



Environmental Factor

Your Online Source for NIEHS News

July 2008

NIEHS Spotlight



Wilson Reports on State of the Institute at May Meeting

On May 29 – 30, the NIEHS National Advisory Environmental Health Sciences Council held its 124th meeting in Rodbell Auditorium.

As the first item on its agenda, the members were presented with an encouraging report ...[read more](#)



Draft BPA Brief Gets Public Comment and Board Review

Less than two months after the eagerly anticipated Draft National Toxicology Program (NTP) Brief on Bisphenol A (BPA) was made publicly

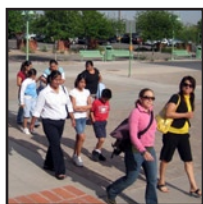
available, the NTP Board of Scientific Counselors (BSC) considered the draft brief as part of its semi-annual ...[read more](#)



NIH Ethicist Tackles “Cutting Edge Consent”

As part of a daylong Institutional Review Board Retreat June 12, NIH ethicist Jerry Menikoff, M.D., J.D., explored the implications of

informed consent during a lecture in Rodbell Auditorium. Menikoff’s talk was titled “Cutting Edge Consent: What Law and Ethics May Require ...[read more](#)

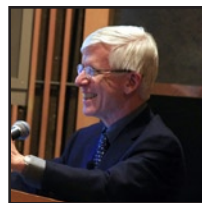


Training Community Health Advocates in South Tucson

Funded in part by the NIEHS Superfund Basic Research Program, the University of Arizona conducted a “Fundamentals of Toxicology” workshop for a group of

community health advocates known as promotoras. A total of 19 female promotoras ...[read more](#)

Science Notebook



Air Pollution Researcher Delivers Distinguished Lecture

The researchers who examine air pollution understand that airborne particles can impact human health.

One of these scientists, Jonathan M. Samet, M.D., presented an overview of the field as part of the NIEHS Distinguished Lecture Series. ...[read more](#)



Research Fellow Reviews Role of Protein Mutations in Mitochondria

On June 11 in Rall Building Conference Room D350, Sherine Chan, Ph.D., presented her research

to the NIEHS Laboratory of Molecular Genetics (LMG) investigators as a part of the LMG Wednesday Seminar Series. ...[read more](#)



Mercury in Compact Fluorescent Lamps Spurs Superfund Research

The Superfund Basic Research Program (SBRP) laboratory of Robert Hurt, Ph.D., director of the

Institute for Molecular and Nanoscale Innovation at Brown University, is studying mercury ...[read more](#)



Nobel Winner Reviews the Greenhouse Effect

One of the pioneers of global warming and greenhouse effect research, F. Sherwood Rowland, Ph.D., spoke on May 22 at the

Research Triangle Park Headquarters as part of the RTI Modern Sciences Seminar Series. ...[read more](#)

NIEHS Spotlight



Cidlowski Honored at ENDO 08

NIEHS Principal Investigator John Cidlowski, Ph.D., was presented with the 2008 Edwin B. Astwood Award at the Endocrine Society's 90th Annual Meeting in San Francisco, June 15 - 18.

Cidlowski is one of eleven distinguished recipients of ENDO 08 Laureate Awards, which the society describes as "the pinnacle of achievement" ...[read more](#)



Library Expands Bioinformatics Support with Fargo Appointment

In late May, the NIEHS Library and Information Services Center added a new resource to its staff with the appointment of former bench scientist

David Fargo, Ph.D., as Bioinformatics Information Specialist. ...[read more](#)



Assistive Technology Aids Federal Employees

"The key words are reasonable and appropriate," explained guest speaker Michael Young during his June 4 presentation in Rodbell Auditorium on

assistive technology and services for federal employees with disabilities. Young's talk, titled "Leading the Way with Accommodations," was sponsored by the NIEHS Diversity Council's Disability Advocacy Committee (DAC). ...[read more](#)

NIH Begins Search for NIEHS Director

NIH is now accepting applications from qualified candidates for the position of director of NIEHS. The closing date for applications is Monday, August 4, 2008. Interested individuals may access the position description and instructions for applications at: <http://www.jobs.nih.gov/vacancies/executive.htm>

Science Notebook



Director's Challenge Study on Breastfeeding and Pulmonary Disease

The June issue of Pediatrics includes the latest findings to emerge from research funded through the NIEHS

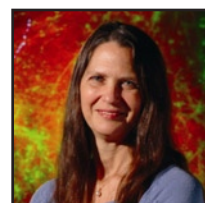
Director's Challenge Program in Integrative Research awarded in October 2006. ...[read more](#)



Long-term Pesticide Exposure May Increase Risk of Diabetes

Licensed pesticide applicators who used chlorinated pesticides on more than 100 days in their lifetime were

at greater risk of diabetes, according to authors of a study published in the May issue ...[read more](#)



Upcoming Distinguished Lecturer Hollis Cline

The 2007 - 2008 NIEHS Distinguished Lecture Series will welcome its next speaker, Hollis T. Cline, Ph.D., at 11:00 a.m. July 8 in

Rodbell Auditorium. ...[read more](#)

Inside the Institute



Homeschoolers Expand Their Understanding of Climate Change

Sometimes, asking is all it takes to open doors. That's what the parents of a team of Triangle-area

homeschoolers found out when they contacted the NIEHS Office of Communications and Public Liaison about a field trip to NIEHS and a workshop on climate change. ...[read more](#)



Summers of Discovery Participants Enjoy Annual Picnic

On June 18, the Summers of Discovery Class of 2008 participants and mentors gathered for the program's traditional

rite of summer at the Annual Picnic on the patio outside the NIEHS Cafeteria. ...[read more](#)



Evergreen Consulting Recognizes Media and Glassware Employees

Just about everyone in the Rall Building at NIEHS has seen the rows of gleaming beakers on display in module D, but

few get to see the hard work that goes on behind closed doors to make sure that labs have the glassware and media they need.[read more](#)



Another Successful Fun-Filled Family Day

Sounds of laughter, popular music from local DJ's and smells of summer grilling on the patio of the NIEHS Rall Building were not the only things

attracting employees and their families to come out for the 3rd Annual Family Day Celebration.[read more](#)

Extramural Research

Extramural Update

Over one hundred parents, families and caregivers of children, along with adolescents and adults with autism spectrum disorders (ASD), took part in a daylong town hall meeting held at the UC Davis Medical Center in Sacramento California on May 3. At the meeting, a diverse range of public opinions were voiced. These comments have been summarized and presented to the Interagency Autism Coordinating Committee (IACC), the federal advisory group charged with coordinating research on autism spectrum disorders (ASD), for consideration during final deliberations for the strategic plan. ...[read more](#)

Extramural Papers of the Month

- [Risks of Coarse Particulate Air Pollution](#)
- [Social Isolation and Possible Implications for Breast Cancer](#)
- [Mapping Gene Expression in the Human Liver](#)
- [Enzyme Variant Identified as a Susceptibility Factor for Heart Failure](#)

Intramural Research

Intramural Papers of the Month

- [Exposure to Pesticides Increases Risk of Diabetes](#)
- [Sox8 Plays an Important Role in Male Fertility](#)
- [The Involvement of DNA Polymerases in Eukaryotic Replication](#)
- [Structures of DNA Polymerase \$\beta\$ Provide the First Glimpse of Pre-Mutagenic DNA Synthesis](#)

Inside the Institute



Discoverers Take Softball Trophy

Retribution was the name of the game as the second annual Friends and Family Softball Tournament concluded Family Day on June 3.

Nearly 80 NIEHS employees and their families came out to support and cheer on their fellow co-workers, as they prepared ...[read more](#)



Friendship the Fish Fry Way

Despite record-breaking heat and a Code Orange ozone-advisory, nearly 100 federal employees gathered under the covered picnic area at the NIEHS ball field on June 5 for the Blacks

In Government (BIG) Annual Fish Fry. Naturally, the perfectly prepared fried flounder, fries, hushpuppies and sides attracted hungry co-workers, ...[read more](#)

Calendar of Upcoming Events

- **June 30 – July 1**, in Rodbell Auditorium, 8:00 – 5:00 — Partnerships for Environmental Public Health Workshop
- **July 2**, in Rodbell Auditorium, 9:00 – 10:30 — Seminar with Nancy Moreno presenting Environmental Health Partnerships to Improve Science Education: Benefits to Research Institutions and Schools Using Real-World Environmental Health Themes in the Classroom
- **July 2**, in Rodbell Auditorium, 11:00 – 12:30 — Summers of Discovery Weekly Seminar: “Inter-alpha-trypsin inhibitor mediates airway hyperreactivity in environmental models of asthma” by Stavros Garantziotis, MD
- **July 8**, in Rodbell Auditorium, 11:00 – 12:00 — Distinguished Lecture Seminar Series featuring Hollis T. Cline, Ph.D., discussing “Mechanisms of Developmental Plasticity in the Visual System”
- **July 9**, in Rodbell Auditorium, 11:00 – 12:30 — Summers of Discovery Weekly Seminar: “Calcium Signaling During Egg Activation” with Carmen Williams, M.D., Ph.D.
- **July 10**, in F193, 1:00 – 2:00 — Laboratory of Structural Biology Seminar Series with Lars Pederson, Ph.D., Topic TBA
- **July 16**, in Rodbell Auditorium, 11:00 – 12:30 — Summers of Discovery Weekly Seminar: “Calcium: Yes, Bones and Teeth, but So Much More” by Jim Putney, Ph.D.
- **July 21 - 22** (Offsite), at the RTP Radisson Hotel, 8:30 – 5:00 — NTP Report on Carcinogens: Expert Panel Meeting Report — Topic: Styrene
- **July 23**, in Rodbell Auditorium, 11:00 – 12:30 — Summers of Discovery Weekly Seminar: Featuring Dale Sandler, Ph.D., discussing “The Sister Study - A Prospective Study of Environmental and Genetic Risk Factors for Breast Cancer in an Enriched Cohort”
- **July 24**, in Rodbell Auditorium, 3:00 – 4:00 — Frontiers in Environmental Sciences Lecture Series featuring Edward “Ted” Emmett, M.D., topic TBA
- **July 30**, in the Rall Building Mall, 9:00 – 12:00 — Summers of Discovery Annual Poster Session
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Wilson Reports on State of the Institute at May Meeting

By Eddy Ball

On May 29 – 30, the NIEHS National Advisory Environmental Health Sciences Council held its 124th meeting in Rodbell Auditorium. As the first item on its agenda, the members were presented with an encouraging report on the progress NIEHS continues to make toward its goal of scientific excellence.

The presentation by NIEHS Acting Director Sam Wilson, M.D., was dominated by the findings of the recent NIH Office of Management Assessment (OMA) review of NIEHS management practices between 2004 and 2007 that was requested by the U. S. House of Representatives Appropriations Subcommittee. Wilson's report outlined the Institute's process and planning for its Corrective Action Plan, which he estimated could be completed and sent to NIH Director Elias Zerhouni, M.D., as early as June.

"We see the OMA report as a positive step in the management of the Institute," Wilson observed. "We can make use of these findings in a very constructive way... to move ahead." When Wilson opened the floor to discussion, member Dan Liebler, Ph.D., asked for "a little more granularity on the discussion of the [findings of the OMA] grants-making subcommittee," which had questioned the Institute's protocol during the review period in regard to what are known as "out-of-rank order" or "raise-to-pay" awards.

According to Wilson, the issue was not the awards themselves, but rather the documentation to justify them. These kinds of decisions, he added, account for only about one percent of all awards at NIEHS. He said these decisions are usually made to encourage new investigators, foster especially innovative research or broaden the Extramural portfolio to meet needs considered important to the NIEHS mission.



Wilson said that NIEHS is proactive in pursuit of its bottom line of "scientific excellence" in all areas of research and has a "future that is stronger than the past."

(Photo courtesy of Steve McCaw)



University of Pittsburgh Department of Pharmacology Chair Bruce Freeman, Ph.D., spoke in support of "out-of-rank" decisions. "We're very glad for our investigators when you reach out and make these special motions of raise-to-pay to support promising research." (Photo courtesy of Steve McCaw)

As Executive Secretary and Acting Director of the Division of Extramural Research and Training Dennis Lang, Ph.D., explained, “The problem we faced was that the justification for those decisions, while done appropriately, were not written down and attached to funding plans that became a part of the final record.”

Lang reinforced Wilson’s commitment to corrective action. “That’s a relatively easy thing to fix,” he said, “and we started doing that a couple of rounds ago, so at the moment I think we are totally in compliance.”

In his review of NIEHS highlights since the last meeting, Wilson lauded the April workshop spearheaded by NIEHS Associate Director Sharon Hrynkow to get NIEHS “to the table during the conversation on climate change, [which is] a key topic in environmental health.” He also recognized the ranking of NIEHS by the Scientist survey of training institutions as one of the best places to work for postdoctoral fellows nationally.

Moving on to the trans-NIH initiative on autism, Wilson described the role of NIEHS in leading a Town Hall Meeting at the University of California Davis in May. The meeting, Wilson explained, was part of the process for development of the NIH Interagency Autism Coordinating Committee (IACC) strategic plan for research. “This Town Hall Meeting was very effective and had the structure that was appropriate for getting input [from the community and research scientists],” he said. “The information will be included in the strategic plan as we move forward” (see [Extramural Update](#)).

In addition, Wilson praised several other important developments:

- Publication of the National Toxicology Program’s Draft Brief on Bisphenol A, which he called “a significant contribution by the NTP in protection of human health”
- The U.S. Japan Cooperative Meeting organized by Associate Director Bill Martin, M.D.
- The Superfund Basic Research Program/Worker Education and Training Program Workshop in April



Other Council members seemed to agree with George Leikauf, Ph.D., who observed after Wilson’s presentation, “I think we’re going in the right direction.” (Photo courtesy of Steve McCaw)



Copeland noted at the beginning of his scientific talk that “mitochondrial medicine is now a [trans-NIH] Roadmap proposal that has just been approved by all NIH directors.” (Photo courtesy of Steve McCaw)



Wilson welcomed two new members to the Council — University of Iowa Civil and Environmental Engineering Professor Gerald Schnoor, Ph.D., above, and U. S. Navy Captain Michael Macinski. (Photo courtesy of Steve McCaw)

· Outstanding research publications, highlighting recent Extramural papers on [polyketide synthase function](#) and [proliferating cell nuclear antigen](#) and Intramural papers on [functional plasticity in hippocampal neurons](#) and [physiological functions of the Krüppel-like zinc finger protein Gli-similar 2](#)

At the request of members, the meeting returned to the two-day schedule format and included more time for discussion than at other recent meetings.



Contractor Kevin Beverly, above, followed the proceedings carefully. Beverly is the executive vice president of Social & Scientific Systems, which supports the Sister Study and the Epidemiology Support Services Contract for the Institute. (Photo courtesy of Steve McCaw)



As this photo of NIEHS Director of Science Policy Joyce Martin, J.D., shows, just because Council meetings are serious business doesn't mean that there's no room for humor.

(Photo courtesy of Steve McCaw)

[Return to Table of Contents](#)

More Time for Discussion... and Science

A more flexible schedule for Council had several benefits for members, not the least of which was an opportunity to hear a talk by [NIEHS Principal Investigator William Copeland, Ph.D.](#) Copeland's talk, "DNA Polymerase λ [Gamma] and Mitochondrial Disease," had been re-scheduled twice. Copeland heads the Mitochondrial DNA Replication Group within the NIEHS Laboratory of Molecular Genetics.

In his introduction of the speaker, Wilson described Copeland's findings as "seminal scientific information that is incredibly exciting."

DNA polymerase gamma ($\text{pol } \lambda$), Copeland explained, functions to replicate mitochondrial DNA, which in turn is responsible for the body's energy production. Defects in mitochondrial DNA (mtDNA) can lead to a long list of diseases that can affect anyone during a lifetime and impact a variety of tissues, especially the heart, brain, liver and kidneys, which are organs that utilize substantial amounts of energy.

Direct mitochondrial diseases affect about 1 in every 2000 births, with about half developing in childhood and the other half presenting in adults, and mitochondrial deficits have a secondary role in many other diseases, such as Parkinson's Alzheimer's, Huntington's and diabetes. About ten percent of autistic children show biomarkers of mitochondrial disease.

Like nuclear DNA, mtDNA is sensitive to mutagens and carcinogens, including some anti-cancer and anti-viral drugs. Because it is the only known DNA polymerase in mammalian mitochondria and a gene frequently found mutated in mitochondrial disease, understanding the role of $\text{pol } \lambda$ dysfunction by mutations in the *POLG* gene may be useful in discovering ways to intervene in mitochondrial disease and other diseases where mitochondrial DNA depletion and mutation play a role.

Copeland explored additional mitochondrial diseases in a [review](#) he published earlier this year in *Annual Review of Medicine*. A report on a [lecture](#) about mtDNA replication by Sherine Chan, Ph.D., a research fellow in Copeland's group, also appears in the Science Notebook section of this issue.

Draft BPA Brief Gets Public Comment and Board Review

By Eddy Ball

Less than two months after the eagerly anticipated [Draft National Toxicology Program \(NTP\) Brief on Bisphenol A \(BPA\)](#) was made publicly available, the NTP Board of Scientific Counselors (BSC) considered the draft brief as part of its semi-annual public meeting on June 11 – 12 at the Research Triangle Park Radisson Hotel. The draft brief represents NTP’s assessment of the risks of BPA exposure for affecting reproduction and development in humans. The draft brief is based on review of an Expert Panel Report issued in August 2007, public comments and new relevant scientific literature.

Chaired by birth defects specialist Gail McCarver, M.D., the meeting gave scientific staff of the NTP Center for the Evaluation of Risks to Human Reproduction (CERHR), who prepared the draft brief, a forum for explaining their conclusions to the BSC. The group also had an opportunity to hear comments on the draft brief from the public as well as receive input from the BSC and several scientists who were designated ad hoc discussants.

The meeting opened with welcome remarks by Acting NIEHS/NTP Director Sam Wilson, M.D., who expressly reinforced “the NTP’s position toward full peer review and toward full public input into the peer review process — and at the same time the commitment toward full transparency. Our aim is to sort through the science and come to the best solution possible based on the scientific information.”

Wilson’s remarks were followed by a review of NTP activities since the BSC’s December 2007 meeting, presented by NTP Associate Director John Bucher, Ph.D. CERHR Director Mike Shelby, Ph.D., then explained the process for preparing the draft brief, presented an overview of the draft brief and explained the NTP’s rationale for reaching its conclusions.

Shelby emphasized several times in his presentation that CERHR reports are assessments of potential effects on human health and should not be confused with regulatory documents. He also articulated the



After presenting his update, Bucher, center, listened intently to the deliberations over the Draft NTP Brief on BPA.

(Photo courtesy of Steve McCaw)



Shelby, center, turned over the program to colleagues following his overview of the draft brief. (Photo courtesy of Steve McCaw)



McCarver kept the meeting moving along, overseeing public comments and focusing BSC deliberation with a series of votes on specific concerns at the end of the day.

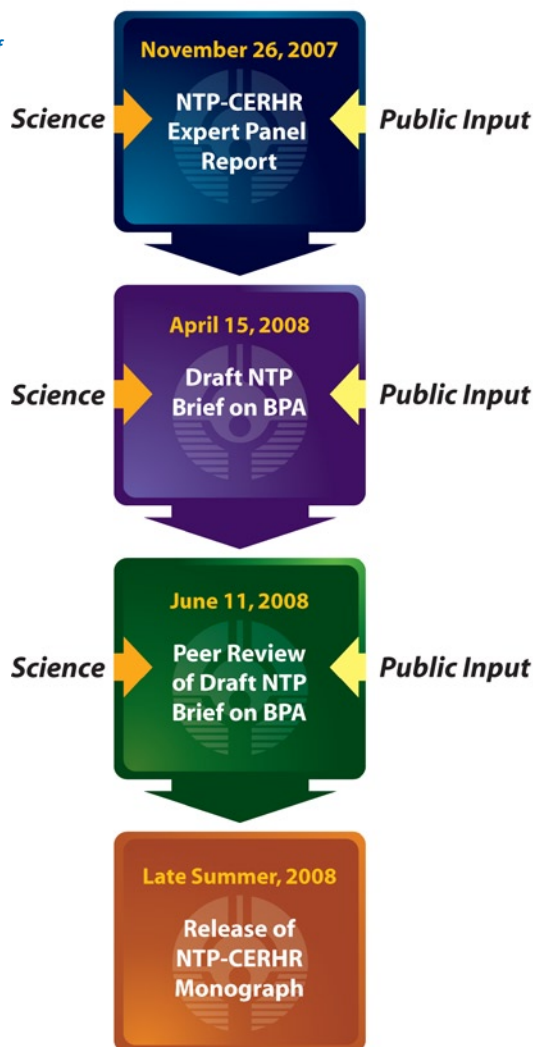
(Photo courtesy of Steve McCaw)

charge to the BSC to evaluate whether the draft is technically correct, clearly stated and supportive of the conclusions. Shelby was followed by Centers of Disease Control and Prevention (CDC) toxicologist Richard Wang, M.D., who presented the [National Health and Nutrition Examination Survey \(NHANES\)](#) study data that support the exposure of more than 90 percent of the population to BPA.

With a few exceptions, the draft conclusions of the NTP were in general agreement with those of the expert panel. The NTP conclusions reflected a higher [level of concern](#) than those expressed by the expert panel for possible effects of BPA on prostate gland, mammary gland and early onset of puberty in exposed fetuses, infants and children. The CERHR staff considered the Expert Panel report and all public comments on the final expert panel report, and reviewed relevant scientific papers that were published subsequent to completion of the expert panel evaluation.

[Click on buttons to view page/pdf](#)

NTP Evaluates BPA



During presentation of the NHANES data on BPA, Wang detailed the strict quality controls on collection and testing that helped to make the data so compelling. (Photo courtesy of Steve McCaw)



CERHR Health Scientist Administrator Kristina Thayer, Ph.D., presented details on the key studies that influenced NTP's conclusions. (Photo courtesy of Steve McCaw)



University of California Berkeley epidemiologist Katherine Hammond, Ph.D., was an active participant in the deliberations and led the BSC discussions of the draft brief. (Photo courtesy of Steve McCaw)

Members of the BSC and ad hoc reviewers engaged in some lively discussion about specific details of the draft brief, but they generally agreed that NTP had done a commendable job of integrating a large amount of sometimes conflicting data into a cohesive draft. The detailed four-hour review was characterized by extensive reference to specific papers on the long list of citations reviewed during preparation of the draft brief. The BSC agreed with most of the conclusions presented in the draft brief, but **recommended** a lower level of concern for possible effects on the mammary gland and puberty in females. Publication of the final NTP Brief on BPA is expected in late summer of this year.

[Return to Table of Contents](#)

NIH Ethicist Tackles "Cutting Edge Consent"

By Eddy Ball

IAs part of a daylong Institutional Review Board Retreat June 12, NIH ethicist Jerry Menikoff, M.D., J.D., explored the implications of informed consent during a lecture in Rodbell Auditorium. Menikoff's talk was titled "Cutting Edge Consent: What Law and Ethics May Require Beyond Current Practice." The event was hosted by David Resnik, Ph.D., J.D., bioethicist in the NIEHS Division of Intramural Research.

[Menikoff](#), who currently serves as the director of the NIH Office of Human Subjects Research, is on leave from his position as a University of Kansas associate professor of Law, Ethics & Medicine in the School of Medicine and associate professor of Law in the School of Law there. He is the author of several books on ethics and the regulation of research with human subjects, including *What the Doctor Didn't Say: The Hidden Truth about Medical Research*.

"It [informed consent] ties into what NIEHS is doing now, particularly in your move toward doing clinical research," Menikoff said as he began his talk. "It is especially applicable to research relating to people who have a clinical problem."

According to Menikoff, participants need to understand that the primary goal of research is to answer a research question. He said patients often enter clinical trials specifically to get treatment they think they could not get otherwise, and they may have unrealistic expectations about the benefits of participating.



Menikoff advocates for expanded disclosure of information to help subjects give truly informed consent.

(Photo courtesy of Steve McCaw)



Matrix Biology Group Principal Investigator Stavros Garantziotis, M.D., center, is the staff clinician at the new NIEHS Clinical Research Center where studies involving human participants are planned. (Photo courtesy of Steve McCaw)

“We have all these rules to protect research subjects,” Menikoff continued, “because research subjects are actually under weaker protections than patients.... Research regulations are designed to make sure that the goal of answering the research question does not inappropriately override the patient’s interest.”

Menikoff maintained that the research community should feel an obligation to give subjects a much more complete and candid explanation about what participating in a study means — and does not mean — for an individual. Invoking the [Nuremberg Code](#) of bioethics, he said that “a person should have ‘sufficient knowledge... to make an understanding and enlightened decision’ about participation.”

For Menikoff, that knowledge includes an understanding of the benefits and risks of participation, as well as appropriate alternatives available elsewhere that could be just as advantageous as anything participants might be able to get in the study. To illustrate his point, Menikoff pointed to the five-year randomized, double-blind Study of Tamoxifen and Raloxifene (STAR), which sought to determine which of the drugs is most effective at preventing breast cancer.

STAR was an example of a situation when getting a “new” therapy, such as Raloxifene, outside the study would in most cases involve no greater risk than getting it in the study, Menikoff explained. By getting a non-standard treatment that is widely available off-label, the patients who wanted the therapy would also have a 100 percent chance of actually getting it, rather than the 50 percent chance they would have in a randomized study.

Menikoff argued that research subjects deserve to be clearly informed of anything about a study that a “reasonable person” would want to know before enrolling.

Using several examples from informed consent forms from clinical studies, Menikoff described how disclosure could improve. “I’m not saying the studies shouldn’t be conducted,” he concluded, “but patients should be told what they need to know.”

[Return to Table of Contents](#)



Because of questions that arose during the discussion of experimental treatments, Resnik, left, and Menikoff were still answering questions from attendees well after the lecture was scheduled to conclude. (Photo courtesy of Steve McCaw)

Training Community Health Advocates in South Tucson

By Denise Moreno Ramírez

Funded in part by the [NIEHS Superfund Basic Research Program](#), the University of Arizona conducted a “Fundamentals of Toxicology” workshop for a group of community health advocates known as promotoras (see text box on page 9). A total of 19 female promotoras and one male promoter ventured to the UA campus for this half-day training session on April 19, 2008.

The program was coordinated by members of the University of Arizona’s (UA) [U.S.-Mexico Binational Center for Environmental Sciences and Toxicology](#) and [Superfund Basic Research Program \(SBRP\)](#) in cooperation with Community Assist of Southern Arizona and Tucson Unified School District. To make the training more accessible for community members, the promotoras were encouraged to bring their children along to the program. Science educational activities were provided by the Flandreau Planetarium Science Center at UA.

UA SBRP Director Jay Gandolfi, Ph.D., and Instituto Tecnológico de Sonora Professor [Mercedes Meza, D.Sc.](#), taught the session while Ms. Rocio Estrella served as the event translator. Most of the participants live in South Tucson, a one square mile city of more than 5,000 residents, mostly Hispanic, which calls itself “the pueblo within a city” and is surrounded entirely by Tucson, Arizona.

The training objective was to increase the promotoras’ level of knowledge in toxicology and epidemiology from both the Mexican and American academic perspective. During the instruction, Gandolfi focused on the fundamentals of toxicology while Meza described epidemiological studies and provided a case study from Sonora’s Yaqui Valley (Valle del Yaqui). Presentations were produced specifically for the promotoras and featured culturally sensitive examples to which they could easily relate. During the training, participants received copies of the presentations and other materials to use as they work in their communities.



While members of the community had to make the physical trek to campus for their training, the curriculum was an effective way of bringing the university to the community and disseminating information that can impact the quality of life in South Tucson.

(Photo courtesy of James Field)



The promotoras and their children enjoyed a breakfast snack as they began their day on campus. While the trainees remained with their instructors, the children went to science activities.

(Photo courtesy of James Field)



Before the training itself began, Meza, center, chatted with participants. (Photo courtesy of James Field)

This training exemplifies the UA's Binational Center and SBRP efforts to decrease the gap between academia and the community. The science generated at UA is being readily translated by the Binational Center and SBRP for citizens — proving to be an effective, empowering tool for communities.

(Since 2005, Denise Moreno Ramírez has served as program coordinator, U.S.-Mexico Binational Center for Environmental Sciences and Toxicology and Superfund Basic Research Program Outreach Core at the University of Arizona.)



Gandolfi, shown in the classroom before the trainees arrived, is UA SBRP director and Binational Center co-director.

(Photo courtesy of James Field)



Estrella, right, is shown with one of the participants. She was on hand to translate for trainees who were not fluent in English.

(Photo courtesy of James Field)

Promotoras — The “Frontline Force” for Health Promotion and Disease Surveillance within Underserved Communities

By Rose Ramos

Promotora, the Spanish word meaning “expert” or “advocate,” is used to describe a lay health advisor within the Latino community. Public health scientists are now appreciating the promotora as a health professional who is perfectly poised to reduce health disparities within underserved Latino communities.

Along the Southwest border of the U.S., the mission of the promotora has been embraced by federal agencies such as the CDC, the NIH, the SBRP and the EPA for community health outreach projects. These projects include increased awareness of the importance of preventive health care, including immunizations and screening for cancer and diabetes. Additionally, promotora-based outreach strategies have included information campaigns regarding environmental exposures to agricultural pesticides and metals, such as lead and arsenic, in abandoned industrial, mining and manufacturing sites.

Promotoras also have served an invaluable role within agricultural migrant communities across the U.S. Recognizing the tremendous barriers to adequate health care among migrant workers and their families, promotoras know that it is their responsibility to equip themselves with knowledge and resources in order to maintain the health of this vulnerable population. Today, the primary objectives of promotoras in the migrant worker communities are to increase prenatal care, reduce the incidence of low birth weight and prevent nutritionally-related disorders among young children.

(Rose Ramos, Ph.D. is NIEHS/NIH Health Disparities fellow working with the NIEHS Metastasis Group.)



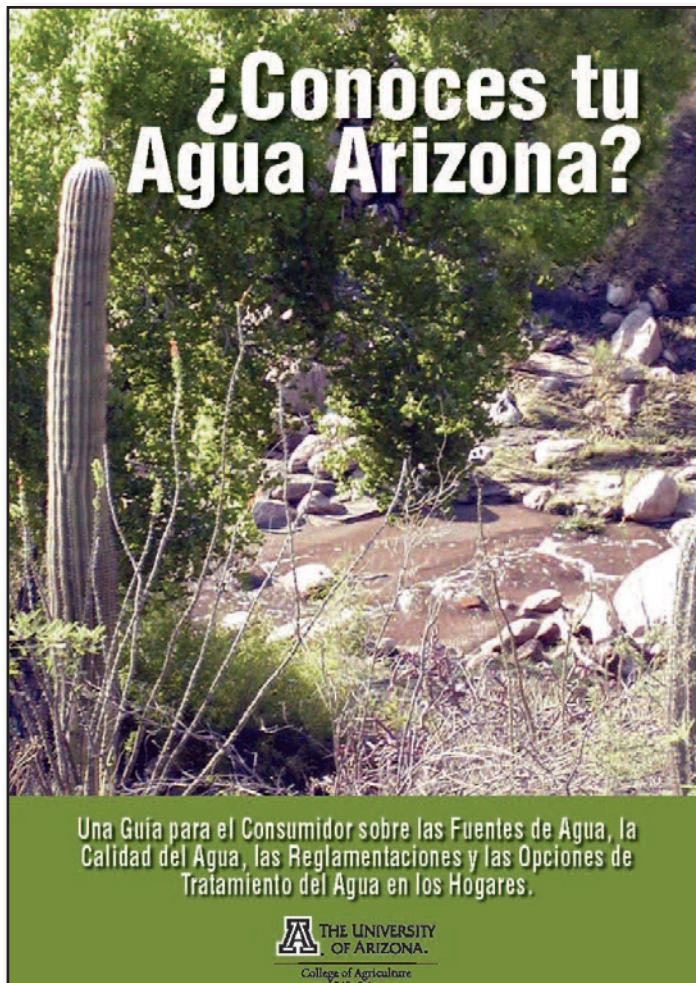
Monica Ramírez, left, and the author, Denise Moreno Ramírez, are shown at an earlier Binational Center event. While trainees learned about likely sources of toxic compounds, their children enjoyed science activities led by the two core coordinators.

(Photo courtesy of James Field)



Mothers escorted the younger children to the classrooms where the science activities were held. (Photo courtesy of James Field)

[Return to Table of Contents](#)



During their training, the promotoras were introduced to the many Spanish-language resources that the program makes available. This booklet, whose title in English means “Arizona: Know Your Water,” is also available as a downloadable [pdf file](#) in English and Spanish.



Although a few children remained behind, once the training began in earnest, most of the promotoras could attend to the instructors because childcare was provided.

(Photo courtesy of the University of Arizona SBRP)

Cidlowski Honored at ENDO 08

By Eddy Ball

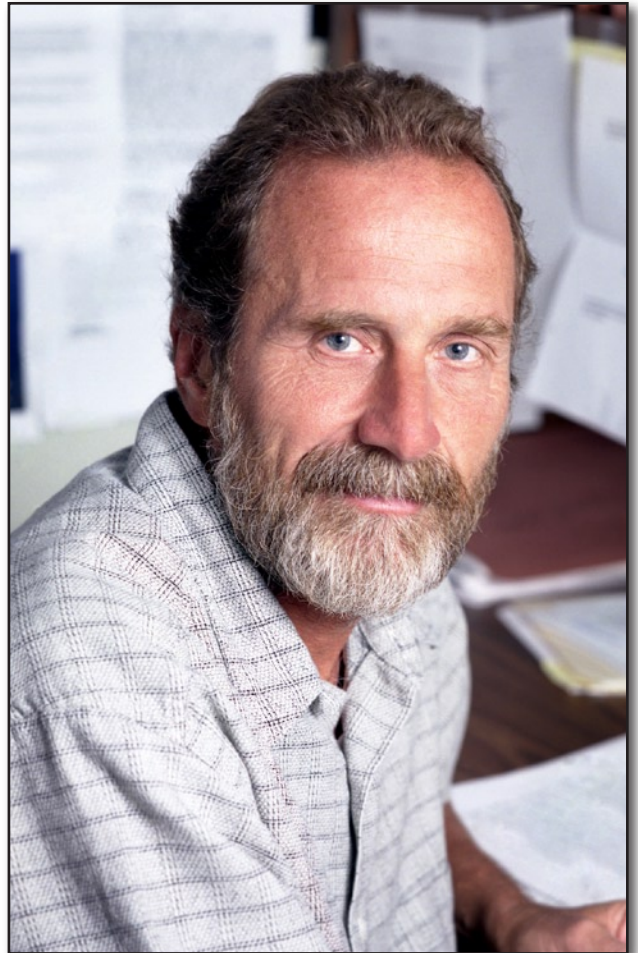
NIEHS Principal Investigator John Cidlowski, Ph.D., was presented with the 2008 Edwin B. Astwood Award at the Endocrine Society's 90th Annual Meeting in San Francisco, June 15 - 18. Cidlowski is one of eleven distinguished recipients of ENDO 08 Laureate Awards, which the society describes as "the pinnacle of achievement in the field of endocrinology."

As part of his award, Cidlowski was invited to present the 2008 Edwin B. Astwood Award Plenary Lecture at the meeting on June 18. He delivered a talk on "The Glucocorticoid Receptor: One Gene, Many Proteins — New Mechanisms for Tissue-Specific Actions of Glucocorticoids."

Cidlowski is the chief of the NIEHS Laboratory of Signal Transduction and head of the [Molecular Endocrinology Group](#). His major research interests are glucocorticoid receptors and their actions on the inflammatory response triggered by environmental stress via steroid hormone action and the regulation of apoptosis in normal and neoplastic cells. He has published more than 250 peer-reviewed articles in leading biomedical journals, as well as several book chapters. Cidlowski served as a professor of Physiology and Biochemistry at the University of North Carolina at Chapel Hill before joining the NIEHS in 1995.

Since 1977, the Endocrine Society has presented the Edwin B. Astwood Award annually to the innovators, educators and practitioners who are transforming endocrinology. Sponsored by Genentech, Inc., the award was established in memory of Tufts University New England Medical Center physician-scientist [Edwin Bennett Astwood, M.D., Ph.D.](#), who died in 1976. Astwood was a physiologist and endocrinologist whose transformative research on the endocrine system is credited with revolutionizing the management of thyroid disease.

[Return to Table of Contents](#)



Edwin B. Astwood Award Winner John Cidlowski
(Photo courtesy of Steve McCaw)

Library Expands Bioinformatics Support with Fargo Appointment

By Eddy Ball

In late May, the NIEHS Library and Information Services Center added a new resource to its staff with the appointment of former bench scientist David Fargo, Ph.D., as Bioinformatics Information Specialist. His appointment is the most recent in a series of developments that have enhanced the library's information services resources for scientists at NIEHS.

According to Director of the Library Dav Robertson, Fargo will help to satisfy a need for bioinformatics support at the NIEHS that was identified in a 2005 assessment of the library. In response to that needs assessment, the library developed its program of "embedded librarians," known formally as informationists, to work more closely with scientists as part of research teams.

Fargo's background includes a doctorate from the Duke University Program in Genetics and Genomics and six years of experience with the University of North Carolina Center for Bioinformatics, serving the UNC system's schools of public health and medicine. In that position, he assessed and disseminated bioinformatics resources statewide to teaching faculty, an effort which involved visiting all 16 campuses to bring together specialists in different disciplines, including the life sciences, statistics, computer science, information technology and mathematics.

During his time at UNC, Fargo also worked in two areas of infrastructure development that should be of special interest to many NIEHS scientists — genome-wide association studies of differential outcomes and next-generation sequencing technologies. Because of experience on the front line of basic research, Fargo said, "I also appreciate what goes on in the laboratory."

As Robertson described the position, it will be evolving as Fargo becomes more familiar with the research going on at NIEHS. "I see this as a consulting role and a collaborative role where he will work very closely with scientists throughout the Institute," Robertson explained, "both those who provide bioinformatics services and those who need those services."

Fargo's services will benefit scientists involved in the increasingly bioinformatics-dependent work in high-throughput screening, toxicogenomics, epigenomics, systems biology and database integration. He will be the NIEHS Library's liaison with the National Library of Medicine and National Center for Biotechnology Information. Additional roles will be bridging the gap between information sciences specialists and research scientists and serving as a resource for information about what bioinformatics tools are available and how well they will work in specific research applications.



Robertson, left, and Fargo look forward to helping investigators take advantage of new and existing resources for managing and analyzing the increasing volumes of data generated by advanced methodologies. (Photo courtesy of Steve McCaw)

“There’s a wide range of needs in the field for making the design of a query better fit the needs of the researcher,” Fargo observed. “Scientists need tools for managing the sea of data [coming from the use of omics methodologies in larger, systems biology type experiments] — to synthesize it, compare it across different experiments and make it usable for life scientists.”

“David has worked with the library at UNC, and he has the service-oriented outlook that is essential to an information service role,” Robertson concluded. “His expertise fills in some gaps in our resources and will complement our team of informationists to enable us to provide a more complete service to the Institute’s scientists.”

[Return to Table of Contents](#)

Assistive Technology Aids Federal Employees

By Shannon Baker

“The key words are reasonable and appropriate,” explained guest speaker Michael Young during his June 4 presentation in Rodbell Auditorium on assistive technology and services for federal employees with disabilities. Young’s talk, titled “Leading the Way with Accommodations,” was sponsored by the NIEHS Diversity Council’s Disability Advocacy Committee (DAC).

Young is manager of the Department of Defense [Computer/Electronic Accommodations Program Technology Evaluation Center \(CAPTEC\)](#). DAC Chair Alicia Moore welcomed the audience, which consisted of both NIEHS and Environmental Protection Agency employees. Young was introduced to by DAC member Luranell (Nell) Burch, Ph.D.

Young immediately grabbed the audience’s attention by asking, “Who has heard of CAPTEC?” With no more than two or three people raising their hands, the response underscored Young’s feeling that CAPTEC is one of the federal government’s best kept secrets.

CAPTEC was established in 1990 to ensure that people with disabilities and wounded service members have equal access to opportunities in the Department of Defense and throughout the federal government. CAP was enacted by the National Defense Authorization Act and currently has partnerships with 65 federal agencies. During the lecture, Young reminded the audience of Section 508 of the Rehabilitation Act — a law that was



Speaker Michael Young reached out toward the audience as he made a point about the cost savings that assistive technology can realize. (Photo courtesy of Steve McCaw)



An audience made up of nearly equal numbers of NIEHS and EPA employees enjoyed the CAPTEC presentation on June 4. (Photo courtesy of Steve McCaw)

enacted to eliminate barriers in information technology and provide disabled employees with electronic and information technology.

Young stressed the need for assistive technology for our country's wounded service men and women and the alliance between CAP and the [North Carolina Assistive Technology Program](#). The program is funded by the state and federal governments to increase access statewide to assistive technology.

An information booth located outside Rodbell A gave attendees an opportunity to see for themselves how some of the assistive technology devices work. Assistive devices available from CAPTEC include new technology to help people with disabilities overcome dexterity, cognitive and communication impairments. CAPTEC provides new technology ranging from modified keyboards to state of the art voice-recognition software.

According to CAP's Disability Profile, 61,448 federal employees have been evaluated and provided with assistive technology since 1990. Young also discussed how disability accommodation aids in employee retention and cuts down on workers compensation costs. He said the average workers compensation claim cost the government \$29,000, while an accommodation averages \$450. CAP supports employees throughout the employment lifecycle to increase recruitment, placement, promotion and retention.

CAP's mission is to provide real solutions for real needs. Young concluded, "We don't want anyone to feel they can't do anything; all they need is the right tools."

"Mr. Young did an outstanding presentation on CAP. Living with a disability in the workplace can be challenging," Moore commented afterwards. "As an employee with a disability, it is helpful for me to know that CAP can provide accommodations and assistive technology that can help me to continue being productive in the workplace. I feel that use of the technology provided by the program would also help to improve my quality of life in the workplace."

The DAC is a standing committee of the NIEHS Diversity Council. Its mission is to improve the employment conditions and quality of life of employees with disabilities, as well as aid visitors to NIEHS facilities. The group sponsors events throughout the year. All employees with or without a disability are welcome to join the DAC. Please contact Alicia Moore (541-7914), JJ Bell-Nichol (316-4519), or Cindy Innes (541-4721) if interested.

For more information about CAP and the agency's programs please visit the website at www.tricare.mil/cap. NIEHS employees who would like more information regarding assistive accommodations should contact EEO Specialists Ginny Ivanoff and Gerard Roman.

(Shannon Baker is a rising senior at Peace College in Raleigh who spent a three-week internship in the NIEHS Office of Communication and Public Liaison. She currently works part time in the NIEHS Office of the Director.)

[Return to Table of Contents](#)



DAC Chair Alicia Moore welcomed Young to NIEHS and presented him with an NIEHS tote bag as a token of the group's appreciation.

(Photo courtesy of Steve McCaw)

Science Notebook

Air Pollution Researcher Delivers Distinguished Lecture

By Robin Arnette

The researchers who examine air pollution understand that airborne particles can impact human health. One of these scientists, Jonathan M. Samet, M.D., presented an overview of the field as part of the NIEHS Distinguished Lecture Series. The seminar was titled “Airborne Particles and Health: What Do We Know in 2008?” and took place in Rodbell Auditorium on June 10. Dale Sandler, Ph.D., chief of the NIEHS Epidemiology Branch and Acting Clinical Director Darryl Zeldin, M.D., senior investigator in the NIEHS Laboratory of Respiratory Biology, co-hosted the event.

Samet is an expert in the areas of health affects of particulate air pollution and ozone, smoking and second-hand smoke, and the epidemiology of lung cancer. He carried out the majority of his work as professor and chairman of the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health, but he recently [accepted](#) the position as director of the University of Southern California (USC) Institute for Global Health and chairman of the Department of Preventive Medicine at the Keck School of Medicine of USC.

Samet prefaced his talk with the comment, “air pollution kills,” and went on to mention several instances when mortality rates increased dramatically as a result of large concentrations of airborne particles within a community. Probably the most studied incident, the London Fog of 1952, occurred because pollution from local factories, diesel buses utilized for public transportation and coal fires used to heat homes became trapped over the city. Thousands of people died during those four days in December and during the following year.

“Children and the elderly preferentially died during this time, but many people who did not fit into that category died too,” Samet said. “From that point we see the rise of air pollution studies, air pollution epidemiology and regulation as a goal for how to prevent such disasters in the rest of the world.”



Samet's talk was interspersed with humorous commentary, including his reference to Gibson's law about scientific discourse. "For every Ph.D.," he quipped, "there is an equal and opposite Ph.D." (Photo courtesy of Steve McCaw)



The Epidemiology Branch was well represented in the audience. Shown here is Visiting Fellow Yang Cao, Ph.D., a member of the Pediatric Epidemiology Group. (Photo courtesy of Steve McCaw)

Samet explained that particulate matter is measured in milligrams per cubic meter (mg/m³) of air, and that particles measuring 2.5 micrometers or less (PM_{2.5}) in aerodynamic diameter are of interest because they are small enough to filter through the respiratory track and reach the alveoli or air spaces in the lungs. A typical room indoors may have 10 mg/m³ of PM_{2.5}, while outside levels may be 25 mg/m³. In cities where the visibility is poor and the air looks gray, the air could contain a hundred times the normal level of particles.

Samet said that Americans spend almost 90 percent of their time indoors, so it seems plausible that the population would be protected from high concentrations of outdoor particulates. However, his research using a typical row house in Baltimore and black carbon as a marker of vehicle exhaust demonstrated that exposure to outdoor pollutants occurs indoors. He said, “We instrumented a row house [with monitoring equipment] during a time when there was a street closure and traffic was higher than usual. Both the indoor and outdoor levels of black carbon were virtually the same. The particles had penetrated the row home.”

Since particle concentration is a major contributor to morbidity, the Environmental Protection Agency (EPA) sets standards and measures the complex mix of particles in the air. Samet and his team have taken this work one step further and have looked for additional factors that determine particle toxicity. His examination suggests other characteristics such as physical configuration, chemistry, surface structure and size are also involved.

In addition to toxicity studies, research by Samet’s group and others has determined a link between air particulates and adverse cardiac function. He is currently working with colleagues at the University of Chicago to study heart failure and asthma models using bioassays.

Samet said that the air pollution research community now agrees that it needs to combine population research with a laboratory approach. “Much of our work has been based upon epidemiological approaches, but we’re starting to do detailed monitoring and use these particles and bioassays to detect differential patterns of responses.”

[Return to Table of Contents](#)



Postdoctoral Fellow Abee Boyles, Ph.D., who works with the Reproductive Epidemiology Group, was also on hand for Samet’s talk. (Photo courtesy of Steve McCaw)



Zeldin fielded several questions from the audience and posed one of his own about the mechanisms of reactive oxygen species triggered by exposure to particulates.

(Photo courtesy of Steve McCaw)

Research Fellow Reviews Role of Protein Mutations in Mitochondria

By Senyene Hunter

On June 11 in Rall Building Conference Room D350, Sherine Chan, Ph.D., presented her research to the NIEHS Laboratory of Molecular Genetics (LMG) investigators as a part of the LMG Wednesday Seminar Series. Chan, who is a Research Fellow in the Mitochondrial DNA Replication Group, spoke on “Proteins at the Mitochondrial DNA Replication Fork.”

Chan’s presentation highlighted the importance of studying mitochondrial DNA (mtDNA) replication in the context of learning more about mitochondrial diseases. “Mutations in genes that encode mtDNA replication proteins cause mitochondrial disease,” explained Chan. “Mitochondrial diseases are associated with defects in the mitochondrial genome or are characterized by any disease that has a large mitochondrial component.”

Chan stressed that as many as 1 in 2000 to 1 in 5000 people — both children and adults — are devastated by mitochondrial myopathies, for which there are currently no cures. Mitochondria are responsible for generating most of the requisite cellular energy. Mitochondrial diseases are characterized by deficits in energy production due to the disruption of oxidative phosphorylation. They include such conditions as progressive external ophthalmoplegia, sensory and ataxic neuropathy, Alpers syndrome, hepatocerebral syndromes and male infertility.

Chan opened her talk by describing work that she has done over the past year in the [Mitochondrial DNA Replication Group](#) headed by Principal Investigator William Copeland, Ph.D. Her presentation focused on three proteins that, along with others, comprise the mitochondrial DNA replication machinery: the catalytic subunit of DNA polymerase gamma (pol γ), its accessory subunit p55 and the mtDNA helicase PEO1. Initial studies by Chan and her colleagues resulted in the biochemical characterization of these proteins. This work greatly advanced the field in the understanding of DNA replication proteins and their involvement in mitochondrial disease.

More than 150 mutations have been found in pol γ that result in mitochondrial disease. The group maintains a [database of all known pol \$\gamma\$ mutations along with their associated clinical phenotypes](#). The genes encoding p55 and PEO1 also have mutations that result in disease states. Chan and other members of the group have expressed and biochemically characterized several of these variant proteins to determine how the mutations affect protein stability and/or function. The aim of the group is to determine the link between the observed protein mutations and the resulting clinical phenotypes.

(Senyene Hunter, Ph.D., is a postdoctoral fellow in the NIEHS DNA Repair and Mitochondrial Damage Group.)

[Return to Table of Contents](#)



Among her accomplishments, NIEHS Research Fellow Sherine Chan was a co-author on a [study](#) linking defects in mtDNA replication to cardiac dysfunction that was selected as an *Intramural Paper of the Month* in June 2007. (Photo courtesy of Steve McCaw)

Mercury in Compact Fluorescent Lamps Spurs Superfund Research

By Melissa Fabiano

The Superfund Basic Research Program (SBRP) laboratory of Robert Hurt, Ph.D., director of the Institute for Molecular and Nanoscale Innovation at Brown University, is studying mercury vapor release from broken and spent compact fluorescent lamps (CFLs). A member of the Hurt Lab at Brown, senior Natalie Johnson, is the lead author on a new study reporting the lab's latest findings, titled "Mercury Vapor Release from Broken Compact Fluorescent Lamps and In Situ Capture by New Nanomaterial Sorbents" (in press, *Environmental Science and Technology*).

The research team found that breakage of a CFL produces mercury vapor concentrations that can exceed the limit of 0.2 microgram per cubic-meter in air for continual habitation by children recommended by the Centers for Disease Control and Prevention (CDC) [Agency for Toxic Substances and Disease Registry](#). The lab also noted that mercury vapor release is greatest at breakage and then decays by the hour. Within a four-day period following breakage, vapor release is greatly reduced but continues at a significant rate.

The study grew out of Johnson's undergraduate award-winning poster displayed in the environmental section of the American Institute of Chemical Engineers' National Meeting in Salt Lake City in November 2007. The poster presented results of an SBRP-funded, independent project titled, "The Characterization and Capture of Mercury Released from Broken Fluorescent Bulbs."

Johnson and colleagues in the [Hurt Lab](#) tested vapor release and capture using nanoscale sorbents, including sulfur, selenium, copper, nickel, zinc, silver, and tungsten disulfide. The adsorption capacities of these elements and compounds varied over a range of more than seven orders of magnitude, from zinc micropowder to unstabilized nano-selenium, depending on sorbent chemistry and particle size.

The research was driven by two important questions in regard to managing mercury in CFLs:

1. What are the implications of direct consumer or worker exposure to mercury vapor from fractured or crushed CFLs?
2. How much mercury is released into the environment at the end of a CFL life?

Johnson and Hurt focused their research on these CFL impacts because of the expected market growth for energy efficient products, and the ways in which CFLs may affect lifestyles following expiration.

The researchers experimented with sorbents of different chemistry and particle size on mercury vapors. They were surprised to find that a few of the common sorbents, such as powdered sulfur or zinc, require enormous amounts of material — greater than 10 kilograms — to treat vapor release for a single CFL, while small quantities of sorbents (for instance, nano-silver and sulfur-impregnated activated carbon forms) have capacities that require less than 1 gram of sorbent to capture the vapor.



Compact fluorescent lamps offer consumers a chance to save on electricity costs. However, the bulbs' mercury content means that it is also important to dispose of them responsibly and to avoid exposure to vapor from broken lamps.

(Photo courtesy of Steve McCaw)

Thus far, Hurt and Johnson have found that when comparing low-temperature mercury vapor sorbents, the most effective is a type of nano-selenium that is capable of capturing CFL vapors at a level of less than 10 milligrams. By using this sorbent, mercury vapor release was reduced by 99 percent compared to an untreated bulb. If a broken CFL was stored in a sealed space with the 10 milligrams of the unstable nano-selenium for 24 hours, nearly complete suppression of mercury vapor could be achieved.

Hurt served as corresponding author on the study. Co-authors from the Hurt Lab included students Shawn Manchester, also a [poster award winner](#), and Love Sarin, along with Senior Research Engineers Indrek Kulaots, Ph.D., and Yuming Gao.

Hurt's lab continues to study methods to improve mercury vapor capture at the time of fracture and vapor release, and vapor stabilization at ambient temperatures by identifying and evaluating high-efficiency sorbents, with a focus on nanosynthesis. With the projected market increase of CFLs, the motivation and support for the development of methods to manage consumer exposure to mercury and its environmental release (upon breakage or disposal) increases with each day, month, and year.

[Return to Table of Contents](#)

Could "Going Green" Give Consumers More Than They Expected?

"Going green" is today's catch-phrase, and American's are becoming aware that even the simplest changes in lifestyle can impact an individual's personal ecological footprint. The number one economically feasible change people can make is investing in compact florescent lamps (CFLs) to replace incandescent light bulbs, but scientists wonder whether CFLs may also harm the environment and how those potential effects could be remediated.

Current studies show that consumers using the newest bulb innovations are reducing their energy use by 75%. These CFLs also pack in more "light" years compared to the incandescent bulbs, increasing the lifetime of bulbs by ten-fold.

Federal legislation calls for phasing out the old-fashioned bulb by 2012. Should this occur, it is essential for researchers to find solutions for effectively disposing of or recycling spent CFLs because of their mercury content. Environmentalists agree that more work must be done on bulb recycling programs. Some retailers will accept expired CFLs, and the [Environmental Protection Agency](#) and [Earth911](#) have sites where consumers can search for other recycling programs near their homes.

Mercury toxicity and lethality is old news; its detrimental effects have been apparent since the 1930s. Today's CFLs underscore mercury's volatile vapor form, which is still a significant health concern — ventilation reduces but does not eliminate this toxicant. Mercury vapor inhalation can cause significant neural damage in developing fetuses and children.

Nobel Winner Reviews the Greenhouse Effect

By Eddy Ball

One of the pioneers of global warming and greenhouse effect research, F. Sherwood Rowland, Ph.D., spoke on May 22 at the Research Triangle Park Headquarters as part of the RTI Modern Sciences Seminar Series. Rowland's talk, "Greenhouse Gases and Climate Change," was sponsored by the RTI Fellow Program and hosted by Senior Fellow R. K. M. Jayanty, Ph.D. Several NIEHS employees were among the audience gathered for the pre-lunch event.

Along with many other honors for his research, Rowland shared the 1995 Nobel Prize in Chemistry with [Paul Crutzen, Ph.D., D.Sc.](#), and [Mario Molina, Ph.D.](#), for their transformative work in atmospheric chemistry. In its [announcement](#) of the prize, the Royal Swedish Academy of Sciences praised the scientists for their "pioneering contributions to explaining how ozone is formed and decomposes through chemical processes in the atmosphere." Their work led to the banning of chlorofluorocarbons (CFC)-based aerosols in 1978.

Rowland began his talk with the events that inspired him to make his 1973 proposal to the U.S. Atomic Energy Commission for funding a predictive study of the atmospheric chemistry of CFC-11, as described in his 1995 [Nobel Lecture](#). "The starting for me in discussing the atmospheric changes that have been discovered in the second part of the 20th century," Rowland said at the beginning of his talk, "was the series of detailed measurements made [of carbon dioxide concentrations between 1958 and 1970]... at two places, Mauna Loa in Hawaii and the South Pole."

These findings set the stage for an accumulation of evidence by Rowland and other scientists that would lead to a [landmark decision in 2007](#) written by Supreme Court Justice John Paul Stevens, reflecting the consensus of scientists about the reality of global warming. "The points [the majority decision made] included the well-documented evidence that the earth is warming, the well-documented evidence that there is a significant increase of carbon dioxide in the atmosphere, and the correlation that respected scientists have found between the two — namely that the carbon dioxide increase is mainly responsible for the temperature increase."



Rowland expressed some hope that legislation and development of alternative energy sources, especially solar, could begin to turn things around. "It is possible for regulation and innovation to do something about what happens in your individual situation."

(Photo courtesy of Steve McCaw)



Lecture host Jayanty, center, also a scientist with research interests in climate change, has known Rowland since Jayanty was a postdoctoral fellow in the early 1970s.

(Photo courtesy of Steve McCaw)

In the years between these two turning points in the discourse about the greenhouse effect, Rowland and his colleagues collected and evaluated some 50,000 air samples at sites throughout the world. The team analyzed concentrations of carbon dioxide and methane, which Rowland described as the “driving gases of greenhouse warming,” as well as a number of other gases, including nitrous oxide and the CFCs, that are affected by human activity and, in their cumulative effects, also contribute to trapping heat in the atmosphere.

Rowland talked in some detail about methane, which has increased significantly due to the activities of humans over the past century from such sources as cattle, rice paddies and landfills. He also observed that the rate at which methane is entering the atmosphere had risen in recent decades. “During the 1980s, what one saw was that there was an increase of about one percent a year of the amount of methane in the atmosphere.”

In addition to analyzing these measurements, according to Rowland, scientists have been able to corroborate the change in the atmosphere by examining trapped air bubbles in glacial core samples from such sites as the Quelccaya Glacier in Peru and the Vostok Glacier in Antarctica. “What you see as you go back in time,” he continued, “is that carbon dioxide and methane levels peak at the same time as temperature.”

Rowland cautioned his audience to avoid putting their faith in “a silver bullet” to stem the rate of global warming. “There may be a dozen things that can be seriously important in trying to control the climate changes that will happen, and it’s worth exploring all of them.”



Because of greater than expected interest in the lecture, RTI decided to move the event from its campus in RTP to a larger venue at the Research Triangle Park Headquarters.

(Photo courtesy of Steve McCaw)

[Return to Table of Contents](#)



NIEHS Director of the Office of Science Policy Joyce Martin, J.D., was drawn to the lecture because climate change is an issue of growing interest to NIEHS policy staff.

(Photo courtesy of Steve McCaw)



Because of its profound economic and health effects, global warming is an interest as well of NIEHS Bioethicist David Resnik, J.D., Ph.D.

(Photo courtesy of Steve McCaw)



NIEHS Superfund Program Administrator Heather Henry, Ph.D., center, listened attentively to Rowland’s account of his 35-year scientific odyssey to develop a body of evidence to convince skeptics that global warming was actually happening.

(Photo courtesy of Steve McCaw)

Director's Challenge Study on Breastfeeding and Pulmonary Disease

By Eddy Ball

The June issue of *Pediatrics* includes the latest findings to emerge from research funded through the NIEHS Director's Challenge Program in Integrative Research awarded in October 2006. NIEHS Laboratory of Respiratory Biology (LRB) Chief Steven Kleeberger, Ph.D., is the principal investigator for the grant, which supports work at NIEHS, the Panamerican INFANT Network at Johns Hopkins University and Fundación INFANT in Buenos Aires, Argentina.

Although some previous research had suggested that gender played a greater role in the protective effect of breastfeeding, the study results were dramatic. Breast-fed females showed a significantly lower (6.5 per cent) rehospitalization rate than males, while formula-fed females experienced a 50 percent rate, pointing to a specific avoidable risk related to gender. For males, breastfeeding made little difference in the rehospitalization rate (18.9 per cent for breast fed versus 18.5 percent for formula-fed).

Johns Hopkins infectious disease specialist Fernando Polack, M.D., was the corresponding author for the *Pediatrics* [study](#), which was led by M. Inés Klein, M.D., an investigator at Fundación INFANT. The research team prospectively analyzed a cohort of 119 preterm infants and young children at high risk for pulmonary disease at two treatment sites in Buenos Aires between 2003 and 2005.

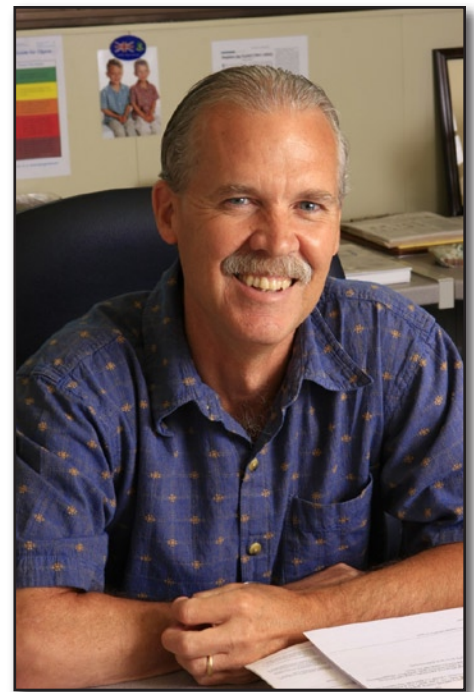
As Polack explained in the paper, the scientists were exploring “the role of gender and breastfeeding on susceptibility to severe acute lung disease among intensively monitored infants at high risk.” The researchers were testing the widely held hypotheses that breastfeeding confers a similar passive protection against serious lung disease to each and every infant, regardless of gender, through transfer from mother to child of immunoglobulin A or of other molecules with specific anti-infective activity.

Writing for the team, Polack identified three important implications of the findings for pediatric research. “They strongly suggest that breast milk protection against acute respiratory infections is not universally conferred by passive transfer of humoral immunity” but in a gender-specific manner instead. They also point to the possibility that a nonspecific modulatory molecule may be involved in protecting infants from several different agents involved in respiratory disease, suggesting a breast milk-mediated critical pathway in the breast-fed girls.

Finally, the findings pinpoint a subset of infants at especially high risk of hospitalization and the strikingly different effects of breast feeding on boys and girls. Although the formula-fed girls represented only 17 percent of infants in the study, they accounted for 48 percent of all hospitalizations during the first episode of acute respiratory disease.

Identifying this especially high-risk group could have an important public health application in prevention and impact infant morbidity in developing countries, where treatment resources can be limited and where hospitalization rates for very low birth-weight infants can be higher than 25 percent during the first year of life.

Now in the second year of a five-year grant, the Director's Challenge Project involves an interdisciplinary approach to understanding respiratory diseases such as bronchopulmonary dysplasia (BPD) among premature infants and the role of specific genes that increase susceptibility to oxidant-induced inflammatory diseases affecting several of the body's systems.



Director's Challenge Grant Principal Investigator Steve Kleeberger

(Photo courtesy of Steve McCaw)

Long-term Pesticide Exposure May Increase Risk of Diabetes

By Robin Mackar

Licensed pesticide applicators who used chlorinated pesticides on more than 100 days in their lifetime were at greater risk of diabetes, according to authors of a [study](#) published in the May issue of the *American Journal of Epidemiology*. The association between specific pesticides and incident diabetes ranged from a 20 percent to a 200 percent increase in risk, said scientists with the NIEHS and National Cancer Institute (NCI).

“The results suggest that pesticides may be a contributing factor for diabetes along with known risk factors such as obesity, lack of exercise and having a family history of diabetes,” said [Dale Sandler, Ph.D.](#), chief of the Epidemiology Branch at the NIEHS and corresponding author on the paper. “Although the amount of diabetes explained by pesticides is small, these new findings may extend beyond the pesticide applicators in the study,” Sandler added.

Some of the pesticides used by these workers are used by the general population, though the strength and formulation may vary. Other insecticides in this study are no longer available on the market. However, these chemicals persist in the environment and measurable levels may still be detectable in the general population and in food products.

Overall, pesticide applicators in the highest category of lifetime days of use of any pesticide had a small increase in risk for diabetes (17 percent) compared with those in the lowest pesticide use category (0-64 lifetime days). New cases of diabetes were reported by 3.4 percent of those in the lowest pesticide use category compared with 4.6 percent of those in the highest category.

Risks were greater when users of specific pesticides were compared with applicators who never applied that chemical. For example, the strongest relationship was found for a chemical called trichlorfon, with an 85 percent increase in risk for frequent and infrequent users and nearly a 250 percent increase for those who used it more than 10 times.

“This is one of the largest studies looking at the potential effects of pesticides on diabetes incidence in adults,” said epidemiologist [Freya Kamel, Ph.D.](#), a researcher in the intramural program at NIEHS and co-author on the paper. “It clearly shows that cumulative lifetime exposure is important and not just recent exposure,” said Kamel. Previous cross-sectional studies have used serum samples to show an association between diabetes and some pesticides.



Lead author Martha Montgomery is a post-baccalaureate fellow in the NIEHS Epidemiology Branch. She won a top prize in poster session competition at the [Eighth Annual Women's Health Research Day](#).

(Photo courtesy of Steve McCaw)



Sandler is the principal investigator for the Agricultural Health Study. (Photo courtesy of Steve McCaw)Health Study Data. (Photo courtesy of Steve McCaw)

The researchers analyzed data from more than 30,000 licensed pesticide applicators participating in the [Agricultural Health Study](#), a prospective study following the health history of thousands of pesticide applicators and their spouses in North Carolina and Iowa. The 31,787 applicators in this study included those who completed an enrollment survey about lifetime exposure levels, were free of diabetes at enrollment, and updated their medical records during a five-year follow-up phone interview. Among these, 1,171 reported a diagnosis of diabetes in the follow-up interview. The majority of the study participants were non-Hispanic white men.

Researchers compared the pesticide use and other potential risk factors reported by the 1,171 applicators that developed diabetes since enrolling in the study to those who did not develop diabetes. Among the 50 different pesticides the researchers looked at, they found seven specific pesticides — aldrin, chlordane, heptachlor, dichlorvos, trichlorfon, alachlor and cyanazine — that increased the likelihood of diabetes among study participants who had ever been exposed to any of these pesticides, and an even greater risk as cumulative days of lifetime exposure increased.

“The fact that all seven of these pesticides are chlorinated provides us with an important clue for further research,” said Kamel. Previous studies found that organochlorine insecticides such as chlordane were associated with diabetes or insulin levels. The new study shows that other types of chlorinated pesticides, including some organophosphate insecticides and herbicides, are also associated with diabetes. The researchers also found that study participants who reported mixing herbicides in the military had increased odds of diabetes compared to non-military participants.

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

[Return to Table of Contents](#)



Kamel, above, is Montgomery's supervisor at NIEHS. She, Sandler and Montgomery collaborated on a 2007 study of pesticide use and age-related macular degeneration using Agricultural Health Study Data.

(Photo courtesy of Steve McCaw)

Upcoming Distinguished Lecturer Hollis Cline

By Eddy Ball

The 2007 – 2008 NIEHS Distinguished Lecture Series will welcome its next speaker, Hollis T. Cline, Ph.D., at 11:00 a.m. July 8 in Rodbell Auditorium. Cline will speak on “Mechanisms of Developmental Plasticity in the Visual System.” The lecture will be hosted by [Serena Dudek, Ph.D.](#), principal investigator and head of the NIEHS Synaptic and Developmental Plasticity Group.

[Cline](#) is a professor and Director of Research at Cold Spring Harbor Laboratory in Cold Spring Harbor, N. Y. Cline received a 2005 [NIH Director’s Pioneer Award](#) to launch a large-scale project to understand the architecture, development and plasticity of brain circuits. She serves as co-chair of the Board of Scientific Counselors of the National Institute of Neurological Disorders and Stroke and is a Council member of the Society for Neuroscience.

Her talk will explore the activity-dependent regulation of dendritic arbor structure and synaptic function in the context of the development of functional neuronal circuits. She will present an overview of visual system development and plasticity from studies of mammalian and non-mammalian vertebrate systems before moving into a discussion of the mechanisms her group has discovered in studies of the *Xenopus* visual system using in vivo imaging, electrophysiology and genetic manipulations.

[Return to Table of Contents](#)



Distinguished Lecturer Hollis Cline

(Photo courtesy of Steve McCaw)

Extramural Update

Autism Town Hall Meeting Report to Be Available Online

Over one hundred parents, families and caregivers of children, along with adolescents and adults with autism spectrum disorders (ASD), took part in a daylong town hall meeting held at the UC Davis Medical Center in Sacramento California on May 3. At the meeting, a diverse range of public opinions were voiced. These comments have been summarized and presented to the Interagency Autism Coordinating Committee (IACC), the federal advisory group charged with coordinating



Participants and their families enjoyed themselves at the UC Davis M.I.N.D. Institute annual holiday party.

(Photo courtesy of Brian Jacobson/Center for Children’s Environmental Health)

research on autism spectrum disorders (ASD), for consideration during final deliberations for the strategic plan. A final version of the meeting report will be made available on the [IACC website](#).

The NIEHS organized this meeting on behalf of the IACC. Investigators and staff from the Center for Children's Environmental Health and Disease Prevention at UC-Davis, a joint program funded by the NIEHS and the US Environmental Protection Agency, galvanized local support from autism researchers and community groups to help ensure a productive meeting. The overall goal of the meeting was to provide an opportunity for additional public input on research priorities for the IACC strategic plan for autism research.

The Town Hall meeting focused on one aspect of the Strategic Plan, treatment research, as this area had dominated public responses to the IACC's previous requests for input. The meeting consisted of two panel discussions, with opportunity for public comment and dialog after each panel. The panels were comprised of treatment researchers, clinicians and service providers and public advocacy representatives.

The morning panel was designed to stimulate discussion about the range of traditional and complementary/alternative approaches that are being used by parents and clinicians to treat children with ASD. Many of these have not been studied in controlled clinical trials and meeting participants were asked for input to help prioritize treatment research to address issues of efficacy and safety. The afternoon session explored interventions for older children and adults with ASD. To date, autism treatment research has been focused primarily on young children, with little attention directed at treatment/interventions for older children, adolescents and adults with ASD. Meeting organizers solicited community views about treatments and intervention across the lifespan to help develop appropriate research questions for this underserved population.

For more information contact [Cindy Lawler, Ph.D.](#)

[Return to Table of Contents](#)

Extramural Papers of the Month

By Jerry Phelps

Risks of Coarse Particulate Air Pollution

A nationwide study of coarse particulate air pollution, defined as 2.5-10 microns in diameter, found some evidence of an association with hospital admissions for cardiovascular disease and no evidence of an association for respiratory disease. Researchers at Johns Hopkins University, supported by NIEHS, conducted the study, the largest on record, for both public health and regulatory purposes.

The study examined associations between daily changes in hospital admission rates for cardiovascular and respiratory outcomes and daily changes in coarse and fine particulate matter concentrations in ambient air in 108 urban counties across the U.S. The study included over 12 million people enrolled in Medicare from 1999-2005.

The Environmental Protection Agency (EPA) regulates the level of fine particulate matter pollution, defined as particles less than 2.5 microns in diameter, but does not currently regulate coarse particulates. Fine particles are generally the result of combustion from automobiles and coal burning power plants. Coarse particles are produced by processes such as mechanical grinding, windblown dust and agricultural practices.

Previous investigation into fine particulate matter pollution by this research team demonstrated a strong link to hospitalization for cardiovascular and respiratory illnesses. According to the researchers, the coarse particle association found in the current study warrants the attention of EPA regulators when the agency readdresses its standard for particles in the air.

Citation: Peng RD, Chang HH, Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. 2008. Coarse particulate matter air pollution and hospital admissions for cardiovascular and respiratory diseases among Medicare patients. JAMA 299(18):2172-9.

[Return to Table of Contents](#)

Social Isolation and Possible Implications for Breast Cancer

NIEHS-supported scientists report that social isolation early in life in laboratory rats is linked to a higher incidence of mammary tumors in mid-life. Their research focused on assessing the effects of isolation on patterns of ovarian development.

Four-week-old rats were housed either in groups of five or in single cages. The isolated rats developed regular ovarian cycles more quickly than the group-housed rats; however, their cycles were shorter than the cycles of the group-housed rats. These differences resulted in more periovulatory surges of estrogen for the isolated rats and a “higher ratio of estrogenized to nonestrogenized days between 60 and 75 days of age when mammary tissue is receptor positive,” even though their mammary development was delayed.

These results suggest that social isolation disassociates two components of puberty by accelerating the maturation of the ovaries while delaying mammary tissue development. At 15 months of age, 100 percent of the isolated animals had tumors as compared to only 33 percent of the group-housed animals.

The researchers suggest that their findings relate to the growing literature on the adverse health outcomes related to girls reaching puberty and experiencing breast development earlier in life than previous generations, possibly leading to an increased risk of certain forms of breast cancer later in life.

Citation: Hermes GL, McClintock MK. 2008. Isolation and the timing of mammary gland development, gonadarche, and ovarian senescence: implications for mammary tumor burden. Dev Psychobiol 50(4):353-360.

[Return to Table of Contents](#)

Mapping Gene Expression in the Human Liver

A large multi-investigator research project to map gene expression in the human liver has yielded more than 6,000 associations between single nucleotide polymorphisms and liver gene expression traits. Many of the identified genes have already been associated with human diseases. Results from this genome wide association study also identified new candidate genes for type 1 diabetes, coronary artery disease and the so-called “bad” cholesterol, or low-density lipoprotein cholesterol.

Genome-wide association study, also known as a GWAS, is a laboratory approach involving the rapid scanning of markers across complete genomes of many people to find genetic variations associated with

particular diseases. Once new genetic associations are identified, researchers can use the information to develop better strategies to detect, treat and prevent the disease.

Four hundred individual human liver samples were used in this study. The researchers profiled more than 39,000 gene transcripts and genotyped 782,476 unique single nucleotide polymorphisms. GWAS reporting associations to disease traits often lack supporting data on the roles candidate susceptibility genes play in disease development. However the NIEHS-backed study provides direct evidence of how integrating genotypic and expression data in mice and humans provides functional support for candidate susceptibility genes.

Citation: Schadt EE, Molony C, Chudin E, Hao K, Yang X, Lum PY, Kasarskis A, Zhang B, Wang S, Suver C, Zhu J, Millstein J, Sieberts S, Lamb J, GuhaThakurta D, Derry J, Storey JD, Avila-Campillo I, Kruger MJ, Johnson JM, Rohl CA, van Nas A, Mehrabian M, Drake TA, Lusis AJ, Smith RC, Guengerich FP, Strom SC, Schuetz E, Rushmore TH, Ulrich R. 2008. Mapping the genetic architecture of gene expression in human liver. *PLoS Biol* 6(5):e107.

[Return to Table of Contents](#)

Enzyme Variant Identified as a Susceptibility Factor for Heart Failure

Researchers from Germany and the U.S. have identified variations in a gene that contributes to heart failure in people with hypertension. The gene, *Ephx2*, codes for the enzyme soluble epoxide hydrolase, which normally degrades specific epoxides.

The third most common cause of death in Western countries, heart failure commonly results from coronary disease and hypertension. It usually develops over a long period of time and is therefore commonly seen in older individuals. When the heart is no longer able to pump enough blood to meet the body's requirements, the heart muscle enlarges in an effort to compensate. Often the heart does not overcome the increased burden and becomes weakened further, especially in cases of pre-existing hypertension.

Using two strains of laboratory rats, one susceptible to hypertension and stroke and the other susceptible to hypertension and heart failure, the researchers observed that the heart failure rats possessed a single nucleotide polymorphism in the *Ephx2* gene that is not present in the stroke prone rats. They conclude that the role of *Ephx2* in the initial stages of heart disease in laboratory animals and humans suggests "a potential avenue for developing new heart failure treatments."

Citation: Monti J, Fischer J, Paskas S, Heinig M, Schulz H, Gösele C, Heuser A, Fischer R, Schmidt C, Schirdewan A, Gross V, Hummel O, Maatz H, Patone G, Saar K, Vingron M, Weldon SM, Lindpaintner K, Hammock BD, Rohde K, Dietz R, Cook SA, Schunck WH, Luft FC, Hubner N. 2008. Soluble epoxide hydrolase is a susceptibility factor for heart failure in a rat model of human disease. *Nat Genet* 40(5):529-537.

(Jerry Phelps is a program analyst in the Program Analysis Branch of the NIEHS Division of Extramural Research and Training. Each month, he contributes summaries of extramural papers to the *Environmental Factor*.)

[Return to Table of Contents](#)

Intramural Papers of the Month

By Robin Arnette

Exposure to Pesticides Increases Risk of Diabetes

Exposure to certain pesticides increased the risk of diabetes in licensed applicators, according to researchers from NIEHS and the National Cancer Institute. The investigation of 33,457 applicators enrolled in the Agricultural Health Study (AHS) is the largest study to date to evaluate potential effects of pesticides on diabetes incidence in adults.

Because previous cross-sectional studies using data from the National Health and Nutrition Examination Survey (NHANES) found associations of diabetes with serum levels of persistent organic pollutants, the researchers wanted to know if there was a similar association between diabetes and lifetime exposure to pesticides. Therefore, they evaluated applicators who reported diabetes for the first time in five-year follow-up telephone interviews, conducted between 1999 and 2003. Previously, at enrollment in 1993 to 1997, applicators had described use of 50 different pesticides, providing information on two primary measures: ever use and cumulative lifetime days of use.

Of 50 pesticides evaluated, seven were associated with an increased incidence of diabetes using both exposure measures. Three of these were organochlorine insecticides (aldrin, chlordane, heptachlor), two were organophosphate insecticides (trichlorfon, dichlorvos), and two were herbicides (alachlor, cyanazine). The strongest association was with trichlorfon: applicators that had used the chemical on more than 10 days in their lifetime had a 2.5-fold increase in risk.

Citation: [Montgomery MP, Kamel F, Saldana TM, Alavanja MC, Sandler DP. 2008. Incident diabetes and pesticide exposure among licensed pesticide applicators: Agricultural Health Study, 1993–2003. *Am J Epidemiol* 167\(10\):1235-1246.](#)

[Return to Table of Contents](#)

Sox8 Plays an Important Role in Male Fertility

Although the transcription factor SOX8 isn't needed during testis development, it is necessary for the maintenance of adult male fertility. The finding came from a collaborative team made up of scientists from NIEHS, the Monash Institute of Medical Research, ARC Centre of Excellence in Biotechnology and Development, the University of Queensland and Merck Research Laboratories. This study provides a framework to determine if SOX8 mutations are involved in the low sperm counts seen in men.

The team generated a strain of *Sox8* knockout mice (*Sox8*^{-/-}) and compared them to heterozygous (*Sox8*^{-/+}) and wild-type control male mice (*Sox8*^{+/+}). Sperm motility was measured at two and five months, while total body weight and testicular weight were measured at two, five and nine months. Testicular tissue was subjected to immunohistochemical staining using Espin and Vinculin, two proteins involved in cell adhesion.

The data demonstrated that loss of SOX8 disturbed the interaction between Sertoli cells and the developing germ cells. This action led to the progressive degeneration of the seminiferous epithelium and decreased activity beyond the first wave of spermatogenesis.

Citation: O'Bryan MK, Takada S, Kennedy CL, Scott G, Harada S, Ray MK, Dai Q, Wilhelm D, de Kretser DM, Eddy EM, Koopman P, Mishina Y. 2008. *Sox8* is a critical regulator of adult Sertoli cell function and male fertility. *Dev Biol* 316(2):359-370.

[Return to Table of Contents](#)

The Involvement of DNA Polymerases in Eukaryotic Replication

For several decades, researchers weren't sure which DNA polymerase copied the leading and lagging strand templates during eukaryotic chromosomal replication. Using the replication fork in *Saccharomyces cerevisiae*, scientists from NIEHS and Washington University School of Medicine have clarified this question by determining that under normal conditions, DNA polymerase δ (Pol δ) copies the lagging strand while DNA polymerase ϵ (Pol ϵ) copies the leading strand. The results suggest a nearly equal strand-specific division of labor between the two polymerases.

The team used a mutant Pol δ allele (L612M) in a yeast genetic system. This mutant was chosen because its error rate is higher for one mismatch, for example T•dGTP, than for its complement A•dCTP, enabling the researchers to assign mutations generated by L612M Pol δ to either the leading or lagging strand. L612M Pol δ mutagenesis was dependent on the orientation of a reporter gene relative to an adjacent replication origin, indicating strand specificity. The identity of the preferentially targeted strand was revealed using the biased error rates of L612M Pol δ . The results imply that greater than 90 percent of L612M Pol δ synthesis was performed using the lagging strand as a template rather than the leading strand.

The researchers also investigated mismatch repair efficiency and intend to further this work by determining if the division of labor varies under different cellular conditions, such as after the replication fork stalls or is blocked.

Citation: Nick McElhinny SA, Gordenin DA, Stith CM, Burgers PM, Kunkel TA. 2008. Division of labor at the eukaryotic replication fork. *Mol Cell* 30(2):137-144.

[Return to Table of Contents](#)

Structures of DNA Polymerase β Provide the First Glimpse of Pre-Mutagenic DNA Synthesis

DNA polymerases read the nucleotide sequence of a “template” strand of DNA as they synthesize a new complementary strand of DNA-obeying Watson-Crick base pairing rules. The synthesis process is highly accurate, but occasionally a polymerase will make an error and insert an incorrect nucleotide into the new DNA strand. This action can lead to an alteration in the genetic material termed a “mutation.” Some mutations are known to be very important in human disease and in conditions such as aging, but insight on how mutations occur during DNA synthesis has remained a mystery.

Researchers at NIEHS used crystallographic structures of DNA polymerase β (Pol β) with right (matched) and wrong (mismatched) nucleotide substrates to gain insight on how mutations are averted during the enzymatic process of DNA synthesis. The team created G-A and C-A mismatches in the Pol β active site by employing a stable nucleotide analog, dAMPCPP, which could bind to the polymerase but not be inserted. Additionally, it was necessary to substitute manganese for magnesium, a divalent metal necessary for DNA synthesis. Kinetic assays revealed that manganese could substitute for magnesium, and increased the binding affinity for the wrong nucleotide to form the pre-requisite ternary complex (Pol β /DNA/nucleotide) crystal.

Surprisingly, the structures revealed that both types of substrates (matched and mismatched) produced the same polymerase conformation. However, the mismatched substrate induced a shift in the template strand that produced an abasic site-like pre-synthesis intermediate. The structures are consistent with mutagenesis studies and provide a strategy to avert misinsertion of the wrong nucleotide. This study sheds light on the specific structural changes necessary during high fidelity DNA synthesis, a process central to DNA repair and replication.

Citation: [Batra VK](#), [Beard WA](#), [Shock DD](#), [Pedersen LC](#), [Wilson SH](#). Structures of DNA polymerase beta with active site mismatches suggest a transient abasic site intermediate during misincorporation. *Mol Cell* 2008 May;30(3):315-324.

[Return to Table of Contents](#)

Inside the Institute

Homeschoolers Expand Their Understanding of Climate Change

By Eddy Ball

Sometimes, asking is all it takes to open doors. That's what the parents of a team of Triangle-area homeschoolers found out when they contacted the NIEHS Office of Communications and Public Liaison about a field trip to NIEHS and a workshop on climate change. The parents thought a visit to NIEHS would help their children prepare for the research-presentation component of the 2008 For Inspiration and Recognition of Science and Technology (FIRST) Lego League Climate Connections Tournament.

On May 30, the students and four homeschooling parents joined NIEHS Public Affairs Officer John Peterson and Associate Director Sharon Hrynkow, Ph.D., for a morning workshop at NIEHS. Peterson organized the event, which featured a talk by Hrynkow highlighting the health risks associated with climate change. Peterson took the visitors through a slide show overview of NIH/NIEHS, facilitated a question-and-answer session about the work at NIEHS and enjoyed a working lunch with the students and parents, where they continued their conversation about the environmental health sciences.

Hrynkow, who is one of the key figures in NIEHS climate change efforts, is experienced in presenting material on the subject to scientists and policy makers. Faced with curious twelve- and thirteen-year-olds, she also proved she was up to the task of talking to, rather than down to, younger listeners and shaping her message to meet their learning styles.

Hrynkow engaged the students with questions until they were comfortable enough to participate on their own and let their own interests guide the discussion during the rest of the presentation. Poised as they were for national competition in the [First Lego League Tournament](#), the homeschoolers were well prepared for the learning experience Hrynkow offered them.

Following Hrynkow's 30-minute presentation, Peterson resumed his discussion with the students



Hrynkow, shown at an earlier meeting, gave the students copies of the reader-friendly booklet, [Understanding and Responding to Climate Change](#), which highlights reports by the Institute of Medicine, the National Research Council and the National Academies of Sciences and Engineering.

(Photo courtesy of Steve McCaw)



Peterson, above, organized the day and gave students insights into the larger context of NIEHS climate change activities. Less than five minutes into his presentation, the students were stopping him to ask questions — setting the tone for a participatory educational experience.

(Photo courtesy of Steve McCaw)

about NIEHS research on ozone/fine particle pollution, the autism-vaccine connection, health effects of mercury and lead, endocrine disrupting compounds and Parkinson's disease. Peterson also talked about the National Toxicology Program's Report on Carcinogens and internship opportunities in the NIEHS Summers of Discovery Program, a topic that parents and children found especially interesting.

According to the parents, experiences like this one are valuable for supplementing the home school curriculum with hands-on, real-life experiences. The complementary educational experiences also help motivate students as they engage in mentor-based programs, such as FIRST, that build science, engineering and technology skills.

FIRST is a non-profit organization whose theme-based science programs on robot building reach over 150,000 young people in the United States and other countries each year. Younger participants build robots using legos, and advanced students progress to using sheet metal and welding to make more complicated machines. The organization enjoys broad-based sponsorship by business and educational groups as well as the participation of thousands of volunteers.

[Return to Table of Contents](#)



Both presenters were a little surprised by how much background the students, such as this young man, brought to the workshop.

(Photo courtesy of Steve McCaw)



This student's study habits were evident as he took notes during Hrynkow's talk.

(Photo courtesy of Steve McCaw)



The parents, who are also these students' primary teachers, seemed to enjoy the workshop as much as their children did.

(Photo courtesy of Steve McCaw)



Describing his efforts to take advantage of resources, such as the NIEHS visit and the FIRST competition, parent Randy Miller, above, explained, "We find curriculum and activities that foster what we want to help them learn."

(Photo courtesy of Steve McCaw)

Summers of Discovery Participants Enjoy Annual Picnic

By Eddy Ball



Summers of Discovery interns and mentors collected in front of the Rall Building for their group photo. Coordinator Charle League is shown in blue sitting in the center of the front row. (Photo courtesy of Steve McCaw)

On June 18, the Summers of Discovery Class of 2008 participants and mentors gathered for the program's traditional rite of summer at the Annual Picnic on the patio outside the NIEHS Cafeteria. The simple, but seasonal, fare included hamburgers and hot dogs with sides of coleslaw and potato and pasta salad.

The picnic takes place at the peak of activity for the students, some of whom have been at NIEHS since late May. In the weeks ahead, interns will be able to attend lectures by Matrix Biology Group Principal Investigator and Clinical Research Unit Staff Clinician Stavros Garantziotis, M.D., July 2; Reproductive Medicine Group Principal Investigator Carmen Williams, M.D., Ph.D., July 9; Calcium Regulation Group Principal Investigator and 2007 Scientist of the Year Jim Putney, Ph.D., July 16; and Epidemiology Branch Chief and Sister Study Principal Investigator Dale Sandler, Ph.D., July 23.

The 2008 Summers of Discovery Annual Poster Session will showcase the work of interns on July 30. Although there are events scheduled in August, the poster session marks the beginning of the participants' exodus, as they move on to the Fall semester at their high schools and colleges.

Photographer Steve McCaw was on site to take a group photo of the young scientists and their mentors as they took a break from food and fellowship to record this important event in their summer experience at NIEHS.

[Return to Table of Contents](#)

Evergreen Consulting Recognizes Media and Glassware Employees

By Eddy Ball

Just about everyone in the Rall Building at NIEHS has seen the rows of gleaming beakers on display in module D, but few get to see the hard work that goes on behind closed doors to make sure that labs have the glassware and media they need. On June 20, for the second year in a row, contract manager Heath Carroll recognized Evergreen workers for their excellent performance during the last evaluation period with a surprise lunch and certificates of appreciation.

NIEHS managers on hand to enjoy chicken and barbeque with the group included Geneticist Jim Mason, Ph.D., Project Officer Jennie Foushee and Assistant Project Officer Essie Jones. Together with Carroll they congratulated employees on a productive year. Even after last year's surprise lunch, most of the members of the Media and Glassware team were nevertheless surprised by the event.

Carroll also gave out tee shirts to everyone at the lunch and permission to leave early that afternoon. The media and glassware employees are a close-knit group with a strong esprit de corps who spent the final few minutes of the event offering to pitch in to help those with work still to complete also get a head start on the weekend.

[Return to Table of Contents](#)

Another Successful Fun-Filled Family Day

By Shannon Baker

Sounds of laughter, popular music from local DJ's and smells of summer grilling on the patio of the NIEHS Rall Building were not the only things attracting employees and their families to come out for the 3rd Annual Family Day Celebration. However, they were enough to transform the auditorium, patio, cafeteria and lakefront from scientific business as usual into a carnival-like playground for kids of every age. The event, organized by Dona McNeil and the Work Life Committee, was held on June 3.

The "Visit North Carolina" travel booths and arts and crafts table were a great start for the program. The 24 booths showcased some of North Carolina's most popular resorts, wineries, tourist attractions



Following their lunch, the group gathered for a photo. Front row, left to right: Janie Shaw, Bonnie Johnson, Ruby Haynes, Cheryl Brooks. Middle row, left to right: Anthony Jackson, Essie Jones, Jennie Foushee, Michael Watkins, Sarah Holmes, Thomas Gillespie. Back row, left to right: Heath Carroll, Lawrence Barbee Jr., Brandon Young, Dennis Malone.

(Photo courtesy of Steve McCaw)



Family Day is an opportunity for all ages to come out and enjoy a summer-like afternoon.

(Photo courtesy of Steve McCaw)

and recreational activities. Several vendors promoted their businesses, while children flocked to the arts and crafts table to take part in “a day at the beach” themed crafts. Sand buckets and metallic rimmed sunglasses were everywhere as children made sunvisors and played with animal-shaped balloons.

Outside on the patio, fellow co-workers participated in ice cooler relay races, water glove tosses, a cake walk and other games. NIEHS Acting Director Sam Wilson, M.D., welcomed everyone and encouraged participation in the events. He also recognized the planning committee and volunteers responsible for the day’s events, as well as thanked everyone for coming out for Family Day.

The cake walk attracted over 20 participants with half of them walking away winners. Winners included Office of the Director Chief of Staff Ebony Bookman, Ph.D., and DIR Special Volunteer Heather Olden who took home pound, lemon and chocolate cakes as prizes. The Wii games in the lobby, as well as Bingo, were also popular attractions as people rushed inside to escape the heat of the day.

The cafeteria offered a discounted menu featuring hot dogs, hamburgers and subs to replenish those getting ready to put their game faces on in the Annual Family Day Softball Tournament. Family Day was a fun-filled event and a good time was had by those who attended. Remembering the atmosphere of laughter and frolic, McNeil commented, “We saw lots of smiles and heard numerous comments about what a great time people had.”

(Shannon Baker is a rising senior at Peace College in Raleigh who spent a three-week internship in the NIEHS Office of Communication and Public Liaison. She is currently working part time in the NIEHS Office of the Director.)



Family Day organizer Dona McNeil apparently had just as much fun at the event as she did planning it.
(Photo courtesy of Steve McCaw)



NIEHS Acting Director Sam Wilson M.D., took a few minutes off from the serious business of running the Institute to watch the festivities.
(Photo courtesy of Steve McCaw)



Well in advance of the Softball Tournament, fans in red came out to show their support for the OD/NTP Toxic Red Tides. (Photo courtesy of Steve McCaw)



Dressed in blue to show her support for the OM Blazin’ Bullets, Cynthia Radford enjoyed being a spectator at the cake walk.
(Photo courtesy of Steve McCaw)



Winning the cake walk was definitely something that excited Heather Olden.
(Photo courtesy of Steve McCaw)



Family Day wouldn't be the same without the good natured banter, oldies but goodies, and beach music provided by the DJ. (Photo courtesy of Steve McCaw)

[*Return to Table of Contents*](#)



Dick Sloane tried to turn the tables on photographer Steve McCaw, but was caught in the act.

(Photo courtesy of Steve McCaw)



These girls found something to smile about as they doubled up on a tricycle.

(Photo courtesy of Steve McCaw)



Julius Thigpen, Ph.D., enjoyed learning about North Carolina's wineries during the travel fair. (Photo courtesy of Steve McCaw)

Discoverers Take Softball Trophy

By Shannon Baker

Retribution was the name of the game as the second annual Friends and Family Softball Tournament concluded Family Day on June 3. Nearly 80 NIEHS employees and their families came out to support and cheer on their fellow co-workers, as they prepared to take on opposing divisions.

The Division of Intramural Research (DIR) Discoverers kicked off the event by defeating former rivals, the Division of Extramural Research and Training (DERT) Devils 11-1. The fun-filled three-inning game was locked in a 1-1 tie, until a last inning hitting spree pushed the DIR Discoverers into the second round. “This year we are getting a little retribution from last year,” boasted DIR team captain Ron Cannon.

As the competition started to heat up, the Office of the Director, National Toxicology Program (OD/NTP) Toxic Red Tides played former champions, the Office of Management (OM) Blazin’ Bullets. Despite OD/NTP’s defensive efforts, the Blazin’ Bullets still proved to be too strong for the Toxic Red Tides and defeated them 3-1. Photographer Steve McCaw managed to score a homerun for the OD/NTP team. Before returning to duty to capture the events unfolding on the NIEHS ball field. OD/NTP Team Captain Chris Portier joked, “OM was lucky; next year we want to test them for steroids.”

DIR and OM moved on for the second year in a row to face off in the final game. Throughout the seven-inning game, the lead changed several times. DIR teammate Eric Tokar hit the ball over the fence, scoring the only homerun in the final game. As the tension grew stronger, DIR ultimately prevailed in the last inning, winning the game 9-5. The inter-divisional trophy was given to DIR for the first time. After the game, Cannon summed it all up with three words, “Retribution was had.”

(Shannon Baker is a rising senior at Peace College in Raleigh who spent a three-week internship in the NIEHS Office of Communication and Public Liaison. She is currently working part time in the NIEHS Office of the Director.)



DIR team player, Eric Tokar took a giant leap of faith for the Discoverers that dropped him and his teammates into the lap of victory over OD/NTP.

(Photo courtesy of Steve McCaw)



DIR Discoverers Team Captain Ron Cannon proves he has what it takes to win. (Photo courtesy of Steve McCaw)



Even in defeat, OD/NTP Toxic Red Tides Team Captain, Chris Portier found ample humor in the antics at the tournament. (Photo courtesy of Steve McCaw)



The lean and mean DIR Discoverers proved they were the “Comeback Kids” after defeating the OM Blazin’ Bullets 9-5 and avenging their loss in last year’s tournament.

(Photo courtesy of Steve McCaw)



NIEHS Acting Director Sam Wilson, who wisely shed his tie for the game, chuckled and chatted with Toxic Red Tides player Sheila Newton.

(Photo courtesy of Steve McCaw)



Although the OM Blazin’ Bullets failed to re-claim the championship title and inter-divisional trophy, they still found reason to smile after their losing battle with DIR.

(Photo courtesy of Steve McCaw)



Blazin’ Bullets team player William Ragland enjoyed a laugh as he tried to escape the heat of the day between games.

(Photo courtesy of Steve McCaw)

[Return to Table of Contents](#)

Friendship the Fish Fry Way

By Shannon Baker

Despite record-breaking heat and a Code Orange ozone-advisory, nearly 100 federal employees gathered under the covered picnic area at the NIEHS ball field on June 5 for the Blacks In Government (BIG) Annual Fish Fry. Naturally, the perfectly prepared fried flounder, fries, hushpuppies and sides attracted hungry co-workers, but the real reason gatherers return every year is to fellowship with one another and raise money for local scholarships.

The nonprofit service organization has been hosting the Annual Fish Fry since 1987, and tickets are usually sold in advance. The organization provides the food for the event, but the refreshments, plates and utensils are donated by members. Along with gathering the supplies, **BIG** members do the cooking and cleaning for the event. NIEHS members, including Kimberly Peterson and Annette Rice, took time away from their busy day to fry up hushpuppies and serve others. **BIG** promotes equity in all aspects of American life, excellence in public service and personal development opportunities for all Americans.

Although the crowd remains largely the same year after year, this year's gathering attracted a few newcomers, along with a group of interns from EPA.

BIG currently has 30 members from the NIEHS, National Center for Health Statistics, Army Research Office, Environmental Protection Agency and other agencies. Membership is open to both government and contract employees of government agencies. Annual dues are \$15 and national dues are \$55 per year. Life membership can be obtained by paying a one time fee of \$300.

BIG donates a portion of its proceeds for scholarships. The proceeds from last year were awarded to the Durham Nativity School. A decision has not yet been made about where the proceeds from this year's fish fry will be donated.

BIG also sponsors Black History Month events each year and is currently working with the Durham Chapter of The Links, Incorporated to collect shoes for scholarships. The Shoes for Scholarship drive was held at NIEHS from June 12-17. The Links were collecting dress, casual and athletic shoes in good condition for both adults and children. The shoes donated will help families in underdeveloped countries. Their goal was to collect 25,000 pairs of shoes with the proceeds going to benefit the Endowed Scholarship Fund at North Carolina Central University.



During most of the event, Kimberly Peterson of NIEHS was hard at work frying French fries. (Photo courtesy of Steve McCaw)



The entrée was fried to golden-brown perfection. (Photo courtesy of Steve McCaw)

Veronica Godfrey, a biologist in the NIEHS Environmental Toxicology Program, has been the local chapter's president for the past two years. When asked about the turnout she replied, "The fish fry was very successful, and our chapter appreciates the support of the entire NIEHS and EPA community."

(Shannon Baker is a rising senior at Peace College in Raleigh who spent a three-week internship in the NIEHS Office of Communication and Public Liaison. She is currently working part time in the NIEHS Office of the Director.)

[Return to Table of Contents](#)



Veterans of several BIG fish fries, the Georges, Margaret of NIEHS and Michael of EPA, worked together on food preparation.
(Photo courtesy of Steve McCaw)



Bill Jirles and Annette Rice took a much deserved break from cooking and enjoyed the fellowship at BIG's Annual Fish Fry. (Photo courtesy of Steve McCaw)



Many of the attendees were veterans of previous fish fries, but newcomers, such as these interns from EPA, are always welcome. Shown, left to right, are Alycia Graves, Tiffiney Benton, and Johnie Blackwell. (Photo courtesy of Steve McCaw)



The e-Factor, which is produced by the Office of Communications and Public Liaison, is the staff newsletter at the National Institute of Environmental Health Sciences. It is published as a communication service to NIEHS employees. We welcome your comments and suggestions. The content is not copyrighted. It can be downloaded and reprinted without permission. If you are an editor who wishes to use our material in your publication, we ask that you send us a copy for our records.

- Director of Communications: [Christine Bruske](#)
- Writer-Editor: [Eddy Ball](#)
- Science Editor: [Robin Arnette](#)