



# Environmental Factor

Your Online Source for NIEHS News

August 2010

## NIEHS Spotlight



### [Grantees Host Sebelius During Gulf Visit](#)

During a community roundtable in New Orleans, HHS Secretary Sebelius engaged in candid discussions about the public health implications of the Gulf oil spill.



### [CDC Taps Portier to Head Programs](#)

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### [EHP Takes Environmental Health Education to the Next Level](#)

Science teachers gathered at NIEHS July 7-8 for a workshop sponsored by the EHP Science Education Program and the UNC Superfund Research Program.



### [Nominations Requested for SOT Anniversary](#)

NIEHS and NTP are helping the SOT mark its 50th anniversary next year with a special poster, banner, and Website commemorating "Benchmarks in Toxicology."



### [Superfund Grantee Wins NASA Fellowship](#)

University of Arizona Superfund Research Translation Coordinator Monica Ramirez will soon transition into a fulltime Ph.D. student, thanks to a NASA space grant fellowship.

## Science Notebook



### [Chromatin Remodeling and the Glucocorticoid Receptor](#)

NCI geneticist Gordon Hager, Ph.D., shared his recent research findings on epigenetic modification of chromatin in an afternoon seminar July 7 at NIEHS.



### [Tox21 Welcomes FDA as Partner](#)

The U.S. Food and Drug Administration (FDA) officially joined Tox21, a powerful federal interagency consortium to advance toxicology in the 21st century.



### [Fellows Honored for Research Excellence](#)

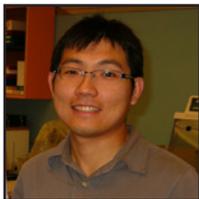
NIEHS set records during the 2011 NIH FARE competition for the numbers of awards to predoctoral fellows and of consecutive awardees.



### [Summer Students Flock to Lecture Series](#)

Half or more of the 50 students in the Summers of Discovery attended the first three seminars in July, proving that the new format was a formula for success.

## NIEHS Spotlight



### [Profiling NIEHS Recovery Act Success Stories](#)

Recipients of NIEHS funding from the American Recovery and Reinvestment Act of 2009 have been able to develop new, or expand existing, research capabilities.



### [NIEHS and the Action Agenda on Chemical Exposures](#)

A dedicated group of NIEHS professionals is helping to create a comprehensive national action agenda on chemicals in the environment.



### [Postdocs Play Key Role in Summer Training](#)

Throughout July, Summers of Discovery students learned about environmental effects on human health in a series of interactive seminars presented by trainees and lab staff.



### [A Fitting Tribute to Colin Chignell](#)

The journal Photochemistry and Photobiology honored deceased NIEHS Principal Investigator Colin Chignell, Ph.D., with a special "Symposium in Print."



### [Staff Recognized with NIH Director's Award](#)

Four NIEHS employees joined representatives from all of the other NIH Institutes and Centers recognized at the 2010 NIH Director's Awards Ceremony July 15.

## Science Notebook



### [Investigating Rare Diseases in Search of a Common Cure](#)

NIH Clinical Center Director John Gallin, M.D., visited NIEHS July 15 to tour the new NIEHS Clinical Research Unit and deliver a presentation as part of the Clinical Director's Seminar Series.



### [NIEHS Launches NanoHealth Signature Program](#)

A novel project is now underway to investigate the health effects of widely used engineered nanomaterials in susceptible populations.



### [NTP Holds Symposium on Pathology](#)

NTP sponsored a satellite session that organizers billed as a "Pathology Potpourri" June 19 as part of the 2010 joint symposium of two toxicologic pathology societies.



### [Chemistry Is Key to Mercury Levels in Saltwater Fish](#)

A new study by NIEHS-funded researchers at Duke University reports on the chemistry of methylmercury (MeHg) degradation in the freshwater and ocean environment.



### [This Month in EHP](#)

The cover of the August issue of EHP features an eye-popping close-up of oil- and dispersant-polluted water to highlight news features on the Gulf oil spill.

## Inside the Institute



### [Campers Engage Hands-on with Nutrition and Fitness](#)

For its fifth annual Science Summer Day Camp June 19, the SEE program took aim at the growing problem of overweight, obesity, and related health issues.



### [Library Pioneer Dav Robertson Retires](#)

NIEHS Library Chief Dav Robertson marked a career milestone on June 29 as friends and colleagues celebrated his retirement after 33 years at the Institute.



### [Veteran Biologist Larry Champion Begins Second Career](#)

Laboratory of Molecular Genetics Biologist Larry Champion made it clear June 29 that he was separating after 30 years of federal service, but not really retiring as he looks forward to teaching fulltime.



### [NIEHS Receives its 20,000th Grant Application](#)

With a special cake to mark the event, the NIEHS Division of Extramural Research and Training celebrated a milestone July 22 — receipt of its 20,000th grant application.

## Extramural Research

### [Extramural Papers of the Month](#)

- [Link Discovered Between Particulate Matter Air Pollution and Sleep-Disordered Breathing](#)
- [Living, Breathing Lung-on-a-Chip](#)
- [Transcription Termination Flips Out](#)
- [Fetal Leydig Cell Protein Regulates Sertoli Cell Proliferation](#)

## Intramural Research

### [Intramural Papers of the Month](#)

- [The Structural Elucidation of the 8odGTP-adenine-pol beta Ternary Complex](#)
- [Cholesterol Trafficking Linked to Inflammatory Response](#)
- [Ozone and TLR4 Lead to Asthma](#)
- [C. elegans Genes Increase Lifespan and Resistance to Cadmium](#)

## Calendar of Upcoming Events

- **August 4** in Rall F193, 11:00 a.m.-12:00 p.m. — Laboratory of Neurobiology Seminar Series with John Hepler, Ph.D., speaking on “RGS14 Integrates G Protein and MAP Kinase Signaling Pathways Important for Hippocampal Synaptic Plasticity and Learning Behaviors”
- **August 5 (Offsite Event)** in the McKimmon Center at North Carolina State University, 1:00-5:00 p.m. — 9th Annual NC State Undergraduate Research Summer Symposium
- **August 16** in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — DERT Director Candidate Seminar, speaker and topic TBA
- **August 17** in Rall Building Mall, 11:00 a.m.-3:00 p.m. — Vendor Trade Show
- **August 20** in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — DERT Director Candidate Seminar, speaker and topic TBA
- **August 27** in Rodbell Auditorium, 2:00 p.m.-3:30 p.m. — Years of Service Ceremony emceed by NIEHS/NTP Director Linda Birnbaum, Ph.D.
- View More Events: [NIEHS Public Calendar](#)

# NIEHS Spotlight

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## Grantees Host Sebelius During Gulf Visit

*By Robin Mackar*

For U.S. Secretary of Health and Human Services (HHS) [Kathleen Sebelius](#), a visit to New Orleans and Grand Isle Beach, La., July 10 was hardly a typical Saturday morning. During a community roundtable at the Deep South Center for Environmental Justice at Dillard University in New Orleans, Sebelius engaged in candid discussions with concerned Louisiana fisherfolk, community leaders, BP oil spill workers, and local government officials about public health and mental health implications of the Gulf oil spill.

NIEHS grantees Beverly Wright, Ph.D., [Deep South](#) executive director, and her colleague Myra Lewis, Ph.D. were the lead organizers of the event, which was also attended by HHS officials James Galloway, M.D., health liaison to the National Incident Command, and Eric Broderick, D.D.S., deputy administrator of the Substance Abuse and Mental Health Services Administration.



*After a round of plain talk and frank discussion, participants posed for a photo. Shown, left to right, are Wright, Edwards, Sebelius, and attendee Gail Edwards. (Photo courtesy of the Deep South Center for Environmental Justice)*

Wright, the moderator of the event, and Lewis are well known in the community and throughout the country for their environmental justice efforts. They were able to gather an impressive group of residents, including New Orleans Mayor Mitch Landrieu, U.S. Representative Joseph Cao (R-LA), graduates from the minority worker training program, Vietnamese community fishers, and other community members.

Deep South receives funding through the NIEHS Worker Education and Training Program (WETP) and oversees safety training programs in several states affiliated with the center. WETP Director Chip Hughes and his staff worked with communications staff at NIEHS and HHS to coordinate the visit.

### Key Areas of Concern

The fishermen and workers identified several key areas of concern during the informal roundtable discussion with the HHS Secretary.

Mental health and economic concerns were at the top of the list of concerns expressed by community members in attendance. Tap Bui, a health outreach coordinator for the Mary Queen of Vietnam Community Development Corporation, provided several examples of how Vietnamese fisherfolk have increasing anxiety and stress levels as they wait by the phone for a call to work. “Having a job and working is a number one priority for Vietnamese fisherfolk, even above their health concerns,” Bui explained. Others said there need to be more mental health services available and to encourage more collaboration among the Veterans Administration hospital systems to provide services to veterans.

Workers also expressed concerns about burning sensations in their eyes and throats. Although they felt they received adequate training to protect themselves, they said they were worried about long-term health effects and wanted more access to health clinics. The workers also complained that the wages being paid were not sufficient for the level of chemicals they may be exposed to.

Another theme that emerged was a desire by the community to have the federal government more involved in the daily response efforts of the oil disaster. Reverend Tyrone Edwards of Zion Travelers Cooperative Center in Plaquemines Parish discussed a disconnect between the needs of the community and BP, especially when it comes to addressing health concerns of the workers and their families. Sebelius was interested in hearing from the mayor and other local leaders about the community's needs for more medical workers.

The Secretary listened intently throughout the meeting, thanked the organizers, and gave a special thanks to the community for coming out on a Saturday morning to share their concerns. "We are committed to working with state, local, and community partners to ensure people have access to needed services," said Sebelius.

Wright closed the meeting by saying the Deep South Center for Environmental Justice will continue to work with HHS, other federal and local government officials, and community leaders to help resolve the critical community concerns raised at the meeting.

"The Secretary's presence with us, and the time she spent talking with us, conveyed a sense of her value for our community and her commitment to the sustainability of our culture and quality of life," Wright said after the visit.

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

[Return to Table of Contents](#)

## NIEHS on Duty in the Gulf

NIEHS continues to play a pivotal role in the Gulf Oil spill response efforts. Some recent highlights include the following:

- The NIEHS Worker Education and Training Program (WETP) effort continued to expand in July. Four more teams of NIEHS trainers were certified in July and are now delivering various BP training modules in Louisiana, Mobile, Ala., and Key West, Fla. Examples of the training being provided include 4-hour courses for workers doing on shore cleanup activities, additional training to Vessel of Opportunity workers, and safety briefings for dock workers.
- To date, approximately 100,000 people throughout the Gulf Coast have been trained by BP or its training contractor PEC/Premier, using NIEHS WETP training materials.
- NIEHS has distributed more than 8,000 "Safety and Health Awareness for Oil Spill Cleanup Workers" guides to front-line responders, instructors, and safety officials.
- WETP continues to perform quality assessments of BP required training and to offer suggestions for improvement.
- NIEHS is gearing up to launch a health study of oil spill clean-up workers and volunteers in late Fall. The Gulf Long-term Follow-up Study (GuLF) is being designed and led by the [NIEHS Epidemiology Branch](#). Initial funding for the study was announced by the NIH director in June ([see story](#)). With much input from local, state, federal agencies, and community partners, the study is expected to evaluate more than 20,000 clean-up workers for a range of possible health effects, including respiratory, neurobehavioral, carcinogenic, immunological, and mental health disorders.

# CDC Taps Portier to Head Programs

*By Larry Lazarus*

Senior Advisor Chris Portier, Ph.D., left NIEHS July 29 to serve as director of two high-profile programs at the Centers for Disease Control and Prevention (CDC). Portier, a 32-year veteran of the Institute, assumes duties as director of the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Center for Environmental Health (NCEH).

Portier said he was motivated to make the career change “due to my focus on direct public health issues during the last several years” and a commitment “to give back to my country and use what I have learned at the NIEHS to improve the health of the American public.”

During his tenure at NIEHS, Portier served in several leadership roles. He was a principal investigator in the Environmental Systems Biology Group, former director of the Environmental Toxicology Program, and former associate director of the National Toxicology Program (NTP).

As senior advisor, Portier was a driving force in the NIEHS global health initiative. He helped design and fund a set of high-profile papers published in the journal *The Lancet* in November 2009 that identified important health benefits of interventions to alleviate global climate change ([see story](#)). He was the NIEHS lead on a white paper, “[A Human Health Perspective on Climate Change](#),” published in April 2010 by a U.S. government-wide global health working group investigating the state-of-the-science on the human health consequences of climate change.

In a congratulatory note about Portier’s new appointment, NIEHS/NTP Director Linda Birnbaum, Ph.D. said, “Over the years, I have often marveled at Chris’ intellectual ability and what I would call brilliance when it comes to big picture visionary thinking. I know I can always count on Chris for new ideas and challenging discussion, which I believe has benefited our Institute in many ways.”

Portier leaves the NIEHS/NTP with the support and admiration of many colleagues and collaborators. In particular, they stressed his committed mentorship, dynamic leadership style, broad understanding and appreciation of basic and applied science, and dedication to using modeling to improve risk assessment.

John Prichard, Ph.D., NIEHS acting scientific director, noted that Portier “led the effort to develop a master plan – a roadmap – for the NTP [due to] his emphasis on mechanistic endpoints, and he set priorities which continue to have a strong impact.” During Portier’s tenure as NTP associate director from 2001-2006, the program put out its landmark document, “[A National Toxicology Program for the 21st Century: A Roadmap for the Future](#).”

Current NTP Associate Director John Bucher, Ph.D., said Portier brought “quantitative rigor” to the NTP by “developing an NTP database and high throughput screening [which] led to the Tox-21 initiative working beyond our dreams.” This sentiment was reiterated by Nigel Walker, Ph.D., NTP deputy program director for science, who remarked, “We are living in the vision he started.”



*In his new role at CDC, Portier will head programs that share important interests in environmental public health with NIEHS. (Photo courtesy of Steve McCaw)*

Portier's mentor and former NTP Associate Director George Lucier, Ph.D., had this to say: "Dr. Portier combines a remarkable intellect with a keen understanding of how to translate science into sound public policy decision-making."

Both Lucier and Birnbaum see Portier's move as an opportunity to strengthen collaborations in addressing environmental causes of human disease. The NCEH/ATSDR is an important member of the NTP, which is an interagency program of the U.S. Department of Health and Human Services.

Explaining the mission of NCEH/ATSDR, Portier added, "The basic concept is anytime anyone needs help about toxic substances in their neighborhood, they call us. The NCEH looks at the people who live in an affected region." Portier said that the scientists and staff at NCEH/ATSDR also serve as boots on the ground as "the nation's first responders for health related issues."

This role involves not only major environmental disasters, such as waste dumps, toxic sites, hurricanes, and oil spills, but also "clusters of environmental health-related cancers," he added. Portier said the NCEH is also the "biomonitoring program for the U.S." and works hand-in-hand with organizations to conduct multidimensional evaluations that assess 450 known environmental chemicals in human blood and urine samples, to aid in understanding exposures in the United States.

(Larry Lazarus, Ph.D., is a principal investigator in the NIEHS Laboratory of Toxicology and Pharmacology.)

[Return to Table of Contents](#)

## EHP Takes Environmental Health Education to the Next Level

*By Thaddeus Schug*

Science teachers from across central North Carolina gathered at NIEHS July 7-8 for a workshop titled "Air, Water and You," sponsored by the [Environmental Health Perspectives \(EHP\) Science Education Program](#) and the [University of North Carolina \(UNC\) Superfund Research Program](#). The workshop was the first in a series of new initiatives designed by EHP to enhance environmental health education in secondary schools.

The 21 attendees engaged in two days of participatory lessons and presentations from scientists who introduced them to new developments in the field of environmental health science. They also went behind the scenes with tours of the Comparative Genomics Lab, where they saw experiments with *C. elegans*, and the NIEHS Clinical Research Unit, where human-subject experiments are getting underway.



*Shown left to right, Sen. Durham County's Jordan High School teacher Stephanie Blochowiak, and Haine demonstrate the effects of body size on internal dose. (Photo courtesy of Steve McCaw)*

The event organizers, EHP Program Manager for Education and Outreach Bono Sen, Ph.D., and UNC Institute for the Environment K-12 Science Education Manager [Dana Haine](#), explained that the EHP lessons promote teaching of interdisciplinary science and encourage students to apply what they've learned in the classroom to

real-life situations. Haine showed teachers how a relatively simple demonstration, such as dropping food coloring into different sized flasks, can teach fundamental lessons about the effects of dose on toxicity.

“The EHP lessons enhance environmental health literacy of the students by engaging them with real-life scenarios and incorporating hands-on and critical thinking activities into the lesson plan,” noted Sen. The teachers also appeared to enjoy the learning experience. “This is the best workshop I’ve been to in years,” said Daniel West, of Wake County’s Middle Creek High School, as he engaged in a version of environmental tic-tac-toe exercise conducted by Duke University Postdoctoral Fellow Michelle Larrea, Ph.D., that turned researching the health effects, regulatory standards, and sources of toxic substances into a game.

### Scientists Teaching Teachers

Experts from NIEHS, the U.S. Environmental Protection Agency (EPA), Duke, and UNC presented lesson modules designed by the EHP Science Education Program to the group of teachers who played the role of middle and high school students. The platform offered an opportunity for teachers to learn from experts and to participate in hands-on learning activities.

Several NIEHS scientists used the workshop as an opportunity to gain valuable teaching experience. Postdoctoral Fellow Sophie Bolick, Ph.D., taught a lesson titled “Risk Factor Roulette,” in which students determined if risks associated with certain diseases were due to environmental, genetic, inherent, or behavioral factors. Biologist Mercedes Arana, Ph.D., presented a lesson on the importance of healthy streams in reducing pollutants, “Streamside Schematic.”

Postdoctoral Fellow Erin Hooper, Ph.D., wrapped up the workshop with a critical thinking lesson called “Consider the Source.” Participant Stephanie Blochowiak of Jordan High School in Durham County applauded Hopper’s approach to evaluating scientific information sources saying, “I think it’s good to bring in the bigger picture.”

The workshop also featured presentations by guest speakers. NIEHS toxicologist Jean Harry, Ph.D., discussed risks associated with toxic exposure to the



*West, center, worked with fellow teachers in an icebreaker Scrabble exercise attempting to name the most environmental risks that begin with a chosen letter. (Photo courtesy of Steve McCaw)*



*EHP Editorial Assistant Mary Collins, Ph.D., conducted a lesson on basic environmental health concepts from the “Educational Resources for Teachers” booklet given to workshop participants. Collins is also an instructor at Durham Technical Community College. (Photo courtesy of Steve McCaw)*



*Haine, above, observed as teachers worked together on a lesson. Her presentation, “Making Superfund Relevant to Students,” drew upon her program’s own outreach efforts with middle and high school students. (Photo courtesy of Steve McCaw)*

brain and nervous system and offered the teachers an overview of the brain's complex structure. Several of Sen's colleagues at EPA, where she completed her postdoctoral fellowship, participated as well, including Ron Williams, Patricia Gillespie, Ph.D., Laura Jackson, Ph.D., and Drew Pilant, Ph.D.

### **EHP has developed hundreds of lessons**

EHP has developed more than 100 high-quality science and interdisciplinary lessons based on selected News and Research articles published in the journal. Although the lessons are aligned with [National Science Education Standards](#) in biology, chemistry, environmental science, geology, and physical science, they highlight the interconnection between human health and the environment. The lessons target students in grades 9–12, although many are also appropriate for undergraduates. All lessons can be downloaded free of charge from the EHP Science Education website.

EHP plans to advance its science education and outreach program by conducting more workshops, developing an interactive website for teachers and students, and adding new lesson resources for teachers.

In comments and evaluations, the teachers praised the organization and scope of the workshop. "I love the format," said Sister Janet Schemmel, head of the science department at Raleigh's Cardinal Gibbons High School.



*Chapel Hill High School teacher Rob Greenberg enjoyed one of the interactive lessons presented by area scientists. "I loved the way everything came together," he said afterwards. "It was wonderful." (Photo courtesy of Steve McCaw).*

## **New Features of the EHP Science Education and Outreach Program**

### **Lesson Plans**

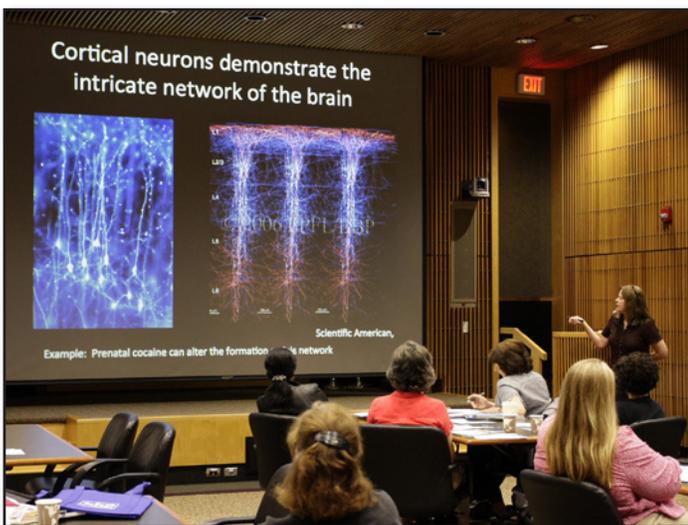
- A core team of lesson-plan developers, including high school and college science teachers as well as environmental health science researchers.
- Lesson plan reviewers, including scientists, educators, and teaching faculty.

### **Website**

- Updated Web site to include, Lesson of the month, student fellowships and awards announcements, book reviews, blogs in which instructors can exchange ideas and experiences, and video links.

### **Workshops**

- Faculty development workshops that incorporate EHP teaching materials
- Workshops on scientific writing and science communication targeted toward graduate students, fellows, and international students
- Expansion of the program to non-Anglophone countries, including Chinese and Spanish translations of existing lessons.



*Harry's slides underscored the concept of the brain as an evolutionary structure with more complex areas developing to moderate and control more primitive areas. (Photo courtesy of Steve McCaw)*



NIEHS Program Administrator Michael Humble, Ph.D., leaned on his experience as a former high school chemistry teacher to demonstrate a lesson about the synergistic effects of mixtures, “Three is a Toxic Number.” (Photo courtesy of Steve McCaw)



Karen Clark, a teacher at Southern Middle School in Aberdeen, analyzed three examples of scientific information for tone and bias during the “Consider the Source” exercise that concluded the workshop. (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.)

[Return to Table of Contents](#)

## Nominations Requested for SOT Anniversary

By Ed Kang

NIEHS and NTP are helping the Society of Toxicology (SOT) mark its 50th anniversary next year with a special poster, banner, and Website commemorating “Benchmarks in Toxicology.” Voting is currently underway at the special “Benchmarks” [Web site](#), where visitors, whether they are SOT members or not, can nominate the most important people, events, and discoveries that have influenced the modern discipline of toxicology.

As in years past, NIEHS and NTP will figure prominently in the presentations, sessions and workshops at the [SOT Annual Meeting](#) March 6-10, 2011 in Washington. At the 50th anniversary celebration, NIEHS, NTP, and the NIEHS journal Environmental Health Perspectives (EHP) will proudly display the “Benchmarks” banner and toxicology timeline. The commemorative poster, banner, and Web site will be available during and after the 2011 SOT conference to individuals, schools, and other public or private institutions.

“From Paracelsus’ declaration that ‘the dose makes the poison’ to high-throughput assays, many people, discoveries and events have shaped the modern field of toxicology,” said NIEHS/NTP Director Linda Birnbaum, Ph.D., who is a benchmark in her own right. Birnbaum is the first woman to lead the NTP and the first toxicologist to head an NIH institute.



“We think this will be a great resource to highlight the formative benchmarks in our field, and we’re excited to have the toxicology community help us shape the project by providing input,” Birnbaum said.

According to SOT, the landmark 50th annual meeting expects to attract more than 7,000 scientists from industry, academia, and government, including confirmed plenary speakers Francis Collins, M.D., Ph.D., director of the National Institutes of Health, and Margaret Hamburg, M.D., commissioner of the U.S. Food and Drug Administration.

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

[Return to Table of Contents](#)

## Superfund Grantee Wins NASA Fellowship

By Eddy Ball

[NIEHS-funded](#) University of Arizona (UA) Superfund Research Translation Coordinator Monica Ramírez will soon transition into a fulltime Ph.D. student, thanks to a space grant fellowship from the National Aeronautics and Space Administration (NASA). The NASA Space Grant program and nominating departments at UA provide six graduate fellowships per year to exceptional graduate students interested in promoting the understanding of science by the public.

Ramírez leaves her role with the [Superfund Research Program \(SRP\) at UA](#) to pursue her degree as she works with the U.S. Environmental Protection Agency (EPA), Arizona Department of Environmental Quality (ADEQ), and the towns of Dewey and Humboldt, Ariz. to determine the quality of vegetables grown in home gardens neighboring the [Iron King Mine and Humboldt Smelter Superfund Site](#).

During her tenure with UA SRP, Ramírez worked with the [U.S.-Mexico Binational Center for Environmental Sciences and Toxicology](#), fostering the growth and development of UA’s unique international outreach program targeting Mexican and Mexican-American communities in the southwestern U.S., U.S.-Mexico border region, and Mexico itself.

Along with colleagues Denise Moreno Ramírez and Rocio Estrella, she organized an innovative science camp, CampCIENCIAS, for students living along the Arizona-Mexico border, and conducted science translation programs that included trainings for community health advocates known as promotoras. Additionally, she has established a solid partnership with EPA Office of Research Development Superfund and Technology Liaison Mike Gill. For the past three years they have been co-hosting an “EPA Seminar Series” bringing SRP science to remediation project managers within EPA Region 9, which includes Arizona, California, Hawaii, Nevada, the Pacific Islands subject to U.S. law, and approximately 140 Tribal Nations, and beyond.



*Ramírez, above, will get used to protective equipment, such as her respirator, as she pursues her research in communities near the Iron King Mine and Humboldt Smelter site. (Photo courtesy of Monica Ramírez and UA SRP)*

As she moves from part-time studies to full-time student status, Ramírez will bring her community-engagement skills to bear on her new work with the [Gardenroots](#) project, which addresses community concerns regarding the quality of produce from home gardens. She will be working with local vegetable gardeners to determine if their soils and vegetable gardens have been impacted by mine tailing waste.

The project aims to empower community members by training them to collect samples from their gardens for micronutrient and metals analyses and informing them about issues related to soil and water quality in Arizona and the Southwestern United States. Ramírez envisions project participants becoming ambassadors for the environment as they expand their understanding of the effects of the environment on their health and quality of their lives, and articulate their concerns about effective remediation efforts.

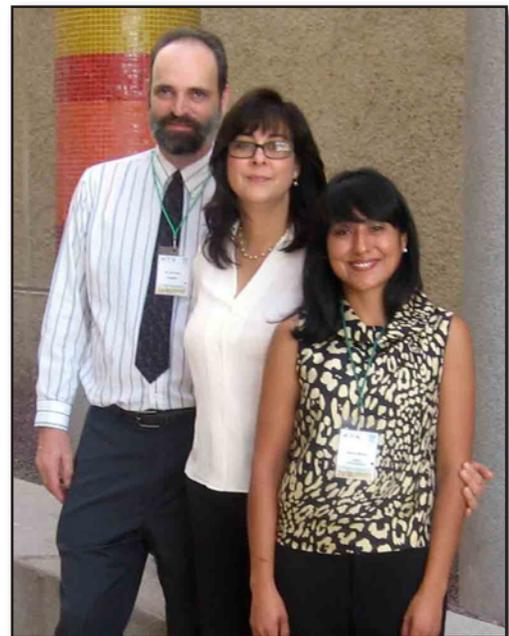


*Abandoned mines on both sides of the U.S.-Mexico border create an environmental hazard as wind and water transport tailings to the soil of nearby communities. (Photo courtesy of Monica Ramírez and UA SRP)*



*A team of UA SRP researchers is shown laying irrigation pipe at the King Mine site, in a phytostabilization trial to determine whether vegetation can keep mine tailings sequestered. (Photo courtesy of Monica Ramírez and UA SRP)*

[Return to Table of Contents](#)



*Three of Ramírez's colleagues posed for a photo at a UA-sponsored Specialized Workshop in Ciudad Obregón, Mexico in 2008 ([see story](#)). Shown left to right are Binational Center Co-director James Field, Ph.D., with Program Coordinators Rocio Estrella and Denise Moreno Ramírez. (Photo courtesy of UA SBRP)*

# Profiling NIEHS Recovery Act Success Stories

By Ed Kang

The influx of resources to the U.S. economy by the American Recovery and Reinvestment Act (ARRA) of 2009 has enabled some of the nation's best scientists to accelerate critical environmental health research – all while creating jobs in communities across the country. Recipients of NIEHS Recovery Act funding have been able to develop new, or expand existing, research capabilities. Their success stories are featured on the NIEHS [Web site](#) and demonstrate a wide diversity of scientific and economic impacts.

ARRA provided \$787 billion to help stimulate the U.S. economy. As part of the effort, NIEHS awarded nearly 350 grants to more than 150 U.S. institutions in 42 states. About \$114 million went to support new two-year research projects, while close to \$50 million went to support existing research. NIEHS also invested \$1.1 million to support summer research positions for students and teachers.

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



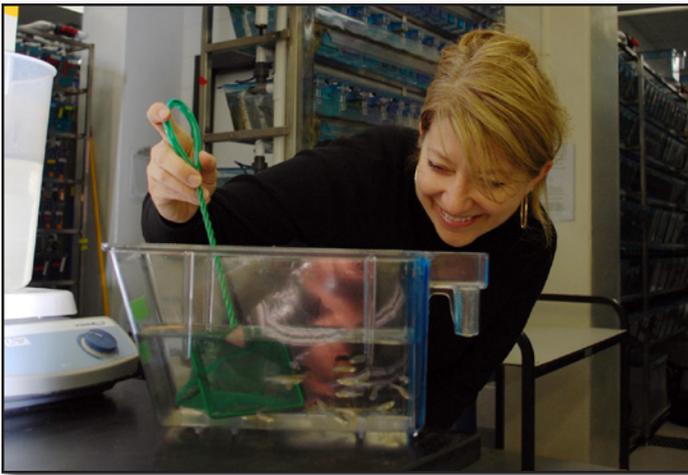
Vicki Kuo, an undergraduate student, and Dalei Wu, Ph.D., a post-graduate researcher, are part of Christoph Vogel's lab at the University of California, Davis studying the effects of environmental toxicants on cells of the immune system. (Photo courtesy of Christoph Vogel)



In the Salinas Valley of California, hundreds of farm workers and their children have been evaluated to determine the effects of pesticides on health. With a Recovery Act grant, Kim Harley, Ph.D., has been able to repurpose the vast collection of data for a study on bisphenol A (BPA), a chemical widely used in the plastics industry. (Photo courtesy of Kim Harley)



High school students from Montana and Idaho show off their research projects, which examined indoor air quality issues in rural communities. In a [podcast](#), Tony Ward, Ph.D., assistant professor at the University of Montana Center for Environmental Health Sciences (CEHS), and others discuss education efforts in rural areas that contribute to the prevention of respiratory diseases such as asthma and lung cancer. (Photo courtesy of Tony Ward)



*Lisa Satterwhite, Ph.D., is creating a strain of tiny zebra fish that act like a bioluminescent signal flare, flashing in the presence of dangerous toxic chemicals. (Photo courtesy of Lisa Satterwhite)*



*Shown, left to right, research technician Bernardine Frankel, graduate student Rebecca Replogle, and research technician Kristen Wilde are part of the [Purdue team](#) studying nutrition and genetic variation. (Photo courtesy of Fleet Lab at Purdue University)*



*Libby, Mont., is an isolated town in the northwestern corner of the state. In a [podcast](#), Brad Black, M.D., director of the Center for Asbestos Related Disease (CARD), talks about the place he lives and works — where 70 years of vermiculite mining has led to asbestos exposure in generations of the town's residents. (Photo courtesy of Brad Black and CARD)*



*The International Chemical Workers Union Council Center (ICWUC) is working with the Coalition of Black Trade Unionists to deliver [training](#) to unemployed or underemployed people in disadvantaged communities. Upon completion of the training, 135 workers, such as the young men in Oakland, Calif. shown above, will be placed into remediation and green jobs. (Photo courtesy of ICWUC)*



*Jocelyn Biagini Myers, Ph.D., is a post-doctoral research associate at the Cincinnati Children's Hospital Medical Center researching pediatric asthma. (Photo courtesy of the University of Cincinnati)*

[Return to Table of Contents](#)

# NIEHS and the Action Agenda on Chemical Exposures

By Eddy Ball

Working behind the scenes for the past 12 months, a dedicated group of NIEHS scientists and environmental public health specialists is helping to create a comprehensive national action agenda on chemicals in the environment. This summer, NIEHS employees joined their colleagues again for meetings of work groups coordinated by a leadership council that includes NIEHS/NTP Director Linda Birnbaum, Ph.D., and NIEHS Senior Advisor for Public Health John Balbus, M.D., who also chairs the Monitoring Work Group.

Launched with fanfare at a meeting attended by some 500 people in Washington June 26, 2009, the [National Conversation on Public Health and Chemical Exposures](#) has mobilized more than 200 specialists, industry representatives, and environmental health advocates to participate on a leadership council and in work groups crafting statements on aspects of the issue. Along with Web dialogues and listening sessions with key stakeholders, the National Conversation has also sought public input and held community conversations throughout the country.

Led by the Centers for Disease Control and Prevention (CDC) and the Agency for Toxic Substances and Disease Registry (ATSDR), the National Conversation's vision is to ensure that chemicals are used and managed in safe and healthy ways for all people. The action agenda — clear, achievable recommendations — will help government agencies and other organizations strengthen their efforts to protect the public from harmful chemical exposures.

According to Balbus, this summer the working groups are finalizing sets of recommendations. "This fall, the Leadership Council will be trying to assimilate all the workgroup reports and other input into a final set of recommendations," he said. "We're working hard to capture the visionary ideas and aspirations of the participants, while also pushing to deliver a set of pragmatic, doable action steps."

The action agenda is slated for release in early 2011. Organizers anticipate that the report will serve as the master plan for measures to implement its recommendations in 2011 and 2012.

In addition to NIEHS leadership and staff, participants with ties to NIEHS serving on work groups include NIEHS grantees, members of NIEHS advisory councils, and representatives of the NIEHS Partners. Staff from the NIEHS intramural and extramural divisions are members of the following work groups:



*Birnbaum, above, and U.S. Environmental Protection Agency Administrator Lisa Jackson were keynote speakers at the June 26, 2009 launch, speaking on the topic "Collaboration is Essential to Strengthening America's Approach to Public Health and Chemical Exposures." (Photo courtesy of Steve McCaw)*



*In his role as NIEHS senior advisor on public health based in Bethesda, Balbus has followed the Conversation in his role as Leadership Council representative and chair of the Monitoring Work Group. (Photo courtesy of Steve McCaw)*

- Scientific Understanding — Neurotoxicology Group Principal Investigator Jean Harry, Ph.D., and Environmental Autoimmunity Group Principal Investigator Frederick Miller, M.D., Ph.D.
- Policies and Practices — Superfund Research Program Analyst Beth Anderson
- Chemical Emergencies — Worker Education and Training Program Director Chip Hughes
- Serving Communities — Susceptibility and Population Health Branch Program Analyst Liam O’Fallon



*Harry is contributing her expertise in neurotoxicology and the effects of chemicals on the development of the brain and nervous system to a work group charged with assessing the kinds of scientific research that are critical to forming the Action Agenda. (Photo courtesy of Steve McCaw)*



*Based in Bethesda, Miller and his group are currently focusing investigations on the systemic rheumatic diseases and the environmental factors, including chemicals, that can trigger their characteristic autoimmune inflammatory response in humans. (Photo courtesy of Steve McCaw)*



*Anderson’s work with the NIEHS Superfund Research Program has given her insight into the most effective ways to meet her group’s charge to “determine prioritized actions that can be taken through legislation, regulation, and policy that will prevent harmful chemical exposures and spur the development and use of safer alternatives.” (Photo courtesy of Steve McCaw)*



*Hughes brings a wealth of experience in mobilizing responses to such emergencies as the World Trade Center attack, Hurricane Katrina, and the Gulf Oil Spill to his role in the Conversation Chemical Emergencies Work Group. (Photo courtesy of Steve McCaw)*



*O’Fallon has been a driving force in NIEHS environmental justice and community-based participatory research programs, as well as the development of its Partnerships for Environmental Public Health program. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

# Postdocs Play Key Role in Summer Training

*By Negin Martin*

Throughout July, NIEHS Summers of Discovery (SOD) students got a chance to learn about environmental effects on human health in a series of interactive seminars designed and presented by teams of postdoctoral fellows ([see story](#)). The series is the result of 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.

According to Klotz and Wilson, the involvement of trainees in the seminars — a new feature this summer — offers students expanded mentoring opportunities and complements trainees' career development experience at NIEHS. "The postdocs gained experience in the delivery aspect of teaching a course on environmental exposures," Klotz said, "but even more importantly, they gained experience in developing the curriculum, learning how to design course content and evaluate whether or not the students learned from it."

Klotz worked with Principal Investigators David Armstrong, Ph.D., and David Miller, Ph.D., last summer laying the groundwork for the new active learning concept. Last fall, Klotz gathered a group of interested postdocs and gave them full reign, with some guidance and mentoring, to teach the workshops this summer and also to develop the theme and design the entire content.

Each week, a general theme tied together all the presentations and exercises. The presenters — postdocs, predocs, and other lab scientists ([see text box](#)) — interspersed the weekly seminars on heavy metals, radiation, and hormones with exercises that emphasized active learning and participation. Students worked in teams at tables in the Institute's Rodbell Auditorium and, for one exercise on solar radiation, even took their learning outside.

According to SOD intern Zach McCaw, the course design was very effective in expanding his understanding of issues in environmental health. "The seminars gave us a glimpse of the diverse perspectives from which the effects of our environment on human health are under investigation," he said. "This introduction to the many pathways that address ambient influences on our wellbeing underscores the numerous opportunities for continued research that needs to be done."



*Erin Hopper, above, was one of the presenters at the "Diet and Hormones" seminar July 20. Her exercise on measuring fat in potato chips also brought home important lessons about designing experiments. (Photo courtesy of Steve McCaw)*



*Mercedes Arana, above, and her colleagues worked the room during the exercises. Arana, who was a postdoc last summer, assisted Principal Investigator Tom Kunkel, Ph.D., who taught the pilot interactive seminar last year. (Photo courtesy of Steve McCaw)*

The series concluded July 27 with a seminar on air pollution, followed by the annual poster session and awards ceremony July 29, which will be the subjects of a report in the September issue of the *Environmental Factor*.

(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences. She recently completed a postdoctoral fellowship with the NIEHS Membrane Signaling Group.)



Bill Fitzgerald brought several items, such as the water jug above, to demonstrate the ubiquity of radiation in the environment. He scanned the jug and a rock with radon with his handheld Geiger counter. (Photo courtesy of Steve McCaw)



Archana Dhasarathy, right, and Sophia Bolick demonstrate that at times “team teaching” could be interpreted literally, as they took turns at the podium. (Photo courtesy of Steve McCaw)

## A Dynamic Team of Instructors

To keep things lively and students attentive, each session involved several scientists from NIEHS labs:

- Intramural Research Training Award (IRTA) Postdoctoral Fellow [Amy Abdulovic, Ph.D.](#), of the DNA Replication Fidelity Group
- Biologist [Mercedes Arana, Ph.D.](#), of the DNA Replication Fidelity Group where she also completed her postdoctoral fellowship
- IRTA Fellow [Sophie Bolick, Ph.D.](#), of the Molecular and Genetic Epidemiology Group
- IRTA Fellow [Abee Boyles, Ph.D.](#), of the Reproductive Epidemiology Group
- Research Fellow [Archana Dhasarathy, Ph.D.](#), of the Eukaryotic Transcriptional Regulation Group
- Radiation Safety Officer Bill Fitzgerald, of the Health and Safety Branch
- IRTA Fellow [Laura Fuhrman, Ph.D.](#), of the Comparative Genomics Group
- IRTA Fellow [Cynthia Holly, Ph.D.](#), of the Macromolecular Structure Group
- IRTA Fellow [Erin Hopper, Ph.D.](#), of the Mass Spectrometry Group
- Biologist [Wendy Jefferson, Ph.D.](#), of the Reproductive Medicine Group
- IRTA Pre-doctoral Fellow [Matthew McElwee](#), of the Comparative Genomics Group
- Biologist [Michelle Sever](#), of the Environmental Cardiopulmonary Disease Group
- IRTA Fellow [Jennifer Sims, Ph.D.](#), of the Eukaryotic Transcriptional Regulation Group
- IRTA Fellow [Jana Stone, Ph.D.](#), of the DNA Replication Fidelity Group
- IRTA Fellow [Danielle Watt, Ph.D.](#), of the DNA Replication Fidelity Group

This summer, Arana, Bolick, and Hopper also made presentations at the [EHP science teacher workshop](#) titled “Air, Water, and You,” and Watt spent a Saturday in June working with students in the [Durham Alumnae Chapter of Delta Sigma Theta Sorority Science and Everyday Experiences](#) program.

# A Fitting Tribute to Colin Chignell

By Eddy Ball

As part of its July issue, the journal Photochemistry and Photobiology honored NIEHS Principal Investigator Colin Chignell, Ph.D., with a “Symposium in Print: Photobiology of the Skin and Eye in Memory of Colin F. Chignell.” Chignell was the longtime chief of the Laboratory of Molecular Biophysics at NIEHS and subsequently a member of the Laboratory of Pharmacology until his unexpected death on July 16, 2008 ([see story](#)).

The special section of the [issue](#) includes an introduction by four of Chignell’s long-time friends and colleagues, including Joan Roberts, Ph.D., professor of chemistry in the Department of Natural Sciences at Fordham University, and Yu-Ying He, Ph.D., an assistant professor in the Department of Medicine at the University of Chicago. Roberts was a longtime faculty member in the Summer of Discovery Program with Chignell, and He was his postdoctoral fellow at NIEHS from 2003-2008. Roberts is working this summer as special volunteer in the NIEHS Free Radical Metabolism Group.

The “Symposium in Print” includes a series of ten papers on topics with strong links to Chignell’s major research interests in skin and eye photochemistry and photobiology, authored by his former colleagues and students at NIEHS and elsewhere. Chignell is an author on five of the papers, including ones written with Roberts, He, and NIEHS Principal Investigator Ron Mason, Ph.D.

”The papers presented are a tribute to the extraordinarily rich interdisciplinary role Colin played during his scientific lifetime and to the wonderful example he set as a caring and thoughtful person,” Roberts and her coauthors wrote in their introduction.

In his announcement to NIEHS employees, Acting Scientific Director John Pritchard, Ph.D., thanked Roberts for her leadership in organizing the special issue and reflected on the legacy of his longtime friend and colleague. “He was a leader in the fields of photobiology and phototoxicity, particularly as light or UV radiation impacted the skin and eyes,” Pritchard wrote. “This issue is a fitting reminder of all he accomplished and how much we miss his scientific expertise and counsel.”

[Return to Table of Contents](#)



*Following his accidental death in the ocean off Myrtle Beach, S.C., Chignell was remembered fondly by his many friends and colleagues. “Colin displayed great versatility in his work, always welcoming new collaborators and always adapting to or leading the way to new scientific developments,” wrote Roberts and co-authors in a November 2008 [tribute](#) in ASP News, a publication of the American Society of Photobiology. (Photo courtesy of Steve McCaw)*

# Staff Recognized with NIH Director's Award

By Robin Arnette

Each year the NIH holds an awards ceremony that recognizes employees who have performed exceptional work on behalf of the agency. On July 15, four NIEHS employees along with representatives from all of the other NIH Institutes and Centers (ICs) joined NIH Director Francis S. Collins, M.D., Ph.D., at the 2010 NIH Director's Awards Ceremony. The festivities took place at the Natcher Conference Center on the main campus in Bethesda, Md.

John Burklow, Associate Director of the Office of Communications and Public Liaison at NIH, served as the master of ceremonies and explained that the NIH Director's Awards "recognized superior performance or special effort significantly beyond regular duty requirements and related directly to fulfilling the mission of the NIH." As Collins presented the plaques, awardees were also congratulated by their individual IC Directors. NIEHS/NTP Director Linda Birnbaum, Ph.D., was on stage during the NIEHS portion of the event.

## Awardees from NIEHS

- Management Analyst Kent Stone received an administrative award for sustained excellence in providing essential administrative support for the NIEHS Division of Intramural Research, while serving in acting roles.
- Administrative Officer Connie Riley won her administrative award for sustained excellence in providing essential administrative support for the NIEHS Division of Intramural Research, while serving in acting roles.
- [Karen Adelman, Ph.D.](#), a principal investigator in the Laboratory of Molecular Carcinogenesis, was recognized in the Scientific/Medical category for her seminal work on the mechanism of RNA polymerase stalling, a regulatory process for rapid change in the transcriptional status of specific genes.
- Senior Advisor Christopher Portier, Ph.D., also received a Scientific/Medical award for his outstanding vision and leadership of an interagency working group in creating a federal research needs report on climate change and health.



*Birnbaum and Collins congratulate two of the four NIEHS winners. From left to right: Birnbaum, Stone, Riley, and Collins. Adelman and Portier were unable to attend. (Photo courtesy of Michael Spencer)*



*Collins displays his musical talent and songwriting ability for the NIH audience. (Photo courtesy of Michael Spencer)*

## NIH Director provided entertainment

Before Collins handed out the plaques, he serenaded the audience with his guitar, using his own rendition of the folk song, “For All the Good People.” The lyrics, modified to fit the occasion, praised not just the awardees, but all NIH’ers for their hard work and commitment.

He introduced the song by saying, “This is a song for all of the good people, and by this I mean all of you and all of the thousands of people who dedicate themselves everyday to the amazing mission of the NIH, to try to find the causes and, ultimately, the treatments, cures, and preventions for those diseases that affect too many.”



*In 2006, Adelman received a Rising Star Early Career Award at the annual NIEHS Science Day. When Collins visited NIEHS this year, he mentioned Adelman as a shining example of the talented young scientists working at the Institute. (Photo courtesy of Steve McCaw)*



*Portier has recently been named as director of the National Center for Environmental Health/Agency for Toxic Substances and Disease Registry at the Centers for Disease Control and Prevention in Atlanta, Ga. ([see story](#)) He assumed his new post on August 1. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

# Science Notebook

## Chromatin Remodeling and the Glucocorticoid Receptor

By Sophie Bolick

Geneticist [Gordon Hager, Ph.D.](#), chief of the Laboratory of Receptor Biology and Gene Expression at the National Cancer Institute, shared his recent research findings on epigenetic modification of chromatin in an afternoon seminar July 7 at NIEHS titled “Rapid Dynamics and Gene Regulation by Nuclear Receptors.”

Hosted by Linda Birnbaum, Ph.D., John Cidlowski, Ph.D., and Ken Korach, Ph.D., Hager discussed his work on how nuclear receptors interact with chromatin and the effect of this interaction on hormone function and the transcription mechanisms involved in many disease processes, including cancer development.

### Chromatin status is important for receptor action

As Hager and his [group](#) investigated the role of SWI/SNF protein remodeling complex glucocorticoid receptor (GR) action, they observed patterns emerging. “What we began to see is a layer of organization at the level of chromatin structure that dictates whether a receptor can gain access and act at those specific sites,” explained Hager. The finding led him to speculate on several specific mechanisms that may be involved.

For one, if a specific remodeling system is necessary, then its presence is critical for the ability of the receptor to work at the site in question. A second possibility is that epigenetic marks on histones or DNA determine chromatin conformation at a given site. Finally, the presence of specific factors that recruit remodeling systems is also needed, he said, because “if the receptor can’t open those sites on its own, then another protein is apparently able to open those sites for them.”

### Mechanisms governing access to GR binding sites

The data generated by his group’s experiments ([see text box](#)) correlated well with the earlier data on GR binding sites. There is a universal overlap between GR binding and hypersensitivity sites. According to Hager, the vast majority of these GR binding events occur at pre-existing DNase hypersensitivity sites, which are already open due to some other process. But, if the chromatin isn’t open and accessible, the GR cannot initiate that activity on its own.



*“We think the dynamics of receptor movement are intimately involved in the remodeling process,” said Hager as he began his talk. He and his group have a long-standing interest in the interaction of nuclear receptors with chromatin. (Photo courtesy of Steve McCaw)*



*The late afternoon lecture drew a number of NIEHS senior investigators, including an attentive Michael Resnick, Ph.D., principal investigator of the Chromosome Stability Group. (Photo courtesy of Steve McCaw)*

As Hager explained, it is thought that there are cell-specific transcription factors that prepare sites for subsequent binding by receptors. Identifying these is an arduous informatics exercise, utilizing *de novo* motif discovery. One example of this is the AP-1 motif present in mammary cells. A c-Jun binding event is equivalent to local DNase hypersensitivity activity in mammary cells. In fact, there is approximately 40 percent overlap between c-Jun binding and GR binding in mammary cells. This is supported by functional evidence using dominant negative forms of AP-1.

### Rapid dynamics of chromatin remodeling processes

The residence time of a receptor on a binding site is very short, involving seconds, rather than minutes or hours. “We feel this [rapid exchange] is very important to the way transcription biology works,” emphasized Hager. This line of thinking led his group to propose a “hit-and-run” model, in which binding events are seen as very transient. When receptor is activated, the result is more frequent events, or hits. When the receptor is inactive, there are infrequent, non-productive hits. GR is not even in the nucleus in the absence of ligand, so very few of these events occur. “We argue ‘hit-and-run’ is a required mechanism for how GR-regulated transcriptional processes work,” Hager concluded.

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

[Return to Table of Contents](#)

## Tox21 Welcomes FDA as Partner

By Robin Mackar

A powerful federal agency collaboration welcomed a new partner this summer. The U.S. Food and Drug Administration (FDA) officially joined the NIEHS/NTP, the National Institutes of Health Chemical Genomics Center (NCGC), and the U.S. Environmental Protection Agency (EPA) July 20 as a partner in Tox21 — the interagency consortium to advance toxicology in the 21st century.

### Cell-specific Mechanism of GR Action

Hager’s group set out to determine whether the SWI/SNF protein-remodeling complex was important for glucocorticoid receptor (GR) action. Surprisingly, knockdown of SWI/SNF activity completely obliterated constitutive hypersensitive sites in a given region, but the GR-induced locus was refractory to SWI/SNF knockdown. These surprising results led to the idea there are either GR-dependent *de novo* sites or constitutive sites, induced in the absence of GR. It was becoming clear that chromatin status of response elements is a major contributor to cell selective GR action at specific genes.

The researchers also used genome-wide mapping of DNase I hypersensitivity sites — a technical advance that has allowed for localized chromatin transitions to be mapped on a much larger scale than before. This is important, Hager explained, because it “gives you a powerful window on what’s going on in terms of regulation with that particular cell type,”

Data generated using this technology shows the receptor always binds at regions of hypersensitivity. When a mammary cell is compared to a pituitary cell, the hypersensitivity sites where receptor binding occurs are constitutively open in both cell types. However, in the instance of a gene active in a mammary cell line, a *de novo* event where chromatin is open on its own is present, creating a hypersensitivity site. This does not occur in the pituitary cell, so the receptor is unable to bind to chromatin.



Tox21 merges federal agency resources (research, funding and testing tools) to develop ways to more effectively predict how chemicals will affect human health and the environment. Tox21 was established in 2008 with a [Memorandum of Understanding \(MOU\)](#) that was expanded this summer to include [FDA](#).

“Using the best science to protect human health and the environment is the ultimate goal of this collaboration,” said Linda Birnbaum, Ph.D., director of the NIEHS and NTP. “The addition of FDA to this effort allows biomedical researchers and regulatory scientists to work together to more rapidly screen chemicals and find more effective ways for protecting the health of the public. The NTP is pleased to bring its toxicology and coordination expertise to bear on making Tox21 a reality.”

Along with Christopher Austin, M.D., director of the NCGC and Robert Kavlock, Ph.D., director of EPA’s National Center for Computational Toxicology, Raymond Tice, Ph.D., chief of the Biomolecular Screening Branch at NIEHS/NTP was instrumental in working with FDA staff to achieve this new MOU. “FDA brings not only its experience in human health effects to the MOU, but the capabilities of the FDA National Center for Toxicological Research will also be key in accelerating our progress in this unique effort,” Tice stated.

FDA will provide additional expertise and chemical safety information to improve current chemical testing methods. “This partnership builds upon FDA’s commitment to developing new methods to evaluate the toxicity of the substances we regulate,” said Janet Woodcock, M.D., director of FDA’s Center for Drug Evaluation and Research.

“This collaboration is revolutionizing the current approach to chemical risk assessment by sharing expertise, capabilities, and chemical information, which will lead to both a faster and deeper understanding of chemical hazards,” said Paul Anastas, Ph.D., assistant administrator for EPA’s Office of Research and Development. “Through the Tox21 collaboration, 2,000 chemicals have already been screened against dozens of biological targets and we are working to increase the number of chemicals to 10,000 by the end of the year.”

A critical part of the Tox21 partnership is the robotic screening and informatics platform at the NCGC that uses fast, automated tests to screen thousands of chemicals a day for toxicological activity in cells.

## What is Tox21?

Tox21 is a collaboration among federal agency partners striving to develop a new paradigm of predictive toxicology by pursuing seven enabling objectives:

- Research, develop, validate, and translate innovative chemical testing methods that characterize toxicity pathways.
- Investigate ways to use new tools to identify chemically induced biological activity mechanisms.
- Prioritize which chemicals need more extensive toxicological evaluation.
- Develop models that can be used to more effectively predict how chemicals will affect biological responses.
- Identify chemicals, assays, computational platforms, and targeted testing needed for the innovative testing methods.
- Complete acquisition in 2010 for a library of more than 10,000 chemicals for quantitative high-throughput screening (qHTS) at the NCGC.
- Implement Phase II of EPA’s ToxCast™ program, which will include the screening of a 700-compound subset of the 10,000 compound library in various mid- and high-throughput assays. ToxCast™ is an initiative launched in 2007 by EPA to revolutionize the agency’s chemical toxicity evaluation procedures. ToxCast™ will use advances in computers, genomics, and cellular biology to speed up toxicity testing and enhance capacity to screen new compounds.

The data generated from the innovative chemical testing methods by the Tox21 partnership will be public and provided to risk assessors to use when making decisions about protecting human health and the environment.

“Our robots screen in a day what would take one person a year to do by hand, allowing a fundamentally different approach to toxicology, which is comprehensive and based on molecular mechanisms,” said Austin.

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

[Return to Table of Contents](#)

## Fellows Honored for Research Excellence

*By Eddy Ball*

NIEHS set records during the 2011 NIH Fellows Awards for Research Excellence (FARE) competition for the numbers of awards to predoctoral fellows and of consecutive awardees. After reviewing 1,030 submissions of research abstracts, the NIH Fellows Committee (FelCom) FARE Subcommittee on July 12 announced 260 awards to fellows in training at the 27 institutes and centers (ICs) that make up NIH.

With 21 [FARE](#) prizes this year, NIEHS fell short by one of the record number of 22 awards earned by its fellows in 2006. Although NIEHS is in the mid-range in terms of size and budget among the NIH institutes, the Institute tied for third place in the total number of awards, surpassed only by the National Cancer Institute and National Institute of Allergy and Infectious Disease.

In his announcement of the NIEHS winners, Deputy Scientific Director Bill Schrader, Ph.D., wrote, “It is particularly gratifying to see that two predoctoral Intramural Training Award (IRTA) students qualified for these awards.” The awards reflect the scientific excellence of the winners, the quality of the NIEHS training and career development program, and the superior mentoring that takes place in the Institute’s labs.

The FARE program is sponsored by the NIH Fellows Committee, Offices of the Scientific Directors, the NIH Office of Research on Women’s Health, and the NIH Office of Intramural Training and Education, and is funded by the Scientific Directors and the Office of Research on Women’s Health. Fellows submit abstracts based their research, which are reviewed and ranked by panels of senior scientists.

The prizes are both an honor and a source of additional support for trainee professional and career development:

- A \$1000 travel award to attend a scientific meeting at which they present their work
- An invitation to present their posters at the annual Research Festival and attend the FARE award ceremony held in October
- Eligibility to serve as judges for the following year’s FARE competition



*Nichols, above, studied toxicology at the University of North Carolina at Chapel Hill. She said of her training, “Conducting my graduate research under Dr. Kleeberger at NIEHS has allowed me to take part in a translation research endeavor, working with a multitude of collaborators and resources to address a critical clinical discrepancy.” (Photo courtesy of Steve McCaw)*

## 2011 NIEHS FARE Honor Roll — Winners, Abstract Titles, and Mentors

Two predoctoral fellows were honored for research excellence:

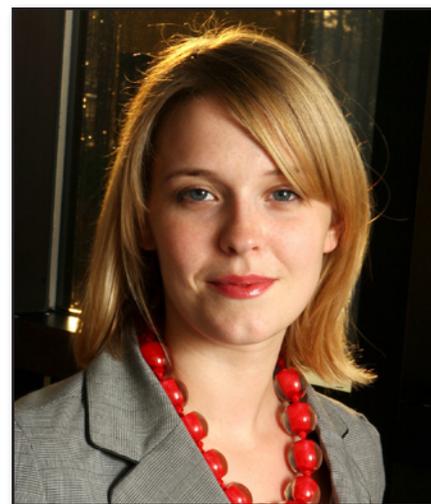
- **Environmental Genetics Group** IRTA Predoctoral Fellow Jennifer Nichols, B.S. — Identifying Candidate Susceptibility Genes in a Murine Model of Bronchopulmonary Dysplasia — Mentor Steve Kleeberger, Ph.D.
- **Molecular Endocrinology Group** IRTA Predoctoral Fellow Lindsay Smith, Ph.D. — Dysregulation of microRNA Expression and Processing During Glucocorticoid-induced Apoptosis of Lymphocytes — Mentor John Cidlowski, Ph.D.

Six postdoctoral fellows took home FARE awards for the second year in a row:

- **Host Defense Group** IRTA Postdoctoral Fellow Jim Aloor, Ph.D. — Leucine Rich Repeats and Calponin Homology Containing Protein 4 (Lrch4), a New Regulator of Lipopolysaccharide Signaling — Mentor Mike Fessler, M.D.
- **Host Defense Group** IRTA Postdoctoral Fellow David Draper, Ph.D. — The Cholesterol Transporter ATP Binding Cassette G1 Regulates Adaptive Immunity in the Lung — Mentor Mike Fessler, M.D.
- **Molecular Endocrinology Group** IRTA Postdoctoral Fellow Erica Lannan, Ph.D. — Identification of a Novel Synergistic Gene Regulation Between Glucocorticoid and Cytokine Signaling — Mentor John Cidlowski, Ph.D.
- **Immunogenetics Group** Research Fellow Hideki Nakano, Ph.D. — Lung Resident CD103+ Dendritic Cells Selectively Prime Th2 Responses to Inhaled Antigens — Mentor Don Cook, Ph.D.
- **Synaptic and Developmental Plasticity Group** Visiting Fellow Ramendra Saha, Ph.D. — Promoter Proximal RNA Polymerase II Stalling May Determine Temporal Expression Kinetics of Neuronal Immediate Early Genes — Mentor Serena Dudek, Ph.D.
- **Intracellular Regulation Group** Research Fellow Xueqian (Shirley) Wang, Ph.D. — Activating PKC $\beta$ 1 at the Blood-Brain Barrier (BBB) Reverses Induction of P-glycoprotein (Pgp) Activity by AhR and Restores Drug Delivery to the CNS — Mentor David Miller, Ph.D.

Another 13 fellows received their first FARE awards this year:

- **DNA Replication Fidelity Group** IRTA Postdoctoral Fellow Amy Abdulovic, Ph.D. — Mechanisms of Mutagenesis in vivo due to Imbalanced dNTP Pools — Mentor Tom Kunkel, Ph.D.
- **Molecular Endocrinology Group** IRTA Postdoctoral Fellow Amy Beckley, Ph.D. — Stress-activated, Hormone-independent Glucocorticoid Receptor Phosphorylation at Serine 134 Preconditions Cells and Alters Their Transcriptional Response to Glucocorticoid Hormones — Mentor John Cidlowski, Ph.D.



*Smith, above, completed her doctorate in toxicology in July at the University of North Carolina at Chapel Hill. She described her pre-doc experience as “unique and overwhelmingly positive... encouraging and collaborative.” She added, “I like it so much here I am staying on for a post-doc.” This fall, Smith begins work with the Intracellular Regulation Group. (Photo courtesy of Steve McCaw)*



*Aloor won a FARE last year for his abstract, “HIV-1 Envelope Protein gp41 Triggers Pro-inflammatory Responses in the Macrophage Through Toll Like Receptors-2 and -4 and Their Adaptors.” (Photo courtesy of Steve McCaw)*

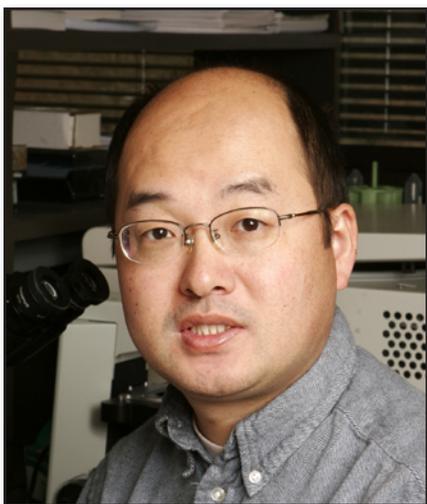
- **Free Radical Metabolism Group** Visiting Fellow Saurabh Chatterjee, Ph.D. — Leptin-redox Stress Synergy Exacerbates Steatohepatitis of Obesity in Environmental Carbon Tetrachloride (CCL4) Exposure — Mentor Ron Mason, Ph.D.
- **Transmembrane Signaling Group** Visiting Fellow Alejandro Colaneri, Ph.D.— A New Perspective on the Mammalian Genome Bimodal Methylation Pattern — Mentor Lutz Birnbaumer, Ph.D.
- **Cell Biology Group** Visiting Fellow Huaixin Dang, Ph.D. — The Nuclear Orphan Receptor TAK1/TR4 Plays a Critical Role in the Development of Obesity, Insulin Resistance, and Inflammation — Mentor Anton Jetten, Ph.D.
- **Mitochondrial DNA Replication Group** Visiting Fellow Rajesh Kasiviswanathan, Ph.D. — Translesion Synthesis Past Acrolein-derived DNA Adduct, Gamma-hydroxypropano-deoxyguanosine, by the Human Mitochondrial DNA Polymerase Gamma Mentor Bill Copeland, Ph.D.
- **Transcriptional Responses to the Environment Group** Research Fellow Sergei Nechaev, Ph.D. — Distribution and Dynamics of Promoter-proximal RNA Polymerase II Stalling Based on Global Sequencing of Short RNAs — Mentor Karen Adelman, Ph.D.
- **Molecular Endocrinology Group** Visiting Fellow Javier Revollo, Ph.D. — Derepression of Gene Expression by the Glucocorticoid Receptor: Silencing of Hes1 is Necessary for the Glucocorticoid Receptor — Mentor John Cidlowski, Ph.D.
- **Synaptic and Developmental Plasticity Group** IRTA Postdoctoral Fellow Stephen Simons, Ph.D. — A Novel Mechanism for Caffeine-induced Cognitive Enhancement — Mentor Serena Dudek, Ph.D.
- **DNA Replication Fidelity Group** IRTA Postdoctoral Fellow Jana Stone, Ph.D. — DNA Polymerase Zeta Can Bypass UV Photoproducts Without Assistance from Another Polymerase — Mentor Tom Kunkel, Ph.D.
- **Immunogenetics Group** IRTA Postdoctoral Fellow Rhonda Wilson, Ph.D. — Reversible Suppression of Ongoing Th2 and Th17 Responses in the Lung by ICOS – ICOS-ligand Interactions — Mentor Don Cook, Ph.D.
- **Biostatistics Branch** Visiting Fellow Sailu Yellaboina, Ph.D. — Computational Prediction and Experimental Validation of Novel Genes Essential for Embryonic Stem Cell Maintenance and Self-renewal — Mentor Raja Jothi, Ph.D.
- **Cell Biology Group** IRTA Postdoctoral Fellow Gary ZeRuth, Ph.D. — Suppressor of Fused Interacts with Gli-similar 3 (Glis3), Inhibits Glis3 Activation of Insulin, and Protects Glis3 Against Speckle Type POZ Protein/Cullin 3-mediated Degradation — Mentor Anton Jetten, Ph.D.



*Draper made an oral presentation, “ABCG1 is a Negative Regulator of Pulmonary Host Defense,” at the 2009 NIH Research Festival symposium on “Cross-regulation of Innate Resistance and Adaptive Immunity.” (Photo courtesy of Steve McCaw)*



*Lannan participated in the 2009 NIH Research Festival symposium on “Understanding Human Immunology” with her oral presentation, “Identification and Classification of Inflammatory Genes Co-regulated by Dexamethasone and TNF-Alpha.” (Photo courtesy of Steve McCaw)*



*Nakano won a FARE last year for his abstract on “The Impact of Surface ALDH1a2 on Pulmonary Dendritic Cells for Generation of Regulatory T Cells Leading to Immunotolerance to Inhaled Antigens.” (Photo courtesy of Steve McCaw)*



*Saha presented his poster, “Rapid Induction of Neuronal Arc Is Mediated by a Promoter Proximal RNA Polymerase-II Stalling Mechanism,” at the 2009 NIH Research Festival. (Photo courtesy of Steve McCaw)*



*Wang was honored last year for her abstract, “The Aryl Hydrocarbon Receptor (AhR) Regulates P-glycoprotein at the Blood-brain Barrier (BBB),” which also earned her two first-place prizes at the annual Society of Toxicology (SOT) meeting (see story) earlier this year. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

## Summer Students Flock to Lecture Series

*By Negin Martin*

The popularity of the first three Summers of Discovery (SOD) seminars in July proved that their new format was a formula for success ([see story](#)). On average half or more of the 50 students participating in this year’s summer program attended each of the seminars.

### Heavy metals — a common health risk in the environment

[Jennifer Sims, Ph.D.](#), opened the SOD seminar series by explaining the outcome of exposure to high doses of heavy metals on human health. Due to their stability and persistence in the environment, arsenic, lead, and mercury are ranked among the most hazardous pollutants. In addition to natural sources, smelting of the ores, incorporation of metal coating in paint, and burning of fossil fuels have increased levels of accumulated metals in the environment, wildlife and humans.



*During the session on “Heavy Metals,” each of the tables featured a microscope that students used to see the effects of cadmium exposure on their roundworms. (Photo courtesy of Steve McCaw)*

Sims gave details of known toxicological responses to heavy metals and finished her talk by introducing *C. elegans* as a model organism for studying metal toxicity. Students examined assigned petri dishes of *C. elegans* with different metal exposure levels to determine the LD50s — the lethal dose that killed half of the population.

Pollution due to release of non-essential metal cadmium into the environment — from discarded old batteries and fossil fuel combustion — and its effect on gene regulation was the topic of the talk by [Laura Fuhrman, Ph.D.](#)

Graduate student [Matthew McElwee](#) introduced SOD interns to the microarray technology. For the last activity of the day, groups of students had to analyze microarray results to determine which genes are up- or down-regulated.

### **Radiation — protecting our genetic stability**

NIEHS Radiation Safety Officer Bill Fitzgerald opened the second session of SOD presentations with an energetic and engaging talk about types and sources of radiation. Students learned about why some atoms radiate and what type of radiation is harmful to health. The first activity prompted students to list at least 10 sources of radiation and rank them based on their ionizing strength.

[Mercedes Arana, Ph.D.](#), and [Danielle Watt, Ph.D.](#), taught interns about the differences between DNA damage and DNA mutations. Environmental insults such as ionizing radiation can damage DNA, but cells are equipped with DNA repair mechanisms that protect genetic stability. During the process of repair, some damage is translated into modifications to the genome that are preserved and passed on to progenies as mutations. Presenters introduced students to the processes involved in DNA replication and repair in cells.

Students also got a chance to test the amount of protection that sunblocks, sunglasses, and clothing offer from cosmic radiation, as they went outdoors with radiation sensitive beads and analyzed the different ways of blocking UV light from sun.

### **Steroids and hormones: natural and unnatural sources of endocrine disruption**

The first speaker for the third week of the SOD series was [Abee Boyles, Ph.D.](#), an epidemiologist who investigates the role of maternal folic acid levels in birth defects. Boyles outlined the debate over the healthy levels of folic acid. In the U.S., grains and cereals are fortified with folic acid to lower the rate of birth



*For Bolick's presentation, the students found bags of common household items on their tables. Their exercise involved evaluating the contents of each item and the potential harm of exposure on human health. (Photo courtesy of Steve McCaw)*



*During the session on "Radiation," students exposed radiation-sensitive beads to sunlight. The exercise got them out of their seats and gave them a tangible demonstration of effective ways to protect against radiation exposure. (Photo courtesy of Steve McCaw)*

defects. However, some question the health effects of cumulative high levels of folate from dietary supplementation. Boyles presented parts of her ongoing research that demonstrate an association between lower levels of maternal folic acid and children with cleft lip and palate.

Endocrine disruptors in common household items was the topic of the second activity conducted by [Sophie Bolick, Ph.D.](#) Students learned about dioxins, phthalates, and bisphenol A in cosmetics and plastics. [Archana Dhasarathy, Ph.D.](#), and [Erin Hopper, Ph.D.](#), instructed students during an activity on how to measure and compare fat content of regular, fat-free, and baked snacks.

At the closing of the third session, students heard a talk by [Wendy Jefferson Ph.D.](#), about genestein, a phytoestrogen in soy. Phytoestrogens are naturally occurring plant steroids that mimic estrogen and have been shown to have a profound effect on the reproductive system. Infants on soy formulas are exposed to high doses of genestein, which raises concern. Jefferson's research on mice has shown that exposure to genestein has adult reproductive outcomes and increases the chance of uterine cancer.

(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences. She recently completed a postdoctoral fellowship with the NIEHS Membrane Signaling Group.)

[Return to Table of Contents](#)

## Investigating Rare Diseases in Search of a Common Cure

*By Thaddeus Schug*

“NIEHS has undergone a remarkable transition with the development of its clinical program and it is very reassuring to see that you have clearly put it together right,” stated [John Gallin, M.D.](#), director of the NIH Clinical Center since 1994. Gallin visited NIEHS July 15, to tour the new NIEHS Clinical Research Unit and deliver a [presentation](#) as part of the Clinical Director's Seminar Series, hosted by NIEHS Acting Clinical Director Darryl Zeldin, M.D.

Gallin, a prominent clinician and researcher of rare diseases, spoke on “The Pipeline of Clinical Research: Spotlight on Rare Diseases.” His seminar



*Summers of Discovery Coordinator Debbie Wilson reminded students of the coming deadline for their abstracts. Despite the pressure they were under to finish their projects, students made the time to attend the seminars. (Photo courtesy of Steve McCaw)*



*In one of his many accomplishments as director of the NIH Clinical Center Gallin pioneered development of the Undiagnosed Diseases Program, which is a trans-NIH initiative focusing on the most puzzling medical cases referred to the NIH Clinical Center in Bethesda, Md., by physicians across the nation. (Photo courtesy of Steve McCaw)*

offered attendees an overview of the clinical program in Bethesda and new insight into the larger public health potential of research into diseases that affect a very small portion of the population.

As Gallin explained, the Clinical Center serves the needs of 17 NIH institutes and is the largest clinical research hospital in the world. Gallin oversaw the design and construction of a new research hospital for the Clinical Center, the Mark O. Hatfield Clinical Research Center, which opened its doors in 2005. He also literally wrote the book and curriculum for clinical research training at NIH, “[Principles and Practice of Clinical Research](#).” Since its inception in 1996, the NIH Clinical Training Program has trained over 19,000 clinical fellows and research investigators.

### Opening the Pipeline for Drug Development

The NIH Clinical Center currently hosts approximately 1,500 clinical research studies, about half of which are clinical trials in phase I or phase II of development. Much of the Clinical Center’s work focuses on rare diseases that the medical industry considers too risky for drug development.

According to Gallin, as few as 1 in 200,000 patients in the United States may have rare or undiscovered illnesses — but they account for about half of NIH’s patients. A central focus of the center is to investigate the possibility that new or existing drugs and protocols that are effective in treating patients with rare diseases could also be used to combat more common illnesses.

NIH has upgraded its drug development and manufacturing facility to “help move ideas from the laboratory bench to the patient faster and more effectively,” said Gallin. “Our hope would be that we could pass the baton on to industry after we get over that so-called valley of death — the gap between when the basic research is finished and when industry sees enough potential in a drug candidate to warrant starting a development program,” he added.

### Researching a Rare Immune Disorder

Gallin’s primary research interest is a rare hereditary immune disorder called chronic granulomatous disease (CGD). Patients with this disease have mutations in oxidase enzymes (NOX) contained in cells of the immune system. These defects make it difficult to create reactive oxygen compounds that phagocytes use to kill ingested pathogens. This defect leads to the formation of granulomata in many organs. Gallin’s laboratory discovered the genetic basis for several forms of CGD and conducted pioneering research that has reduced life-threatening bacterial and fungal infections in CGD patients.



*Zeldin, left, and Gallin hope to team together to share resources. “I hope that we can combine what is going on here at NIEHS and what is going on in Bethesda to strengthen our overall clinical programs,” Gallin told the audience. (Photo courtesy of Steve McCaw)*



*Research Fellow Hong Li, Ph.D., (left) and Technical Laboratory Manager Kevin Gerrish, Ph.D., were among those in a near capacity audience for the Clinical Director’s Seminar series held in Rodbell Auditorium. (Photo courtesy of Steve McCaw)*

According to Gallin, CGD affects about 1 in 200,000 people in the United States, with about 20 new cases diagnosed each year. Most people with CGD are diagnosed in childhood, usually before age 5. Early diagnosis is important since these people can be placed on antibiotics to ward off infections before they occur.

Gallin's discoveries of the defective genes within CGD patients has led to identification of several NOX isoforms in more common diseases. "It turns out that NOX proteins are found in many tissues of the body, and they are aligned with many inflammatory disease states, such as atherosclerosis, ischemia, and heart disease," he explained. These findings support Gallin's vision of investigating rare diseases in search of a common cure.

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction and a regular contributor to the Environmental Factor.)



*According to Gallin, the NIH Clinical Center covers 35 acres on the 302-acre NIH campus in Bethesda. (Photo courtesy of NIH)*

[Return to Table of Contents](#)

## Rare Disease Research Leads to Big Discovery

As young clinical fellows at NIH from 1968 to 1970, Michael Brown, M.D., and Joseph Goldstein, M.D., were fascinated by patients displaying a hereditary condition that caused excessive levels of cholesterol to build up in their blood. The disease produced severe atherosclerosis, leading to heart attacks in early childhood. The condition is very rare — affecting one in a million people — so the chance that they would see cases like this in any other clinical setting was extremely small.

Brown and Goldstein decided to build a research program with a mission to determine how genes control cholesterol levels in the blood, and why some people have almost no cholesterol and others have dangerously high levels. Brown later said, "If we hadn't seen those patients at NIH, we would have never known about this illness and we would never have worked on the problem."

In their later collaborations on the studies of familial hypercholesterolemia at the University of Texas Southwestern Medical School, they made use of serum samples gathered many years earlier at NIH. In 1985 Brown and Goldstein won the Lasker Award and the [Nobel Prize](#) for their discovery of mechanisms regulating cholesterol metabolism, laying the foundation for interventions to control cholesterol levels and help prevent the onset of cardiovascular disease for millions of patients.

# NIEHS Launches NanoHealth Signature Program

By Eddy Ball

Six months ago a team of investigators led by NIEHS Clinical Research Unit Medical Director and Matrix Biology Group Head [Stavros Garantziotis, M.D.](#), began preliminary studies for a novel, interdisciplinary and interagency project now underway to investigate the health effects of widely used engineered nanomaterials (ENM) in susceptible populations.

ENMs are increasingly found in medications, cosmetics, electronics, and other consumer products, creating environmental as well as occupational exposures. The study is one of several launched in the past year in response to the [NIH Nanoscience and Nanotechnology in Biology and Medicine Program](#).

## Public health potential

According to Garantziotis, the research will have important public health implications. “The unique physicochemical characteristics of nanomaterials enable new applications,” he wrote in a summary of the project, “but may also engender new health risks, particularly in vulnerable populations, such as individuals with pre-existing lung disease.” Understanding more about modes of action, he added, could also lead to improved efforts to better design safety into the ENMs to which humans are most commonly exposed.

The physical, chemical, and biological properties of ENMs, which range in size from roughly 1 to 100 nanometers, differ from the properties of individual atoms and molecules, or of bulk matter.

According to the NIH booklet [“Nanotechnology at the National Institutes of Health,”](#) nanoscale devices smaller than 50 nanometers can easily enter most cells, while those smaller than 20 nanometers can move out of blood vessels as they circulate through the body — raising concerns among many environmental health scientists about their potentially harmful health effects.

## A three-phase approach

Over the next three years, Garantziotis and colleagues in the Clinical Research Unit (CRU) will engage in bidirectional collaborations with the National Toxicology Program (NTP), labs in the NIEHS intramural program, and the U.S. Environmental Protection Agency (EPA) as they explore the effects of exposure among healthy and susceptible populations to ENMs that are already present in the atmosphere, as part of the Intramural NanoHealth Signature Program. The team will study the effects in cells tissue, animals, and human subjects.

According to Garantziotis, the research team will test the hypothesis that selected engineered nanomaterials induce pulmonary inflammation and that asthmatic individuals are particularly susceptible to engineered nanomaterial effects, in a translational exposure model with three aims:

- Exposing human bronchial epithelia and alveolar macrophages — native lungs cells donated by healthy volunteers — to ENMs *ex vivo* to evaluate inflammation and cell toxicity



*Like many scientists, Garantziotis is intrigued by the applications of nanotechnology, but concerned about how much is still unknown about ENMs. “The problem,” he said, “is that we just don’t know what the health effects may be.... A dose which may be innocuous for a healthy person may have adverse effects in a susceptible person, such as an asthmatic.” (Photo courtesy of Steve McCaw)*

- Comparing the *ex vivo* response to ENMs of human bronchial epithelia and alveolar macrophages between healthy and asthmatic individuals to understand whether pre-existing disease alters the effect of ENMs on human cells
- Performing controlled chamber exposures of human volunteers to select ENMs of interest to assess the potential for effects on lung function and inflammation

### **A three-pronged collaboration across divisions and agencies**

This novel collaboration will pilot nanomaterial research in the NIEHS intramural program among clinical and basic researchers and introduce translational research collaboration among the NTP [Nanotechnology Safety Initiative](#), the NIEHS extramural program and its grantees working on ENMs, and the U.S. Environmental Protection Agency (EPA), where bronchoscopy and controlled exposures of human subjects will take place.

Garantziotis said he expects information transfer to be robust and bidirectional. “We will compare our findings to animal toxicology findings from NTP and EPA,” Garantziotis added, “to establish the relevance of the animal models.” Animal studies may also suggest ENMs for further human testing, and investigators in the extramural consortium will likewise benefit from, and contribute to, ongoing clinical research.

## **A Precedent-Setting Network of Collaboration**

The Nanohealth and Safety Initiative includes five components — materials science research, basic biology, pathobiology research, informatics, and training — that draw upon the talents of scientists from throughout NIEHS and its grantee community. In his presentation to NIEHS/NTP Director Linda Birnbaum, Ph.D., Garantziotis offered special thanks to 12 of his colleagues:

- Andrew Ghio, M.D., pulmonologist and clinical researcher at the EPA, who is collaborating in the human study component of the project
- Erika Gutierrez, predoctoral fellow in the NIEHS Clinical Research Program, who is performing *ex vivo* experiments on human cells using ENMs
- Ron Herbert, D.V.M., Ph.D., leader of the NTP Pathology Support Group who is assisting in the analysis of results
- Ivy Ji, Ph.D., scientist at the University of California, Los Angeles (UCLA) and the California NanoSystems Institute
- Pat Mastin, Ph.D., acting deputy director of the Division of Extramural Research and Training
- Sri Nadadur, Ph.D., DERT health scientist administrator overseeing the nanotechnology grants portfolio
- Andre Nel, M.D., professor of Medicine, Pediatrics and Public Health at UCLA, chief of the UCLA Division of NanoMedicine, and NIEHS grantee researching [ENMs](#)
- Annette Rice, a biologist working in the NIEHS Clinical Research Program who is performing *ex vivo* experiments on human cells using ENMs
- Sally Tinkle, Ph.D., NIEHS senior science advisor and lead in interagency and trans-NIH working groups on NanoHealth issues
- Nigel Walker, Ph.D., NTP deputy program director for science and lead for the NTP Nanotechnology Safety Initiative
- Darryl Zeldin, M.D., acting director of the NIEHS Clinical Research Program
- Jeffrey Zink, PhD, distinguished professor of chemistry at UCLA

# NTP Holds Symposium on Pathology

By Mamta Behl

Several NIEHS pathologists participated in the 2010 joint symposium of the Society of Toxicologic Pathology (STP) and the International Federation of Societies of Toxicologic Pathologists (IFSTP) June 19–24 in Chicago. As part of the annual meeting, NTP sponsored a satellite session encompassing what organizers billed as a “Pathology Potpourri,” featuring several noteworthy presentations as well as a talk on proposed [International Harmonization of Nomenclature and Diagnostic \(INHAND\) Criteria for Lesions in Rats and Mice](#).

The symposium chair, NTP Pathologist Susan Elmore, D.V.M., opened the session with a warm welcome. This interactive symposium has become a popular pre-meeting event for attendees of the annual STP symposium with the objective of providing continuing education on the fine points of interpreting pathology slides and generating lively and productive discussion of the challenges and pitfalls involved.

## Striving for accurate identification and diagnosis

A longstanding debate in the field of pathology involves the ability to distinguish among different liver lesions. Rodney Miller, a pathologist with Experimental Pathology Laboratories, Inc., addressed this question in a talk titled “Rat and Mouse: Are They Really That Different?” Miller explored the issue in terms of liver lesions in different rodent species by displaying a set of case studies and then asking pathologists in the room to vote on the diagnosis.

Miller’s talk compared and contrasted the diagnosis of several lesions such as hepatocholangiocarcinomas, hepatoblastomas, hepatocellular carcinomas, and hepatocholangiomas in rats and mice. Miller focused on specific diagnostic differences in hepatocholangiocarcinomas and metastatic lesions in F344/N rats and B6C3F1 mice.

Elmore followed with a talk that highlighted case studies on the identification of amorphous eosinophilic substances within the kidney and nasal septum, “What Is That Pink Eosinophilic Material?” Elmore presented a series of slides and asked pathologists to cast a vote on their diagnosis. Interestingly, “amyloid” topped the list as a diagnosis for the amorphous eosinophilic material, although Elmore subsequently presented a series of stained slides and electron microscopic images revealing the absence of amyloid. In Elmore’s take home message, she said, “Not everything that is amorphous and eosinophilic should be diagnosed as amyloid.” She left the pathologists with an important lesson about what she described as traditional “knee-jerk” diagnoses.

An introduction to INHAND criteria of central and peripheral nervous system (CNS/PNS) proliferative lesions by Alys Bradley, head of pathology for preclinical services at Charles River Laboratories — United Kingdom, provided an overview on the different INHAND terminologies. Bradley opened the talk by explaining the INHAND project and the role of the INHAND nervous system working group. She went on to discuss the identification and distinction between benign and malignant lesions in the nervous system, such as ependymomas, medulloblastomas, papillomas, schwannomas, and astrocytomas, and concluded her talk by providing the audience a plethora of well-defined information on the characterization of CNS/PNS lesions.



*Elmore is a board-certified veterinary pathologist and staff scientist in the NTP Pathology Group. (Photo courtesy of Steve McCaw)*

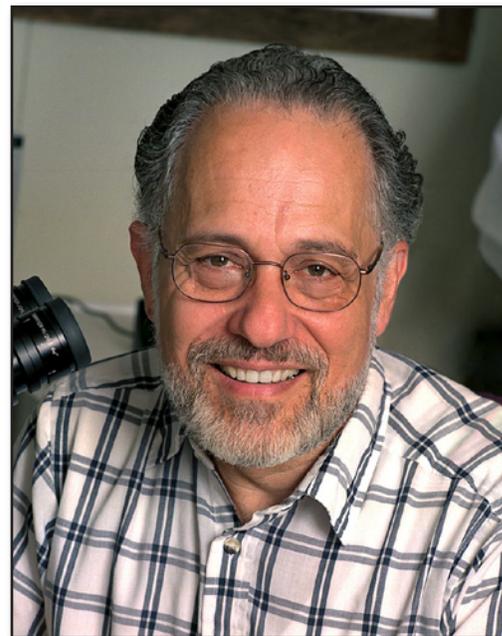
Concluding the agenda was pathologist Bob Maronpot, Ph.D., an independent consultant and retired NTP scientist, who highlighted the challenges associated with distinguishing cholangiofibrosis from cholangiocarcinoma. Cholangiocarcinoma is regarded as a neoplasm of the bile ducts, which drain bile from the liver into the small intestine, and is often difficult to distinguish histopathologically from its precursor cholangiofibrosis.

Maronpot presented slides with case studies of various bile duct lesions, such as cholangiomas, cystic cholangiomas, cholangiofibrosis, cystic cholangiofibrosis, and cholangiocarcinoma-intestinal type. He then asked pathologists in the room to cast their vote on a diagnosis. The attendees offered several thoughtful answers with different rationales for diagnosis.

After he explained the pathogenesis and potential mechanisms involved with formation of the lesions, Maronpot closed by reminding his audience about the need for careful consideration when it comes to diagnosis. “The challenge [here] is to be able to distinguish between cholangiofibrosis and cholangiocarcinoma,” he said.

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

[Return to Table of Contents](#)



*Maronpot is a board-certified veterinary pathologist and toxicologist who has designed, conducted, and evaluated animal carcinogenesis studies for 40 years, including 26 years at NIEHS/NTP. (Photo courtesy of Steve McCaw)*

## Chemistry Is Key to Mercury Levels in Saltwater Fish

*By Eddy Ball*

Saltwater fish, especially large ones higher up in the food chain, are known to contain high levels of methylmercury even though seawater contains very low levels as compared to fresh water. For that reason, the U.S. Food and Drug Administration [advisory](#) on mercury in fish cautions against any consumption of Shark, Swordfish, King Mackerel, or Tilefish by women who may become pregnant, pregnant women, nursing mothers, and young children.

A new study by NIEHS-funded researchers at Duke University reports on the chemistry of methylmercury (MeHg) degradation in the environment and could explain how this organometal persists in seawater.

Published online in the journal Nature Geoscience, the [findings](#) point to the benefits of more research into how the differences between the rates of photodecomposition of MeHg in fresh and saltwater



*Hsu-Kim, shown in her lab, conceived the study, supervised the research, and carried out speciation calculations. (Photo courtesy of Duke University Photography)*

environments affect accumulation of MeHg in the tissues of fish and shellfish — and ultimately the humans who may endanger their health by consuming them.

### **Sunlight and dissolved organic matter speed up degradation**

“The most common way nature turns methylmercury into a less toxic form is through sunlight,” said principal investigator [Heileen Hsu-Kim, Ph.D.](#), in a June 27 press release issued by Duke University. “When it [MeHg] is attached to dissolved organic matter, like decayed plants or animal matter, sunlight more readily breaks down the methylmercury.

“However, in seawater, the methylmercury remains tightly bonded to the chloride, where sunlight does not degrade it as easily,” Hsu-Kim explained. “In this form, methylmercury can then be ingested by marine animals.”

In the experiments that led to publication of their study, Hsu-Kim and first author Tong Zhang, a doctoral student in [Hsu-Kim’s research group](#), tested the effects of photoreactive intermediates on the decomposition of MeHg by sunlight. Sunlight falling on dissolved organic matter generates a highly reactive form of dissolved oxygen that drives the process of photolytic degradation.

The researchers measured decomposition rates of different MeHg-ligand complexes in saltwater and freshwater. They calculated and compared the degradation rates of MeHg linked to sulfur-containing ligands, such as glutathione, mercaptoacetate, and humic acid that are found in freshwater, to the rates of MeHg-chloride complexes that predominate in saltwater.

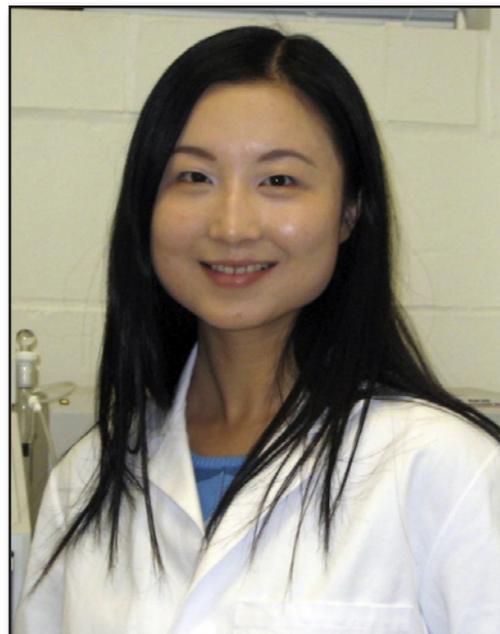
According to the researchers, the rates of decomposition in freshwater with high enough concentrations of humic acid were relatively rapid, while MeHg photodecomposition rates in saltwater were considerably slower, by at least an order of magnitude. These differences help explain why the lower concentrations of MeHg present in saltwater actually pose a greater risk to health because of their persistence in the marine environment.

### **Public health implications of understanding photodecomposition**

The authors point to the public health implications of mercury concentrations in saltwater fish. “The exposure rate of mercury in the U.S. is quite high,” Hsu-Kim explained. “A recent epidemiological survey found that up to 8 percent of women had mercury levels higher than national guidelines. Since humans are on the top of the food chain, any mercury in our food accumulates in our body.”

The researchers are hopeful that this kind of research may lead to secondary prevention measures to limit exposure to MeHg. “With this new understanding of how photodemethylation occurs, we can improve efforts to predict mercury cycling in the aquatic environment and prevent bioaccumulation of MeHg in food webs,” they concluded.

The research by Hsu-Kim and Zhang is the latest of nearly 70 publications associated with the NIEHS grant to principal investigator Richard Di Giulio, Ph.D., for the [Center for Comparative Biology of Vulnerable Populations](#) at Duke. The grant is administered by NIEHS Program Administrator Les Reinlib, Ph.D.



*Tong Zhang carried out all experiments and data analysis. The experiments were part of the work on her thesis topic, “Role of sulfur-coordination on rates of mercury methylation and demethylation.” (Photo courtesy of Heileen Hsu-Kim and Duke University)*

“The Duke Center works with federally-supported investigators to try to understand why certain people develop disease when challenged with environmental agents and others remain healthy,” Reinlib said. “This study extends the Center’s focus on biological, physiological, and social aspects of vulnerability that may alter the effect of environmental toxins on human health.”

*Citation:* Zhang T, Hsu-Kim H. 2010. Photolytic degradation of methylmercury enhanced by binding to natural organic ligands. *Nat Geosci* 3(7):473-476.

[Return to Table of Contents](#)

## This Month in EHP

By Eddy Ball

The cover of the August issue of [Environmental Health Perspectives \(EHP\)](#) features an eye-popping close-up of oil-polluted water to highlight its news features on the *Deepwater Horizon* disaster. The news article “Between the Devil and the Deep Blue Sea: Dispersants in the Gulf of Mexico” describes the use of these chemicals as a high-stakes gamble — a tradeoff of one set of ecologic effects for another. A second story, “Emergency Responder Health: What Have We Learned From Past Disasters?” explores how scientists and policy makers are using past experiences to learn ways to better protect emergency responders.

In this month’s [podcast](#), Dana Wetzel, Ph.D., program manager at Mote Marine Laboratory, discusses her research on dispersant use and the questions that still remain to be answered about its health effects.

The August issue is also the journal’s annual “Reviews in Environmental Health” issue. Among the 13 reviews included in this issue are:

- Biomonitoring Suggests Widespread BPA Exposure
- Understanding Patterns of Environmental Disease
- Health Impacts of a Shift from Cars to Bikes
- Methylmercury: Lessons Learned
- A Niche for Infectious Disease in Environmental Health

[Return to Table of Contents](#)



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# Extramural Papers of the Month

By Jerry Phelps

- [Link Discovered Between Particulate Matter Air Pollution and Sleep-Disordered Breathing](#)
- [Living, Breathing Lung-on-a-Chip](#)
- [Transcription Termination Flips Out](#)
- [Fetal Leydig Cell Protein Regulates Sertoli Cell Proliferation](#)



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

## Link Discovered Between Particulate Matter Air Pollution and Sleep-Disordered Breathing

In a study co-funded by NIEHS, the National Heart, Lung, and Blood Institute, and the U.S. Environmental Protection Agency, researchers at the Harvard School of Public Health report for the first time a link between particulate matter air pollution and sleep-disordered breathing (SDB), a known contributor to cardiovascular diseases.

SDB includes conditions such as apnea and hypopnea and affects approximately 17 percent of U.S. adults, many of whom are not aware that they have a problem. The current studies included more than 3,000 subjects and found novel evidence for temperature and pollution effects on SDB. Increases in apnea and hypopnea were associated with short-term temperature increases in all seasons and with increases in particulate matter air pollution in the summer months.

Specifically, increases in particulate matter of less than ten micrometers in size were associated with about a 13 percent increase in the Respiratory Disturbance Index and with a 20 percent increase in the amount of time the blood oxygen saturation fell below 90 percent.

Air pollution and SDB are independently associated with increased risk for cardiovascular diseases, strokes, and other major health conditions. Further research is necessary to determine whether particulate matter air pollution produces its negative effects, at least in part, by promoting sleep-disordered breathing.

*Citation:* [Zanobetti A, Redline S, Schwartz J, Rosen D, Patel S, O'Connor GT, et al. 2010. Associations of PM10 with Sleep and Sleep-disordered Breathing in Adults from Seven U.S. Urban Areas. Am J Respir Crit Care Med. Epub ahead of print. doi:10.1164/rccm.200912-1797OC \(See story\)](#)

[Return to Table of Contents](#)

## Living, Breathing Lung-on-a-Chip

In response to the NIH Nanoscience and Nanotechnology in Biology and Medicine Program, NIEHS-supported researchers have developed a device that mimics a living and breathing human lung on a microchip roughly the size of a quarter.

The device has the potential to be a valuable research tool for testing the effects of environmental agents, as well as the absorption, safety, and efficacy of drug candidates. The device may help accelerate and reduce the expense of drug development, which can cost more than \$2 million per substance.

The lung-on-a-chip device uses a new approach to tissue engineering that places tissue from the lining of the alveoli and blood vessels that surround them across a porous membrane. Air flows across the lung cells while culture medium, mimicking blood, is pumped through the capillaries. Mechanical stretching of the device mimics the expansion and contraction of the lungs during breathing.

The researchers tested the device by introducing *E. coli* bacteria on the lung cell side of the device while allowing white blood cells to flow through the capillaries. The lung cells detected the bacteria, and, through the porous membrane, activated the blood vessel cells, which caused an immune response resulting in the movement of white blood cells to the air chamber where they killed the bacteria.

The team is also working to build other model systems to mimic the intestinal system, bone marrow, and cancer models.

*Citation:* Huh D, Matthews BD, Mammoto A, Montoya-Zavala M, Hsin HY, Ingber DE. 2010. Reconstituting organ-level lung functions on a chip. *Science* 328(5986):1662-1668.

[Return to Table of Contents](#)

## Transcription Termination Flips Out

Miguel Garcia-Diaz, Ph.D., recipient of an NIEHS Pathway to Independence Award (K99/R00), reports the determination of the structure of a mitochondrial termination factor called MTERF1. Mitochondrial termination factors are a family of proteins implicated in mitochondrial transcription — the coordination between transcription and replication and the regulation of mitochondrial protein synthesis. Human MTERF1 is responsible for transcription termination in the mitochondria.

Combined with functional studies, the structure reveals that upon binding MTERF1 unwinds the DNA double helix and promotes base flipping, the rotation of a single base to the outside of the helix, and that this reorganization is essential for termination. The analyses show how MTERF1 recognizes specific DNA sequences and provides a context for understanding the mechanistic consequences of two pathogenic mitochondrial DNA mutations.

Further experiments are planned to address whether the two mutations, G3249A and G3242A, result in transcriptional differences and if these alterations fully explain the clinical phenotype.

*Citation:* Yakubovskaya E, Mejia E, Byrnes J, Hambardjieva E, Garcia-Diaz M. 2010. Helix unwinding and base flipping enable human MTERF1 to terminate mitochondrial transcription. *Cell* 141(6):982-993.

[Return to Table of Contents](#)

# Fetal Leydig Cell Protein Regulates Sertoli Cell Proliferation

NIEHS-supported trainee Denise Archambeault reports a newly discovered function for a fetal Leydig cell-produced protein called Activin A.

The protein, which is a member of the transforming growth factor beta (TGF-beta) protein superfamily, acts directly on Sertoli cells to promote proliferation during late embryogenesis. Prior to this discovery, it was thought that fetal Leydig cells, which produce testosterone, served only to masculinize the embryo and did not function in testis morphogenesis.

In the research team's experiments, which genetically disrupted the gene that encodes for Activin A specifically in fetal Leydig cells, testis cord elongation and expansion due to decreased Sertoli cell proliferation failed to occur. Disruption of TGF-beta signaling in Sertoli cells led to testis cord dysgenesis and proliferative deficits similar to those in the Leydig cell-specific Activin A knockout mice.

These results indicated that Activin A is the major TGF-beta protein that acts directly on Sertoli cells. The effects last into adulthood, resulting in low sperm production and abnormal testicular development. These findings challenge the existing paradigm that fetal testis development is solely under the control of the Sertoli cells.

*Citation:* Archambeault DR, Yao HH. 2010. Activin A, a product of fetal Leydig cells, is a unique paracrine regulator of Sertoli cell proliferation and fetal testis cord expansion. Proc Natl Acad Sci U S A 107(23):10526-10531.

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

[Return to Table of Contents](#)

## Intramural Papers of the Month

*By Robin Arnette and Jeffrey Stumpf*

- [The Structural Elucidation of the 8odGTP-adenine-pol beta Ternary Complex](#)
- [Cholesterol Trafficking Linked to Inflammatory Response](#)
- [Ozone and TLR4 Lead to Asthma](#)
- [C. elegans Genes Increase Lifespan and Resistance to Cadmium](#)

## The Structural Elucidation of the 8odGTP-adenine-pol beta Ternary Complex

NIEHS researchers have solved the first crystal structure of human DNA polymerase beta (pol beta) with 8-oxo-7,8-dihydro-2'-dGTP (8odGTP) paired with the template base adenine. The structure, published in Nature Structural & Molecular Biology, revealed that the *syn* conformation of 8odGTP binds to the *anti* conformation of adenine, causing a planar arrangement that mimics nonmutagenic base pairs.

The structure confirms that the *syn* conformation is stabilized by three interactions: a Hoogsteen hydrogen bond between 8odGTP and adenine, a hydrogen bond between 8odGTP and a pol beta asparagine that is crucial for the incorporation of 8odGTP, and the stabilization of the entire complex through an intramolecular hydrogen bond within 8odGTP.

Incorporating 8odGTP opposite cytosine is nonmutagenic, but it is much less efficient than incorporation opposite adenine. The researchers modeled the nonmutagenic incorporation of 8odGTP opposite cytosine and showed that this would result in a steric clash between the *anti* conformation of 8odGTP and the sugar phosphate backbone of the incoming nucleotide.

The elucidation of the incoming 8odGTP-template adenine-pol beta complex is important because 8odGTP, a highly mutagenic lesion produced by oxidative stress, may contribute to carcinogenesis and aging. 8odGTP preferably binds with adenine during replication and, without repair, results in an A-to-C transversion.

*Citation:* [Batra VK](#), [Beard WA](#), [Hou EW](#), [Pedersen LC](#), [Prasad R](#), [Wilson SH](#). 2010. Mutagenic conformation of 8-oxo-7,8-dihydro-2'-dGTP in the confines of a DNA polymerase active site. *Nat Struct Mol Biol* 17(7):889-890.

[Return to Table of Contents](#)

## Cholesterol Trafficking Linked to Inflammatory Response

Investigators from the NIEHS Laboratory of Respiratory Biology report that Myeloid Differentiation Primary Response Protein 88 (MyD88), an adaptor protein in innate immunity signaling pathways, is required for cholesterol export from cells and couples cholesterol export to inflammation. They found that MyD88-dependent inflammatory signals are elicited in macrophages by apolipoprotein A-I (ApoA-I), the major protein component of high-density lipoprotein (HDL) particles.

The model presented in this study holds that ApoA-I induces signals in the macrophage that require the presence of Toll-like Receptors (TLRs), cell surface receptors that normally recognize bacterial-derived lipid ligands. TLR2 and TLR4 then recruit MyD88, activating the transcription factor nuclear factor-kappaB and inducing pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha). Notably, the authors find that MyD88 is also required for the macrophage to export cholesterol to apoA-I. This action occurs, at least in part, through a feedback effect of MyD88-derived TNF-alpha upon the macrophage.

This work supports a new paradigm in which the innate immune response acts as a physiologic signal in cholesterol homeostasis. Whereas inflammation is generally thought to promote atherosclerosis, the authors provide evidence that immune pathways may also be required for removal of cholesterol from vessel walls. This work may provide future insights in the connection between inflammation and diet.

*Citation:* [Smoak KA](#), [Aloor JJ](#), [Madenspacher J](#), [Merrick BA](#), [Collins JB](#), [Zhu X](#), et al. 2010. Myeloid differentiation primary response protein 88 couples reverse cholesterol transport to inflammation. *Cell Metab* 11(6):493-502.

[Return to Table of Contents](#)

## Ozone and TLR4 Lead to Asthma

Epidemiologic evidence suggests that high levels of ozone, a key component of air pollution, contribute to the increased prevalence of asthma. Investigators from NIEHS and Duke University Medical Center have recently found that ozone activates pulmonary dendritic cells through a Toll-like receptor 4 (TLR4)-dependent mechanism. The investigators propose that this activation can lead to allergic sensitization and ultimately to asthma.

Members of the research team studied the effect of ozone exposure on allergic sensitization to an inhaled protein, ovalbumin (OVA). They found that mice exposed to OVA alone did not become sensitized to it and were unresponsive to subsequent exposures to this protein. However, mice exposed to both ozone and OVA became sensitized because upon subsequent exposure to OVA, they developed allergic pulmonary inflammation and produced high levels of inflammatory cytokines. The authors further showed that ozone could activate pulmonary dendritic cells, which are critical cells in the initiation of allergic responses.

When *tlr4*-deficient mice were used in the same type of experiment, they displayed very low levels of airway inflammation and cytokine production. This finding suggests that ozone-mediated allergic sensitization through the airway occurs through a TLR4-dependent mechanism.

*Citation:* Hollingsworth JW, Free ME, Li Z, Andrews LN, Nakano H, Cook DN. 2010. Ozone activates pulmonary dendritic cells and promotes allergic sensitization through a Toll-like receptor 4-dependent mechanism. *J Allergy Clin Immunol* 125(5):1167-1170.

[Return to Table of Contents](#)

## *C. elegans* Genes Increase Lifespan and Resistance to Cadmium

A new study by NIEHS investigators reports that nuclear localized metal responsive (*numr*)-1 and *numr*-2, two novel *Caenorhabditis elegans* genes associated with resistance to metal toxicity, are also involved in increasing the lifespan of the organism. Their research further suggests that the expression of these genes is regulated by the insulin-IGF-like signaling pathway.

The investigators determined that both genes exhibited nearly identical nucleotide sequences and that *numr-1/-2* mRNA levels experienced a sevenfold increase following exposure to cadmium. They also discovered that the cellular pattern of *numr-1* and *numr-2* expression was both tissue specific and dependent on the type of metal exposure. In the absence of metal, *numr-1/-2* was expressed in a subset of neurons in the *C. elegans* head, tail and vulva. Exposure to cadmium increased the expression of *numr-1/-2* in the intestine, while exposure to copper increased expression in the pharynx.

A knockdown of *numr-1/-2* increased the nematode's sensitivity to cadmium, while over-expression increased the worm's resistance to metals and its lifespan, both in the presence and absence of metal. Although the upstream regulators of *numr-1/-2* have not been identified, the two genes have binding sites for DAF-16 and SKN-1, two transcription factors that are involved in the insulin-IGF-like signaling pathway and that regulate the expression of several stress-response genes.

*Citation:* Tvermoes BE, Boyd WA, Freedman JH. 2010. Molecular characterization of *numr-1* and *numr-2*: genes that increase both resistance to metal-induced stress and lifespan in *Caenorhabditis elegans*. *J Cell Sci* 123(Pt12):2124-2134.

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

[Return to Table of Contents](#)

# Inside the Institute

## Campers Engage Hands-on with Nutrition and Fitness

By Eddy Ball

For its fifth annual Science Summer Day Camp June 19, the [Durham Alumnae Chapter of Delta Sigma Theta Sorority](#) Science and Everyday Experiences (SEE) program took aim at the growing problem of overweight, obesity, and related health issues. As they have in years past, NIEHS staff generously volunteered their time and expertise to help make the summer camp a success.

Developing this year's theme "Blast Into Scientific Exploration for the 21st Century: Healthy Lifestyles," the camp offered 19 children in the fourth to eighth grades a fun-filled, hands-on immersion into healthy eating and fitness, completely free of charge, during the half-day program held at the Durham Alumnae Delta House.

According to Durham [SEE](#) chair Sharon Beard and co-chair Joan Pakenham, Ph.D., who are colleagues at NIEHS, the healthy lifestyles program embraces First Lady Michelle Obama's [Let's Move: America's Move to Raise a Healthier Generation of Kids](#), launched earlier this year. "We wanted to help parents and campers understand why it's important for diet to be a major concern in the household to have everyone eating healthier," Beard explained.

This year's camp attracted a record 35 NIEHS, Delta, parent, and community volunteers who organized and conducted the program. A returning component in the program was the SEE Parental Involvement Workshop, supported by former NIEHS scientist Marian Johnson-Thompson, Ph.D. The goal was to introduce parents and caregivers to the world of interactive hands-on science, an important part of the camp's emphasis on family involvement in learning and health, with an opening presentation by Leatrice Martin-Short, director of the Duke Heart Center Community Outreach and Education Program. Organizers designed many of the activities, Beard explained, so they could be done as a family unit as campers' families integrated what they learned into their everyday lives.



Beard, front and center, welcomed campers, as current and former NIEHS employees stood in the background. Visible behind Beard, left to right, are Amber Haynes, Undi Hoffer, Ph.D., Elena Braithwaite, Ph.D., and Pakenham. (Photo by Laura Hall)



Campers gathered in front of one of the tents donated by Fisher Funeral Parlor in Durham. Jeter led campers in health and fitness rotations for the entire family. (Photo by Laura Hall)

Conspicuously absent from this year's camp were the standard fare of pizza, soft drinks, and packaged snacks, both for volunteers and participants, as campers enjoyed a healthy breakfast, lunch, and snacks in the course of activities on science, nutrition, health, and fitness. Following a welcome from Deloris Hargrow, president of the Durham Alumnae Chapter, a camp overview by Beard, and a health and fitness warm up led by NIEHS volunteer Shawn Jeter, campers went to the first of three hands-on science, nutrition, and health activities.

Led by Pakenham, module one, "Understanding Your Body — Health and Nutrition Needs," explored the U.S. Department of Agriculture's revised food pyramid and health guidelines for human body's fuel needs and taught campers how to use body mass index and waist circumference as health guidelines. The module brought home the message that poor nutrition has direct effects on health problems, such as cardiovascular disease and diabetes. Topics Pakenham and colleagues covered during this module included "Assessing Your Risk for Disease," "How Much Do I Need to Eat," "Fats, Sugar and Salt," and making healthy choices when eating at fast food restaurants.

Module two, "Nutrition Made Simple — Healthy in the Kitchen," was led by Martin-Short with assistance from Delta volunteer Lillian Horne, M.D., a physician in private practice, and Erica Strickland, a student at Johnson and Wales University College of Culinary Arts. The activity leaders showed campers and parents how to make such heart-healthy snacks as smoothies, fruit kabobs, hummus, homemade salsa, and Greek salad.

In module three, Jeter led campers in health and fitness rotations for the entire family, such as Zumba, line dancing, Wii, toning and stretching, and hula hoops.

SEE is a national initiative of Delta Sigma Theta Sorority to encourage African-American children to gain competency and interest in science, mathematics, and technology, by involving them in hands-on science activities that are fun and thought provoking. These activities demonstrate to the children that people use science and math in their every day lives.

## NIEHS Volunteers

When it comes to science education outreach and community service, NIEHS employees are generous group. As they have in the past, this year several of the Institute's current and past employees answered the Delta call for summer camp volunteers:

- Beth Anderson, program analyst with the Superfund Research Program
- Martha Barnes, program analyst with the Program Analysis Branch
- Sharon Beard, Worker Education and Training Program (WETP) industrial hygienist
- Elena Braithwaite, Ph.D., staff scientist in the Comparative Genomics Group
- Amber Haynes, predoctoral fellow in the Clinical Research Unit
- Undi Hoffler, Ph.D., former postdoctoral fellow with the National Toxicology Program (NTP)
- Shawn Jeter, technical information specialist with the NTP
- Joan Pakenham, Ph.D., director of the NIEHS Office of Human Research Compliance
- Jim Remington, program analyst with the WETP
- Veronica Godfrey Robinson, biologist with the NTP
- Marian Johnson-Thompson, Ph.D., former director of Education and Biomedical Research Development
- Danielle Watt, a postdoctoral fellow in the DNA Replication Fidelity Group



NIEHS Intramural Research Training Award Fellow Danielle Watt, Ph.D., offered her expertise during an activity about reading and understanding food labels. (Photo by Laura Hall)



As Watt, right, holds a measuring cup of grains, volunteers talk about merits of fresh foods and whole grains, such as quinoa, which campers were able to sample. Standing left to right, are Hoffer, Braithwaite, and Pakenham, who led the activity. Haynes, not shown, was also a volunteer for this activity. (Photo by Laura Hall)



Martin-Short, left, and Horne helped campers learn about heart-healthy cooking for the family. "Campers and parents were allowed to engage hands-on, by preparing simple, low cost, fresh, healthy foods," said Martin-Short. (Photo by Laura Hall)



Johnson and Wales culinary student Erica Strickland, right, shared her expertise as campers got hands-on experience making healthy snacks. Strickland is completing an internship in the Duke University Community Service program. (Photo by Veronica Godfrey Robinson)



Seven of the NIEHS volunteers posed for a group photo at the end of this year's successful camp. Shown, left to right, are Braithwaite, Hoffer, Watt, Martha Barnes, Pakenham, Beard, and Haynes. (Photo by Veronica Godfrey Robinson)

# Library Pioneer Dav Robertson Retires

By Eddy Ball

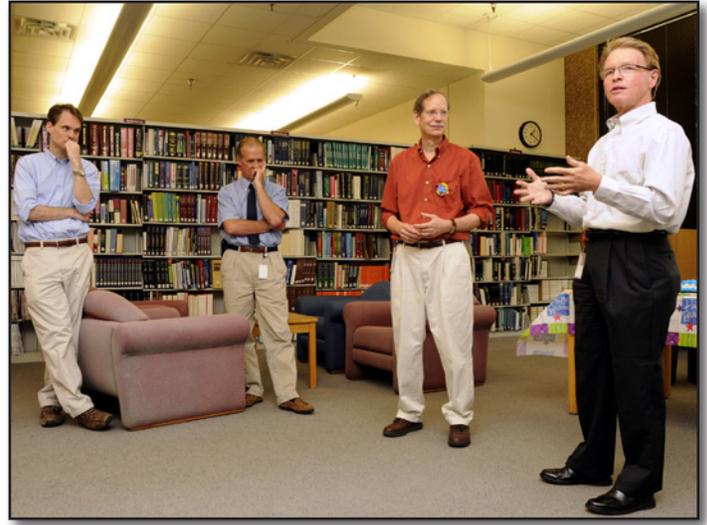
NIEHS Library and Information Services Branch Chief Dav Robertson marked a career milestone on June 29 as friends and colleagues celebrated his retirement after 33 years at the Institute. Robertson enjoyed a round of tributes from well-wishers gathered in the NIEHS Library commons, ranging from members of the NIEHS leadership and the library staff to lab-based scientists and some of the former interns whose careers he did so much to shape.

Robertson, whose final day at NIEHS was July 2, joined the library staff in 1977 at legendary Building 18 on the former North Campus, following two years of federal service with the U.S. Environmental Protection Agency and a stint with the Peace Corps in Korea. He was named chief of the library in 1988.

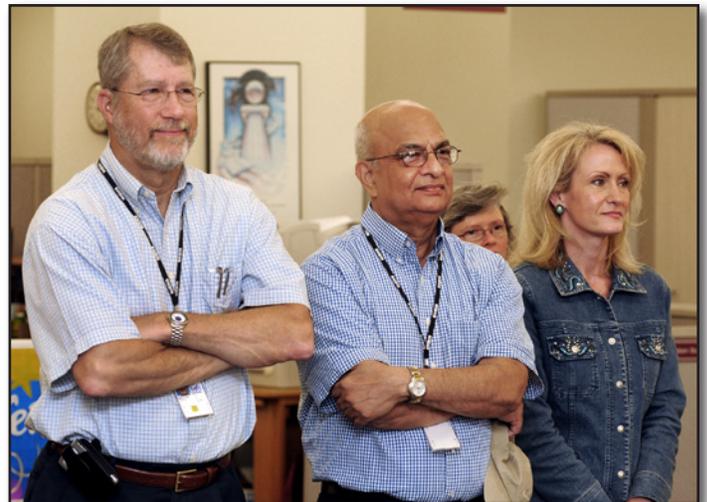
During his 22 years at the helm, Robertson was the guiding force in the transformation of the NIEHS Library from a traditional repository of printed information to a state-of-the-art electronic-based special library capable of tailoring its services to the changing needs of the NIEHS scientific community. His eagerness to embrace new information services technologies led to NIEHS being one of the first Medline search centers. He has continued to keep the library at the cutting edge of science with recent initiatives to meet the needs of the growing number of large-team, bioinformatics-supported research efforts at NIEHS.

As they formed a circle for a round of tributes to Robertson, many of the guests spoke in turn about his long and successful career as head of the library. Acting Deputy Director Steve Kleeberger, Ph.D., presented Robertson with a special issue of the NIEHS Environmental Factor. The issue celebrated thirty years of the many library activities and accomplishments that had appeared in the newsletter since it was established in 1978.

While Kleeberger praised Robertson for creating a library with “all the things academic institutions would kill for” and former Acting Director Sam Wilson, M.D., honored the library chief’s “thoughtful, innovative approach,” tributes for Robertson also focused on his management style and winning personality.



*Deary, right, recalled the ways Robertson empowered his staff and championed the cause of the library. Shown with Deary, left to right, are NIEHS Library Bioinformatics Information Specialist David Fargo, Ph.D., Kleeberger, and Robertson. (Photo courtesy of Steve McCaw)*



*NIEHS Acting Scientific Director John Pritchard, Ph.D., left, NTP General Toxicology Group Leader Rajendra Chhabra, Ph.D., center, and Christine Flowers, director of the NIEHS Office of Communication and Public Liaison, reflected the diversity of the guests at Robertson’s retirement party. (Photo courtesy of Steve McCaw)*

As NIEHS Special Advisor Allen Dearry, Ph.D., said, “Dav exemplifies the kind of person we all like to have as a leader..., [one who] does a great job of crediting his staff.” Bill Suk, Ph.D., director of the NIEHS Center for Risk and Integrated Sciences, added, “The one person you always looked forward to seeing was Dav.”

When Robertson’s turn to speak came about, not surprisingly, he downplayed his many accomplishments with his characteristic modesty. “If you’ve got a good staff,” he said, “it’s easy to look good.”

Guests enjoyed light refreshments and cake, as they mingled and watched a video collage of Robertson and the library.



*Deputy Associate Director of Management Chris Long, left, talked with Robertson’s wife, Eliza, who is the library director at the National Humanities Center. (Photo courtesy of Steve McCaw)*



*Eliza Robertson, center, posed with reference intern Ruth Finch, left, and Information Systems Librarian Alisa Haggard, right. (Photo courtesy of Steve McCaw)*



*Past, present, and future at the NIEHS Library converge as NIEHS retiree Ralph Hester, left, posed with NIEHS Biomedical Librarian Stephanie Holmgren, retiree Larry Wright, Ph.D., and Robertson. Holmgren assumed duties as acting chief on July 6. (Photo courtesy of Steve McCaw)*



*Robertson smiled as he sliced a cake featuring an image of NIEHS as part of its icing. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

# Veteran Biologist Larry Champion Begins Second Career

By Eddy Ball

Laboratory of Molecular Genetics (LMG) Biologist Larry Champion made it clear June 29 that he was separating after 30 years of federal service, but not really retiring. As Champion told a group of more than 50 friends and colleagues attending his going away party in the NIEHS cafeteria, he'll begin teaching full time August 16, after teaching as an adjunct for several years.

Party organizers created a program to honor their longtime coworker, which opened with piano accompaniment by Jennie Foushee, project officer for the glassware media group. Emcee Essie Jones, a biological aide in Champion's group and assistant project officer, led off tributes to her colleague with a fond remembrance of their years together. She spoke for Champion's many friends at NIEHS, when she observed, "Larry will be well missed by me and a lot of people in this room."

Tributes from Champion's colleagues included a performance of "You've Been Faithful" by tenor George Kimble, a retired NIEHS electrician. After his song, Kimble told Champion, "Now it's your time to be blessed." Colleague Dee Anderson read her poem, "I Hate to Say 'Goodbye,'" and Michael Watkins gave a heartfelt expression of thanks on behalf of his fellow glassware media employees. LMG Drosophila Chromosome Structure Group Principal Investigator Jim Mason, Ph.D., gave his colleague of more than three decades a framed certificate of appreciation and a lapel pin as mementos.

When it was her turn to speak, Foushee presented the retiree with a signed photo of NIEHS and a cash gift from friends to help Champion "remember us forever." NIEHS retiree Ann Kersey handed Champion a hat embroidered with the words "Retired and Loving It" and a card to "Celebrate Good Times," as a recording of the Kool and the Gang song played in the background.

Cafeteria employee Lakesia Register recalled the many mornings she greeted Champion and Jones at breakfast and noted the need "to find Essie a new breakfast partner." She said she always enjoyed seeing Champion and appreciated his genuine friendliness and unfailing courtesy, even when things weren't quite up to par.

Organizers concluded the tributes with a video remembrance of Champion over the course of his decades of service at NIEHS, accompanied by a recording of the Impressions' hit song, "Keep on Pushing."

Fellowship and reminiscences continued as more guests arrived to offer their congratulations to Champion on his career at NIEHS and his future teaching. Visitors then tackled the generous buffet that spread across eight tables at the front of the cafeteria.



*Sporting the new addition to his wardrobe, Champion was clearly pleased by the turn out of people wishing him luck in his new career and sharing fond memories of their time together at NIEHS. (Photo courtesy of Steve McCaw)*



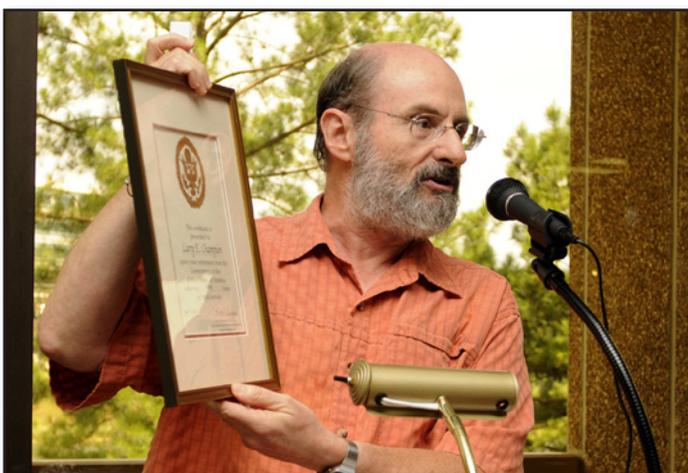
*Jones, above, smiled as she recalled working with Champion. The two provided lab support for quality control of glassware media. (Photo courtesy of Steve McCaw)*



*After reading her poem to the audience, Anderson gave Champion a framed copy of her tribute. (Photo courtesy of Steve McCaw)*



*Kimble, left, joined Foushee after his vocal performance. Speaking of his own retirement, Kimble said that these days he tells friends, "Don't call me before 9:30." (Photo courtesy of Steve McCaw)*



*Mason, who showed the audience Champion's certificate, was Champion's first and only supervisor at NIEHS. Mason once told Champion that he was hired because of his self-confidence.*



*Foushee smiled as she held up the signed photo of NIEHS she presented to Champion. (Photo courtesy of Steve McCaw)*



*Old friends Champion and Kersey hugged after she presented him with her gift. (Photo courtesy of Steve McCaw)*



*This watermelon fruit basket on display showed the love and care that organizers put into their impressive afternoon spread. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

# NIEHS Receives its 20,000th Grant Application

The NIEHS Division of Extramural Research and Training (DERT) celebrated a milestone July 22 — receipt of the Institute’s 20,000th grant application. Since its founding in the mid-sixties, the number and rate of new grant applications the Institute receives each year has grown steadily. More than 30 years elapsed prior to the receipt of grant number ES010000 — the 10,000th application — while it took only 19 years for the next ten thousand applications to arrive.

DERT Program Analyst Jerry Phelps organized a small contest to see who could pick the date grant number ES020000 would be received and catalogued in the IMPACII database. DERT Grants Management Specialist Michelle Victalino won a \$10 gift certificate to a local ice cream parlor by selecting May 29, which turned out to be closest date.

Victalino and Phelps celebrated July 19 along with DERT Health Scientist Administrator Annette Kirshner, Ph.D., who described herself afterwards as “the big loser.” Although Kirshner selected February 10, the farthest from the actual date, she didn’t seem to mind losing too much — she got to have ice cream anyway!

DERT employees celebrated the milestone event with a special cake they enjoyed after their quarterly staff meeting July 22.

## Application milestones

- ES000001 – approximately 1965
- ES005000 – 1988
- ES010000 – 1999
- ES015000 – 2006
- ES020000 – 2010

[Return to Table of Contents](#)



*Victalino, left, and Kirshner enjoyed their prizes at Rita’s — a local ice cream parlor. (Photo by Jerry Phelps)*



*As DERT Health Scientist Administrator Janice Allen, Ph.D., waited for her piece of the cake, Victalino and Kirshner savored their victories once again. (Photo by Eddy Ball)*



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