



Environmental Factor

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September 2010

NIEHS Spotlight



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[New breast cancer committee to set federal research agenda](#)

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[NIEHS joins NC oil spill forum](#)

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[Applying Superfund expertise to the Gulf oil spill](#)

Kim Anderson, Ph.D., of the Oregon State University (OSU) Superfund Research Program (SRP) is tracking the long-term chemical impact of the Deepwater Horizon oil spill in the Gulf of Mexico.



[Superfund trainee awarded EPA fellowship](#)

NIEHS-funded trainee Alissa Cordner, a Ph.D. student at Brown University, has been awarded a highly competitive EPA STAR Graduate Fellowship.

Science Notebook



[Keystone lecture explores the challenges of mixtures research](#)

During his visit to NIEHS June 23, biochemist Andreas Kortenkamp, Ph.D., spoke on "Mixtures: The Future of Toxicology Research, Testing and Risk Assessment."



[Students showcase Summers of Discovery research](#)

Participants in the NIEHS Summers of Discovery program brought to fruition several weeks of working toward a successful presentation at the annual poster competition.



[MAGE-11 regulation of androgen receptor](#)

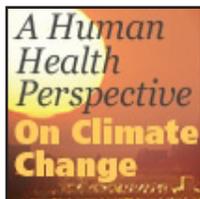
On Aug. 3, the NIEHS Receptor Mechanisms Discussion Group welcomed Elizabeth Wilson, Ph.D., its most recent guest and an expert on androgen receptor regulation.



[Study on early puberty advances breast cancer research](#)

A new study led by NIEHS-funded investigators adds to widespread concern that girls are increasingly entering puberty at an earlier age.

NIEHS Spotlight



[NIH announces climate change and health funding](#)

In a funding opportunity announcement issued July 27, NIEHS announced a new trans-NIH program to fund research on climate change and human health.



[DERT director finalists visit NIEHS](#)

During a very busy week Aug. 16-20, employees at NIEHS had an opportunity to hear from the finalists for position of director of the NIEHS extramural program.



[Superfund grantee honored by entomology group](#)

Veteran NIEHS Superfund Research Program grantee Bruce Hammock, Ph.D., has added yet another prestigious honor to his long list of achievements.



[Newton to chair National Children's Study committee](#)

Continuing the NIEHS leadership presence in the National Children's Study (NCS), Sheila Newton, Ph.D., will chair the NCS Interagency Coordinating Committee.



[NIEHS scientists help Milwaukee students imagine](#)

Sylvia Hewitt and April Binder, Ph.D., were among some 50 volunteers at the first annual Society for the Study of Reproduction pre-meeting outreach day July 29.



[Former trainee builds mentoring program at NCSU](#)

When Shweta Trivedi, Ph.D., was in the middle of her fellowship at NIEHS, little did she know that she would one day build a highly successful mentoring program at NCSU.

Science Notebook



[High-throughput screening of mitochondrial toxicity](#)

The NTP hosted a talk by Craig Beeson, Ph.D., July 30 on "High-Throughput Respiriometric Assay for Mitochondrial Biogenesis and Toxicity."



[Atrazine causes abnormalities in male rats](#)

A new NIEHS-funded study shows that male rats prenatally exposed to low doses of atrazine, a widely used herbicide, are more likely to develop prostate inflammation.



[NIEHS-led study advances predictive genomics](#)

A new NIEHS-led study shows that genomic indicators in the blood can serve as diagnostic biomarkers predictive of drug-induced liver injury.



[Unruly protein may shape learning and memory](#)

Neurobiologist John Hepler, Ph.D., shared exciting findings about a protein found in the mouse hippocampus, where spatial learning and memory formation occur.



[Summers of Discovery ends with module on air pollution](#)

The program concluded its lecture series July 27 with a module on air pollution presented by three NIEHS postdocs and an NIEHS laboratory biologist.

NIEHS Spotlight



[Roman to head EEO](#)

Gerard Roman will lead support services to NIEHS as the Institute's Equal Opportunity and Diversity Management specialist, according to an Aug. 23 announcement by NIH.

Inside the Institute



[Feds Feed Families with a half ton of help from NIEHS](#)

This summer, NIEHS joined a government-wide effort to alleviate severe shortages of non-perishable items at food banks across the nation.



[New NIEHS signs include NTP](#)

NIEHS underwent a minor facelift in July and August when workers installed new signs on campus that include NTP for the first time.



[Fellows enjoy food and fellowship at Lake Crabtree picnic](#)

High temperatures and an overcast morning did nothing to dissuade approximately 50 fellows and their families from turning out for an afternoon of fun August 14.



[Army gains as NIEHS loses Gentry](#)

Friends and colleagues gathered August 10 to wish Supervisory Contract Specialist Melissa Gentry the best in her new job at the Army Research Office.



[Ivanoff heads west for new adventures](#)

At the end of August, NIH Equal Employment Opportunity (EEO) Specialist Ginny Ivanoff left her position at NIEHS for a new job in Little Rock, Ark.

Science Notebook



[This month in EHP](#)

EHP tackles environmental issues in the Arctic in this month's news with a stunning cover depiction of an eerie frozen landscape and two timely feature articles.



[DNA Repair Videoconference Seminar Series begins](#)

The popular NIH series is broadcast live on the second Tuesday of each month between September and June to 14 linked sites across the country.



[Upcoming distinguished lecturer Patricia Donahoe](#)

On Sept. 14, NIEHS will host a talk by Patricia Donahoe, M.D., on the potential of Mullerian Inhibiting Substances in ovarian cancer treatment.

Extramural Research

[Extramural papers of the month](#)

- Polyfluoroalkyl chemicals linked to ADHD
- Circadian clock in pancreas linked to diabetes
- *In utero* BPA exposure leads to epigenetic alterations
- Vitamin A treatment and lung disease in pre-term lambs

Intramural Research

[Intramural papers of the month](#)

- The absence of SIRT1 produces an inflammatory response
- Dyslipidemia and the TLR response
- Cohesin prevents genome instability by restricting DNA repair to sister chromatids
- Oxidized (bi)sulfite leads to reactive sulfur species and protein radical formation

Calendar of Upcoming Events

- **Sept. 1-2** in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — National Advisory Environmental Health Sciences Council fall meeting — public portions Webcast
- **Sept. 7** in the Executive Conference Room, 12:00-1:00 p.m. — Receptor Mechanisms Discussion Group, featuring Yoshiaki Tsuji, Ph.D., exploring “A New Regulatory Mechanism of CREB and ATF1 by HIPK2 in Cellular Genotoxic Response”
- **Sept. 8-9** in Keystone 1003AB, 8:30 a.m.-4:30 p.m. — “Autism and the Environment: New Ideas for Advancing the Science” — Webcast
- **Sept. 13** in Rodbell Auditorium, 8:30 a.m.-4:30 p.m. — High Throughput Screening Pathways Identification Meeting
- **Sept. 14-16 (Offsite Event)** in the Natcher Conference Center on the NIH campus in Bethesda, Md., 8:30 a.m.-5:00 p.m. — International Workshop on Alternative Methods to Reduce, Refine, and Replace the Use of Animals in Vaccine Potency and Safety Testing
- **Sept. 14** in Rodbell Auditorium, 11:00 a.m.-12:30 p.m. — Distinguished Lecture Seminar Series with Patricia Donahoe, M.D., discussing “Chemotherapeutic Agents vs. Mullerian Inhibiting Substance on Stem/Progenitor Cells in Human Ovarian Cancer”
- **Sept. 15 (Offsite Event)** in Building 106 Rooms 1A/1B at the National Center for Environmental Health/Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention, in Chamblee, Ga., 10:00-11:30 a.m. — Agency for Toxic Substances and Disease Registry Seminar Series, with Celia Chen, Ph.D., addressing “Ecological Factors Controlling Metal Bioaccumulation and Trophic Transfer in Aquatic Food Webs”
- **Sept. 16** in Rodbell Auditorium, 2:00-3:00 p.m. — Carter Van Waes, M.D., Ph.D., speaking on “Molecular Pathogenesis and Therapy of Subsets of Tobacco Related Head and Neck Cancers”
- **Sept. 20** in Rall F193, 11:30 a.m.-12:30 p.m. — Laboratory of Molecular Genetics Seminar Series, with Vivian Cheung, M.D., speaking on “Genetic analysis of radiation-induced changes in human gene expression”
- **Sept. 24** in Rodbell Auditorium, 1:00 p.m.-2:00 p.m. — National Postdoc Appreciation Day and NIEHS Trainees Assembly General Assembly Meeting
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Senate hearing focuses on autism research

By Ed Kang

In an August 3 hearing, the U.S. Senate Committee on Environment and Public Works Subcommittee on Children’s Health met to discuss the state of research on environmental factors related to autism and related disorders. Held in the Dirkson Senate Office Building in Washington and broadcast live on C-SPAN3, the [hearing](#) focused on the “State of Research on Potential Environmental Health Factors with Autism and Related Neurodevelopment Disorders.”

Linda Birnbaum, Ph.D., director of NIEHS/NTP, and Paul Anastas, M.D., assistant administrator of the U.S. Environmental Protection



NIEHS enjoyed a high profile at the hearing, with testimony by Birnbaum, above, and researchers funded by NIEHS. (Photo courtesy of Steve McCaw)

A video player thumbnail showing a play button over a video frame of two women. To the right of the frame, the text reads: "Linked video: [Dr. Birnbaum's testimony describes NIEHS autism research](#)". Below the frame, it says "(Launches in new window)". At the bottom left, there is a "Download Media Player: Quicktime" link with a small icon.

Agency (EPA) Office of Research and Development, were joined by veteran NIEHS grantees Issac Pessah, Ph.D., and Bruce Lanphear, M.D., to offer their perspectives on the latest advances and areas for opportunity in autism research.

Pointing to the suffering of families and the billions of dollars of economic impact from disease-related expenditures, Sen. Barbara Boxer, D-Calif., chair of the Committee on Public Works, noted the urgency surrounding science’s search for answers. “Research is especially important now, since some data indicates that the occurrence of autism is growing,” said Boxer, referring to a Centers for Disease Control and Prevention estimate that 1 in 110 U.S. children have symptoms of autism spectrum disorder (ASD).

Lanphear, director of the Cincinnati Children’s Environmental Health Center, noted the changing landscape of scientific understanding surrounding childhood disease and development. “The findings from research on some of the most thoroughly studied and widely dispersed environmental toxicants indicate that exposure to exceedingly low levels are risk factors for the ‘new morbidities’ of childhood — intellectual impairments, behavioral problems, asthma, and preterm birth,” he said. “Indeed, there is often no apparent threshold and, in some cases, the effects appear to be greater at the lowest levels of exposure.”

Lawmakers address clusters, chemical reform

Boxer explained Congress’s intent to focus on legislation. “When these disorders appear in concentrations or clusters, it may be an indication that environmental factors are playing a role in making people sick,” she said.

To help address the issue, Boxer said she is introducing legislation to ensure that federal agencies are coordinating their efforts on disease clusters as effectively as possible. “My bill will also require EPA to upgrade data tracking systems to strengthen the federal government’s ability to investigate disease clusters,” she added.

Boxer also referenced the Safe Chemicals Act of 2010, which Senator Frank Lautenberg, D-N.J., introduced earlier this year. The bill, an overhaul of the Toxic Substances Control Act of 1976, would strengthen the way the federal government regulates toxic chemicals by requiring the chemical industry to prove the safety of their chemicals before introducing them to market.

Pessach, who has led the University of California (UC), Davis Center for Children’s Environmental Health since 2001, supports limiting exposure to harmful chemicals to mitigate or prevent autism in susceptible individuals. “Only by bringing together the concerted effort of multidisciplinary teams of scientists can we identify which of the more than 80,000 commercially important chemicals currently in production promote developmental neurotoxicity,” he stated.

According to Anastas, EPA Administrator Lisa Jackson has emphasized strengthened chemical management as a top priority. “Research to better understand the environmental contributions to ASD and other disorders will help us develop policies and actions to reduce them,” he explained. “We must also develop safer chemicals to reduce and prevent adverse effects to children’s health.”

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

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Birnbaum describes autism research efforts funded by NIEHS

Two large research efforts are co-funded by NIEHS to better understand the causes and contributing factors for autism or developmental delay, Birnbaum told the subcommittee.

The Childhood Autism Risks from Genes and the Environment (CHARGE) study is the first large-scale human population case-control study of children with autism. Researchers at UC Davis are looking at a wide range of environmental exposures and their effects on early development in three groups of 1,600 California children: children with autism, children with developmental delay who do not have autism, and children from the general population. Heavy metals are one of the classes of exposure being investigated.

“Perhaps the most interesting new findings from the CHARGE study relate immune system alterations in children to the development of autism,” said Birnbaum. “These findings point to the need for further study on the interface of the immune and nervous systems in autism etiology.”

In another NIEHS-funded project, the Early Autism Risk Longitudinal Investigation (EARLI) study, researchers at the Drexel University School of Public Health are enrolling mothers who have a child with autism and are pregnant again. This longitudinal study, one of the largest of its kind, will follow 1,000 mothers during their pregnancy and their new babies through age three to identify prenatal, neonatal, and early postnatal exposures that may influence risk of developing autism.

September workshop to target environmental factors and autism

A workshop will be held September 8 on the campus of NIEHS to identify opportunities to accelerate research on environmental factors and autism. Discussion will focus on recent advances in autism research, emerging tools and technologies in environmental health sciences, and analogies to successful approaches in other environmentally mediated diseases.

This workshop is a joint effort between the National Institute of Environmental Health Sciences and Autism Speaks. A full agenda and list of presenters is available [online](#).

New breast cancer committee to set federal research agenda

By Ed Kang

A newly formed advisory committee will develop and coordinate a strategic federal research agenda on environmental and genetic factors related to breast cancer.



Established by the Breast Cancer and Environmental Research Act of 2008, the 19-member Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC) will review all breast cancer research efforts conducted or supported by federal agencies, including the U.S. Department of Health and Human Services, the National Institutes of Health, the U.S. Department of Defense, and the U.S. Environmental Protection Agency. Additionally, the committee will create a comprehensive plan to expand opportunities for collaborative, multi-disciplinary research, and develop a summary of advances in federal breast cancer research.

The committee’s voting membership consists of seven representatives of federal agencies; six non-federal scientists, physicians, and other health professionals from clinical, basic, and public health sciences; and six advocates for individuals with breast cancer.

“The broad range of expertise and insight of these individuals will ensure the federal research portfolio continues to advance our understanding of the critical links between our environment, our genes, and our health,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program (NTP).

In addition to Birnbaum and National Cancer Institute (NCI) Director Harold Varmus, M.D., the business of the committee will be facilitated by Gwen Collman, Ph.D., interim director of the NIEHS Division of Extramural Research and Training, and Deborah Winn, Ph.D., deputy director of the NCI Division of Cancer Control and Population Sciences.

The first meeting of the IBCERCC will take place Sept. 30 – Oct. 1, 2010 in the Washington, D.C., area.

Federal Representatives	
Christine Ambrosone, Ph.D.	Member, Board of Scientific Advisors, National Cancer Institute, and Professor of Oncology, Roswell Park Cancer Institute
Sally Darney, Ph.D.	Acting National Program Director, Human Health Research Program U.S. Environmental Protection Agency
Suzanne Fenton, Ph.D.	Reproductive Endocrinologist National Institute of Environmental Health Sciences
Vivian Pinn, M.D.	Director, Office of Research on Women’s Health National Institutes of Health
Marcus Plescia, M.D., M.P.H.	Director, Division of Cancer Prevention and Control Centers for Disease Control and Prevention
Gayle Vaday, Ph.D.	Program Manager, Breast Cancer Research Program, Congressionally Directed Medical Research Programs, U.S. Department of Defense
Shelia Hoar Zahm, Sc.D.	Deputy Director, Division of Cancer Epidemiology and Genetics National Cancer Institute

Non-Federal Representatives (Scientists, Physicians, and other Health Professionals)	
Michele Forman, Ph.D.	Professor of Epidemiology The University of Texas M.D. Anderson Cancer Center
Michael Gould, Ph.D.	Professor of Oncology University of Wisconsin–Madison
Sandra Haslam, Ph.D.	Professor of Physiology Michigan State University
Ronda Henry-Tillman, M.D.	Medical Director, Women’s Oncology Clinic and Director, Cancer Control Arkansas Cancer Research Center, University of Arkansas for Medical Sciences
Kenneth Portier, Ph.D.	Statistician American Cancer Society
Cheryl Walker, Ph.D.	Professor of Carcinogenesis The University of Texas M.D. Anderson Cancer Center
Non-Federal Representatives (Advocates)	
Janice Barlow, P.H.N., C.P.N.P.C.	Executive Director Zero Breast Cancer
Beverly Canin	President Breast Cancer Options
Alice Chang, Ph.D.	President and Co-Founder Academy for Cancer Wellness
Karen Joy Miller	Founder and President Huntington Breast Cancer Action Coalition
Laura Nikolaides, M.S.	Director, Research & Quality Care Program National Breast Cancer Coalition
Jeanne Rizzo, R.N.	President and CEO Breast Cancer Fund

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

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NIEHS joins NC oil spill forum

By Eddy Ball

While the experts think it’s unlikely oil from the Gulf will reach the shores of North Carolina, the state is coordinating a comprehensive response just in case it does.

Organized by the University of North Carolina at Chapel Hill (UNC-CH) and co-hosted by the North Carolina State University College of Veterinary Medicine, the [“One Health” Forum on NC Oil Spill Response, Recovery, and Health Effects](#) July 29 drew approximately 100 citizens and officials to a full-day meeting and workshop in Chapel Hill, including NIEHS Workers Education and Training Program (WETP) Director Chip Hughes.

Forum attendees were a diverse group, ranging from experts from the UNC Gillings School of Global Public Health, marine scientists, medical professionals, U.S. Coast Guard (USCG) senior staff, and N.C. coastal county managers to business and tourism representatives, state officials, and concerned citizens. They gathered at the Friday Center in Chapel Hill to learn more about the impact of oil spills on people, animals, and the economy, and to explore the ways they can position North Carolina to be a step ahead of the ripple effects of the Gulf oil spill and similar disasters in the future.



In the weeks following the Deepwater Horizon explosion, Hughes spent time on the ground in Louisiana and Alabama with members of his WETP team. WETP grantees trained the trainers of workers involved in the cleanup effort. (Photo courtesy of UNC Gillings School of Global Public Health)



Hughes reports on NIEHS initiatives

Hughes is part of the federal response to the Gulf oil spill. He and his staff are coordinating training for thousands of workers involved in the cleanup efforts. Hughes spoke of lessons learned in past disasters, including the World Trade Center attack, Hurricane Katrina, and the Deepwater Horizon spill, during his presentation on [“Oil Spill Health Effects.”](#)

In his presentation, Hughes reviewed NIEHS efforts to help keep workers safe during oil spill response and cleanup operations. He also urged his audience to keep in mind that, as dramatic as the immediate effects of a disaster are, it’s important to keep in mind the long-term health effects that emerge long after the media have turned their attention elsewhere.

“We’re still seeing the impact of 9/11 and Katrina on the health of responders,” he said, “and it’s certain that the effects of oil and dispersant as well as the trauma experienced by people in the region will impact health in the Gulf and beyond for years to come.”

Presenting a catalogue of NIEHS activities in response to the Gulf oil spill, Hughes pointed to the more than 100,000 people throughout the Gulf Coast who have been trained by BP or its training contractor PEC/Premier, using NIEHS WETP training materials. NIEHS has distributed more than 10,000 [“Safety Awareness for Oil Spill Cleanup Workers”](#) guides to frontline responders, instructors, and safety officials.

Looking years ahead, he said, NIEHS is gearing up to launch a health study of oil spill clean-up workers and volunteers in late fall. The Gulf Workers Study (GuLF) is being designed and led by the NIEHS



Organizer Bill Gentry, above, is a faculty member of the UNC Gillings School of Global Public Health, assistant director of executive programs, and an expert in community preparedness and disaster management. (Photo courtesy of UNC Gillings School of Global Public Health)

[Epidemiology Branch](#) with special funding announced in June by NIH Director Francis Collins, M.D., Ph.D. With much input from local, state, federal agencies, and community partners, the study is expected to evaluate more than 20,000 cleanup workers for a range of possible health effects, including respiratory, neurobehavioral, carcinogenic, immunological, and mental health disorders.



USCG Lt. Shannon Scaff is the incident management chief at Sector North Carolina. He presented an [overview of USCG pollution response](#), with an emphasis on the North Carolina coast. (Photo courtesy of UNC Gillings School of Global Public Health)



Julie Casani, M.D., is the director at the N.C. Division of Public Health, Office of Public Health Preparedness and Response. Her [presentation](#) outlined the systems in place for mounting a response to the public health effects of an oil spill in North Carolina. (Photo courtesy of UNC Gillings School of Global Public Health)

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Applying Superfund expertise to the Gulf oil spill

By Angela Spivey

Kim Anderson, Ph.D., of the NIEHS-funded Superfund Research Program (SRP) at Oregon State University (OSU) is tracking the long-term chemical impact of the Deepwater Horizon oil spill in the Gulf of Mexico. Using novel sampling devices, [Anderson](#) and her research team are monitoring air and water levels of polycyclic aromatic hydrocarbons (PAHs) along the coast of four Gulf states.

Anderson's early samples showed that after the April 20 spill, the level of PAHs in the water in Louisiana rose 40-fold during the month of May. PAHs are present in oil in small amounts and are known carcinogens.

The passive sampling devices that Anderson's team employs — biological response indicator devices for gauging environmental stressors (BRIDGES) — were developed as part of an SRP grant. The sampling devices sequester and measure the dissolved fraction of a contaminant, which enables the researchers to focus on only the chemicals that are active or bioavailable, while disregarding those that are merely present.



Linked video:
[NIEHS grantees deploy sensing devices in the Gulf](#)

(Launches in new window)

Download Media Player:  Flash 

Results of this sampling campaign will be used to link environmental exposures to biological responses in the environment and reduce uncertainties found in risk assessments of such disasters. The study will be the first assessment of the concentrations as well as spatial and temporal distributions of bioavailable oxygenated PAHs in an active oil spill.

The devices enable the researchers to study the possibility that chemical dispersants that were used to mitigate the oil spill may increase the bioavailability and toxicity of PAHs. The devices sequester and measure not only PAHs, but also oxygenated PAHs, which can form from photo-reactions and microbial degradation of PAHs, and may be more bioavailable than PAHs.

OSU has created a dedicated [Web page](#) on its SRP oil spill activities and resources. Anderson's work was recently featured in [USA Today](#), where she likened the oil leak to a chemical spill in the ocean.

The OSU BRIDGES project is funded in part by an NIEHS SRP [grant](#) and an NIEHS Environmental Health Sciences Center [grant](#).

(Angela Spivey is a freelance writer for the NIEHS Superfund Research Program and Worker Education and Training Program.)



Members of the OSU team gathered beside to the waters of the Gulf of Mexico. Shown, left to right, are students Sarah Allan and Steven O'Connell, Anderson, and student Kevin Hobbie. (Photo courtesy of Kim Anderson and OSU)



Allan prepares passive samplers for deployment in the Gulf of Mexico. (Photo courtesy of Kim Anderson and OSU)



Student Lane Tidwell loads passive samplers into the air deployment apparatus. (Photo courtesy of Kim Anderson and OSU)



OSU student Steven O'Connell deploys a water sampler. (Photo courtesy of Kim Anderson and OSU)

Superfund trainee awarded EPA fellowship

By Angela Spivey

NIEHS Superfund Research Program trainee Alissa Cordner, a Ph.D., a student at Brown University, has been awarded a highly competitive U.S. Environmental Protection Agency (EPA) STAR Graduate Fellowship. Cordner will receive up to \$37,000 per year for up to three years for general support of her studies and research on the social implications of flame retardant chemicals.

Cordner is questioning scientists, activists, regulators and policy makers, participants in biomonitoring studies, and industry representatives to understand how these different stakeholders interpret and characterize the risks and hazards of flame retardants, and how those interpretations influence their actions, including any effects they may exert on chemical policy decisions.



Cordner, above, can look forward to generous support from EPA as she completes her doctorate. (Photo courtesy of Alisa Cordner)

“This fellowship will allow me to interview people working on flame retardant issues around the country, and to understand how all these different stakeholders perceive risk and incorporate those perceptions into their daily lives,” Cordner said. “I think it’s wonderful that the EPA acknowledges the importance of this type of work on the risks and hazards of emerging contaminants.”

Cordner works with sociology and environmental studies professor Phil Brown, Ph.D., who directs the Community Outreach Core of Brown University’s NIEHS Superfund Research Program.

Masters and doctoral candidates in environmental studies compete for the STAR fellowships through a rigorous review process. The fellowships help defray the ever-increasing costs associated with studies leading to advanced degrees in environmental sciences.

Since the program began in 1995, EPA has awarded approximately 1,500 STAR fellowships to students in every U.S. state and most territories pursuing degrees in traditionally recognized environmental disciplines, as well as other fields such as social anthropology, urban and regional planning, and decision sciences.

(Angela Spivey is a freelance writer for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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NIH announces climate change and health funding

By Eddy Ball

In a funding opportunity announcement (FOA) issued July 27, NIEHS announced a new program to fund research on climate change and human health, leading an effort that involves ten other NIH institutes and offices (ICs). The program, called “[Climate Change and Health: Assessing and Modeling Population Vulnerability to Climate Change](#),” will fund research for up to two years.

The earliest date that applications could be accepted for the grants was August 28. A second and third round of applications will be accepted beginning April 24, 2011 and April 24, 2012. Letters of intent should be sent to NIEHS Program Administrator [Caroline Dilworth, Ph.D.](#) Electronic submission is required.

According to the FOA, a better understanding of how climate change will alter human health risks in the United States and globally, and who will be most vulnerable to adverse health effects, is critical for reducing or preventing illness and death. The ultimate goal of the research program is to help inform climate change adaptation and public health interventions to reduce the current and future vulnerability of various at-risk populations.

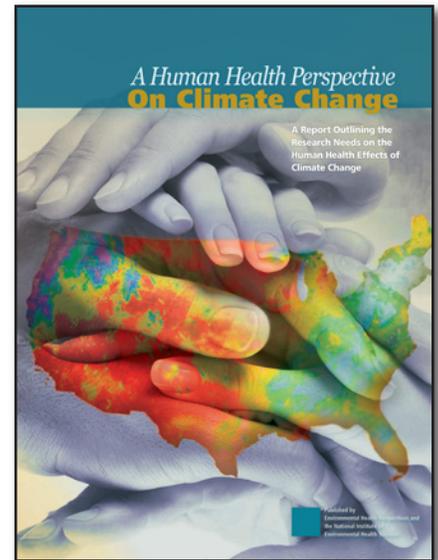
The program has its roots in recent workshops and papers coordinated by several NIH ICs, including NIEHS, to identify research needs on the human health impacts of climate change. NIEHS was the lead for NIH on an ad hoc Interagency Working Group on Climate Change and Health (IWGCCCH) that recently released a [white paper](#) outlining research needs for eleven categories of human health consequences of climate change.

The white paper expressed concerns about the effects of climate change on asthma and respiratory disease, cancer, cardiovascular disease and stroke, foodborne diseases and nutrition, human developmental effects, mental health and stress-related disorders, neurological diseases and disorders, vectorborne and zoonotic diseases, waterborne diseases, and weather-related morbidity and mortality. The report underscored the need for more research to assess and characterize population vulnerability to adverse health impacts due to climate change.

Participating ICs will consider applications related to their [specific research interests](#) as described in the FOA:

- [Fogarty International Center \(FIC\)](#)
- [National Heart, Lung, and Blood Institute \(NHLBI\)](#)
- [National Cancer Institute \(NCI\)](#)
- [National Center on Minority Health and Health Disparities \(NCMHD\)](#)
- [National Institute on Aging \(NIA\)](#)
- [Eunice Kennedy Shriver National Institute of Child Health and Human Development \(NICHD\)](#)
- [National Institute of Biomedical Imaging and Bioengineering \(NIBIB\)](#)
- [National Institute of General Medical Sciences \(NIGMS\)](#)
- [National Library of Medicine \(NLM\)](#)
- [Office of Behavioral and Social Sciences Research \(OBSSR\)](#)

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The interagency working group report was published April 21. NIEHS was the NIH lead on the white paper, which helped drive the new funding opportunity

DERT director finalists visit NIEHS

By Eddy Ball

During a very busy week Aug. 16-20, employees had an opportunity to hear from the finalists for the position of director of the NIEHS Division of Extramural Research and Training (DERT). The talks, hosted by NIEHS/NTP Director Linda Birnbaum, Ph.D., gave the finalists an opportunity to showcase their qualifications for heading what is, in terms of budget, the largest division at the Institute.

The candidates spent a full day at NIEHS, presenting their seminars and meeting with various NIEHS leadership, staff, trainee, and constituency groups. Employees took to heart Birnbaum's invitations to attend the talks in Rodbell Auditorium Aug. 16, 18, and 20.

The finalists, all of them distinguished senior science administrators with ties to NIH, discussed their areas of expertise, trying to demonstrate, as well as describe, the strengths they could bring to this key leadership position at NIEHS. DERT is organized into seven branches and centers and is composed of 60 full-time federal employees. Each year, the extramural program is responsible for awarding approximately 874 research grants for a total of approximately \$388 million.

The candidates and their topics

- Aug. 16 — Gwen Collman, Ph.D., interim director of the NIEHS DERT, gave a talk titled "The Power of the NIEHS Extramural Program." Collman used her home-court advantage as she addressed the many aspects of power enjoyed by the current NIEHS extramural effort with a catalogue of the program's accomplishments, including its extensive grantee base, its impact on the direction of scientific research, and its network of partners worldwide.
- Aug. 18 — Sudhir Srivastava, Ph.D., chief of the Cancer Biomarkers Research Group at the National Cancer Institute (NCI), described his experiences in a talk on "Working Across Boundaries: Making Collaboration Work in Translational Research." Srivastava shared lessons he learned coordinating the NCI Early Detection Research Network to launch a presentation on strategies for integrating partners and interest groups in a wide-ranging collaborative effort with translational impact.



Birnbaum, above, took extensive notes during the series of talks and facilitated the question-and-answer sessions as NIEHS employees queried candidates about a variety of topics. (Photo courtesy of John Maruca)



Collman gestured as she listed a number of outstanding researchers and partners who collectively empower the extramural program at NIEHS. (Photo courtesy of Steve McCaw)

- Aug. 20 — Rudolph Parrish, Ph.D., a professor in the Department of Bioinformatics and Biostatistics at the University of Louisville School of Public Health, explored the “Era of Complexity in the Environmental Health Sciences: Perspective on Extramural Research and Training.” Parrish drew upon his extensive experience in clinical trials as he addressed the potential of and challenges facing the extramural program at NIEHS, ranging from predictive toxicology to research into the health effects of endocrine disrupting compounds.



Srivastava is an accomplished cancer researcher and editor of the journals Disease Markers and Cancer Biomarkers, but he told the audience, “I’m still a student.” (Photo courtesy of Steve McCaw)



Parrish underscored the enormous importance of DERT and his passion, perseverance, and vision in the pursuit of quality science that will make a difference in public health. He said his motto is to “model like a scientists, but test like an engineer.” (Photo courtesy of John Maruca)



DERT staff, such as Program Analyst Liam O’Fallon, above, were on hand to experience how those who would lead handle themselves in the public venue. (Photo courtesy of Steve McCaw)



The series was also well attended by employees from other divisions, including Comparative Medicine Branch Chief Diane Forsythe, D.V.M., above. (Photo courtesy of Steve McCaw)



Division of Intramural Research Principal Investigators Ken Korach, Ph.D., right, and Walter Rogan, M.D., center, attended the series. Korach asked questions of two of the speakers. (Photo courtesy of Steve McCaw)



DERT Acting Deputy Director Pat Mastin, Ph.D., waited at the audience microphone after asking Parrish about applications of genome-wide association studies in environmental health research. (Photo courtesy of John Maruca)

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Superfund grantee honored by entomology group

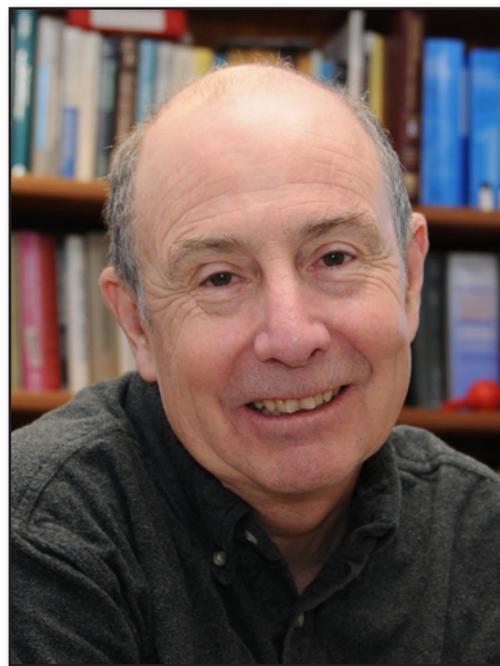
By Eddy Ball

Veteran NIEHS Superfund Research Program (SRP) grantee Bruce Hammock, Ph.D., has added yet another prestigious honor to his long list of achievements. In a July 28 [press release](#), the Entomological Society of America (ESA) announced the election of Hammock as one of ten new ESA fellows who will be recognized during [Entomology 2010 — ESA's Annual Meeting](#) Dec. 12-15 in San Diego.

Founded in 1889, ESA is a non-profit organization committed to serving the scientific and professional needs of more than 6,000 entomologists and individuals in related disciplines. ESA's membership includes representatives from educational institutions, government, health agencies, and private industry. ESA fellows are recognized authorities in their fields, and this year's group includes three from the University of California system — Hammock, UC Davis colleague Thomas Scott, Ph.D., and Thomas Miller, Ph.D., of UC Riverside.

ESA fellow Bruce Hammock

[Hammock](#) is a distinguished professor of entomology at the UC Davis, who was elected to the National Academy of Sciences in 1999. He joined the UC Davis faculty in 1980 and currently holds a joint appointment in cancer research with the UC Davis Medical Center.



Hammock, above, is a scientific polymath — a divergent thinker who negotiates disciplinary boundaries as easily as he crosses a street to get to class. (Photo courtesy of UC Davis)

Funded continuously by NIEHS for more than 30 years, Hammock directs the Superfund Research and Training Program, as well as the NIH Training Program in Biotechnology and the NIEHS Combined Analytical Laboratory at UC Davis, where he has performed extensive research into applications of metabolomics methodologies.

An odyssey from basic to translational research

Trained as an insect developmental biologist, Hammock has expanded his research interests to include drug development and advanced laboratory analysis. In his early SRP-funded work, his laboratory pioneered the use of transition state theory to inhibit enzymes with small molecules and recombinant viruses as green pesticides, as well as the use of immunochemistry for pesticide analysis.

From his time as a graduate student, Hammock's laboratory has focused on xenobiotic metabolism, especially the role of enzymatic esterases and epoxide hydrolases. Current projects involve examining the role of esterases in insecticide resistance and human metabolism of pyrethroids, the active compound in many insecticides. His laboratory has applied this research, as Hammock explored the use of inhibitors of epoxide hydrolases as drugs to treat diabetes, inflammation, ischemia, and cardiovascular disease.

Hammock's findings have significant potential in the treatment of human disease. His group has demonstrated that increasing serum levels of the fatty acid 12-(3-adamantan-1-yl-ureido)-dodecanoic acid (AUDA) effectively blocks the enzyme soluble epoxide hydrolase (sEH) that is implicated in the hypertension and inflammation. A drug he developed — a compound known as AR9281 — is now in Phase II human clinical trials and promises to be the first novel treatment for hypertension and cardiovascular disease in the last 25 years ([see UC Davis story](#)).

In a 2008 study, Hammock and his colleagues also demonstrated that raising AUDA levels to block effects of sEH has potential applications in treating the side effects of the chemotherapeutic agent cisplatin in the kidneys of mice ([see story](#)). According to the study's authors, this novel approach may represent the first significant advance in clinical management of acute renal failure since the development of dialysis.

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A distinguished career in science, teaching, and playing

Hammock received the UC Davis Faculty Research Lecture Award in 2001 and the Distinguished Teaching Award for Graduate and Professional Teaching in 2008. He has also been honored with the Frasch and Spencer Awards of the American Chemical Society as well as the Alexander von Humboldt Award, one of the most prestigious in the field of agriculture.

Author or coauthor of more than 760 peer-reviewed publications, Hammock is the principal investigator on three NIEHS grants: [Biomarkers of Exposure to Hazardous Substances](#), which funds the SBR Center at UC Davis; [Hydrolytic Enzymes in the Metabolism of Toxins](#); and [Metabolomic Study of Ozone and Nitronaphthalene Toxicity](#).

Hammock is an engaging lecturer with a wry sense of humor who has spoken several times at NIEHS, including a distinguished lecture in October 2007 ([see story](#)). Those fortunate enough to know Hammock realize that he understands the importance of playing, as well as working hard ([see UC Davis story](#))

Newton to chair National Children’s Study committee

By Thaddeus Schug

Continuing a long-standing leadership presence for NIEHS in the [National Children’s Study \(NCS\)](#), Sheila Newton, Ph.D., director of the NIEHS Office of Policy, Planning, and Evaluation, will chair the Interagency Coordinating Committee (ICC). Newton, who initially joined the ICC in 2003, will serve a yearlong appointment as chair beginning in September. The [Eunice Kennedy Shriver National Institute of Child Health and Human Development \(NICHD\)](#) is the lead NIH institute for the study in partnership with NIEHS.

The NCS is the largest long-term study of environmental and genetic influences on children’s health ever conducted in the United States. By following 100,000 children from before birth to age 21, researchers hope to better understand how children’s genes and their environments interact to affect their health and development.

“The NCS is entering a new stage in development,” Newton said. “It is important that the community understand that the study is alive and well, and that we are changing focus a little to field test and reframe some of the components of the vanguard study.”

The vanguard phase of the study is being retooled to provide guidance on a wide range of operational issues, to inform decision making when the main study gets underway. “The idea is that these efforts will accelerate development and deployment of the main study,” Newton continued.

In addition to NICHD and NIEHS, other lead agencies for the study include the Centers for Disease Control and Prevention (CDC) and the U.S. Environmental Protection Agency (EPA). The ICC, which oversees broad study issues and ensures interagency collaborations, consists of members from all four lead agencies.

In her role as chair of the ICC, Newton is responsible for setting the program agenda, interfacing with the program office, and making sure the ICC’s work moves forward and all that all voices are heard. “It is the role of ICC to ensure the NCS stays aligned to the interests of the lead agencies,” she said.

NIEHS has maintained a visible presence on the ICC since the study was authorized by Congress as part of the Children’s Health Act of 2000. Past NIEHS ICC members include Gwen Collman, Ph.D., acting director of the NIEHS Division of Extramural Research and Training (DERT), and Principal Investigator Matthew Longnecker, M.D., Sc.D. Currently, both Newton and DERT Health Scientist Administrator Kimberly Gray, Ph.D., hold positions on the ICC. In addition, NIEHS Senior Advisor Allen Dearry, Ph.D., serves on the NCS Advisory Committee, the federally chartered body of external advisors for the study.

The NCS will eventually involve 100,000 families followed over a 21-year period, in 105 study counties served by an estimated 40 centers nationwide. Biomedical and environmental samples will be stored at a central repository, and, along with clinical and lifestyle questionnaire data, they will be analyzed to provide insights into the environmental causes of such conditions as birth defects, premature birth, asthma, diabetes, childhood cancers, and autism.



Newton, above, has served on several high-profile federal advisory committees. (Photo courtesy of Steve McCaw)

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

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NIEHS scientists help Milwaukee students imagine

By Eddy Ball

NIEHS scientists Sylvia Hewitt and April Binder, Ph.D., were among some 50 volunteers at the first annual Society for the Study of Reproduction (SSR) pre-meeting outreach day July 29. The daylong hands-on learning experience for local students at Marquette University Biological Campus featured fun labs and other activities organized around the theme, [Imagine: The Science of Reproduction and You](#).

Hewitt is a senior biologist and Binder is an Intramural Research Training Award postdoctoral fellow in the NIEHS [Receptor Biology Group](#) headed by Chief of the NIEHS Laboratory of Reproductive and Developmental Toxicology (LRDT) Ken Korach, Ph.D. Both were authors on posters presented at the meeting. Hewitt was co-author on two abstracts from the Receptor Biology Group, and Binder was first author on an abstract from her Washington State University doctoral program.

Hewitt said part of her motivation for volunteering came from experiences working with youth at her church. Binder said she was interested in working together and networking with other members of SSR, as well as having a chance to share her enthusiasm about reproductive science with the students.

Targeting groups under-represented in science and technology

Supported by a grant from the Burroughs Wellcome Fund and sponsored by SSR, Marquette University, University of Wisconsin (UW)–Madison, and UW–Milwaukee, Imagine attracted approximately 150 students, many of them minority students at inner city schools. Some of the students were participants in summer programs at Marquette and UW–Milwaukee and members of the local YMCA Youth Leadership Academy.

Students could participate in three of the program's six fun labs, have lunch with SSR graduate students, and sign up to attend SSR scientific sessions with their new mentors. Hands-on activities ranged from dissection of a sheep brain to an artificial insemination exercise using a life-size model cow. In the afternoon, students heard from a career panel of SSR graduate students and a research career panel of SSR members, who helped the students imagine a future for themselves as clinicians and researchers.

The busy day closed with a motivational presentation by UW–Madison graduate student [Beverly Hutcherson](#), who did her part to develop the workshop theme with a talk titled, "You Can Do It!" Hutcherson graduated from



Hewitt said she learned of the volunteer opportunity through a conversation with Jorgensen following her talk on gonad development at NIEHS last November. The talk was part of the LRDT Seminar Series. (Photo courtesy of Steve McCaw)

Milwaukee's predominately black Harold S. Vincent High School and Marquette University. She is a former Advanced Opportunity Fellow studying polycystic ovary syndrome as part of her master of science program.

An idea whose time has come

The workshop was the brainchild of organizer [Joan Jorgensen, D.V.M., Ph.D.](#), a professor in the UW School of Veterinary Medicine. Jorgensen took advantage of scientists, students, and trainees who planned to attend the 2010 SSR Annual Meeting and were willing to arrive in Milwaukee a day or two early to help set up wet labs and work with students. She also brought along information about the veterinary program at UW.

Hewitt said, "It was fun to be a part of outreach day," and she plans to volunteer for next year's workshop to be held just before the 2011 SSR meeting in Portland, Ore. Binder, who also chaperoned students arriving at the workshop by bus, said, "I love the energy and enthusiasm of the kids, and I hope to be involved again next year. It's a great way to learn how to explain your science to people with limited science backgrounds and, hopefully, motivate youth to explore scientific careers in the future."

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Binder has been at NIEHS only a few months, but she's already complementing her training at the bench with career development experiences in other areas of science. (Photo courtesy of Steve McCaw)

Former trainee builds mentoring program at NCSU

By Bono Sen

When former postdoctoral fellow Shweta Trivedi, Ph.D., was taking advantage of her many mentoring opportunities at NIEHS, little did she know that she would one day be building a highly successful mentoring program of her own at North Carolina State University (NCSU). As she enters her second year as head of [VetPAC, the Veterinary Professions Advising Center](#), Trivedi's program stands out as a model for other universities in maximizing retention and placement of pre-veterinary students.

[Trivedi](#) received her veterinary training in India and her Ph.D. in immunology at the NCSU College of Veterinary Medicine. During her two years as a fellow at NIEHS, Trivedi was a member of the Environmental Genetics Group headed by Principal Investigator Steven Kleeberger, Ph.D. Trivedi left NIEHS in 2009 to accept a position as a teaching assistant professor at NCSU. Once there, she was charged with setting up a program for pre-vet students modeled on the university's HealthPAC, the Health Professions Advising Center, created three years earlier.

Trivedi says the mentoring she received from Kleeberger and Diane Klotz, Ph.D., director of the Office of Fellows Career Development, helped her immensely in setting up the innovative program within the NCSU College of Agriculture and Life Science.

"VetPAC is unique in that very few land-grant universities offer such a centralized advising program for their pre-vet students," said Trivedi. In her capacity as the director of VetPAC, she advises students and develops new programs in partnership with local and international organizations to enhance the students' pre-vet training experience.

VetPAC has teamed up with the Wake County Animal Center to provide pre-vet undergraduate students the opportunity to experience all aspects of care for shelter animals. For those students interested in wildlife conservation and management, Trivedi has created a new study abroad program where the students can participate in a two-week-long program at the Wildlife Institute of India studying tiger rehabilitation in the national parks of India.

By enriching her program with resources such as the new Vet-PAC library, invited-speaker seminars, and individual mentoring that she developed during her first year at NCSU, Trivedi's objective is to expose the students to the expanse of the veterinary profession and to help them get accepted to their veterinary school of choice. "I am also working on our Website, so that students can begin to build their portfolios toward vet school application," she said.

Trivedi's vision for the program and her ability to anticipate students' needs are already paying off. In her first year alone, she placed 28 VetPAC advisees into various DVM programs across the country. She said she expects the number to grow as more students learn about VetPAC and take advantage of its network of resources.

Besides advising, Trivedi also has teaching responsibilities. She teaches anatomy and physiology as well as animal science to 100-140 students each semester. She hopes to add research to her list of responsibilities soon. For now, though, she is thoroughly enjoying her role as a mentor.

(Bono Sen, Ph.D., is the science education and outreach program manager for the NIEHS journal Environmental Health Perspectives.)

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Roman to head EEO

By Eddy Ball

NIH Hispanic Employment Program Manager Gerard Roman will lead support services to NIEHS as the Institute's NIH equal opportunity and diversity management specialist, according to an Aug. 23 announcement by NIH. He fills a void created with the departure of former NIH Equal Employment Opportunity (EEO) Specialist Ginny Ivanoff, ensuring a continuity of equal opportunity and diversity promotion management for the Institute's employees and managers.

Roman said of his new role, "It's good to be once again connected to the NIEHS. ... In this added role, I look forward to becoming more involved in serving as a liaison to the services provided to the NIEHS by the NIH Office of Equal Opportunity and Diversity Management (OEODM)."

As part of OEODM, Roman works with a team of professionals who manage equal opportunity and diversity promotion for an 18,000-person NIH workforce. At NIEHS, he will assist with action items related to national and internal reports on equal opportunity and diversity, provide information sessions for managers and supervisors, work on disability employment issues, and help mediate employee and management concerns.



Former postdoc Shweta Trivedi, above, now works at the other end of the mentoring lifeline. She credits her experiences as a fellow at NIEHS with preparing her for a challenging and exciting career path. (Photo courtesy of Steve McCaw)

“There’s never a boring minute,” Roman said of the job. “Most of our work at OEODM is typically performed behind the scenes.”

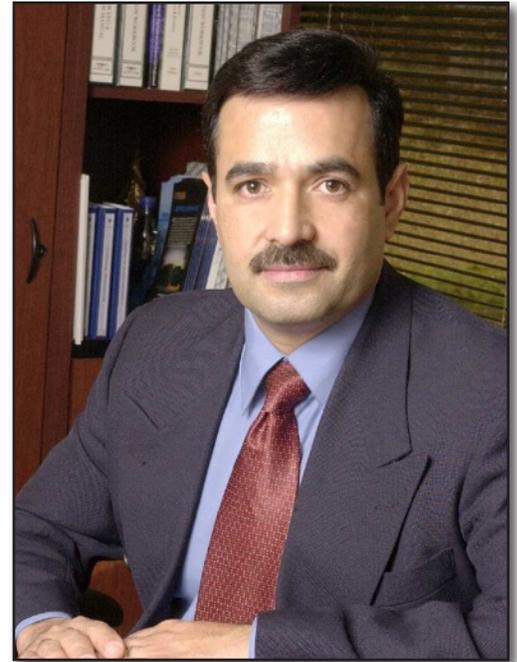
Roman has worked in the field of equal opportunity and diversity promotion for nearly 20 years. In 1990, while serving in the Army Roman was selected for training and a special assignment at the Department of Defense Equal Opportunity Management Institute. His last assignment was as the senior equal opportunity staff advisor for three installations overseas servicing more than 15,000 military service members, Department of Defense civilians, and local nationals.

Following a distinguished 20-year military career and two years of civilian federal service, Roman joined NIEHS in 2002. He became part of the NIH OEODM after the office underwent reorganization in 2006.

Roman has completed training in EEO and human relations, with equal opportunity advisor, equal employment officer, and equal employment specialist resident courses from the Department of Defense Equal Opportunity Management Institute. He has a B.S. from Troy State University in Alabama and a master’s in human relations from the University of Oklahoma. Roman is now completing his final research project for a Ph.D. in human services from Walden University.

“Over the years, I’ve seen how the functions of equal employment opportunity have expanded from overseeing civil rights and equal employment protections, to more involvement in the intricate area of workforce diversity,” Roman explained. “In my new role here at NIEHS, I am committed to providing the most professional support possible and help the employees who make NIEHS a great place to work.”

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NIH Hispanic Employment Program Manager Gerard Roman takes on the added responsibilities of EEO Specialist at NIEHS. (Photo courtesy of Steve McCaw)

Keystone lecture explores the challenges of mixtures research

By Melissa Kerr

Biochemist Andreas Kortenkamp, Ph.D., spoke as a part of the Keystone Science Lecture Seminar Series during his visit to NIEHS June 23. Kortenkamp's presentation, titled "Mixtures: The Future of Toxicology Research, Testing and Risk Assessment," explored the different approaches and many challenges involved in mixtures research. The presentation was hosted by NIEHS Health Scientist Administrator Jerry Heindel, Ph.D.



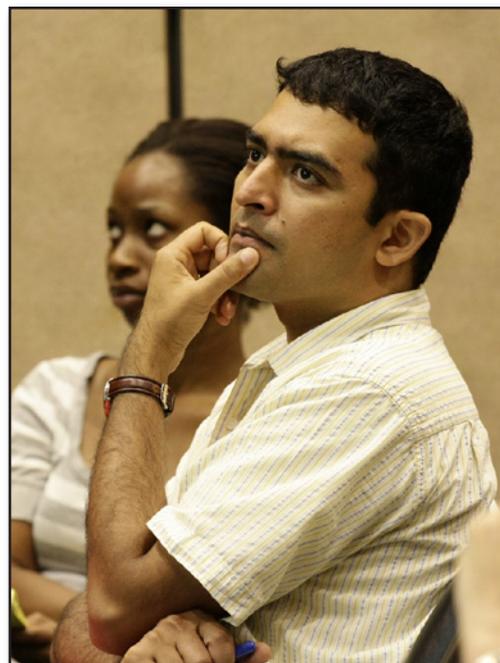
Kortenkamp is well known for his seminal paper in the mixtures field, "Something from 'nothing'" — which demonstrated the significant mixture effects of eight weak estrogenic chemicals combined at concentrations below the level of no observed effect concentrations. (Photo courtesy of Steve McCaw)



Looking to future directions in extramural program research

[Kortenkamp](#) has a worldwide reputation as an expert and pioneer within the field of chemical mixture research. His recent research follows endocrine disrupting compounds in the environment and the possibility that these chemicals contribute to the rising incidence of breast and testicular cancer. Kortenkamp is a professor and the head of the Centre of Toxicology in the School of Pharmacy at the University of London. He is also head of the mixtures consortium at the European Union.

As Heindel explained in his introduction, NIEHS scientists recently gathered to discuss future directions for NIEHS-supported research in chemical mixtures and to "figure out what we [at NIEHS] can really do to move forward in this field and have a big impact." In the at-capacity audience were scientists from throughout the Institute with interests in mixtures research, including several members of intramural and extramural programs, as well as the National Toxicology Program, including Chief of the NTP Biomolecular Screening Branch, Ray Tice, Ph.D., and NTP Associate Director John Bucher, Ph.D.



Kortenkamp's talk attracted scientists from throughout NIEHS, such as Intramural Research Training Award (IRTA) Fellow Arun Pandiri, Ph.D., who works in the Investigative Pathology Group. (Photo courtesy of Steve McCaw)

Defining "mixtures" and designing studies of their effects

Kortenkamp began his lecture by specifying his definition of mixtures in relation to the thousands of chemicals in the environment

that may end up in human tissue. “How can we deal with co-exposure to a large number of chemicals and how can we assess their effects?” he asked. As he described the ways a scientist could assess a particular mixture, Kortenkamp said he prefers a component-based analysis. A central concern in current mixture research is assessing whether a group of chemicals act in an additive fashion or antagonistically.

Delving into the history of multiple-chemical studies, Kortenkamp identified inconsistencies in past investigations. In general, he explained, human toxicology studies were inadequately designed and the combination effects indeterminate, whereas ecotoxicology studies were more adequately designed and the combination effects were evident. A large part of the problem, he said, was a tendency to not use a hypothesis.



Also intrigued by the talk were, left to right, NTP IRTA Fellow Erik Tokar, Ph.D., Epidemiology Branch IRTA Fellow Todd Jusko, Ph.D., Summers of Discovery intern Arielle Sloan, and NTP Staff Scientist Retha Newbold. (Photo courtesy of Steve McCaw)

The critical need for prioritizing and grouping chemicals

The current problem lies, according to Kortenkamp, in prioritizing and grouping chemicals. As yet, guidelines for grouping criteria are unclear. The U.S. Environmental Protection Agency groups chemicals according to similarity of mechanisms, while Kortenkamp argues that chemicals should be grouped by common adverse outcomes. Referring to endocrine disruption as an example, he said, “It doesn’t matter very much by which detailed molecular mechanism androgen action in fetal life was disturbed, because the outcome will be similar.”

According to Kortenkamp, there is an unfortunate trend among scientists to stick with one major chemical component despite the thousands of other possibilities in the environment. For example, many toxicologists have considered that *pp*'DDE, the main metabolite of the parent compound *pp*'DDT, is linked to breast cancer. However, Kortenkamp said his research indicates that it contributes very little. He said that seven chemicals explained more than 90 percent of expected combination effects in his experiments, and *pp*'DDE was very far down the list, compared to several others that have not been as well researched.



As Heindel, right, demonstrated, one purpose of the Keystone Lecture Series is to offer administrators insight into future directions for the extramural grants portfolio by hosting guest speakers who are experts in fields of interest. (Photo courtesy of Steve McCaw)

As he looked to the future of chemical mixtures research, Kortenkamp said he hopes to see a decline in the trend of researching “your favorite chemical.” He would like to see the development of a more useful way for defining a mixture of concern. He also said that exploring what he calls the dirty dozen chemicals should be a high priority, as should investigating fractionations of compounds and focusing on additional endpoints.

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

Students showcase Summers of Discovery research

By Melissa Kerr

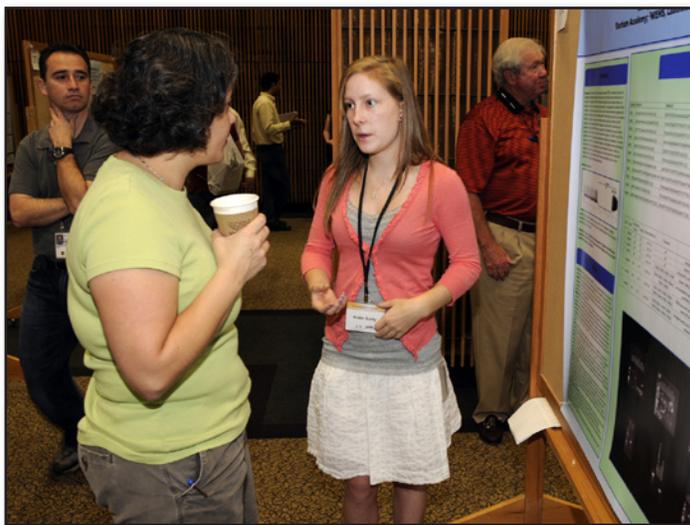
Participants in the NIEHS Summers of Discovery (SOD) program brought to fruition several weeks of working with mentors to develop the necessary data for a successful presentation at the program's annual poster competition. Held in the Institute's Rodbell Auditorium July 29, the event showcased the work of the 41 students who displayed the results of their summer work in Institute labs. For the Institute's scientific community, the annual SOD poster session is a time to reach out to the next generation of biomedical researchers and be reminded of the youthful curiosity that inspired their own careers in the field.

At the poster session, fellow students, postdoctoral fellows, and NIEHS scientists negotiated the labyrinth of presentation boards, each with an abstract and a proud first author eager to explain the results. It was the interns' time to show off what they had learned during the summer and share their enthusiasm about the science involved.

With the help of the SOD program, each summer NIEHS continues to mentor and excite future scientists. Interns are paired with mentors based on their individual interest and spend the summer working on a research project. It's not unusual for interns' summer projects to eventually become peer-reviewed publications or presentations at scientific meetings.

For some of the participants, the program offers a chance to experience the inner workings of a laboratory for the first time. As SOD coordinator Debbie Wilson noted, this summer there were twice as many high school students as last year.

For others, the internship can be potentially career changing. Melissa Ricker, an undergraduate student at North Carolina State University, said of the experience, "This has opened a new door for me." She expressed gratitude toward her mentor, Robert London, Ph.D., calling the experience "the best summer of my life." She said London's instruction and knowledge, as well as his humor, guided her as the summer progressed.



The poster session is an opportunity for young scientists to get a taste of what they're sure to spend much of their careers doing — explaining and defending their science before other scientists. Durham Academy student Kristin Sundy, right, talks with NIEHS Biologist Mercedes Arana, Ph.D., of the DNA Replication Fidelity Group. (Photo courtesy of Steve McCaw)



Catherine Hollister, left, a student at Cardinal Gibbons High School in Raleigh, posed with her proud mother, Piedmont Research Center Vice President Beth Hollister, center, and Comparative Medicine Branch Microbiologist Julius Thigpen, Ph.D. Thigpen was one of Hollister's mentors and second author on her study. (Photo courtesy of Steve McCaw)

During the poster session, each young scientist must articulate the contents of his or her poster and the research involved, as well as field questions and observations from senior scientists. For Eason Lee, winner of the undergraduate division of the poster session, the process of determining a question and then finding an answer through the scientific method was a great reward. “The constant repeating of experiments, the discussions and pointed questions of the poster session, and the excitement of seeing a new or successful result — that’s the essence of the research I’m glad I got to experience this summer.”

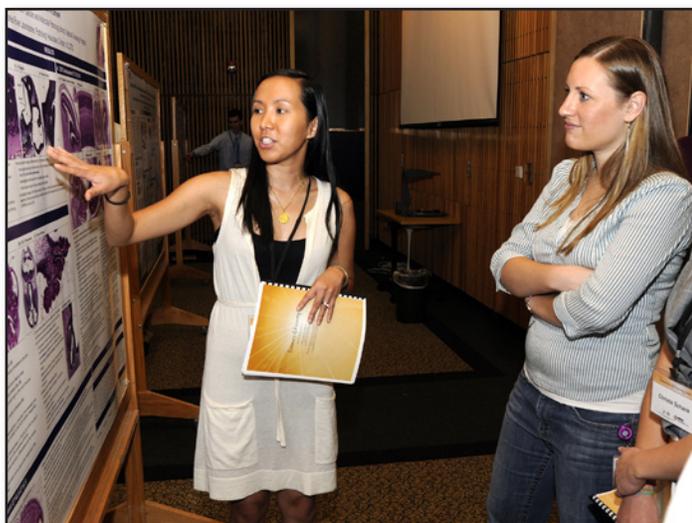
Later in the day, NIEHS Deputy Director Bill Schrader, Ph.D., presented awards for the best posters (see text box). Schrader opened the ceremony by saying, “Science is fun.” He said he hoped that the students were able to foster and expand an interest in science, as he prepared to name the winners in the high school, undergraduate, and graduate categories.

The posters were judged by postdoctoral fellows on the quality of the science, the poster presentation, and the oral presentation. Diane Klotz, Ph.D., director of the NIEHS Office of Fellows’ Career Development, spoke to the students about the success of the poster presentations and said, “The postdocs were overwhelmingly impressed with the level of science.” Klotz closed the ceremony by inviting the students to keep in touch with her and let her know how they progress as they pursue the exciting discoveries that science has to offer.

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



High school division poster winner Sawyer Bowman, right, explained his research to NIEHS DNA repair expert Mike Resnick, Ph.D., principal investigator in the Chromosome Stability Group. (Photo courtesy of Steve McCaw)



North Carolina State University (NCSU) veterinary student Vivian Chen, Ph.D., described her work on an atlas of brain histology to fellow SOD interns. She worked this summer with her NTP mentors, Pathology Group Staff Scientist Susan Elmore, D.V.M., and Biologist Julie Foley, and Charles River Laboratories representative James Morrison. (Photo courtesy of Steve McCaw)



Brian Rogers, left, talks with fellow intern Adrian Russell. Rogers’ poster won first place in the graduate division. (Photo courtesy of Steve McCaw)



Non-scientists, such as Ethics Coordinator Jackie Stillwell, right, also enjoyed learning about the students' summer research. NCSU student Julie Wofford explained her analysis of mite allergen in the NIEHS Nuclear Resonance Imaging facility. (Photo courtesy of Steve McCaw)



Holding his first place award in the undergraduate division, Duke University student Eason Lee posed with NIEHS Deputy Scientific Director Bill Schrader, Ph.D. Lee said of his summer at NIEHS, "I was able to do a project that combined engineering design while also probing a biological question." (Photo courtesy of Steve McCaw)



After the awards were presented, interns had a chance to enjoy the traditional end of summer ice cream social in the NIEHS cafeteria. (Photo courtesy of Steve McCaw)

And the winners are...

- High School — Sawyer Bowman, a student at the Woodlawn School in Davidson, N.C., studied correlation in Quantitative High Throughput Screening (qHTS) data. The challenge he faced was finding ways to identify patterns and interpret the large amounts of data that the qHTS approach produces, as well as how to represent the data. Bowman was mentored by NTP Biomolecular Screening Branch Chief [Raymond Tice, Ph.D.](#), and Staff Scientist Keith Shockley, Ph.D.
- Undergraduate — Eason Lee, a student at Duke University's Pratt School of Engineering, studied ways to extend the viability of the brain capillaries in order to manipulate blood-brain barrier function. On his project, "A superfusion system extended the viability three-fold and has the potential to further extend the viability with slight alterations to the procedure," Lee worked with mentors [David Miller, Ph.D.](#), NIEHS principal investigator and chief of the Laboratory of Toxicology and Pharmacology, and Intracellular Regulation Group Staff Scientist Ronald Cannon, Ph.D.
- Graduate — Brian Rogers, a student at the Howard University School of Medicine, studied the use of global gene expression profiling in relation to development and progression of hepatocellular carcinoma (HCC). He found that dysregulation of several genes within mice paralleled HCC in humans, therefore providing a more effective model to study the human disease. NIEHS Investigative Pathology Group Leader [Mark Hoenerhoff, Ph.D.](#), was the principal investigator on Roger's study, which included eight coauthors from the NTP Cellular and Molecular Pathology Branch, NIEHS Biostatistics Branch, and NIEHS Laboratory of Toxicology and Pharmacology.

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MAGE-11 regulation of androgen receptor

By Sophie Bolick

On August 3, the NIEHS Receptor Mechanisms Discussion Group welcomed Elizabeth Wilson, Ph.D., the most recent speaker in its monthly lecture series and an expert on androgen receptor regulation. Hosted by Ken Korach, Ph.D., and John Cidlowski, Ph.D., Wilson discussed her work in a talk on “Regulation of Androgen Receptor Transcription by MAGE-11.”

Wilson, who is a professor at the University of North Carolina at Chapel Hill School of Medicine, reported on her research on the primate-specific melanoma antigen gene protein-A11 (MAGE-11). She discussed the discovery of MAGE-11, as well as its binding partners and potential involvement in the development and treatment of prostate cancer.

Androgen receptor binding

The androgen receptor (AR) is a member of the nuclear receptor family of steroid hormone receptors. AR binds with high affinity and specificity the active androgens, testosterone and dihydrotestosterone, which can be disrupted by environmental agents. Similar to other members of the steroid receptor family, AR is comprised of domains important for hormone and DNA binding.

The crystal structure of AR (see text box) shows that the AR ligand binding domain is capable of interacting with the p160 coactivator LXXLL motif as well as its own amino terminal FXXLF motif.

According to Wilson, this competition for the ligand binding domain “sets up a dilemma for the androgen receptor because, on the one hand, AR wants to be activated by p160 coactivators. On the other hand, AR has an FXXLF motif within its own structure that binds with higher affinity the same AF2 hydrophobic groove that binds the coactivator LXXLL motif.”

Identification of MAGE-11

To address this dilemma, Wilson proposed “that perhaps a protein exists that binds the FXXLF motif and interferes with the AR amino/carboxy interaction and allows the activation of function 2 (AF2) site [in the ligand binding domain] to bind a coactivator.” Using a yeast two-hybrid screen to approach this experimentally, she identified MAGE-11.

MAGE-11 stabilizes AR in the absence of ligand because it can bind the FXXLF motif. MAGE-11 is an



Wilson, above, shared the excitement of her detective work identifying a previously unappreciated player in hormone receptor activity. Her groundbreaking work on MAGE-11 has resulted in a number of publications over the past few years. (Photo courtesy of Steve McCaw)



Questions and comments from the audience provide for an open exchange of ideas on the first Tuesday of each month, as the Receptor Mechanisms Discussion Group hosts guest speakers in the informal setting of the NIEHS Executive Conference Room. (Photo courtesy of Steve McCaw)

AR co-regulator that co-localizes with AR in nuclei of human Sertoli cells, endometrium, and granulosa cells. Due to its lack of expression in the mouse and rat, there is a need to establish biological systems to allow study of MAGE-11 in the human.

AR and MAGE-11 in prostate cancer

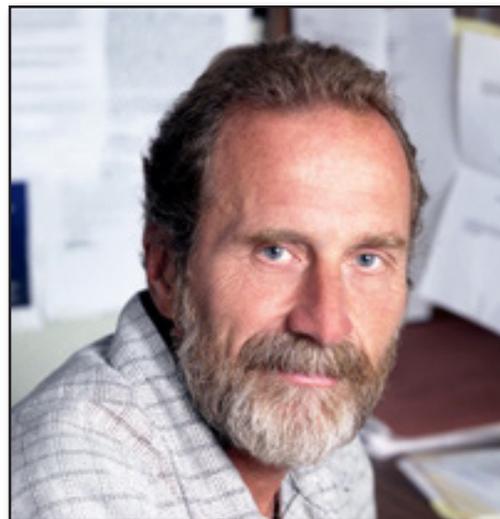
As Wilson explained, the AR is important at all stages of prostate cancer development and progression. There is an increase in the levels of the AR coactivator TIF2 and MAGE-11 in castration-recurrent prostate cancer. One mechanism for this increase in expression is thought to be due to DNA methylation. The CpG island in the MAGE-11 promoter is extensively methylated in human benign prostatic hyperplasia (BPH) and androgen-dependent prostate cancer, but is hypomethylated in castration-recurrent prostate cancer patient samples.

Tissue microarray studies of patient biopsies stained for MAGE-11 protein expression show evidence for some MAGE-11 staining in BPH samples, even though the MAGE-11 promoter is highly methylated in these samples. While the reason for this may be related to the cell cycle-dependent expression of MAGE-11, it is evident from these studies that MAGE-11 protein expression increases with prostate cancer progression.

MAGE-11 interaction with co-regulators

A series of experiments using AR deletion mutants demonstrated the interaction of MAGE-11 with coactivators TIF2 and CBP/p300. MAGE-11 links the amino terminal region of AR with the p300 histone acetyltransferase to increase AR transcriptional activity. A series of FXXLF-like motif interactions mediate the formation of a transcription complex containing AR, MAGE-11, p300, and TIF2 that is modulated by the AR amino/carboxy interaction.

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



Co-host John Cidlowski is chief of the NIEHS Laboratory of Signal Transduction and principal investigator of the [Molecular Endocrinology Group](#). (Photo courtesy of Steve McCaw)



Co-host Kenneth Korach is chief of the NIEHS Laboratory of Reproductive and Developmental Toxicology and principal investigator of the [Receptor Biology Group](#). (Photo courtesy of Steve McCaw)

Crystal structure of androgen receptor ligand binding domain resolved

The amino terminus of the AR contains an FXXLF motif. The AR ligand binding domain in the carboxyl-terminus contains an AF2 hydrophobic region that interacts with the AR FXXLF motif (the AR amino/carboxy interaction) and with LXXLL motifs of p160 coactivators. In collaboration with Robert Gampe of GlaxoSmithKline, Wilson resolved the crystal structure of the AR ligand-binding domain bound to R1881 and FXXLF or LXXLL peptide. The interaction between the AR FXXLF motif with AF2 suggests an anti-parallel orientation of AR dimers, in which the amino terminus of one AR monomer is oriented across from the carboxy terminus of the opposing monomer.

Study on early puberty advances breast cancer research

By Eddy Ball

A new study led by NIEHS-funded investigators adds to widespread concern among parents, physicians, and researchers that girls are increasingly entering puberty at an earlier age. The study was co-funded by the National Cancer Institute (NCI) and led by two NIEHS grantees — University of Cincinnati (UC) pediatrician [Frank Biro, M.D.](#), first author, and Mount Sinai School of Medicine preventive medicine and oncological sciences specialist [Mary Wolff, Ph.D.](#), principal investigator.

The findings also support a protocol for use in large-scale studies by the NIEHS/NCI [Breast Cancer and the Environment Research Centers \(BCERC\)](#) that examine environmental factors involved in the development of breast cancer. While the study set out to report the maturation status of a cohort of 1,239 girls at ages 7 and 8 years — and their findings are dramatic ([see text box](#)) — a significant outcome was a pubertal assessment protocol that could add reliability and standardization across multiple sites for longitudinal studies of larger, nationally representative cohorts.

“What causes earlier onset of puberty isn’t entirely clear at this time, but we are looking closely at several different potential factors, including genes and environmental exposures, as well as how those two may interact with each other,” said Biro in a UC HealthNews report. Biro is the director of adolescent medicine at Cincinnati Children’s Hospital Medical Center and a professor of pediatrics at the UC College of Medicine.



*Biro was one of three physicians involved in training clinical staff to evaluate breast and pubic hair development in the subjects.
(Photo courtesy of the University of Cincinnati)*

According to the researchers, a number of epidemiological studies have found a significant association between early onset of pubertal maturation and increased risk of developing breast cancer — possibly due to greater lifetime exposure to female hormones and the susceptibility of rapidly developing breast tissue to environmental exposures. Past studies, however, have used different criteria to evaluate sexual maturation in girls.

Determining onset of puberty

The new study successfully implemented a clinical assessment method for using measurement of breast and pubic hair development in determining the onset of puberty. Teams of physicians, nurse practitioners, and research staff examined girls in East Harlem, the Cincinnati metropolitan area, and the San Francisco Bay area, after training in a standardized protocol and scoring criteria.

Investigators and study coordinators used what is known as the Marshall and Tanner criteria to measure breast maturation and pubic hair stages in the subjects. Clinical staff underwent a training program with the three physicians involved in the study, including the review of photographs of anonymous girls at various stages of development, and then performed dual examinations of a group of peripubertal girls. At each of the sites, one of the three physicians also performed inter-rater assessments for quality assurance to maintain comparability among the centers.

By minimizing measurement error between sites and examiners, the researchers sought to better account for differences among sites that may be influenced by environmental exposures and dietary patterns.

Looking ahead

The researchers were candid about the weaknesses of their study, which include a small cohort, possible recruitment bias, and baseline differences in maturation by site. However, the consistency of assessment across the three BCERC sites was a major accomplishment, overcoming some of the methodological limitations in earlier studies.

“The ability to capture with reasonable accuracy the timing and tempo of pubertal breast maturation in this prospective study,” they concluded, “should allow us to pool data for detecting associations between specific factors, including diet and environmental chemicals with variations in patterns of pubertal maturation.”

Citation: [Biro FM, Galvez MP, Greenspan LC, Succop PA, Vangeepuram N, Pinney SM, et al.](#) 2010. Pubertal Assessment Method and Baseline Characteristics in a Mixed Longitudinal Study of Girls. *Pediatrics*. [Epub ahead of print]

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A disturbing trend for the next generation of young women

Anecdotal accounts from parents and physicians, as well as associations found in epidemiological studies, point to progressively earlier maturation among young girls today than among young girls studied 10 to 30 years earlier. According to the study led by Biro and Wolff, girls in their cohort showed high rates of breast stage 2 development at age 7 and 8:

- At age 7, 23.4 percent of black non-Hispanic girls, 14.9 percent of Hispanic, and 10.4 percent of white girls had reached stage 2
- At age 8, the rates had as much as doubled, with 42.9 percent of black non-Hispanic, 30.9 percent of Hispanic, and 18.3 percent of white girls measured at stage 2.

The study reports that higher BMI, older age, black race, and being from the Harlem or Cincinnati site were also associated with breast stage 2 or greater development. The proportion of white girls with stage 2 development at age 7 was more than twice that reported in a 1997 study of the Pediatric Research in Office Settings Network.

The authors note that earlier maturation in girls is associated with breast and endometrial cancer, hyperinsulinemia, and elevated blood pressure. It is also associated with potentially harmful psychological effects, such as low self-esteem, eating disorders, suicide, and engagement in risky behavior.

High-throughput screening of mitochondrial toxicity

By Mamta Behl

The NTP Biomolecular Screening Branch (BSB) hosted a talk by Craig Beeson, Ph.D., July 30 on “High-Throughput Respiriometric Assay for Mitochondrial Biogenesis and Toxicity” as part of the [NTP High-Throughput Screening Initiative](#). Beeson described the results he has obtained using the Seahorse Bioscience XF analyzer for real-time measurement of mitochondrial function in adapted primary cultures of renal proximal tubular cells.

As an associate professor in the Department of Pharmaceutical and Biomedical Sciences and the director of the Metabolomics Core and Drug Design and Synthesis Core at the Medical University of South Carolina, [Beeson](#) focuses on the biochemical networks responsible for the regulation of energy metabolism and cellular proliferation and their potential applications in the areas of predictive toxicology and drug discovery.

Mitochondrial toxicity assays in the Tox21 partnership

“The BSB is evaluating mitochondrial toxicity as a potential toxicity pathway using *in vitro* studies as part of its high-throughput screening initiative,” NTP molecular toxicologist and lecture host [Scott Auerbach, Ph.D.](#), said of the branch’s decision to invite Beeson to speak at NIEHS.

The NTP, NIH Chemical Genomics Center (NCGC), and U.S. Environmental Protection Agency (EPA), along with their most recent partner, the U.S. Food and Drug Administration (FDA), are striving to advance the state of [toxicity testing in the 21st century](#) through a consortium known as Tox21. The consortium is seeking to identify new mechanisms of chemical activity in cells, effectively prioritize the backlog of untested chemicals for more extensive evaluations, and develop better predictive models of human response to such toxicants as industrial and environmental chemicals and drugs.



“RPTCs cultured under standard conditions in which they are stationary with glucose medium have basal oxygen consumption rates 100-fold lower than those for RPTCs cultured under optimized conditions in which they were shaken with lactate as media,” explained Beeson. (Photo courtesy of Steve McCaw)

Overcoming limitations in current mitochondrial cell-based assays

Although many drugs and chemicals are mitochondrial toxicants, according to Beeson, assessing mitochondrial function has posed a challenge for investigators, because there is no direct high-throughput assay for mitochondrial function. In addition, the current cell-based models of mitochondrial toxicity are inadequate, because immortalized cell lines have lost differentiated function and are highly glycolytic, with minimal aerobic metabolism and altered mitochondrial physiology.

Beeson said that although roughly half of the drugs with FDA black box warnings for hepatotoxicity or cardiotoxicity also have documented mitochondrial effects, the same level of attention has not been given for nephrotoxicity, despite the frequency of loss in renal function due to adverse drug effects and xenobiotic exposure.

To address this issue, Beeson’s group adapted primary renal proximal tubular cells (RPTCs) as a model to study mitochondrial loss following oxidative injury. “In contrast to immortalized cells, RPTCs are robust primary cells, which are completely differentiated and polarized with good brush border enzyme activity and sodium-dependent glucose transport,” Beeson explained. “The RPTCs are somewhat unique among differentiated tissues in that they have some capacity for repair and regeneration,” he added. Beeson described the use of multiple endpoints, such as basal and uncoupled respiration rates, and provided examples of compounds that induce increased uncoupled respiration, confirming that it is a biomarker of mitochondrial biogenesis.



Auerbach, above, moderated active discussion on potential upstream energy stress depletion signals which, in turn, may alter the ATP/AMP ratio in the mitochondria. (Photo courtesy of Steve McCaw)

Collaborative efforts for a promising future

Beeson provided examples of loss of respiratory capacity of the mitochondria in degenerative diseases such as retinitis pigmentosa and macular degeneration, as well as the development of novel molecular models, known as pharmacophores, that serve as computational templates for discovering drugs to use in their treatment. “Our strategy involves looking at protection of the uncoupled rate for new molecules in the prevention of these disorders,” concluded Beeson.

The lively discussion enabled researchers at the NTP to identify several areas of mutual interest where collaborations might be possible. “One area of immediate interest is in applying Dr. Beeson’s mitochondrial toxiphore descriptor model to the Tox21 10K-compound library that will be tested for mitochondrial toxicity in high-throughput mode at the NIH Chemical Genomics Center,” said BSB Chief [Ray Tice, Ph.D.](#)

Citation: [Beeson CC, Beeson GC, Schnellmann RG](#). 2010. A high-throughput respirometric assay for mitochondrial biogenesis and toxicity. *Anal Biochem* 404(1):75-81. Epub ahead of print.

(Mamta Behl, Ph.D., is a research fellow in the NTP Toxicology Branch.)



Beeson was the latest in a series of speakers Tice has invited to NIEHS whose research has direct bearing on the high-throughput screening initiative. “Given our interest in identifying mitochondrial toxicants, we are very pleased that Dr. Beeson found the time in his busy schedule to present his research findings and meet with key NTP staff,” Tice said. (Photo courtesy of Steve McCaw)

The Seahorse technology for high-throughput screening

The limitation in the availability of high-throughput real-time assays to assess mitochondrial function poses additional restrictions in the screening of mitochondrial toxicity. The existing high-throughput assays often use alterations in mitochondrial gene expression thereby leading to false negatives and false positives due to lack of correlation between messenger RNA and [biogenesis](#). To circumvent this problem, the [Seahorse Biosciences XF](#) analyzer was recently introduced. Using this technique, researchers can measure shifts between aerobic respiration and glycolysis as a result of genetic, pharmacologic, or physiologic manipulation simultaneously and non-invasively using a medium- to high-throughput platform.

Beeson’s laboratory utilized the Seahorse technology to demonstrate that known toxicants produced concentration-dependent changes in respiratory capacity. “Mitochondrial damage is a phenotypic stress response and is detected prior to cell death, suggesting its role in capturing chronic toxicity,” he explained.

According to Auerbach, investigators at NIEHS can access the Seahorse analyzer through one of NTP’s contractors.

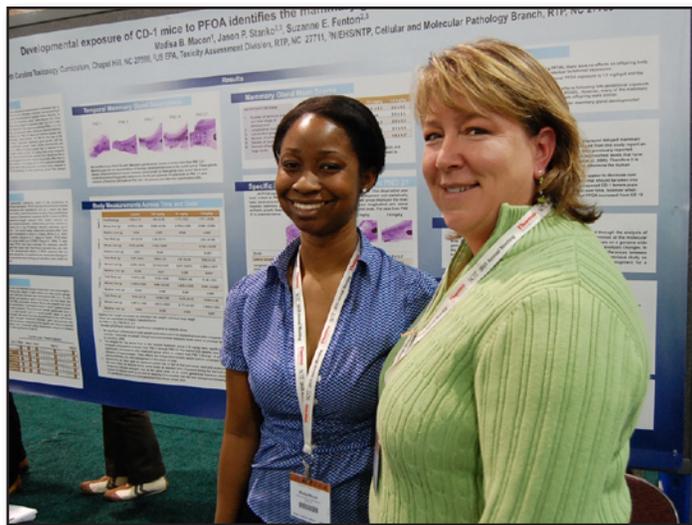
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Atrazine causes abnormalities in male rats

By Robin Mackar

A new NIEHS-funded study shows that male rats prenatally exposed to low doses of atrazine, a widely used herbicide, are more likely to develop prostate inflammation and to go through puberty later than non-exposed animals. The research adds to a growing body of literature on atrazine, an herbicide predominantly used to control weeds and grasses in crops such as corn and sugar cane. Atrazine and its byproducts are known to be relatively persistent in the environment, potentially finding their way into water supplies.

The research was led by NIEHS scientists Suzanne Fenton, Ph.D., and Jason Stanko, Ph.D. Fenton began the work as a researcher at the United States Environmental Protection Agency (EPA), but completed the research at NIEHS, working closely with NIEHS pathologists. Both NIEHS and EPA provided financial support for the [study](#).



Fenton, right, joined student Madisa Macon during the poster presentation at the Society of Toxicology meeting earlier this year. (Photo courtesy of Ed Kang)

The study, which is available online and will be featured on the cover of *Reproductive Toxicology*, found that the incidence of prostate inflammation rose from 48 percent in the control group to 81 percent in the male offspring who were exposed to a mixture of atrazine and its breakdown products prenatally. The severity of the inflammation increased with the strength of the doses. Puberty was also delayed in the animals that received atrazine.

The doses of atrazine mixture given to the rats during the last five days of their pregnancy are close to the regulated levels in drinking water sources. The current maximum contamination level of atrazine allowed in drinking water is 3 parts per billion. The doses given to the animals were 0.09 (or 2.5 parts per million), 0.87, or 8.73 milligrams per kilogram body weight.

“We didn’t expect to see these kinds of effects at such low levels,” Fenton said. She adds that this is the second paper to show low dose effects of atrazine metabolite mixtures. Fenton was the senior author on a 2007 paper which demonstrated low doses of the atrazine mix delayed mammary development in female siblings from the same litters used in this current study.

“It was noteworthy that the prostate inflammation decreased over time, suggesting the effects may not be permanent,” said David Malarkey, D.V.M., Ph.D., an NIEHS pathologist and co-author on the paper.

Fenton points out that these findings may extend beyond atrazine alone, and may be relevant to other herbicides found in the same chlorotriazine family, including propazine and simazine. All three of the herbicides create the same set of breakdown products.

Fenton says more research is needed to understand the mechanism of action of the chlorotriazines and their metabolites on mammary and prostate tissue. “These tissues seem to be particularly sensitive to the effects of atrazine and its breakdown products,” Fenton added. “The effects may be due to the stage of fetal development at the time the animals were exposed.”

“We hope that this information will be useful to the EPA as it completes its risk assessment of atrazine,” said Linda Birnbaum, Ph.D., NIEHS/NTP director.

Fenton will present her research findings in September to the EPA, as part of its reassessment of atrazine. EPA announced in 2009 that it had begun a comprehensive new evaluation of atrazine to determine its effects on humans. At the end of this process, the agency will decide whether to revise its current [risk assessment](#) of atrazine and whether new restrictions are necessary to better protect public health.

Citation: [Stanko JP](#), [Enoch RR](#), [Rayner JL](#), [Davis CC](#), [Wolf D](#), [Malarkey DE](#), [Fenton SE](#). Effects of prenatal exposure and prostate development of male Long Evans rats. *Reprod Toxicol*. Epub ahead of print. DOI:10.1016/j.reprotox.2010.07.006

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

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NIEHS-led study advances predictive genomics

By Thaddeus Schug

In a new study published online July 30, a team of 23 investigators led by NIEHS bioinformatician Pierre Bushel, Ph.D., shows that genomic indicators in the blood can serve as diagnostic biomarkers predictive of drug-induced liver injury (DILI).

The study, which points to potential applications in the clinical setting and in drug discovery, provides a proof of principal for ongoing efforts by the MicroArray Quality Control Phase II (MAQC-II) project led by Leming Shi, Ph.D., of the U.S. Food and Drug Administration (FDA) National Center for Toxicological Research (NCTR) to develop best practices for microarray gene expression utilization in biomarker discovery.

According to the authors of the [study](#), drug-induced hepatotoxicity results in thousands of emergency room visits each year and is the major cause for a drug to be withdrawn from the market, have its use restricted, or be required to use a warning label. They explain that DILI is difficult to diagnose in its early stages with serum markers currently in use or by liver biopsy.

“There’s a huge need to put better information in the hands of clinicians, and I think genomics is an important tool for helping us reach that goal,” said one of the coauthors of the study, Rick Paules, Ph.D. Paules is a senior scientist and principal investigator in the Laboratory of Toxicology and Pharmacology and director of the NIEHS Microarray Core facility.



Bushel is head of the Microarray and Genome Informatics Group in the NIEHS Biostatistics Branch. With his colleague, Paules, Bushel has been instrumental in spearheading the Toxicogenomics Integrated with Environmental Science series of international conferences. (Photo courtesy of Steve McCaw)

The NIEHS-led study is one of 11 papers published in a special August 2010 issue of The Pharmacogenomics Journal (TPJ) by researchers in the MAQC-II consortium. Bushel, Paules, National Toxicology Program Scientific Administrator Jennifer Fostel, Ph.D., and other NIH members are also co-authors on a [summary report](#) of the entire MAQC-II project published online July 30 in Nature Biotechnology.

Genomic indicators predict a phenotype of toxicity

To test the utility of genomic indicators for predicting very early stage DILI, the team used a unique data set from the MAQC-II project that was generated by the NIEHS National Center for Toxicogenomics (NCT) and contributed by Paules, consisting of gene expression data from two tissues in rats — blood and liver. They found that by analyzing genomic indicators in the blood as biomarkers, they could predict liver necrosis or hepatic cell death across a variety of chemical compounds that target the liver, as shown by histology of liver samples after rats had developed frank DILI.

The researchers compared results on two microarray platforms for profiling the liver data and were able to predict DILI with as great as 92.1% accuracy. In an independent validation component of the study, they also showed that these genomic biomarkers predicted acetaminophen-induced liver injury with a high accuracy, as well as predicted liver injury induced by two non-therapeutic chemical compounds with an accuracy that was slightly lower than with acetaminophen.

“Our results strongly support the claim that genomic indicators in the blood can serve as biomarkers of necrosis as a form of a chemically-stressed adverse effect on the rat liver, and give credence to the acquisition of gene expression signatures from minimally invasive biomaterial sources potentially for diagnostic testing of DILI in humans,” explained Bushel.

Reflecting on the long history of pioneering research in toxicogenomics at NIEHS, Paules concluded, “While the challenges of developing signatures to utilize as clinical biomarkers of specific adverse effects are great, the prospects have never been brighter. We really hope to provide better science for better treatment of disease.”

The study’s findings underscore the potential for using microarray gene expression technology as a means to individually tailor drug treatments to a patient’s genome. Use of diagnostic genomic indicators is also likely to speed up development of high-throughput drug screening assays. Ultimately, genomic medicine could reduce the costs and duration associated with clinical trials, which often spell death for promising new drugs.

Citations: [Huang J, Shi W, Zhang J, Chou JW, Paules RS, Gerrish K, et al. 2010. Genomic indicators in the blood predict drug-induced liver injury. Pharmacogenomics J 10\(4\):267-277.](#)

[The Microarray Quality Control Consortium. 2010. The MicroArray Quality Control \(MAQC\)-II study of common practices for the development and validation of microarray-based predictive models. Nat Biotechnol. Epub ahead of print. doi:10.1038/nbt.1665](#)

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



This spring the Society of Toxicology recognized Paules with the 2010 Leading Edge in Basic Science Award “for his work in the integration of genomics into the investigation of the molecular basis of injury and disease processes,” describing him as “a visionary ... who has diligently positioned NIEHS at the forefront of the field.” (Photo courtesy of Steve McCaw)

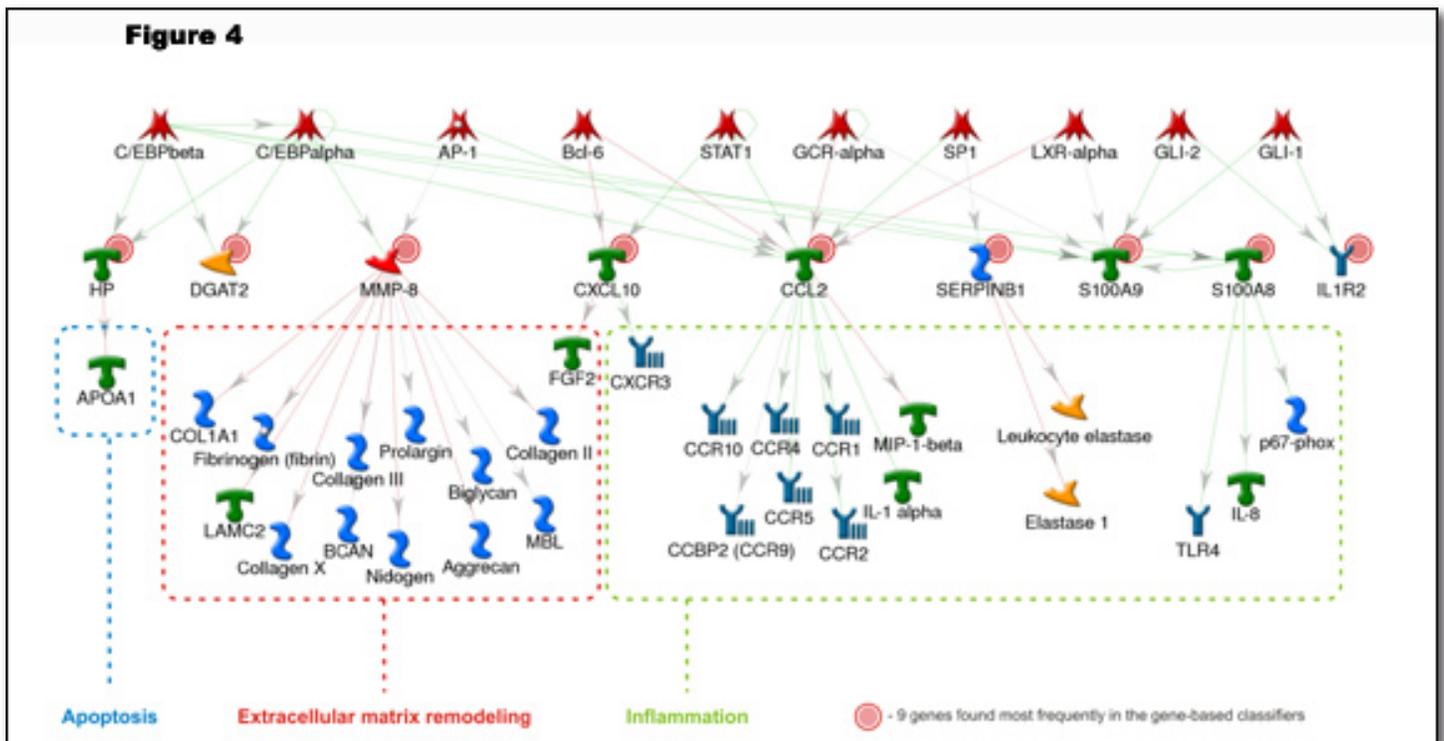


Figure 4 – Network analysis of the upstream and downstream regulation. The nine genes (marked with solid circles) are direct targets of 10 transcription factors. The downstream genes belong to three processes implicated in liver injury. (Figure courtesy of Nature Publishing Group, Pierre Bushel, and Rick Paules)

Moving forward – the SEQC project

Despite the highly successful efforts of the NIEHS-led team, several of the other teams experienced difficulty in deriving classifiers from certain microarray clinical studies for prediction of certain clinical end-points. In an editorial accompanying the 11 papers in TPJ, William Slikker Jr., Ph.D., observed, “Quality control and appropriate bioinformatics processing will remain a challenge for any new high-throughput molecular technology.”

These challenges also led the editors of the two Nature-published journals to conclude, “The results from this large-scale project involving participants from academia, industry, and governmental agencies will likely be useful for developing classifiers for data from high-throughput assays other than DNA microarrays.”

As phase II of the MAQC project nears its end, FDA plans a third phase, MAQC-III, also called the Sequencing Quality Control (SEQC) project. The SEQC project aims to assess the technical performance of next-generation sequencing platforms by generating benchmark datasets with reference samples. They also plan to evaluate the advantages and limitations of various bioinformatics strategies in RNA and DNA analyses.

NIEHS will continue its productive partnership with the FDA and other agencies to extend the successes of MAQC-II and to look further into the quality and reproducibility of next generation sequencing through SEQC. “This is another example of how NIH and FDA are working together to advance translational and regulatory science,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program. “I’m proud of the role NIEHS investigators played in this important undertaking.”

Unruly protein may shape learning and memory

By Emily Zhou

In an Aug. 4 seminar at NIEHS, neurobiologist John Hepler, Ph.D., shared exciting findings about a protein found in the mouse hippocampus, where spatial learning and memory formation occur. Part of Hepler's research is in collaboration with NIEHS Synaptic and Developmental Plasticity Group Principal Investigator [Serena Dudek, Ph.D.](#), investigating how expression of the regulator of guanine nucleotide binding protein (G protein) signaling 14 (RGS14) may regulate the synaptic plasticity involved in learning and the formation of memories.

Dudek hosted Hepler's discussion of "RGS14 as a novel integrator of unconventional G protein and MAPkinase signaling important for hippocampal function," as part of the Laboratory of Neurobiology Seminar Series. Together, the [Hepler](#) and Dudek labs have shown that RGS14 acts as a natural suppressor of CA2 synaptic transmission and of hippocampal spatial learning and memory.

Previous studies by the Hepler lab have advanced the understanding of emerging signaling mechanisms of G proteins and RGS proteins. More recently, the group's efforts have focused on novel functions of RGS proteins as integrators of receptor and G protein signaling.

Hepler and his colleagues are currently exploring several aspects of RGS protein biology, including signaling roles of RGS proteins in isolated primary hippocampal neurons and slices; regulated dynamic localization of RGS proteins in neurons; RGS protein regulation of spine and dendrite morphology and associated behavioral outputs; and RGS regulation of receptor signaling in neurons and glia.

RGS14 — not a well-behaved RGS protein

According to Hepler, the established model for G protein signaling pathways proposes that hormone- and neurotransmitter-stimulated receptors activate heterotrimeric G proteins ($G\alpha$ and $G\beta\gamma$ subunits) to elicit responses on downstream effectors. To accelerate the rate of guanine triphosphate (GTP) hydrolysis, RGS proteins serve as GTPase activating proteins (GAPs) that bind to active $G\alpha$ -GTP, thereby returning $G\alpha$ to the inactive $G\alpha$ -GDP form and terminating G protein signaling to effectors.

All RGS protein family members share an RGS domain, but differ in the presence of other unique domains. RGS14 contains an RGS domain that interacts with active Gai/o and a GPR/GoLoco motif that interacts with inactive $Gai1/3$. According to Hepler, RGS14 is not "well behaved" because it can bind both active and inactive $G\alpha$ subunit.



Hepler emphasized that "recent studies, including our own, indicate that neurotransmitter GPCR and G proteins engage a growing list of newly appreciated yet poorly understood proteins and linked signaling pathways to carry out their cellular functions." (Photo courtesy of Steve McCaw)

Ties to Chapel Hill and NIEHS

Hepler earned his Ph.D. in neurobiology at the University of North Carolina at Chapel Hill where he trained with a distinguished scientist in G protein signaling, Kenan Professor T. Kendall Harden, Ph.D. Hepler then moved to the University of Texas Southwestern Medical Center for a postdoctoral fellowship with Alfred G. Gilman, M.D., Ph.D., who shared the 1994 Nobel Prize in Medicine, for the discovery of G proteins, with Martin Rodbell, Ph.D., of NIEHS.

RGS14 – the memory gene

Immunohistochemistry and *in situ* hybridization analyses by the Hepler lab used staining to show the presence of RGS14 protein and mRNA in the mouse hippocampus, where spatial learning and memory formation occur. Hepler also demonstrated that knockout mice lacking the RGS14 gene/protein show a marked enhancement in spatial learning and enhanced object memory, with no differences in open-field locomotor, startle reflex, and anxiety behaviors that are not dependent on hippocampal synaptic plasticity.

Further experiments by the Hepler lab found evidence that RGS14 is most highly enriched at postsynaptic spines and dendrites of pyramidal neurons of the enigmatic *Cornu Ammonis 2* (CA2) region of the hippocampus.

RGS14 integrates unconventional G protein and MAPkinase signaling

In searching for signaling mechanisms responsible for this RGS14 learning phenotype, Hepler and colleagues determined that RGS14 acts as a scaffold that binds both H-Ras and its effector Raf kinases. By doing so, RGS14 inhibits growth factor mediated MAPkinase signaling through sequestering Ras and Raf. However, when inactive $G\alpha$ binds RGS14, the conformation of RGS14 protein changes so that it no longer can bind Ras and Raf, allowing its signaling to MAPkinase.

Since H-Ras/Raf and ERK signaling are important for synaptic plasticity, Hepler postulates that RGS14 serves as a scaffold that integrates and modulates $G\alpha_i$ and Ras/Raf/ERK-signaling in the CA2 to regulate synaptic plasticity, learning, and memory. In one of his lighter moments, Hepler suggested that Homer Simpson's stupidity might result from his fully functional RGS14 phenotype, while his bright and multi-talented daughter, Lisa, might have an RGS14 knockout phenotype.

(Yixing [Emily] Zhou, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction.)

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Summers of Discovery ends with module on air pollution

By Melissa Kerr

The Summers of Discovery (SOD) program concluded its redesigned lecture series July 27 with an interactive session on air pollution, presented by three NIEHS postdoctoral fellows and an NIEHS laboratory biologist. It was the final module in a series of four crafted by a special committee of postdoctoral fellows ([see related story](#)).

The series is a collaboration between organizers Diane Klotz, Ph.D., director of the NIEHS [Office of Fellows Career Development](#), and Debbie Wilson, coordinator of the [Summers of Discovery](#) and Special Programs, who served as facilitator at each of the seminars.



When Dudek, above, was nominated for a Society of Biological Psychiatry award in 2009, Acting Chief of the NIEHS Laboratory of Neurobiology David Armstrong, Ph.D., described her as “one of the youngest luminaries in one of the most dynamic and distinguished fields in neuroscience.” (Photo courtesy of Steve McCaw)

In this concluding module, postdoctoral fellows Jana Stone, Ph.D., Amy Abdulovic, Ph.D., and Cynthia Holley, Ph.D., worked with Michelle Sever, a biologist in the NIEHS Laboratory of Respiratory Biology, to teach students about the sources and potential health effects of inhalation exposure to particles and gases. The four scientists split the session into presentations about different aspects of air pollution, interspersed with table activities and discussions to enrich the learning experience.

Environmental exposure and indoor air quality

Stone opened the session by discussing both man-made and natural sources of air pollution. She explained what the Air Quality Index represents and how to reduce the effects of exposure. Staying inside, she pointed out, does not eliminate exposure because indoor air pollution can also be an issue. Stone asked students to look at several filter papers that were on the tables where they were sitting. The papers had been slathered in Vaseline and set at various places in the community at various times during the spring. The students identified pollen, cat hair, and road construction dust.

In response to earlier SOD lecture student comments asking for more details from specific research, Sever described an investigation dealing with the German cockroach and how a person's exposure to the allergen-producing cockroach could correlate with occurrences of asthma. The study followed ways to rid a household of cockroach infestation, including different methods of extermination, cleaning, and household education. She said that clearing the living space of cockroaches would clear the air of the allergen, but the study also found that simple extermination alone wasn't enough. A much more focused and thorough approach was necessary for a long-term solution.

Large-scale events lead to government regulation and policy

Next to take the podium was Abdulovic, who spoke on gaseous air pollution. The start of government involvement in relation to air pollution began following the Great London Smog of 1952. The acceleration of illness and death due to the smog prompted Parliament to take action in the form of research, thereby leading to the Clean Air Act of 1956. Turning the lecture toward more current issues, Abdulovic enlightened the students about both protective and harmful effects of ozone. She concluded with a visual demonstration of the amount of carbon dioxide a car releases into the atmosphere during a year.

Holley brought the session to its close by raising issues of air pollution and public policy. She gave a brief history on the relationship between the U.S. government and pollution issues. She said the Clean Air Act of 1963 was the first federal regulation enacted by Congress to control air pollution on a national level. The establishment of the U.S. Environmental Protection Agency came in 1970, followed by an increase in funding for programs and research. Holley closed with



Holley, shown at the podium, was also an instructor earlier in the series (see story). (Photo courtesy of Steve McCaw)



Abdulovic was chair of the committee of postdocs who set about redesigning the summer training last fall. (Photo courtesy of Steve McCaw)

an exercise challenging the students to develop catchy slogans about air pollution. NIEHS fellows voted on the slogans by email and selected “Drive less, breathe more!” due to the simplicity of the message.

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



Like other members of the committee, Stone helped with exercises at earlier sessions in the series. (Photo courtesy of Steve McCaw)



Sever was able to offer students specific examples of NIEHS air pollution research and its relevance to public health issues. (Photo courtesy of Steve McCaw)

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This Month in EHP

By Eddy Ball

Environmental Health Perspectives (EHP) tackles environmental issues in the Arctic in this month’s news with a stunning cover depiction of an eerie frozen landscape and two timely feature articles. “The Changing Landscape of Arctic Traditional Food” looks at trends in the diet of northern Canada’s Inuit population, with the increased intake of processed foods, pollution of traditional food sources, and the impact of climate change. “Cold Hard Cache: The Arctic Drilling Controversy” examines concerns about the safety of moving forward with exploratory drilling in the Arctic in the aftermath of the Gulf oil spill.

In this month’s two-part **podcast**, host Ashley Ahearn talks about the public health legacy of the World Trade Center attack with NIEHS-funded researchers Phil Landrigan, M.D., and Paul Lioy, Ph.D.

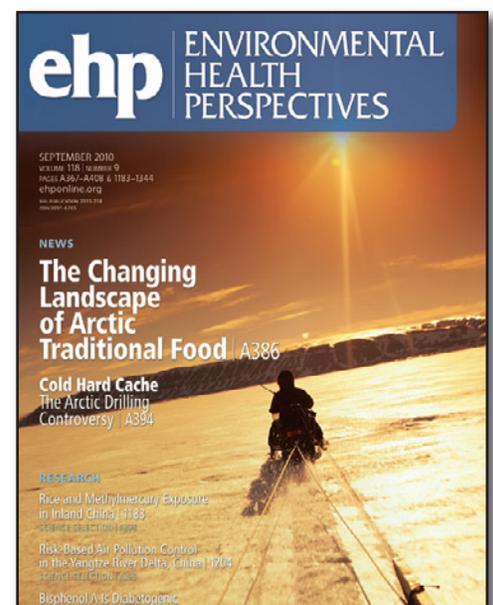
Among the research studies included in this issue are:

- Rice and Methylmercury Exposure in Inland China
- Risk-Based Air Pollution Control in the Yangtze River Delta, China
- Bisphenol A Is Diabetogenic in Mice
- Air Pollution and Type 2 Diabetes

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<http://twitter.com/ehponline>



DNA Repair Videoconference Seminar Series begins

By Jeff Stumpf



Researchers at NIEHS will again participate in the popular NIH DNA Repair Videoconference Seminar Series beginning Sept. 7. Broadcast live on the second Tuesday of each month, between September and June, at 12:30 p.m., the videoconference links 14 sites at academic and government institutions throughout the country.

At NIEHS, the lectures are shown in the Rall building B200 conference room, where attendees can ask questions and make comments via a teleconference connection. The webcasts are archived by NIH, and currently, more than 140 past lectures, many including lecture slides, are available [online](#).

DNA repair is a major research interest in several groups in the Institute's laboratories of Molecular Genetics, Structural Biology, and Molecular Carcinogenesis. Their insights into DNA repair have advanced research in the genetic and environmental causes of human diseases.

The seminar series features 45-minute lectures, originating from one of several locations by prominent scientists in the repair field. Each year, one of the spring seminars highlights three short presentations by young investigators. The final seminar of the year provides historical perspectives of DNA repair research by showcasing excerpts from the past 15 years of DNA repair videoconferences.

[Kenneth Kraemer, M.D.](#), senior investigator in the Dermatology Branch at the National Cancer Institute (NCI), co-hosts the videoconference program. "It's a nice way of communicating and seeing one another without the expense of traveling," Kraemer said.

The series is one of the ways that the more than 1500 members of the [NIH DNA Repair Interest Group](#) collaborate and share their findings with each other. The group also maintains a [listserv](#) that interested scientists can join, and it sponsors several conferences and events each year.

History of the DNA repair videoconference

The interest group began 25 years ago as a series of meetings between Kraemer and his former NCI colleague [Vilhelm Bohr, M.D., Ph.D.](#), who is now chief of the Section on DNA Repair at the National Institute on Aging. When Bohr moved to his current position at the NIA facility in Baltimore in 1995, continuing the collaboration became cumbersome. "We tried commuting back and forth, but that didn't work very well," said Kraemer.

A screenshot of a video player interface. On the left, there is a video thumbnail with the following text: "DNA Repair Interest Group", "History of DNA Repair: Four Decades of DNA Repair at NIH and the First Twenty-Five Years of the DNA Repair Interest Group", "Natcher Conference Center", "Wil Bohr, NIA, NIH and Ken Kraemer, NCI, NIH", "June 15, 2010", and "1:04:28". On the right, there is a "Linked video:" section with the text: "History of DNA Repair: Four Decades of DNA Repair at NIH and the First Twenty-Five Years of the DNA Repair Interest Group". Below the video player, there is a "Download Media Player: Flash" button with a download icon and a link icon.

DNA repair videoconference seminars at NIEHS

Because of the great depth of research at NIEHS on DNA repair, the Institute's scientists have played an important role in the lecture series for many years.

In September 2009, Dmitry Gordenin, Ph.D., a staff scientist in the Chromosome Stability Group, gave a [talk](#) on his latest study on the nonrandom cluster of mutations that arise after exposure of ultraviolet light. Gordenin showed that mutation clusters occur around regions that were single-stranded during irradiation.

In May, Scott Lujan, Ph.D., a postdoctoral IRTA trainee in the Replication Fidelity Group, participated in one of the young investigator presentations. Lujan presented evidence supporting the hypothesis that two different DNA polymerases replicate leading and lagging strands throughout the entire genome.

Videoconferencing began 15 years ago and has blossomed into today's large national network. The topics of the lectures range from clinical observations of diseases related to DNA repair to molecular studies of the proteins involved.

Several highlighted lectures in this series include the description of mutations that lead to Xeroderma Pigmentosa and the cloning of the ATM protein kinase that is mutated in patients with Ataxia Telangiectasia.

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

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Upcoming distinguished lecturer Patricia Donahoe

By Angelika Zaremba

NIEHS will welcome the first speaker in its 2010-2011 Distinguished Lecture Series Sept. 14, when Patricia Donahoe, MD, addresses the potential of Mullerian inhibiting substance (MIS) in ovarian cancer treatment. Hosted by NIEHS Principal Investigator and Chief of the Laboratory of Reproductive and Developmental Toxicology Kenneth Korach, Ph.D., Donahoe will discuss "Chemotherapeutic Agents vs. Mullerian Inhibiting Substance on Stem/Progenitor Cells in Human Ovarian Cancer."

[Donahoe](#) is the Marshall K. Bartlett Professor of Surgery at Harvard Medical School, the director of Pediatric Surgical Research Laboratories at Massachusetts General Hospital, an associate member of the Broad Institute, and a senior faculty member at the Harvard Stem Cell Institute. She served as president of the Boston Surgical Society and is president-elect of the American Pediatric Surgical Association.



Donahoe has been honored many times for her work on MIS. Her dream is to see it developed as a therapeutic agent for ovarian and other reproductive cancers. (Photo courtesy of Patricia Donahoe)



Linked video:
[Patricia Donahoe, M.D., Pinpointing the Genetic Causes of Birth Defects](#)

(Launches in new window)

Download Media Player:  Silverlight [L2](#)

Donahoe was elected to membership of the National Academy of Sciences and the National Institute of Medicine. The National Cancer Institute and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development have funded her seminal research continuously for 30 years.

The [Donahoe group](#) specializes in developmental biology and genetics. One of the group's major focuses is the potential of MIS, also known as anti-Mullerian hormone, as an anticancer agent. During development, this gonadal protein hormone causes regression of Mullerian structures in fetal males. The group discovered that as a naturally occurring growth inhibitor, MIS inhibits cell growth and induces apoptosis in ovarian cancer cells and other reproductive tumors.

Donahoe's laboratory is also investigating the differences between ovarian somatic stem cells and ovarian cancer stem cells. The group is interested in the molecular mechanisms of sex differentiation and is searching for gene defects that cause congenital anomalies. One of the group's goals is to design in utero pharmacologic therapies to reduce the severity of abnormalities at birth.

MIS is now in development as a novel treatment for cancer, and preclinical tests are underway in preparation for phase I clinical trials in human ovarian cancer patients.

(Angelika Zaremba, Ph.D., is a visiting postdoctoral fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

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Extramural papers of the month

By Jerry Phelps

- [Polyfluoroalkyl chemicals linked to ADHD](#)
- [Circadian clock in pancreas linked to diabetes](#)
- [In utero BPA exposure leads to epigenetic alterations](#)
- [Vitamin A treatment and lung disease in pre-term lambs](#)



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

Polyfluoroalkyl chemicals linked to ADHD

NIEHS-funded researchers report finding a link between exposure to polyfluoroalkyl chemicals (PFCs) and attention deficit hyperactivity disorder (ADHD) in children.

PFCs are highly stable compounds used in a variety of industrial and commercial applications, such as stain resistant coatings, food packaging, fire-fighting foams, and non-stick surfaces for cookware. The research team used data from the National Health and Nutrition Examination Survey (NHANES) to compare PFC levels in blood samples taken from 571 children ranging in age from 12 to 15. Forty-eight of the children were reported to have ADHD. An earlier report of NHANES data suggests that more than 98 percent of the US population has measureable amounts of PFCs. Because of the compounds' stability, it can take years for PFCs to be eliminated from the body.

Other research suggests that PFCs may be developmental neurotoxicants. *In vitro* studies show the compounds affect nerve cell differentiation, and *in utero* rodent studies linked PFCs to reductions in thyroid hormone, which is known to regulate brain development.

The authors are careful to point out that, at the present time, there is no evidence that PFCs cause ADHD. But given the persistence and prevalence of these compounds in the environment, further investigation into whether PFCs cause ADHD and other behavioral disorders is merited.

Citation: Hoffman K, Webster TF, Weisskopf MG, Weinberg J, Vieira VM. 2010. Exposure to polyfluoroalkyl chemicals and attention deficit hyperactivity disorder in U.S. children aged 12-15 years. *Environ Health Perspect*. Epub ahead of print.

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Circadian clock in pancreas linked to diabetes

New research by NIEHS grantees at Northwestern University published in the prestigious journal *Nature*, reports that the circadian clock in pancreatic islet cells regulates the production of insulin. If the clock or, more specifically, the genes that regulate it are faulty, the result is diabetes.

The researchers report the insulin-secreting beta cells have their own dedicated clock, which regulates the behavior of genes and proteins involved in insulin production and secretion on a 24-hour cycle. The researchers created transgenic mice with the clock genes knocked out. The animals developed impaired glucose tolerance, had abnormally low levels of insulin, and went on to develop diabetes.

The team concludes that the variation seen in insulin secretion in humans and susceptibility to diabetes are likely related to the clock mechanism. They report an association between the changes of the cycling of the clock within the pancreas itself and disease. They plan to continue research in this area to determine if the clock can be modulated, which may lead to a better understanding of circadian rhythm or better treatments for diabetes.

Citation: [Marcheva B, Ramsey KM, Buhr ED, Kobayashi Y, Su H, Ko CH, et al.](#) 2010. Disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinaemia and diabetes. *Nature* 466(7306):627-631.

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In utero BPA exposure leads to epigenetic alterations

Researchers at the Yale University School of Medicine report that *in utero* exposure to bisphenol-A (BPA) causes diminished methylation of the estrogen response element of the *Hoxa10* gene. This finding suggests that permanent epigenetic alteration of estrogen response element sensitivity to estrogen may be a general mechanism by which endocrine disrupting chemicals exert their actions.

BPA is a known endocrine-disrupting chemical. It binds to the estrogen receptor, tricking the cells' machinery into thinking they are being signaled by estrogen to act in a prescribed manner. The *Hoxa10* gene is a homeobox gene that controls uterine growth and development. A homeobox is a DNA sequence found in genes that are involved in the regulation of patterns of development. These sequences are found in animals and plants.

In this study, pregnant mice were treated with BPA. *Hoxa10* and protein expression were increased by 25 percent in the reproductive tracts of mice exposed *in utero*. DNA methylation of *Hoxa10* was significantly reduced in both the promoter and intron regions of the gene after BPA exposure. The decrease in methylation led to an increase in binding of the estrogen receptor alpha to the estrogen response element of the gene.

Citation: [Bromer JG, Zhou Y, Taylor MB, Doherty L, Taylor HS.](#) 2010. Bisphenol-A exposure in utero leads to epigenetic alterations in the developmental programming of uterine estrogen response. *FASEB J* 24(7):2273-2280.

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Vitamin A treatment and lung disease in pre-term lambs

Neonatal Chronic Lung Disease (CLD) often occurs in premature babies who are chronically maintained on mechanical ventilation until their lungs have developed enough to breath normally. The disease is characterized by incomplete development of the lungs and a thickening of lung tissues. Even with improved procedures for ventilation, neonatal CLD continues to be a major cause of mortality and long-term morbidity in premature infants. Administration of vitamin A has improved the respiratory outcome of premature infants, but there is little information to suggest the mechanisms by which this occurs.

A multidisciplinary team of researchers from Utah, California, Pennsylvania, and Texas reports that a variety of growth factors and cellular components are modulated by vitamin A administration in premature lambs managed with mechanical ventilation. Gene expression of tropoelastin and deposition of elastin was decreased in treated lambs, while vascular endothelial and other growth factors were increased.

The researchers conclude that vitamin A treatment partially improves lung development in chronically ventilated preterm neonates by modulating these factors. They speculate that treatment approaches that could potentially enhance these effects may lead to more complete alveolar development and capillary growth, such that gas exchange will be improved in premature infants.

Citation: [Albertine KH, Dahl MJ, Gonzales LW, Wang ZM, Metcalfe D, Hyde DM, et al. 2010. Chronic lung disease in preterm lambs: Effect of daily vitamin A treatment on alveolarization. Am J Physiol Lung Cell Mol Physiol 299\(1\):L59-L72.](#)

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

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Intramural papers of the month

By Jeffrey Stumpf and Robin Arnette

- [The absence of SIRT1 produces an inflammatory response](#)
- [Dyslipidemia and the TLR response](#)
- [Cohesin prevents genome instability by restricting DNA repair to sister chromatids](#)
- [Oxidized \(bi\)sulfite leads to reactive sulfur species and protein radical formation](#)

The absence of SIRT1 produces an inflammatory response

NIEHS scientists have determined that SIRT1, a member of the NAD⁺-dependent deacetylase family of proteins called sirtuins, provides protection against chronic inflammation by controlling the acetylation of nuclear factor kappa B (NF-κB), a transcription signaling pathway involved in the innate immune response. The finding may lead to treatment therapies for chronic inflammatory conditions such as obesity, insulin resistance, and type 2 diabetes.

For its *in vivo* work, the research team generated a myeloid-specific SIRT1 knockout mouse model (Mac-SIRT1 KO) and demonstrated that the absence of SIRT1 resulted in hyperacetylated NF-κB, which led to an increase

in the transcription of proinflammatory genes in macrophages. When the Mac-SIRT1 KO mice were fed a high-fat diet, their liver and fat tissue displayed an increased amount of macrophage infiltration. This condition predisposed the mice to the development of systemic insulin resistance.

Using bone marrow-derived macrophages from wild-type and Mac-SIRT1 KO, the investigators confirmed their results *in vitro*. The Mac-SIRT1 KO cells also exhibited hyperacetylated NF- κ B levels. Taken together, these data show that SIRT1 is an important mediator between environmental stress and immune system activation.

Citation: [Schug TT, Xu Q, Gao H, Peres-da-Silva A, Draper DW, Fessler MB, et al. 2010. Myeloid deletion of SIRT1 induces inflammatory signaling in response to environmental stress. Mol Cell Biol. Epub ahead of print. doi:10.1128/MCB.00657-10](#)

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Dyslipidemia and the TLR response

Dyslipidemia, an abnormal amount or quality of fats in the blood, induces opposite effects on host defense, depending on whether infection occurs inside the lung or elsewhere in the body. A new NIEHS-funded study — performed by investigators from NIEHS, the National Heart, Lung and Blood Institute, the University of Vermont College of Medicine, and Wake Forest University — represents the first published *in vivo* evidence that macrophages have increased surface expression of lipid rafts and TLR4, the lipopolysaccharide (LPS) receptor, during dyslipidemia.

Following inhalation of either LPS or *K. pneumoniae*, neutrophil recruitment to and cytokine induction in the airspace were both attenuated in dyslipidemic mice, and clearance of bacteria from the lung was impaired. In contrast, the researchers found that during dyslipidemia bacteria were cleared more efficiently from the bloodstream and peritoneum, due to more robust inflammatory responses in these body compartments.

Macrophages from the peritoneum, in which cholesterol levels increased during dyslipidemia, had increased lipid rafts associated with increased TLR4 expression and function. By contrast, macrophages from the airspace, in which cholesterol was maintained at a constant level during dyslipidemia, had normal responses and rafts. Taken together, the data suggest that the airspace may be a privileged immune site, thereby uniquely sensitive to the effects of dyslipidemia.

Citation: [Madenspacher JH, Draper DW, Smoak KA, Li H, Griffiths GL, Suratt BT, et al. 2010. Dyslipidemia induces opposing effects on intrapulmonary and extrapulmonary host defense through divergent TLR response phenotypes. J Immunol 185\(3\):1660-1669.](#)

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Cohesin prevents genome instability by restricting DNA repair to sister chromatids

NIEHS researchers have reported that reduction in yeast sister chromatid cohesion complex, or cohesin, decreased survival and permitted recombination between homologous chromosomes when exposed to low

level radiation. While supporting current models in which the tethering of sister chromatids together following replication promoted DNA double-strand break repair via recombination, they showed that cohesin was limiting and that a small reduction placed the cell at risk for inappropriate recombination.

This study utilized an innovative method of decreasing protein amounts by maintaining only one copy of the essential cohesin subunit gene *MCD1* in tetraploid yeast strain, thereby causing a three- to four-fold reduction as compared to wildtype tetraploid strains. This approach provided the opportunity to assess essential gene products under conditions of natural gene regulation and enabled the impact of variation in protein levels on cellular function to be addressed.

Restraining homologous recombination to copies of the same sequence in sister chromatids effectively protects genomic stability in response to DNA breaks. However, this study demonstrated that when the cohesin level was reduced, opportunities for recombination between homologous sequences across the genome were increased, which can lead to nonallelic recombination and rearrangements, as well as loss of heterozygosity. These types of genetic instabilities are important in the etiology of some genetic disorders and cancers.

Citation: [Covo S, Westmoreland JW, Gordenin DA, Resnick MA](#). 2010. Cohesin is limiting for the suppression of DNA damage-induced recombination between homologous chromosomes. *PLoS Genet* 6(7):e1001006.

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Oxidized (bi)sulfite leads to reactive sulfur species and protein radical formation

A recent study by NIEHS researchers published in the July issue of *Environmental Health Perspectives* provides evidence that sulfite and (bi)sulfite, commonly used as food preservatives, can be oxidized into reactive free radicals that result in protein oxidative damage. Oxidative damage is proposed to lead to tissue injury in allergic reactions due to byproducts of sulfur dioxide.

Sulfite and (bi)sulfite are two ionized forms of the major pollutant sulfur dioxide that are used to prevent food spoilage. Using electron paramagnetic resonance, optical spectroscopy, oxygen uptake, and immune-spin trapping, the investigators were able to show that the oxidase activity of copper, zinc-superoxide dismutase oxidizes (bi)sulfite into the reactive sulfur species peroxymonosulfate anion radical and sulfate anion radical.

(Bi)sulfite is approved by the FDA, despite its association with allergies, asthma, and anaphylactic shock. Mechanisms for (bi)sulfite toxicity have been unclear. However, deficiencies in the mitochondrial enzyme sulfite oxidase cause abnormally high levels of sulfite in plasma resulting in toxicity. This study reports that protein damage by free radical formation caused by oxidized (bi)sulfite should be considered as a possible cause for (bi)sulfite toxicity.

Citation: [Ranguelova K, Bonini MG, Mason RP](#). 2010. (Bi)sulfite oxidation by copper, zinc-superoxide dismutase: Sulfite-derived, radical-initiated protein radical formation. *Environ Health Perspect* 118(7):970-975.

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

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Inside the Institute

Feds Feed Families with a half ton of help from NIEHS

By Eddy Ball

This summer, NIEHS joined a government-wide effort to alleviate severe shortages of non-perishable items at food banks across the nation. The goal of the 2010 [Feds Feed Families](#) initiative is to gather 1,200,000 pounds of food nationwide for families in need, with NIH striving to collect 13,000 pounds.

During August, donors and volunteers at NIEHS reached out to do their part to make the food drive a success, contributing a total of 1,051 pounds of non-perishables in an impressive display of generosity and concern for others.



Feds Feed Families volunteers show that being generous can also be a lot of fun. NIEHS Health Scientist Administrator Mike Humble, Ph.D., clowns around as he drops off food for the drive. Shown with him, left to right, are Robinson, Michelle Owens, Jirles, and Rachel Frawley. (Photo courtesy of Steve McCaw)

Linked video:
[First Lady Michelle Obama calls on you to serve](#)
(Launches in new window)

Download Media Player: Flash

Organized by the NIEHS Office of Management (OM), [Research Triangle Park, N.C. Chapter of Blacks In Government \(BIG\)](#), and [American Federation of Government Employees \(AFGE\) Local 2923](#), volunteers at NIEHS collected food during July and August for the Durham Rescue Mission and the Food Bank of Central and Eastern North Carolina. AFGE Local 2923 donated approximately 400 pounds of the overall total for the food drive.

AFGE Local President Bill Jirles and BIG Past President Veronica Godfrey Robinson served as co-chairs on the food drive along with co-chair Monya Wells of the NIEHS OM.

As the NIEHS effort gained momentum, employees from across the Institute ([see text box](#)) made donations, helped with collections and delivery, and worked to publicize the food drive. The NIEHS effort ran from Aug. 2-18, with volunteers gathering donations from drop boxes and curbside collections on Aug. 4 and Aug. 18.

Heavy lifters in the NIEHS Feds Feed Families food drive

Along with a sincere “thank you” to the many generous NIEHS employees and contractors who contributed food to make the food drive such a success, co-chairs Wells, Jirles, and Robinson recognized the central core of food drive volunteers. These are the folks who helped with lining up carts, emptying collection boxes, delivering the food to Durham Rescue Mission and the Food Bank of Central and Eastern North Carolina, and doing the behind-the-scenes work that got food from donor’s pantries to the people who need it:

- William Boyd, OM Administrative Services and Analysis Branch
- Rachel Frawley, National Toxicology Program
- Margaret George, Transmembrane Signaling Group
- Myra Westmoreland, OM Administrative Management Branch
- Elliott Gilmer, Conference Facilities Coordination, Raven Contractor
- VeeVee Shropshire, OM Health and Safety Branch
- Jackie Osgood, Program Specialist, Kelly Contractor
- Michelle Owens, Division of Extramural Research and Training Office of the Director
- Alyson Scoltock, Molecular Endocrinology Group
- Cheryl Thompson, Office of Communications and Public Liaison

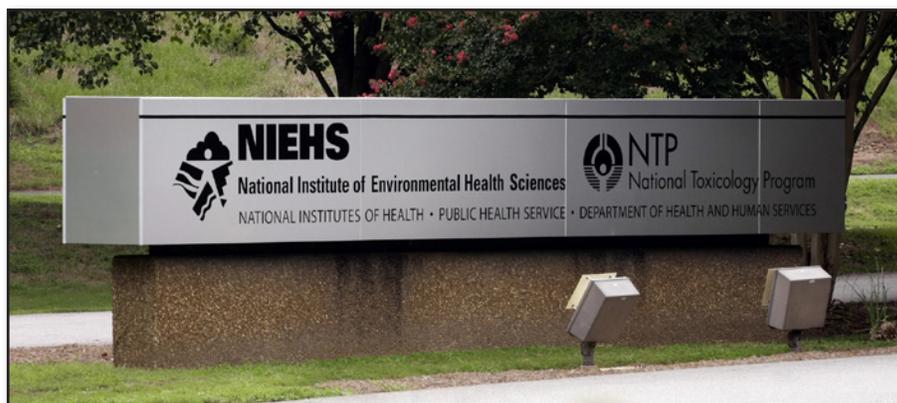
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New NIEHS signs include NTP

By Eddy Ball

NIEHS underwent a minor facelift in July and August when workers installed new signs on campus that include NTP for the first time. The new signs employ a sharp contrast between black and off-white, giving them a certain retro charm and eye-catching appeal, while at the same time balancing abstract elements for a more modern look than the signs they replaced.

Photographer Steve McCaw has taken many photos using the NIEHS sign as a backdrop, and he was able to provide some file photos to show how the public face of the Institute has changed over the years, as its signage evolved to reflect the growing importance of its work.



First impressions count. The new sign appears at the T.W. Alexander Drive entrance to campus, welcoming visitors to the world headquarters of cutting-edge environmental public health research. (Photo courtesy of Steve McCaw)



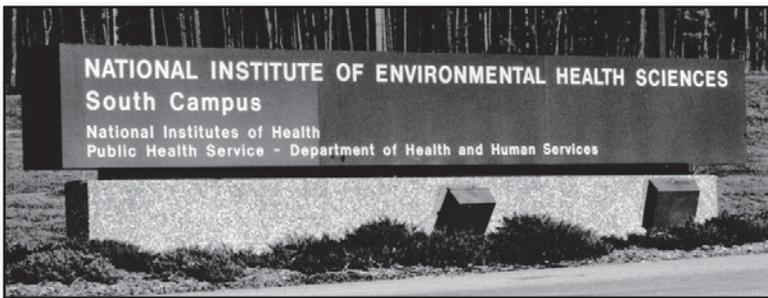
With finishing touches applied, the new sign on the Rall Building is a negative image of the sign at the campus entrance. (Photo by Eddy Ball)



The old sign, now replaced, did not include the NTP and showed an outdated NIEHS logo. (Photo courtesy of Steve McCaw)



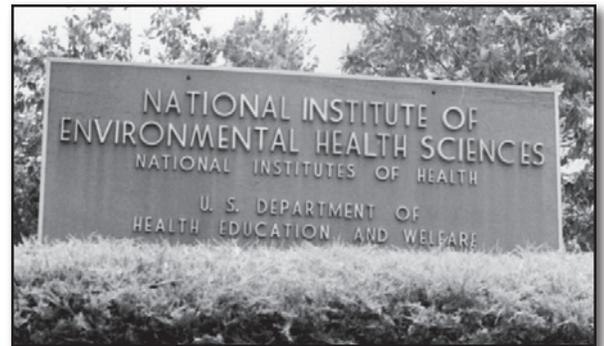
In the 1990s, the main building sign was made up entirely of words, which offered a sharper contrast with the building, but lacked the visual interest of the logo-wording mix that replaced it. (Photo courtesy of Steve McCaw)



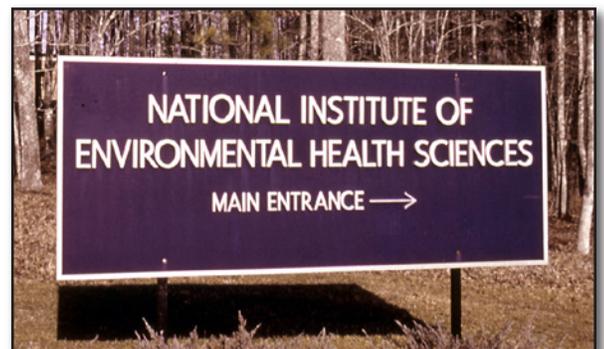
This earlier sign at the NIEHS entrance was an improvement over its predecessors and featured lighting, but it also reflected an agency still not quite certain about how to communicate its image. (Photo courtesy of Steve McCaw)



The new directory signs also feature the color contrast of the other signs. (Photo courtesy of Steve McCaw)



NIEHS toyed briefly with the tombstone look, as it moved away from one of its first efforts, below, to put a public face on its work. (Photo courtesy of Steve McCaw)



One of the first signs announcing NIEHS to visitors was a small, plain, and obviously temporary affair, matching the lackluster rented headquarters on the old North Campus. (File photo courtesy of Steve McCaw)

Fellows enjoy food and fellowship at Lake Crabtree picnic

By Sophie Bolick

A summer of record high temperatures and an overcast morning did nothing to dissuade approximately 25 fellows and their families from turning out for an afternoon of fun on Aug. 14. Early morning clouds gave way to sunny skies and gentle breezes in the late afternoon for the First Annual NIEHS Trainees Assembly (NTA) Summer Picnic at Lake Crabtree Park.

“The NTA wanted to organize an activity that got fellows away from lab work, publishing, and the job search — if only for an afternoon. We also wanted to provide an opportunity for fellows to socialize with people they may pass in the hallway every day,” said Allison Schorzman, Ph.D., a fellow with the Mass Spectrometry Group and organizer of the event.

Children enjoyed the park playground and bounce house, while adults took advantage of the sand volleyball court and horseshoe pits. Fellows showcased their culinary talents with a variety of excellent side dishes and desserts, which rounded out the entrees of fried chicken and barbecue.

Tammy Collins, Ph.D., a fellow in the Mitochondrial DNA Replication Group, stated, “It was a great opportunity to get to know fellows from other labs while enjoying some good ol’ NC BBQ.” She added, “I hope to see the NTA continue to offer social events such as this to help build community among trainees.”

Raj Gosavi, Ph.D., a fellow with the Structure and Function Research Group in the Laboratory of Structural Biology, organized an impromptu game of volleyball. Of their efforts, he commented, “Perhaps none of us were playing on the level of professionals, but nevertheless it was fun and was certainly competitive. There were people on my team with whom I had never interacted before, which also made it interesting.”

The NIEHS NTA is an organization created and governed by fellows. One of the missions of the NTA is to foster communication among fellows at social events such as the monthly coffee hours, the annual Postdoc Appreciation Day, and this picnic. Schorzman summed it up best by stating, “What better way to get to know people than over good food and a beautiful view.”

(Sophie Bolick, Ph.D., is a postdoctoral fellow with the Genetic and Molecular Epidemiology Group in the Laboratory of Molecular Carcinogenesis.)



Fellows took a break from the lab to showcase their volleyball skills on a Saturday afternoon at Lake Crabtree Park. (Photo courtesy of Allison Schorzman)



Left to right above, David Draper, Ph.D., Schorzman, and Collins shared a laugh as they filled their plates with fried chicken and barbecue before moving on to the potluck dishes. (Photo courtesy of Xiaoqing Chang)



Fellows relaxed in the shade and allowed their meals to settle as they caught up with old friends and made new ones. (Photo courtesy of Allison Schorzman)



There was no shortage of activities for children. They enjoyed the bounce house as well as the playground and lake. (Photo courtesy of Allison Schorzman)

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Army gains as NIEHS loses Gentry

By Eddy Ball

Friends and colleagues gathered Aug. 10 to wish departing Office of Acquisitions (OA) Supervisory Contract Specialist Melissa Gentry the best in her new job at the Army Research Office (ARO). While testimonials, food, and fellowship dominated the going away party, speakers who came to celebrate Gentry's contributions also lamented the Institute's loss of one of its much beloved senior contract specialists to another agency.

In their talks about how much Gentry will be missed, several of those speakers took advantage of having Don Gula in the audience. Gula is a longtime friend and colleague of Gentry and was an NIEHS employee for 20 years when he took a job at ARO in 2009. Some of the speakers joked that Gula had played a part in persuading Gentry to take her new job.

Gentry's supervisor and event emcee, Gary Delaney, opened the party by saying that he promised Gentry he would not throw a "Gula-Bash" of embarrassing tributes, while at the same time referring to all the accomplishments he said "I can't talk about." To keep his promise to Gentry, Delaney opened the floor for spontaneous tributes from those who hadn't been a party to his promise.

As Delaney said afterwards, he didn't realize that this informal Gula-Bash would also turn into something of a good-natured Gula-Roast.



Gentry's popularity meant that virtually every seat at the party was filled and the back wall of the Keystone conference room lined with friends and admirers. (Photo courtesy of Steve McCaw)

In a show-stealing stand-up routine that kept the audience laughing, Jimmy Bryant, a contract specialist in the OA, wove references to Gula into a monologue in praise of his colleague. Bryant said of Gentry, “She’s good people,” as he offered example after example of her humor, dedication, and professionalism. He punctuated his tribute with several good-natured jabs at Gula, saying, “I’m not happy with Don,” and concluding, “He has really, really worked my nerves.”

By the time she had listened to fond memories and farewells from so many of her friends at NIEHS, including a poem composed by OA colleague Vondia (Collete) Malone, Gentry was almost in tears. She managed to maintain her composure long enough, however, to move the party on to the refreshment table, as she talked individually with friends from throughout NIEHS.

Bryant clearly spoke for many in the room about a future at NIEHS without Gentry, when he recalled the words she used to encourage him in times of stress and frustration. “She said, ‘Jimmy, trust and believe.’”



Delaney, standing, started things off with a monologue in which he referred to all the good things about Gentry that he promised not to talk about. (Photo courtesy of Steve McCaw)



One of the first tributes was the poem “Stepping Out,” composed and written by Malone, above. (Photo courtesy of Steve McCaw)



Bryant, left, hugged Gentry following his tribute to his longtime — and much shorter — colleague and mentor. (Photo courtesy of Steve McCaw)



OA colleagues posed for a group photo. Shown, left to right, are Bryant, Dianne Gray, Tanya Shields, Wanda Holliday, and Kim Holmes. (Photo courtesy of Steve McCaw)



Shown above, left to right, are Shields, Holmes, and Holliday enjoying Bryant's narrative of his experiences working with Gentry. (Photo courtesy of Steve McCaw)



Seated from left to right, Administrative Officer Margarita Roque and Gula joined Rose Anne McGee and Kathy Ahlmark of the NIEHS Division of Extramural Research and Training. (Photo courtesy of Steve McCaw)



Gula, above, inadvertently set himself up for a roast by saying that gaining Gentry at the ARO was "like getting your first choice in an NFL draft." (Photo courtesy of Steve McCaw)



Administrative Officer Charletta Fowler, left, was just one of many from other branches of the Office of Management who paid tribute to Gentry's work during her 21 years at NIEHS. (Photo courtesy of Steve McCaw)

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Ivanoff heads west for new adventures

By Eddy Ball

At the end of August, NIH Equal Employment Opportunity (EEO) Specialist Ginny Ivanoff left her position at NIEHS for a new job in Little Rock, Ark., after living in the Raleigh-Durham area for the past 13 years. Ivanoff, who will lead the Army Corps of Engineers EEO program there, joined friends and colleagues for an informal going-away party Aug. 20 in the observation suite in the Keystone Building.

Along with food and best wishes from individuals, the event featured a running narrative by the wild-mannered Ivanoff about her plans to pursue new adventures in the nation's heartland. She sets out to build an EEO program there and the kind of employee-driven diversity program that she helped implement at NIEHS.

Surrounded by her many well-wishers, Ivanoff talked about her years stationed at NIEHS and reflected on the irony of her return to the Corps, which rified her from a previous job in Wilmington. "So why am I going back to them?" she joked. "I don't know. ... I'm actually taking a pay cut for the first four months because I'm going off the Raleigh-Durham pay chart."

On a more serious note, Ivanoff described all the positive things about her new job in Little Rock, including the cultural opportunities there, the state's natural beauty, and a Tai Chi studio literally a block from her office. And, she said, "The cost of living is much lower [and] real estate is a steal."

"Everything I could ask for is literally falling into my lap with this job," she said. In addition to the cultural attractions of Little Rock, Ivanoff said she'll enjoy exploring the lower-brow aspect of the state's culture and joked about the name of the small town of Toad Suck, near Conway in central Arkansas. She added that she also looks forward to site visits to Corps offices throughout her district.

As Ivanoff talked about her tenure at NIEHS, she recalled her long and productive relationship with the NIEHS Diversity Council, many of whose members were at the party.

"I took my job seriously, even though it seemed as though I never took anything seriously," Ivanoff said at one point. "Maybe that was the secret of my success."



As people began to filter into the party, Ivanoff, left, chatted with Acting Deputy Director Steve Kleeberger, Ph.D. (Photo by Eddy Ball)



The atmosphere was congenial and the refreshments abundant, as well-wishers socialized and enjoyed the food. (Photo by Eddy Ball)



As she cut her cake, Ivanoff joked, “Do I need to cut a piece for everyone?” (Photo by Eddy Ball)



Speaking for his colleagues on the Diversity Council, chair Brad Collins, left, thanked Ivanoff for her dedication to equal opportunity and diversity at NIEHS. He also presented her with several presents and mementos from her colleagues. (Photo courtesy of Steve McCaw)

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