus fatness and diabetes risk

By Melissa Kerr

A new exercise program at the NIH in Bethesda, Md., encourages employees to participate in more heart-healthy behavior and has the added advantage of helping researchers learn more about diabetes and obesity. National Heart, Lung, and Blood Institute (NHLBI) investigator [Richard Cannon, M.D.](#), explained in an NIEHS Clinical Director's Lecture Series presentation Feb. 7 that data from the NHLBI Keep the Beat worksite wellness program is leading to new insights into how diabetes and obesity affect the body.

"This is a relatively new field for me, diabetes in the workforce," Cannon explained. "This is of public health importance because the prevalence of obesity is high and is increasing."

Cannon has been on the staff of NHLBI since 1979. He is currently clinical director in the Institute's Division of Intramural Research, and head of the Clinical Cardiology Section in the Cardiology Branch. Colleague Darryl Zeldin, M.D., NIEHS acting clinical director, hosted Cannon's talk on "Diabetes Risk in the Workforce: NHLBI's Keep the Beat Program."

Promoting health at the job site

[Keep the Beat](#) was designed to help promote a heart-healthy lifestyle through diet and exercise. NHLBI is utilizing this program to provide employees with a great deal of Web-based information on diet, a physical activity room, pedometers, and walking maps of the Bethesda campus, along with menu tips to help increase overall health.

Cannon and his team used Keep the Beat enrollment data in research on insulin sensitivity in non-diabetic overweight and obese subjects. Cannon worked closely with scientists at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), as the team evaluated 141 middle-aged overweight and obese women, 89 African-American and 52 white.

During their exercise program, subjects were tested for exercise oxygen consumption and carbon dioxide release, adipose tissue or body fat by DEXA scanning, and insulin sensitivity, among other measures of cardiac health. They will be tested again at the conclusion of their six-month program.

Fit versus fat

Cannon's research focused specifically on truncal fat, because it seems to have the strongest correlation to insulin sensitivity. Truncal fat, he said, is responsible for adipokines, signaling proteins that help to regulate insulin transport. The greater the truncal fat, Cannon explained, the higher a person's resistance to insulin. However, "Fitness does matter," Cannon insists, especially in African-American overweight and obese women. "There clearly is a relationship between cardiac respiratory fitness and insulin sensitivity that is independent of truncal fat."

Cannon was particularly interested in results that indicated previously unrecognized differences between white women and African-American women. He found a significant difference of 20 percent in oxygen consumption



Cannon was making his first trip to NIEHS. He told the audience, "This is not high science. This is old-fashioned clinical research, sort of gumshoe clinical research." (Photo courtesy of Steve McCaw)

and treadmill exercise duration between African American women and white women. “Although black women have greater muscle mass than white women, for any given muscle mass measure, African-Americans have worse exercise performance than whites,” he said. In reviewing the data, he found an interesting deviation from the conventional wisdom that more muscle equates with better health. He found instead that in obese black women, the greater the muscle mass, the more resistant the muscle is to insulin. This was not the case in white obese women.

However, despite their poorer exercise performance, African-American women show a positive relationship between lean mass and insulin resistance, while white women do not.

Cannon said that he plans to continue this line of investigation into patterns of insulin sensitivity and racial differences in the impact of obesity on health. “There are some interesting questions with regards to genetic determinants of insulin sensitivity that hopefully we’ll address in future research,” he said, “maybe in collaboration with some people here [at NIEHS].”

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

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Kensler discusses bench to tea-time research on Nrf2

By Jeffrey Stumpf

During his guest lecture at NIEHS Feb. 7, toxicologist Thomas Kensler, Ph.D., provided a new twist to the age-old axiom about eating your vegetables. Invited by Laboratory of Molecular Genetics (LMG) trainees, the University of Pittsburgh and Johns Hopkins University professor discussed the molecular and culinary implications of his research on Nrf2.

Kensler, who is a project leader on an NIEHS [grant](#), described his progress on studies that identified chemopreventive environmental agents, including sulforaphane, a chemical that is isolated from cruciferous vegetables such as broccoli.

A variety of stresses are involved in carcinogenesis, including metabolic stress, oxidative stress, and DNA damage. Transcription factors, such as Nrf2, induce the expression of proteins that protect the cell. Kensler discussed how inducing Nrf2 provides protection against diseases and suggested that Nrf2 is a potential prophylactic target.

Nrf2 expression increases only in response to environmental stresses. Kensler explains that the key to regulating Nrf2 is a complex between Keap1 and the ubiquitin ligase system that targets proteins for degradation. Under normal circumstances, Keap1 binds to Nrf2 and promotes the quick degradation of Nrf2. Environmental agents such as reactive aldehydes, as well as chemopreventive agents such as sulforaphane disrupt, Keap1, thereby preventing the destruction of Nrf2 and triggering the induction of protective genes.



Kensler enjoyed audience reaction, as he described the strange brew his team tested in people living in a part of China with a very high incidence of liver cancer. (Photo courtesy of Steve McCaw)

Nrf2 pathway's three-tiered approach to damage: Prevention, control, repair

Kensler explained the importance of Nrf2 in disease prevention using the example of its inhibition of aflatoxin-induced liver tumors in rats. Nrf2 activates glutathione S-transferases that are used to detoxify aflatoxin. In mice without Nrf2, damage by aflatoxin increased along with sensitivity to carcinogenesis. Alternatively, reducing the amounts of Keap1 increased Nrf2 and was chemoprotective.

In addition to prevention, Kensler showed evidence that Nrf2 activates the pathway involved in removing DNA damage that occurs because of UV or oxidative damage. Nrf2 also induces proteins that increase proliferation of liver cells when tissue needs to be repaired.

Reducing cancer risk with broccoli? Clinical trials are brewing

The fact that the Nrf2-inducing chemical, sulforaphane, is in broccoli sprouts begs an obvious question. How much broccoli must someone eat to mimic the protection against carcinogenesis demonstrated in the lab? “Depending on the variety of broccoli, about 500 grams,” Kensler explained. “It’s about one head of broccoli, which is too much to consistently eat in a day.”

Kensler and his colleagues offered a possible alternative — broccoli tea. The sprouts contain all of the glucoraphanin, the precursor to sulforaphane, in the plant, making it possible to be brewed into a tea and to provide a more practical method of ingestion.

To test the potential protective effects of broccoli tea, Kensler is leading a clinical trial in Qidong, a Chinese city where liver cancer is 25-fold more prevalent than in the population only 100 kilometers away. In addition to hepatitis B, exposure to aflatoxin-contaminated food is a major cause of liver cancer.

Volunteers in the clinical trials drank broccoli tea in a controlled tea house, and despite a bitter bite to the brew, there was 100 percent compliance. Measures in the urine excreted from the volunteers indicated that there was an average 50-fold increase in uptake of sulforaphane, but this amount varied among people.

Although early results showed only mild decreases in DNA damage, people with greater uptake of sulforaphane had fewer DNA damage adducts. This finding provides hope for the future of food-induced chemoprotective therapies, especially in poorer regions.



NIEHS Visiting Fellow Deepa Sambandan, Ph.D., foreground, was lecture host. Sambandan is a trainee in the LMG Environmental Genomics Group, headed by Principal Investigator Doug Bell, Ph.D. (Photo courtesy of Steve McCaw)



NIEHS Principal Investigator Leping Li, Ph.D., was one of several Chinese scientists who attended the talk. (Photo courtesy of Steve McCaw)

“When one thinks about broad-based intervention in Qidong, China or sub-Saharan Africa and other areas endemic for liver cancer, efficacy is clearly very important, but what is more important are the factors of cost, practicality, and tolerability,” Kensler stated. “Using Western-based approaches and interventions are not going to work in those populations.”

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

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Bell, above, was one of several LMG principal investigators who joined their trainees for Kensler's presentation. (Photo courtesy of Steve McCaw)

Paper described as “tour de force” featured in microbiology journal

By Ernie Hood

A new paper from the [NIEHS Human Metabolism Group \(HMG\)](#) that describes for the first time a key transcriptional mechanism for regulation of drug and lipid metabolism in the human liver has been awarded “Spotlight” status by the journal *Molecular and Cellular Biology*, which is published by the American Society for Microbiology.

“[Med25 is required for RNA polymerase II recruitment to specific promoters, thus regulating xenobiotic and lipid metabolism in human liver](#)” was published online in December 2010 and in the journal in February. HMG scientists Ritu Rana, Ph.D., and Sailesh Surapureddi, Ph.D., were co-lead authors, along with senior author and HMG Principal Investigator Joyce Goldstein, Ph.D., intern Wayne Kid Kam, and Stephen Ferguson of Invitrogen Corporation/CellzDirect. One reviewer called the paper “a tour de force [that] provides very convincing data...that will be of considerable interest to the transcription community.”

Identifying a master switch for xenobiotic, drug, and chemical metabolism

The article reports the results of a series of experiments focusing on the novel role of the Med25 protein in regulating the expression of sets of genes in the cytochrome P450 family drug metabolism and those involved in fatty acid metabolism. Using microarray and imaging methods, mainly in primary human hepatocytes, which are a model for human liver, the researchers were able to demonstrate that “Med25 interacts with hepatocyte nuclear factor 4alpha (HNF4alpha) [a liver enriched receptor], and it up-regulates or regulates specific genes, including those involved in drug metabolism and lipid metabolism,” Rana explained.



Rana is a visiting fellow in the Human Metabolism Group, which is part of the NIEHS Laboratory of Toxicology and Pharmacology. (Photo courtesy of Steve McCaw)

Med25 does so by changing the composition of the HNF4 α -bound transcriptional complex from an inactive to an active state, recruiting RNA polymerase II to the specific sites to initiate transcription and the expression

of the specific genes involved. That specificity is crucial. The liver controls a wide variety of metabolic processes, but “when Med25 levels are manipulated, the only metabolisms that seem to be affected are drug and lipid metabolisms,” said Surapureddi. “Co-activators had been predicted to do that for a long time, and this is the first paper to show that.”

“It’s a master switch for certain genes,” said Goldstein. “If Med25 was not there, you’d have a number of genes that wouldn’t be responding to environmental chemicals, or clinical drugs you’re taking with your morning coffee.” Gene silencing techniques and up-regulation of the gene confirmed the necessity of Med25 to the process. “This was the first paper to show that if Med25 is not there, polymerase II cannot come, whatever other genes are there or not, it doesn’t matter,” said Surapureddi. “If Med25 is silenced and the other genes are normal, we cannot get polymerase II to the transcription complex.”

When the team up-regulated or silenced Med25 and then ran microarray tests to identify which sets of genes were expressed, they discovered, said Rana, “Not all HNF4alpha-regulated genes were regulated by Med25. It’s kind of a sub-categorizer — it’s Med25 giving specificity to HNF4alpha to up-regulate a specific subset of genes.”

Although there are no immediate clinical or translational implications of the research, the Med25 revelations are nonetheless significant discoveries to help elucidate cellular mechanisms involved in the all-important drug and lipid metabolic processes. And the impact of the protein may extend beyond just those mechanisms, according to Goldstein. “My guess is that this will have far-reaching implications to other genes, beyond those in just drug metabolism and lipid metabolism,” she said.

Although Rana is leaving NIEHS shortly to assume another postdoctoral position at Yale University, the Med25 line of research in the HMG will continue, as the team seeks to characterize phosphorylation status involved with Med25 and HNF4alpha.

Citation: [Rana R](#), [Surapureddi S](#), [Kam W](#), [Ferguson S](#), [Goldstein JA](#). 2011. Med25 is required for RNA polymerase II recruitment to specific promoters, thus regulating xenobiotic and lipid metabolism in human liver. *Mol Cell Biol* 31(3):466-481.

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

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Surapureddi is a staff scientist with the group. (Photo courtesy of Steve McCaw)



Goldstein is an ISI Highly Cited Author in Pharmacology, a member of the Faculty of 1000, and board certified by the American Board of Toxicology. (Photo courtesy of Steve McCaw)



Intern WayneKid Kam, right, described early findings from the group’s work on Med25 at the 2008 Summers of Discovery poster competition. (Photo courtesy of Steve McCaw)

This month in EHP

By Matt Goad

Engineered nanoparticles are being added to an increasing number of consumer products, but the long-term safety of these materials is still unknown, and pinpointing exactly which products contain them is not always easy. The March issue of [Environmental Health Perspectives \(EHP\)](#) examines this topic in its feature article, “Engineered Nanoparticles in Consumer Products: Understanding a New Ingredient.”

This issue’s second news story, “Alberta’s Oil Sands: Hard Evidence, Missing Data, New Promises,” discusses the conclusions of a new Royal Society of Canada report that analyzed the published science around the environmental and human health impacts of oil-sands development.

In the [podcast](#) for the month, Peter Goering, Ph.D., secretary of the Society of Toxicology (SOT), tells host Ashley Ahearn about the process of selecting the people and events represented in the “Benchmarks of Toxicology” poster developed by EHP, NIEHS, the National Toxicology Program, and the SOT, to commemorate the society’s 50th anniversary.

Among the reviews and research included in this issue of EHP are:

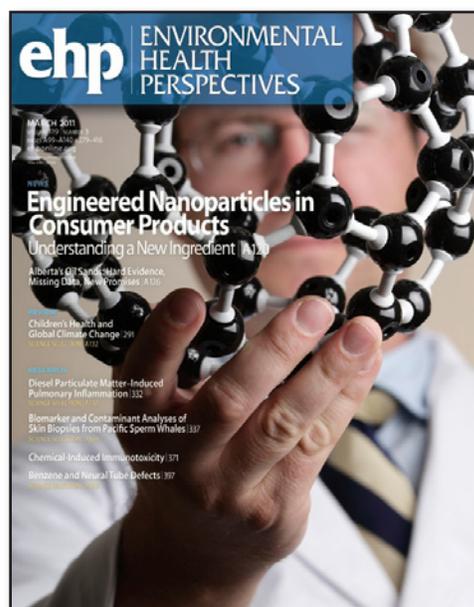
- Children’s Health and Global Climate Change
- Diesel Particulate Matter-Induced Pulmonary Inflammation
- Biomarker and Contaminant Analyses of Skin and Blubber Biopsies from Pacific Sperm Whales
- Chemical-Induced Immunotoxicity
- Benzene and Neural Tube Defects

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

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NIEHS extends deadline for scientific director applications

By Eddy Ball

NIEHS has extended the application deadline for the position of director, Division of Intramural Research ([scientific director](#)), to March 31, 2011. The Institute is seeking exceptional candidates with an M.D., Ph.D., or equivalent terminal degree, as well as demonstrated scientific leadership and extensive scientific accomplishments, to lead the Division of Intramural Research (DIR). The scientific director oversees a staff of approximately 800 employees and an annual budget of around \$110M.



The scientific director is part of the top leadership team at NIEHS, who sets the priorities of the intramural research program and advises the Institute's director on the scientific direction of NIEHS. DIR is organized into four scientific programs, including 12 laboratories and branches conducting laboratory, clinical, and population-based research.

Interested candidates should send a cover letter including a brief description of research and administrative experience, a one-page vision statement for leading DIR, curriculum vitae with bibliography, and full contact information for three to five individuals who may be contacted to provide letters of reference to: Stephanie Jones (DIR-11-01), Office of Human Resources, NIH, PO Box 12233, MD K1-01, Research Triangle Park, NC 27709; or via email to collinsonj@od.nih.gov by March 31, 2011.

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Alternative testing panel to meet in Bethesda

By Warren Casey

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), which is headquartered at NIEHS, is convening an international peer review panel March 29-30 in the Natcher Conference Center on the NIH campus in Bethesda, Md. The panel will evaluate results from an international validation study of an *in vitro* test method using a human cell line to detect endocrine disrupting compounds (EDCs).

The meeting is free and open to the public. Those wishing to attend the meeting should [register online](#) by March 15.

The objective of this validation study, which included laboratories from the U.S., Europe, and Japan, was to assess the accuracy and reliability of the BG1Luc4E2 estrogen receptor transcriptional activation test (BG1Luc ER TA) for the qualitative detection of substances with *in vitro* human estrogen receptor agonist or antagonist activity.

The peer review panel will evaluate data from the NICEATM-led international study, along with draft recommendations developed by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) on the usefulness and limitations of the BG1Luc ER TA test method for identifying potential EDCs.

Federal agencies are developing programs to identify and assess the effects of endocrine disrupting chemicals, in response to concern about the potential health effects of substances that could interfere with normal endocrine function.

The U.S. Environmental Protection Agency, in support of the Food Quality Protection Act and the Safe Drinking Water Act amendments, initiated the Endocrine Disruptor Screening Program (EDSP) program, a three-tiered screening approach to assess the potential of pesticides and environmental contaminants to affect the endocrine systems of humans and wildlife. The BG1Luc ER TA test method may be appropriate to meet the ER TA testing requirement in Tier 1 of this program.

(Warren Casey, Ph.D., is the deputy director of NICEATM.)

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Extramural papers of the month

By *Jerry Phelps*

- [Rapid evolution in Hudson River tomcod](#)
- [Elevated plasma cytokines in children with autism spectrum disorder](#)
- [Glutathione variant linked to lung function growth](#)
- [Interactions of lifetime lead exposure and stress](#)



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

Rapid evolution in Hudson River tomcod

New research findings by NIEHS grantees suggest that Hudson River tomcod have undergone rapid evolution in response to industrial contamination of the river with polychlorinated biphenyls over the last 50 years. Natural selection, the driving process in evolution, usually takes place over thousands of years, but the research team reports that this is the first example in vertebrate animals of such a rapid evolutionary change.

The research team of NIEHS and Superfund Research Program grantees found changes in the gene that codes for the aryl hydrocarbon receptor 2 (AHR2), which is important in mediating toxicity in early life stages. The AHR2 protein in the Hudson River fish is missing two amino acids, which causes a weaker bond between the receptor and PCBs, a necessary step in the metabolism of the compound. The variant is found in about 95 percent of the Hudson River fish and in about 5 percent of tomcod in two smaller streams in Connecticut and on Long Island. The variant can't be found at all in fish further down the Hudson.

Because the Hudson River fish is resistant to the toxic effects of PCBs, they are able to accumulate more of the chemical without becoming sick. However, this evolutionary adaptation is not all good news for the ecosystem. Since the fish can bioaccumulate the compound at higher levels, consumption of them by other fish can lead to transfer of PCBs up the food chain.

Citation: [Wirgin I, Roy NK, Loftus M, Chambers RC, Franks DG, Hahn ME](#). 2011. Mechanistic Basis of Resistance to PCBs in Atlantic Tomcod from the Hudson River. *Science*; doi:10.1126/science.1197296 [Online 17 February 2011].

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Elevated plasma cytokines in children with autism spectrum disorder

New research findings report an altered plasma cytokine profile in children with autism spectrum disorders (ASD) compared to typically developing children. Elevated cytokine levels were directly correlated with impaired communication skills and aberrant behavior, and demonstrate that immune alterations in ASD are associated with the severity of the condition.

ASDs are characterized by impairment in social interactions, communication deficits, and repetitive behaviors. These disorders have been on the rise for the past 25 years, but no definitive cause has been found. Cytokines are small cell-signaling proteins that are secreted by glial cells of the nervous system and numerous cells making up the immune system that modulate immune responses.

The authors report a significant shift in cytokine profiles among children with ASD, which suggests that ongoing inflammatory responses may be linked to behavioral disturbances. These findings need to be confirmed in larger studies, but they do suggest that the characterization of immunological markers may have important implications for diagnosis and therapeutic interventions to treat core symptoms and behavioral impairments associated with ASD.

Citation: [Ashwood P, Krakowiak P, Hertz-Picciotto I, Hansen R, Pessah I, Van de Water J.](#) 2011. Elevated plasma cytokines in autism spectrum disorders provide evidence of immune dysfunction and are associated with impaired behavioral outcome. *Brain Behav Immun* 25(1):40-45.

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Glutathione variant linked to lung function growth

Scientists at the University of Southern California report that variations in one of four genes in the glutathione metabolism pathway is associated with differences in susceptibility to adverse effects of air pollutants on lung function growth. Glutathione is the most abundant intracellular antioxidant. It is an important defense mechanism in the lung in response to oxidative air pollutants and inflammation.

The gene, known as *GSS*, codes for glutathione synthetase. Polymorphisms in this gene and others in the pathway have been shown to be associated with reductions in lung function. Variation in *GSS* was found in 48 percent of the study population of 2,106 children from 12 Southern California cities.

The study results demonstrate that children with *GSS* variation were differentially susceptible to lung function growth deficits associated with air pollutants including nitrogen dioxide, particulate matter, elemental carbon, organic carbon, and ozone. The authors conclude that these findings place added emphasis on the identification of strategies for reducing levels of urban air pollutants for susceptible populations.

Citation: [Breton CV, Salam MT, Vora H, Gauderman WJ, Gilliland FD.](#) 2011. Genetic variation in the glutathione synthesis pathway, air pollution, and children's lung function growth. *Am J Respir Crit Care Med* 183(2):243-248.

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Interactions of lifetime lead exposure and stress

Recent laboratory-based research, by NIEHS-supported investigators at the University of Rochester and the Environmental and Occupational Health Sciences Institute, confirms earlier epidemiologic studies that low-level lead exposure and chronic stress interact to cause behavioral and cognitive deficits.

Female laboratory rats were exposed to lead in their drinking water for two months prior to breeding and throughout gestation. At gestation day 16 and 17, some of the pregnant rats were subjected to a restraint stress procedure consisting of three 45-minute sessions. At weaning, offspring pups were provided with unlimited access to food and given the same drinking water regimen that their dams had received. Subsets of the offspring were used for various laboratory tests and some were subjected to a variety of stressors and behavioral tests, including a fixed interval reward test.

Subject data suggest that lead and prenatal stress effects shift high numbers of test subjects towards the high end of the normal range of fixed interval performance values. These findings were consistent with a dose-response type of lead and stress additivity. The authors conclude that altered fixed interval performance represents behavioral inefficiency and possibly dysfunctional energy use.

Citation: Rossi-George A, Virgolini MB, Weston D, Thiruchelvam M, Cory-Slechta DA. 2011. Interactions of lifetime lead exposure and stress: behavioral, neurochemical and HPA axis effects. *Neurotoxicology* 32(1):83-99.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training.)

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Intramural papers of the month

By Ritu Rana, Matt Goad, and Robin Arnette

- [Uncontrolled neuroinflammation drives progressive neurodegenerative disorders](#)
- [Interleukin-10 protects against ozone-induced lung inflammation](#)
- [Mutations resulting from subtle chemical “trickery”](#)
- [Categorizing heterogeneous myositis syndromes by phenotype](#)

Uncontrolled neuroinflammation drives progressive neurodegenerative disorders

Researchers at NIEHS reported that persistent neuroinflammation caused by uncontrolled activation of brain immune cells known as microglia, leads to the gradual loss of neurons in Parkinson’s disease.

Previous studies had shown that Parkinson’s disease is a progressive neurodegenerative disorder characterized by chronic neuroinflammation and the gradual loss of dopamine neurons. The authors used three different neurotoxins (1-methyl-4-phenylpyridinium, lipopolysaccharide, and rotenone) to mimic Parkinson’s disease

models. They found that though these toxins were sufficient to generate acute neurotoxicity in neuron-enriched cultures, microglia are required for the progressive neurodegeneration.

Mechanistic studies showed that high-mobility group box 1 (HMGB1) protein, released by activated microglia and damaged neurons, interacts with macrophage antigen complex 1 (Mac1) present on microglia and activates the nuclear factor-kappaBeta (NF- κ β) pathway. The activated NF- κ β pathway produces various inflammatory factors contributing to chronic neuroinflammation. HMGB1-Mac1 interaction also activates NADPH oxidase and inducible nitric oxide synthase (iNOS) enzymes releasing many reactive free radicals causing oxidative insult to the neurons.

Researchers further showed that HMGB1 fails to activate NF- κ β and NADPH oxidase signaling pathways in Mac1-deficient microglia, suggesting Mac1 is a potential therapeutic target for the treatment of Parkinson's disease.

Citation: [Gao HM, Zhou H, Zhang F, Wilson BC, Kam W, Hong JS](#). 2011. HMGB1 acts on microglia Mac1 to mediate chronic neuroinflammation that drives progressive neurodegeneration. *J Neurosci* 31(3):1081-1092.

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Interleukin-10 protects against ozone-induced lung inflammation

A collaborative study between NIEHS, the University of North Carolina, and Michigan State University demonstrates the mechanism by which Interleukin-10 (IL-10) protects lung inflammation from ozone (O₃)-exposure. The study identified some potential pathways and their downstream molecular events that are involved in anti-inflammatory effect of IL-10 against ozone toxicity.

Researchers compared wild-type and IL10-deficient mice for their lung inflammatory response against O₃ assault and found that loss of IL10 enhanced O₃-induced inflammation and injury to the lung. Results showed that O₃ exposure increased infiltrating neutrophils and enhanced cellular proliferation in centriacinar regions of the lung in IL-10 null mice as compared to wild-type. Researchers suggested that IL-10 provides lung protection from O₃ by modulating nuclear activity of nuclear factor-kappaBeta (NF- κ β) and expression of inflammatory mediators such as macrophage CD86 and macrophage inflammatory protein 2 (MIP2). Higher activity and expression of inflammatory mediators were observed in IL10-deficient mice upon O₃ exposure.

Furthermore, using microarray and pathway analyses, scientists identified three IL-10 affiliated pathways that are involved in IL10-mediated anti-inflammatory activity. Researchers also found novel genes that may be potentially contributing to O₃-mediated pulmonary inflammation and could serve as potential therapeutic targets against O₃-induced pathogenesis.

Citation: [Backus GS, Howden R, Fostel J, Bauer AK, Cho HY, Marzec J, Peden DB, Kleeberger SR](#). 2010. Protective role of interleukin-10 in ozone-induced pulmonary inflammation. *Environ Health Perspect* 118(12):1721-1727.

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Mutations resulting from subtle chemical “trickery”

Using X-ray crystallography, NIEHS researchers have determined that human DNA polymerase can incorporate a guanine-thymine (G•T) mismatch during DNA synthesis that is structurally similar to the correct adenine-thymine (A•T) base pair. The results, published in a February 2011 issue of PNAS, are the first evidence of DNA bases forming mismatches with correct Watson-Crick geometry, which can potentially lead to mutations. In addition, the typical sources of environmental stress on DNA, such as exposure to UV light or chemical toxins, don't cause these mutations. They happen spontaneously.

James Watson and Francis Crick first proposed the spontaneous base substitution mutation theory in their Nature papers describing the structure of the DNA double helix in 1953. The hypothesis was difficult to test, so evidence supporting it remained elusive for 58 years. Because the authors were able to study DNA at the atomic level, they were able to provide support for the idea.

The investigators assert that understanding how a DNA polymerase generates mutations may not only help scientists discern the cause of disease, but also may improve drug design since DNA polymerases commonly serve as targets of pharmaceutical agents.

Citation: [Bebenek K, Pedersen LC, Kunkel TA](#). 2011. Replication infidelity via a mismatch with Watson-Crick geometry. *Proc Natl Acad Sci U S A* 108(5):1862-1867. [Story](#)

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Categorizing heterogeneous myositis syndromes by phenotype

In a recent issue of JAMA, NIEHS researchers argue for the systematic grouping of idiopathic inflammatory myopathies also known as myositis syndromes.

The research team concluded that understanding and categorizing the many mutually exclusive and stable myositis phenotypes will aid in deciphering the mechanisms by which these conditions arise in humans, and help in interpreting and anticipating care. The authors encourage incorporation of phenotype status into future investigations of pathogenesis and therapy.

Myositis syndromes are systemic autoimmune diseases defined by chronic muscle weakness and inflammation of unknown etiology, and result in significant morbidity and mortality. The most common forms are polymyositis, dermatomyositis, and inclusion body myositis.

Citation: [Rider LG, Miller FW](#). 2011. Deciphering the clinical presentations, pathogenesis, and treatment of the idiopathic inflammatory myopathies. *JAMA* 305(2):183-190. [Story](#)

(Ritu Rana, Ph.D., is a visiting fellow in the NIEHS Laboratory of Toxicology and Pharmacology Human Metabolism Group. Matt Goad is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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Inside the Institute

Revisiting an almost forgotten chapter of local black history

By Matt Goad

As part of the NIEHS Black History Month celebration Feb. 2, employees had an opportunity to take part in a history project about the black experience in Durham, N.C., and found themselves right in the middle of the making of a new documentary.

The NIEHS Diversity Council and the Research Triangle Park (RTP) chapter of Blacks In Government (BIG) sponsored a screening of the documentary in progress about the nearby area of downtown Durham once known as the Hayti community, “Hayti: The Heritage — The Legacy of Black America.”

Hayti was the center of a vibrant black community during most of the 20th century. Black-owned businesses thrived in Hayti until suburban flight and urban renewal efforts in the 1970s killed it off.



The creators of “Hayti: The Heritage – The Legacy of Black America,” right to left, Kelvin D. Allen, Jaisun McMillian, and Beverly Washington Jones, Ph.D., took part in the discussion after screening the film in Rodbell Auditorium. (Photo courtesy of Steve McCaw)

 **Linked video:**
[Watch footage from the Hayti documentary \(08:38\)](#)
(Launches in new window)
Download Media Player:  Flash 

The film comes to NIEHS

Event facilitator and NTP biologist Veronica Godfrey Robinson, chair of the Diversity Council’s Black History Month Committee and secretary of the RTP Chapter of BIG, attended a screening at the [Hayti Heritage Center](#) earlier this year and decided NIEHS employees could benefit from seeing it.

“While Duke has done some positive things in the Durham community,” Robinson said, “there are also other groups making important contributions to the quality of life and culture in that vibrant city.”

The documentary is work in progress, said producers Jaisun McMillian, Victor Stone, and Kelvin Allen, and project historian Beverly Washington Jones, Ph. D., who all attended the NIEHS showing.



Veronica Godfrey Robinson listened to the discussion about Hayti. Seated beside her is Diversity Council chair and NTP chemist Brad Collins. (Photo courtesy of Steve McCaw)

They were here not only to answer questions and give out information, they said, but also to draw on the knowledge of NIEHS employees who remember Hayti and to get advice on how to improve the film.

The producers hope to turn the 20-minute film they have now into a 56-minute documentary with three parts — the past, the present, and the future.

After the screening in the NIEHS Rodbell Auditorium, the producers answered questions and listened to comments from NIEHS employees for about an hour.

“The thing that impressed me the most was the interest that people had in that time period,” McMillian said after the discussion, “and it tells me that our mission is a good one.”

Allen pointed out that the story of “Black Wall Street” in Durham and some of the bigger businesses of Hayti is well known. He wants to tell the story of the underbelly of Hayti — the blue-collar workers and Mom-and-Pop stores.

“That’s a part of the story that we really wanted to tell,” Allen said.

Spirit of community

One theme that came through in both the film and the discussion following was that there was a strong sense of community and cooperation in the old Hayti, something that ironically was lost as desegregation provided for upward mobility for some African-Americans and allowed them to move into the suburbs.

The producers said they hoped this project would help bring back that sense of community.

“When I think about Hayti, I think about a spirit,” Jones said. “I think about a community. And though the demolition came, our role is to rekindle that spirit.”

(Matt Goad is a contract writer in the NIEHS Office of Communications and Public Liaison.)



Michael Watkins, a media and glassware contractor at NIEHS, made a comment during the discussion after the film. (Photo courtesy of Steve McCaw)



John Schelp, special assistant to the director in the Office of Education Outreach, talked about report card day in the community, when children in Hayti were expected to show neighbors their report cards. If they had A's, they got a nickel. That spirit of community has been lost, he said. (Photo courtesy of Steve McCaw)



Acting Associate Director for Management Chris Long, center right, was on hand to show management’s support for the celebration. Seated beside him are Budget Officer Laurie Johnson, left, and media and glassware contractor Bryan Haynes, right. (Photo courtesy of Steve McCaw)



Like many younger Durham residents and transplants in the audience, Contract Specialist Wanda Holliday was interested in learning more about Hayti, which almost completely disappeared when the Durham Freeway joined I40 and I85 — and split Durham in half. (Photo courtesy of Steve McCaw)



RTP Chapter of BIG President and NIEHS Biologist Annette Rice, center, said the documentary was an excellent way to celebrate Black History Month. “The documentary was a historic re-visiting to what Durham was like for African Americans during segregation,” she said. “It was representative of the ways the community worked together on all levels.” (Photo courtesy of Steve McCaw)

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Green leader featured at Black History Month event

By Eddy Ball

In its celebration of Black History Month, NIEHS neighbor, the U.S. Environmental Protection Agency (EPA) hosted a talk by sustainability specialist George Benjamin Brooks, Ph.D., Feb. 15 in the agency’s Research Triangle Park conference center.



Linked video:

[Watch Brooks in action in ‘Grandma was Green’ \(09:22\)](#)

(Launches in new window)

Download Media Player: Flash

The event opened with the Southern High School Dance Company’s lively review of African American dance, from early African to Hip Hop. The audience of nearly 200 included employees from EPA and NIEHS, as well as students from three Durham, N.C. high schools — Southern, Riverside, and Northern.



Members of the Southern High School Dance Company began their review with a traditional African dance. (Photo courtesy of Chuck Gaul, SRA International)

As Brooks quipped in opening remarks, he was charged with presenting a talk that would reinforce this year’s Black History theme — African Americans and the Civil War — as well as inspire a new generation of scientists and engineers while exploring the potential of green technology. “And I’m supposed to do all that in 30 minutes,” he told the audience.

Remarkably, Brooks accomplished his task, and he could hardly have enjoyed a more receptive audience, one that gave him an enthusiastic ovation following his presentation.

Tracing sustainability throughout the African American experience

“You can tell that I’m a preacher’s kid,” Brooks said as he launched his talk with an account of his parents. Brooks father was a Presbyterian minister who started the prototype of the Head Start Program at his Phoenix, Ariz. Southminster Church, and his mother was a virologist and high school science teacher.

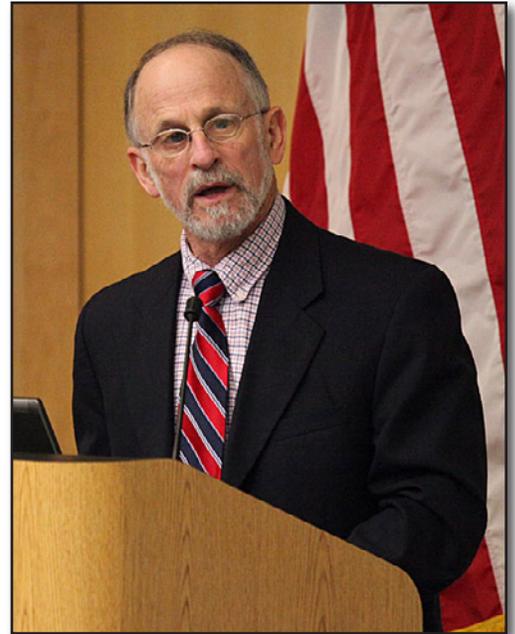
Often speaking with the rhythm of a revivalist minister, Brooks developed themes from his “Grandma was Green” videos and motivational talks to underscore how African Americans faced the experience of slavery and Jim Crow era sharecropping by acting on the wisdom and values of their African ancestors. He pointed to six principles of sustainability that his grandmother and other African Americans used for generations to shape their daily lives and their work:

- Do unto others as you would have them do unto you.
- Begin with the end in mind.
- Make the most of what you’ve got.
- Do no harm.
- Always seek to make things better.
- Make it happen.

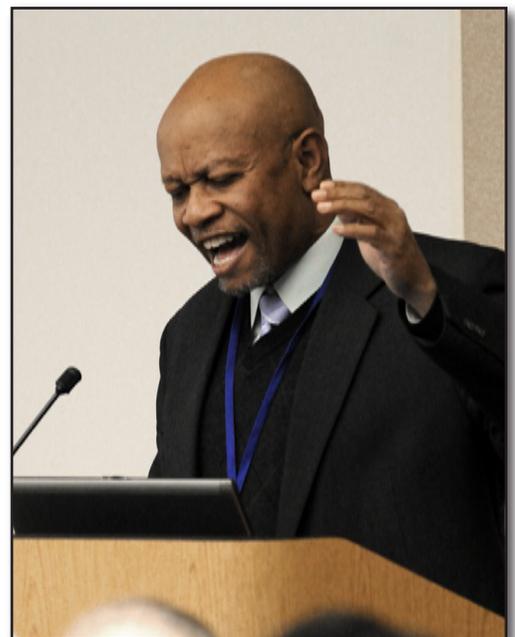
A message for the next generation

In the course of a talk that ranged from slave gardens and the contributions of George Washington Carver to sustainable agriculture, to community renaissance in the South Mountain Village section of Phoenix to leading-edge green science, engineering, technology, and design, Brooks never lost sight of the young people sitting in the first few rows of the auditorium. By the end of the presentation, the high schoolers were his primary focus as he challenged them to make a better world.

“See what the needs are and then figure out a way to do it,” Brooks urged his young listeners. “Learn how to build institutions.”



EPA leader Harold (Hal) Zenick, Ph.D., said that Brooks brings a timely message that parallels EPA’s own green vision. Zenick is the director of the National Health and Environmental Effects Research Laboratory in the Office of Research and Development. (Photo courtesy of Chuck Gaul, SRA International)



Brooks’ oratorical style clearly has its roots in the church his father ministered. (Photo courtesy of Steve McCaw)

He closed with a quote from Harriet Tubman, “Every great dream begins with a dreamer,” and recited a Kenyan proverb. “Treat the earth well. It was not given to you by your parents. It was loaned to you by your children,” he said.

Although he used the word “sustainability” throughout his talk, Brooks said he was still searching for a better term. He said he wants something that denotes the sense of progression and making things better that is inherent in his grandmother’s six principles, while also communicating the important quality of environmental stewardship.



Brooks, center, joined EPA-RTP Black Employment Program Management (BEPM) Champion Frederick Thompson, left, and BEPM Manager Sheila Lee, right. (Photo courtesy of Chuck Gaul, SRA International)



The library at EPA featured a special display of books, photos, and other literature in recognition of Black History Month. (Photo courtesy of Steve McCaw)

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Chinese delegation visits NIEHS

By Matt Goad

NIEHS welcomed a delegation from China to help celebrate the Chinese New Year and foster good will between China and the United States, during a tour and reception held Feb. 16. The delegation was in North Carolina as part of a Chinese acrobatic show performing at Duke University.

As he welcomed the delegation to NIEHS, Deputy Scientific Director William T. Schrader, Ph.D., mentioned that the Year of the Rabbit, which began Feb. 3, is supposed to be a year of international cooperation and friendship.

Schrader noted that of 225 postdoctoral fellows at NIEHS, 27, or about 10 percent, are from China. Many of those fellows attended the reception at the NIEHS cafeteria in the Rall Building.



Leping Li noted that the delegation from China that visited NIEHS in February happened to be in North Carolina during a full moon, which in the Chinese calendar represents a time for family. (Photo courtesy of Steve McCaw)

Environmental Health Perspectives International Program

Manager Hui Hu translated Schrader's talk into Mandarin Chinese for the delegation.

Spirit of cooperation

The leader of the Chinese delegation, Rupei Ma, vice minister of the Overseas Chinese Affairs Office, also spoke of cooperation between the two nations.

"I'm really impressed with the science here," Ma said as members of the delegation along with NIEHS scientists and postdoctoral fellows lined up for a buffet of dumplings, chicken wings, and egg rolls.

"The research they're conducting at the institute is leading environmental health research," Ma continued. "On behalf of the delegation, I would like to wish the best to all the staff of the institute. I'm hoping the research here and the work that is done here can help continually improve human health and eventually bring harmony and peace to the world."

Ma also noted that he was impressed with the high number of Chinese postdocs at NIEHS and hopes they can improve the level of research at NIEHS and cooperation between China and the U.S.

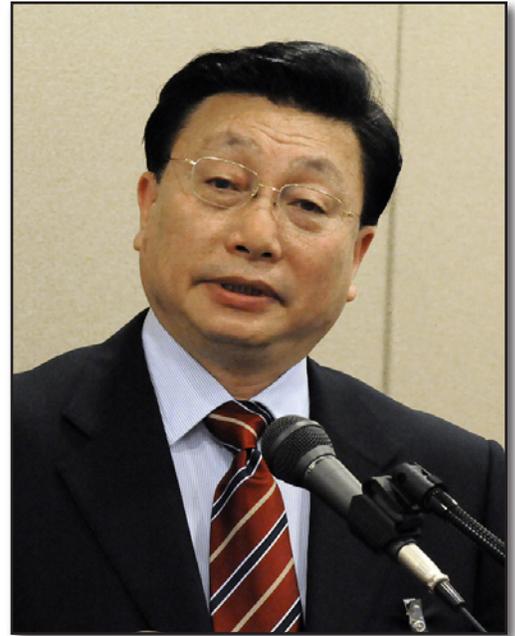
Ma presented Schrader with a gift of a silk painting of a flowering branch that Schrader said would be prominently displayed at NIEHS to commemorate the visit.

Also speaking from NIEHS were [Leping Li, Ph.D.](#), principal investigator with the Biostatistics Branch, who welcomed the delegation, and Hui Hu, who gave the delegation a statistical portrait of the Triangle region of North Carolina.

Xiaofeng Zheng, Ph.D., a Chinese postdoctoral fellow in the NIEHS [Stem Cell Biology Group](#) who attended the reception, said he hoped NIEHS research would be able to help his native country as it experiences a mass migration from the countryside to the city.

"We need more technology to help the Chinese government establish environmentally friendly cities," Zheng said.

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



Ma spoke of a spirit of cooperation between the United States and China that grows as NIEHS scientists from China work with U.S.-born researchers. (Photo courtesy of Steve McCaw)



As she did during a similar visit by a Chinese delegation in 2008, Hui Hu served as translator for the visitors. (Photo courtesy of Steve McCaw)



Chinese journalists interview NIEHS Principal Investigator Honglei Chen, M.D., Ph.D. (Photo courtesy of Steve McCaw)



As the attendees prepared to enjoy refreshments, Ma, center with red tie, joined Schrader and Chinese NIEHS principal investigators. Shown, left to right, are Guang Hu, Ph.D., Schrader; Leping Li, Ma; Chen, and Xiaoling Li, Ph.D. (Photo courtesy of Steve McCaw)



Members of the delegation shared Chinese and American dishes with NIEHS employees. (Photo courtesy of Steve McCaw)

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