

November 2012

NIEHS Spotlight



[Birnbaum gives keynote at Chesapeake Bay watershed meeting](#)

NIEHS/NTP Director Linda Birnbaum, Ph.D., spoke at the Oct. 10 annual meeting of the Pesticides and the Chesapeake Bay Watershed Project in Reisterstown, Md.



[WETP promotes logic model concept for training assessment](#)

A workshop at NIEHS Oct. 11-12 aspired to fundamentally transform ways of thinking about worker health and safety training evaluation, as well as share best practices.



[Superfund marks 25th year of advancing health and wellbeing](#)

The annual meeting of the NIEHS Superfund Research Program Oct. 22-24 in Raleigh was an occasion for celebrating accomplishments and looking to the future.



[NIEHS welcomes Scholars Connect charter cohort](#)

A new internship program to foster the engagement of minority scholars with the environmental health sciences officially launched Sept. 17 at NIEHS.



[Mobile technologies poised to aid training and emergency response](#)

Several representatives of leading-edge organizations visited NIEHS Oct. 9 to demonstrate innovative public health applications for mobile technologies.

Science Notebook



[Designing the next generation of sustainable chemicals](#)

Scientists committed to developing green solutions for replacing problem chemicals in the marketplace gathered at a meeting Oct. 15-17 in Tarrytown, NY.



[NTP panel reviews outcomes of women treated for cancer while pregnant](#)

During its meeting at NIEHS Oct. 1-2, the panel conducted in-depth discussions and concurred by unanimous vote on each of the NTP's five main findings.



[Fellows and scientists stand out at NIH Research Festival](#)

NIEHS scientists and trainees presented talks and posters at the annual event Oct. 9-12 at the Natcher Conference Center in Bethesda, Md.



[Kunkel steps away from administrative role as LSB lab chief](#)

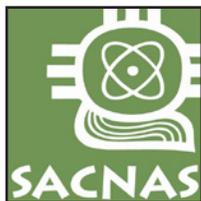
As of Oct. 1, lead researcher Thomas Kunkel, Ph.D., is devoting himself full time to research as head of the DNA Replication Fidelity Group.



[NIEHS researchers gather to combat obesity](#)

The connection between chemicals and obesity was the focus of an NIEHS grantee meeting Oct. 3-4 at the Ann Arbor Regent Hotel in Michigan.

NIEHS Spotlight



[Reaching out to Hispanic, Native-American, and other minority students](#)

Ericka Reid, Ph.D., and Anshul Pandya, Ph.D., represented NIEHS at the nation's premier conference for Hispanic and Native-American science students.



[Workshop addresses the millions who die yearly from household air pollution](#)

Representatives of several agencies and organizations joined researchers at a Household Air Pollution Research Training Institute Oct. 9-12, co-sponsored by NIEHS.



[Building bridges between risk assessment and environmental justice](#)

A meeting Oct. 15 may be one sign of a new working relationship between environmental justice advocates and risk assessment scientists.



[GuLF STUDY makes final call for study participants](#)

Workers and volunteers who helped with the 2010 Deepwater Horizon oil spill cleanup have until Dec. 31 to sign up to be a part of the historic study.



[Hardworking postdoc receives prestigious Pathway to Independence Award](#)

Trainee Ramendra Saha, Ph.D., became the latest NIEHS beneficiary of this early-career support Oct. 1, when the National Institute of Mental Health announced his award.

Science Notebook



[Getz uncovers exciting new trends in cancer genomes](#)

Gad Getz, Ph.D., provided a glimpse of the exciting new world of identifying and treating cancer in his talk Oct. 5 at NIEHS.



[Gabbay Foundation honors bisphenol researchers](#)

Three NIEHS grantees are this year's recipients of the Jacob Heskel Gabbay Award in Biotechnology and Medicine for their work on the health effects of bisphenol A.



[Genomics day highlights the new resources available to intramural researchers](#)

NIEHS celebrated Genomics Day Sept 27 by showcasing new resources for high-throughput assessment and the advanced research those resources make possible.



[Bacterial protein in house dust spurs asthma](#)

A bacterial protein in common house dust may worsen responses to indoor allergens, according to research conducted by scientists at NIEHS and Duke University.



[Dioxin exposure causes transgenerational health effects](#)

A new study finds that dioxin affects not only the health of an exposed rat, but also unexposed descendants through a mechanism of epigenetic transgenerational inheritance.

NIEHS Spotlight



[HHS workshop aims to speed up public health emergency response](#)

Experts from NIEHS and nearly two dozen other federal agencies gathered Sept. 25 on the NIH campus in Bethesda, Md. to carry out a critical mission.



[Hispanic heritage month celebration promotes diversity united](#)

NIEHS observed Hispanic Heritage Month Oct. 3 with a program featuring Elizabeth Yeampierre, J.D., a civil rights attorney and community leader in Brooklyn, N.Y.



[Veterinary group recognizes animal welfare as specialty](#)

The American Veterinary Medical Association announced Sept. 19 its approval of animal welfare as a certification for veterinary specialists.



[NIEHS grantee meets with stakeholders to discuss aquatic toxicity project](#)

Researchers at the Colorado School of Mines hosted a multimetallic project meeting and Superfund site visit Sept. 23-25 for stakeholders.



[Love of science and exemplary leadership define Mason's tenure at NIEHS](#)

After a 34-year career at the bench, James "Jim" Mason, Ph.D., will step away from his role as leader of the *Drosophila* Chromosome Structure Group.

Science Notebook



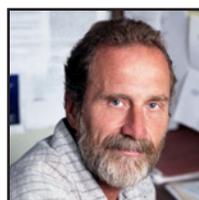
[Van Oijen visualizes DNA replication of single molecules](#)

University of Groningen professor Antoine van Oijen, Ph.D., dazzled NIEHS researchers with images of DNA replication proteins altering single DNA molecules in real time.



[Bisphenol A linked to lower thyroid hormone levels in newborn boys](#)

A new study funded in part by NIEHS reports that exposure to BPA during pregnancy may affect thyroid hormones levels in pregnant women and newborn boys.



[NIEHS researchers describe important cell signaling mechanism](#)

Understanding this signaling mechanism could lead to more precisely targeted therapeutic interventions that have increased efficacy and fewer side effects.



[Household contaminants associated with childhood respiratory problems](#)

Two NIEHS-funded studies from Columbia University report new findings that link exposures to chemicals found in the home with childhood respiratory problems.



[Exploring regulatory mechanisms in the fruit fly genome](#)

In an Oct. 2 talk at NIEHS, Kami Ahmad, Ph.D., discussed findings from his work on epigenetic control of gene expression and development in a *Drosophila* model.

NIEHS Spotlight



[With death of Arlen Specter, NIH loses a faithful supporter](#)

News of the death of former Sen. Arlen Specter (D-Pa.) Oct. 14 saddened many at NIH who had worked with him over the years to advance biomedical research.



[NIH-funded program opens new doors for scientists with disabilities](#)

NIEHS staff and scientists gathered Oct. 15 for a unique presentation on enhancing access to biomedical laboratories for people with disabilities.

Inside the Institute



[CFC races toward \\$115K goal](#)

With proceeds from a bake sale Oct. 2, the Combined Federal Campaign at NIEHS had raised nearly \$32,200, as of Oct. 29, toward its 2012 goal.



[Memorial to Frank Kari dedicated at University of Illinois](#)

Along with his memorial tree at NIEHS, toxicologist Frank Kari, Ph.D., is remembered by the Dr. Frank W. Kari Walkway and Ponds Restoration Project at his alma mater.



[Durham Magazine highlights NIEHS/EPA early learning center](#)

This summer, Durham Magazine writer Mark Griffin profiled the First Environments Early Learning Center in a story titled "Eat (And Grow) Your Veggies."

Science Notebook



[Study offers insight into HIV metal and ligand binding](#)

A discovery by scientists in the NIEHS Laboratory of Structural Biology opens the door for developing new treatments for human immunodeficiency virus.



[Committee recommends using fewer animals in eye hazard testing](#)

An interagency committee administered by NTP has transmitted recommendations to federal agencies on reducing animal use for identifying chemical eye hazards.



[New study describes mechanism of anticancer drug resistance](#)

NIEHS researcher Scott Williams, Ph.D., thinks he may have discovered how some malignant cells resist aggressive pharmaceutical treatment.



[This month in EHP](#) ▶ Audio

The November issue of Environmental Health Perspectives highlights mercury exposures from mining and the immediate and long-term effects of dam removal.

Calendar of Upcoming Events

- **Nov. 1-2**, in Rodbell Auditorium — Nov. 1, 8:30 a.m.-4:15 p.m.; Nov. 2, 9:00-11:30 a.m. — NIEHS Science Days
- **Nov. 3 (offsite event)**, at Duke University Levine Science and Research Center, B101, 4:00-5:00 p.m. — Seminar on “Genetics of variation in human gene expression,” by Vivian Cheung, M.D.
- **Nov. 6**, in the Executive Conference Room, 12:00-1:00 p.m. — Receptor Mechanisms Discussion Group featuring Albert Baldwin, Ph.D., exploring “Roles of IKK and NF-kappaB in oncogenesis”
- **Nov. 8 (offsite event)**, at the William and Ida Friday Center for Continuing Education in Chapel Hill, N.C. — Genetics and Environmental Mutagenesis Society annual fall meeting, [register](#)
- **Nov. 14**, in Rodbell A, 10:00-11:00 a.m. — Keystone Science Lecture Seminar Series, speaker and topic TBA
- **Nov. 15**, in the 101 mall area, 9:30-11:30 a.m. — America Recycles
- **Nov. 15 (offsite event)**, at the Natcher Conference Center on the NIH campus in Bethesda, Md., 8:00 a.m.-4:00 p.m. — Building Interdisciplinary Research Careers in Women’s Health Symposium, [webcast](#)
- **Nov. 15 (offsite event)**, at the University of North Carolina at Chapel Hill, 1131 Bioinformatics Auditorium, 10:30-11:30 a.m. — Seminar on “The many roles of VEGF in the adult” by Patricia D’Amore, Ph.D.
- **Nov. 16**, in Rodbell A, 11:00 a.m.-12:00 p.m. — Laboratory of Reproductive and Developmental Toxicology Seminar Series, featuring Vargheese Chennathukuzhi, Ph.D., discussing “Pathogenesis of uterine leiomyomas: new molecular mechanisms”
- View More Events: [NIEHS Public Calendar](#)

Extramural Research

[Extramural papers of the month](#)

- [Non-coding DNA variants may link early exposures with later health problems](#)
- [Reversible epigenetic changes associated with bee behavior](#)
- [Fetal BPA exposure harms reproductive health in primates](#)
- [Assay quantifies effects of DNA damage on transcription](#)

Intramural Research

[Intramural papers of the month](#)

- [New treatment allows medicines to cross blood-brain barrier](#)
- [Neuromodulators may affect learning and memory](#)
- [Inverse relationship between allergy and heart attack](#)
- [Low-level p53 expression reveals supertransactivating response element sequences](#)

NIEHS Spotlight

Birnbaum gives keynote at Chesapeake Bay watershed meeting

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., spoke at the Oct. 10 annual meeting of the [Pesticides and the Chesapeake Bay Watershed Project](#) in Reisterstown, Md.

Birnbaum's talk explored the health effects of exposure to low doses of endocrine-disrupting chemicals (EDCs), as she has in other venues before groups of scientists. But, her audience this time also included politicians, government regulators, advocacy groups, farmers, and residents who live and work along what is America's largest estuary and one of its most diverse.

According to the [state of Maryland](#), Chesapeake Bay's drainage basin covers more than 64,000 square miles with water, waste products, and runoff entering the bay from more than 150 rivers and streams in the District of Columbia and six states, potentially impacting the lives of some 17.5 million people who live there.

People in the basin are accustomed to hearing warnings about industrial pollution and parasite-laden shellfish, but Birnbaum's presentation outlined an emerging paradigm of dose response to endocrine-active chemicals in pesticides and other products that can also impact human and animal health now and for generations to come.

Should we be concerned?

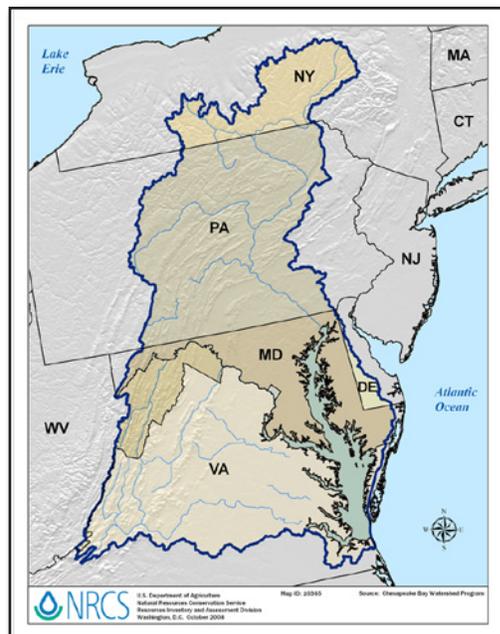
Right at the beginning of her talk, Birnbaum posed the question on virtually everyone's mind about the dramatic increases in rates of complex and chronic diseases with a known environmental component. Reports of testicular cancer, hypospadias, breast cancer, low sperm count, diabetes, autism, asthma, and attention deficit hyperactivity disorder, she noted, have increased as much as 50 percent or more in recent years.

Genetic changes don't occur that quickly in a population, she said, but over recent decades, the environment, from the chemicals in our homes to the food we eat, has changed fundamentally.

"There are unanticipated effects of exposure to toxic chemicals," she told the audience, and our research must extend to health endpoints beyond cancer and birth defects. "NIEHS is supporting research on the developmental origins of obesity and the theory that environmental exposures during development play an important role in the current epidemic of obesity, diabetes, and metabolic syndrome," Birnbaum said.



Environmental exposures during windows of susceptibility, such as during infant and child development, may trigger health effects that manifest years or even decades afterwards, Birnbaum told the audience. (Photo courtesy of the University of Illinois)



This U.S. Department of Agriculture watershed map shows the portions of the six states whose runoff flows into the Chesapeake Bay.

EDC exposure at home, at work, at play

This new research, Birnbaum continued, is based on a conceptual shift in thinking about chemical exposure to pesticides and other EDCs. “Whereas we used to think that higher doses are bad and lower doses are not as bad, we now know that low-dose effects from some chemicals that can act like hormones can have a substantial impact on our health,” she explained. She also said that new research has pointed to the persistence of susceptibility long after exposure, through epigenetic alterations in gene expression.

These changes in gene expression are increasingly linked to later development of obesity, diabetes, and neurological disease. Birnbaum pointed with pride to NIEHS research that has led to banning or limiting use of some pesticides, as well as to ongoing work by grantees, the Agricultural Health Study, and the National Toxicology Program (NTP) on additional long-term effects of exposure.

Commitment to public health

While the focus of the meeting was pesticides, Birnbaum’s presentation also covered the range of activities at NIEHS and NTP, from the development of predictive toxicology and studying the challenges of global climate change, to emerging issues related to nanotechnology, fracking, and health effects from the Gulf oil spill. She also shared with her audience the key components of the NIEHS 2012-2017 strategic plan, as they shape environmental health science research, translation, and their impact on public health.

Birnbaum closed with a new vision for NIEHS and NTP that maximizes resources through partnerships with sister NIH institutes and federal agencies, and addresses complex diseases and complex environmental impacts through transdisciplinary approaches.

An interagency cross-disciplinary effort toward improving watershed health

The Pesticides and the Chesapeake Bay Watershed Project meeting lineup of speakers and panelists reflected a convergence of several different scientific and regulatory interests.

In her invitation to Birnbaum, Executive Director of the Maryland Pesticide Network Ruth Berlin said, “Dr. Birnbaum’s March 14 commentary on low-dose effects of chemicals — particularly endocrine disruptors — generated a great deal of attention among our stakeholders and their colleagues.”

Because of this interest, Birnbaum ended up sharing the podium with U.S. Environmental Protection Agency environmental scientist Greg Allen and Wye Research and Education Center aquatic toxicologist Daniel Fisher, Ph.D. Allen previewed the upcoming report from EPA’s Chesapeake Bay Project, scheduled for release in November, on the impact of toxic contaminants on the bay watershed, while Fisher shared his recent work on the environmental impacts of contaminants, including the endocrine disruptive effects of land-applied poultry litter.

An afternoon panel discussion brought together Allen, who facilitates the project’s Research and Data Gaps Working Group, with colleagues from other project working groups:

- University of Maryland Farm Management Specialist and organic farmer Erroll Mattox, who facilitates the Project’s Collaborating with the Agricultural Community
- National Oceanic and Atmospheric Administration Research Fishery Biologist Andrew Leight, Ph.D., who facilitates the Preventing Pesticides from Entering the Watershed Working Group
- Andrew Fellows, Chesapeake regional director of Clean Water Action in Washington, D.C., and mayor of College Park, Md., who facilitates the Laws and Policies Working Group

EPA Environmental Protections Specialist Lee Tanner, who facilitates the Increasing Demand for Healthier Alternatives Working Group, had been scheduled to participate, but was unable to attend the workshop.

Citation: [Birnbaum LS](#). 2012. Environmental Chemicals: Evaluating Low-Dose Effects. *Environ Health Perspect* 120(4):a143-a144.

“Our job doesn’t stop with the publication of scientific results,” she concluded. “We have an obligation to help translate the fruits of our research investments into public health interventions, policy, and preventive clinical practice, to provide the best protection of human health.”

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WETP promotes logic model concept for training assessment

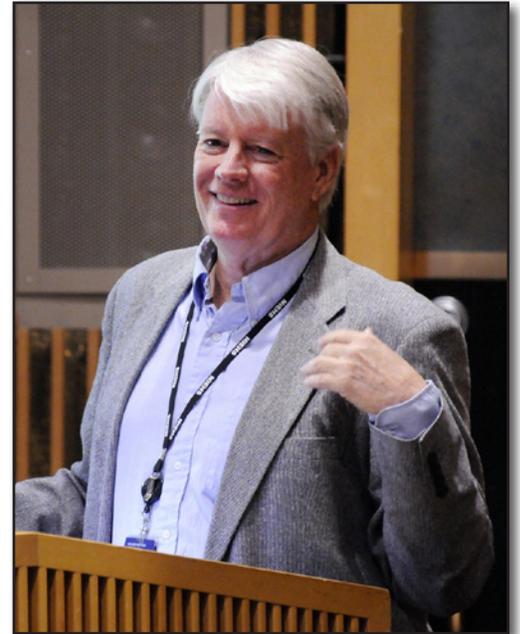
By Eddy Ball

A workshop at NIEHS Oct. 11-12 aspired to fundamentally transform ways of thinking about worker health and safety training evaluation, as well as share best practices. More than 100 grantees and contractors attended the workshop, which was part of the [annual meeting](#) of the [NIEHS Worker Education and Training Program \(WETP\)](#).

The workshop developed a theme that WETP Director Chip Hughes introduced in his opening comments on the importance of being able to demonstrate the effectiveness of worker health and safety training and its value to the nation. “Program evaluation has always been a core part of our mission.”

As veteran evaluator Ruth Ruttenberg said during a panel session on evaluation tools and methods, “Training only matters if it makes a difference.” Her challenge, and the challenge of the other panelists and presenters, involved helping participants think critically about how they design training and how they can develop metrics to show its impact on workers on the job, at home, and in the larger political context of their lives.

Following Hughes’ introduction, WETP grantee Craig Slatin, Sc.D., presented a big-picture keynote address on “Current and Future Safety and Health Training Expectations Under 21st Century Workplace and Socioeconomic Conditions.” In the face of economic restructuring that continues to impact job security, Slatin explained, the objectives of training can be difficult to realize. “We try to get workers’ voices out through the training,” he said, “[but the question of] how far do I push is always in workers’ minds.”



Hughes could joke about Kirkpatrick, even as he described the WETP dilemma when it comes to evaluation. “We have one foot in the real world,” he observed, “and one foot in the academic world.” (Photo courtesy of Steve McCaw)

Something old, something new — Kirkpatrick and logic models

Hughes’ introduction, and nearly every presentation at the workshop, acknowledged the tremendous contribution and continuing relevance of the four-level model of training course evaluation first published by University of Wisconsin Professor Emeritus [Donald Kirkpatrick, Ph.D.](#), in 1959. Modified over the years by the author and his partners, Kirkpatrick’s [framework](#) breaks down evaluation into how well learners respond, what they learn specifically, how much training influences performance, and whether the education program accomplished its original organization goals.

Not surprisingly, Kirkpatrick’s influence is also evident in the WETP logic model, which was the topic of presentations by NIEHS Division of Extramural Research and Training program analyst and evaluation specialist Kristi Pettibone, Ph.D., WETP program analyst Jim Remington, and WETP senior intern Hannah Leker, as well as a hands-on group exercise involving a collective effort to flesh out a logic model for their own programs.

The logic model reflects Kirkpatrick’s striving for exhaustive analytical precision, as it helps users construct a timeline flow chart of inputs, activities, outputs, and impacts — short term, midterm, and long term. The WETP handout also included mission and organizational priorities from the [WETP 2008-2113 strategic plan](#) as a benchmark for planning activities.

Numbers, narratives, and post-training audits

Early in the workshop, panelist Sue Ann Sarpy, Ph.D., introduced the concept of 360-degree evaluation. She described the feedback evaluation scheme as a multisource system that includes all stakeholders, including the director, students, employers, program coordinator, and community members, and also serves as a continuing quality improvement instrument. Sarpy’s approaches range from questionnaires and open-end questions, to focus groups and success stories to help lend a human touch to other metrics, as well as strengthen the case for support.

The 360-degree approach can also involve audits of trainees after they’ve completed training, with a checklist of behaviors observed. Yale University project manager Thomas Ouimet warned against the number one fatal assumption — attending equates with learning — as he advocated for on-the-jobsite followup observations. Like many of his co-presenters, Ouimet is a strong advocate of blended training, such as e-learning simulation, role playing, and case studies, as well as blended assessment with instruments matched to Kirkpatrick’s levels of evaluation.

As he wrapped up the meeting, Hughes looked toward funding realities, and the aging of the current group of experienced health and safety program operators and trainers. The workshop title,



Slatin lamented what he called a 40-year effort to reduce worker power that has resulted in the unemployment, or chronic underemployment, of some 23 million workers in the U.S. (Photo courtesy of Steve McCaw)

Worker safety and health training — a 25-year odyssey

Although the workshop focused on evaluation as a defensive strategy in an atmosphere of flat and even declining budget resources, participants have a rich history of accomplishment to build on, as they make their case. “You have to prove to somebody what you already know is true,” Hughes said to the audience. He also reflected on the quality of what crowd-source knowledge trainers can bring to the effort.

Keynote rappateur Eula Bingham, Ph.D., of the University of Cincinnati, framed her talk on evaluation in historical terms. “Let people know that you’re saving lives,” she said, “[by] helping us to tell the people it was all worthwhile.”

National Institute for Occupational Safety and Health researcher Paul Schulte, Ph.D., added, “WETP is one of the unsung heroes of this country.” Looking ahead to the potential for taking an effective program, with a proven track record, to an even higher level, Don Elisburg, J.D., of the National Clearinghouse for Worker Safety and Health Training, talked optimistically about what the talent on display during the workshop could mean for the future of worker training. “Looking at what everybody has done with these projects is mind-blowing,” he said.

“Prove It Makes a Difference,” referred both to the immediate, as well as long term, health of worker training. “The impact on the next generation is one of our big challenges for the future,” he said.



An author of the NIEHS Partnerships for Environmental Public Health Evaluation Metrics Manual (see story), Pettibone helped lead the group activities that resulted in creation of the WETP logic model. (Photo courtesy of Steve McCaw)



Looking back on the successes of worker training, Ruttenberg told participants, “We should have had an epidemic from cleaning up hazmat, but we didn’t.” She added that, today, there are first responders in every state in the U.S. (Photo courtesy of Steve McCaw)



Jamie Kirkley, Ph.D., of Wisdom Tools Enterprises, underscored the importance of precise analysis of training design and desired outcomes. “Don’t teach them [trainees] to swim, if you end up testing them on diving,” she told the participants. (Photo courtesy of Steve McCaw)



Occupational Safety and Health Administration training director Cathy Cronin called for active, job-focused training. She said instructors should devote about one-third of class time to lecture and two-thirds to interaction. (Photo courtesy of Steve McCaw)



Schulte said that employers should look at worker safety and health training as one part of a comprehensive risk management program. (Photo courtesy of Steve McCaw)



Elisburg is but one of several veterans of the program who are looking at retirement in the near future. Looking ahead, he encouraged trainers to keep in mind the very different learning styles of the next generation of workers. (Photo courtesy of Steve McCaw)

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Superfund marks 25th year of advancing health and wellbeing

By Eddy Ball

The annual meeting of the NIEHS Superfund Research Program (SRP) Oct. 22-24 in Raleigh, N.C., was an occasion for celebrating accomplishments and looking to the future.

The meeting, which attracted some 350 researchers and trainees from across the nation, was hosted by SRP grantees at the University of North Carolina at Chapel Hill and Duke University.

As SRP Director Bill Suk, Ph.D., held up the program's commemorative booklet during the opening ceremony Oct. 22, he spoke with pride about the program's long list of successes. He described the landmark program as mature at 25, but he also looked to the challenges ahead. "I want to thank you for 25 years of a good time," he told the audience, as he set the stage for four distinguished speakers who would offer their visions of next steps for the SRP. "Now we have to figure out the encore."

Partners in prevention and remediation

Leading the slate of speakers was NIEHS/NTP Director Linda Birnbaum, Ph.D., who emphasized the importance of SRP interaction with the U.S. Environmental Protection Agency (EPA). Pointing to the SRP focus on applied transdisciplinary research, community engagement, and outreach, Birnbaum said, "SRP is a pretty unique program within NIH."

As a program built on the principle of interagency partnerships, SRP has worked over the years to build productive relationships with EPA, which oversees hazardous waste cleanup at Superfund sites, and the Agency for Toxic Substances and Disease Registry (ATSDR), which shares SRP's public health mission. On the agenda with Suk, to kickoff the meeting, were Chris Portier, Ph.D., director of the CDC National Center for Environmental Health and the ATSDR, and Lisa Feldt, deputy assistant administrator of the EPA Office of Solid Waste and Emergency Response (OSWER).

In his overview of ATSDR, Portier focused on his agency's track record of community engagement. He pointed to almost 9,000 communities in the U.S. where ATSDR has been engaged, including the 1,220 where it is currently involved. "We want to work with the community from the beginning," he said, as he offered to help SRP programs identify productive contacts in their communities.



"There are a lot of young people who are the future of the program," Suk told the audience during his introduction. At the morning break on the first day of the meeting, he spent time talking with several of the trainees. (Photo courtesy of Steve McCaw)



Birnbaum praised the innovative applications of Superfund research. "I love the phytoremediation program," she said, pointing to the development of alternative ways to clean up Superfund sites. (Photo courtesy of Steve McCaw)

As a biostatistician with more than three decades experience at NIEHS and NTP, Portier is understandably interested in new directions in toxicology. “It’s time for us to change with the research,” he said, which provided a natural transition to remarks by Feldt.

Feldt also spoke along the lines of taking advantage of new developments to revisit chemicals at Superfund sites and advancing community engagement. “I’m really focused on the ground,” she said, where research findings move from the lab to viable use in the field. Both because of their joint mission and increasingly strained resources, Feldt said, the partnership of what she described as the Superfund triumvirate will continue to be critical to success.

Friend of Superfund reflects on successes and challenges

In his survey of SRP, keynote speaker Philip Landrigan, M.D., specifically addressed “Why We Need a Superfund Research Program.” Landrigan, the dean for global health at Mount Sinai School of Medicine, brought his background as a pediatrician, epidemiologist, and global public health scholar to bear on his description of where SRP had come from and his vision for where he sees it going in years to come.

“I guess waste is a primate thing,” he began. “What’s new is what’s in our waste today.” Because of the chemical revolution of the last 50 years, he said, the U.S. has more than 15,000 federally managed hazardous waste sites across the country, located within one mile of where some 11 million people make their homes — a disproportionate number of them minorities and people socioeconomically disadvantaged.

As he surveyed the successes and heroes of SRP, Landrigan looked beyond the borders of the U.S. to future collaborations with other countries where, he said, “There’s going to be lots of Superfund work to be done.” He noted that at least 20 percent of deaths in developing countries are directly attributable to environmental exposures to such things as lead in gasoline, asbestos, pesticides, and e-waste.



Looking back on the quarter century of collaboration among the Superfund partners, Feldt said, “Together, you have made great progress.” (Photo courtesy of Steve McCaw)



As he moved into his description of SRP as a model for developing countries facing a growing hazardous waste problem, Landrigan told attendees, “It [SRP] is the envy of the world.” (Photo courtesy of Steve McCaw)



Before he left the meeting to return to Atlanta, Portier, right, reconnected with grantee Ivan Rusyn, Ph.D., of the University of North Carolina-Chapel Hill. (Photo courtesy of Steve McCaw)



Grantees Rebecca Fry, Ph.D., of UNC, left, and Jay Gandolfi, Ph.D., of the University of Arizona, talked during the break. Gandolfi is retiring at the end of the year from his post as director of the SRP there. (Photo courtesy of Steve McCaw)



A smiling Baker, left, held her Wetterhahn plaque, as Collman, one of the ranking female scientists at NIEHS, beamed with shared pride in the accomplishments of SRP trainees. “I’m very proud to have this outstanding program as part of our portfolio,” Collman said during her introductory remarks. (Photo courtesy of Steve McCaw)

The future of SRP

Along with their presentations and plenary sessions, SRP annual meetings set aside time for celebrating award-winning trainees — what Landrigan rightly called the future of public health.

NIEHS Division of Extramural Research and Training Director Gwen Collman, Ph.D., introduced the 2012 winner of the coveted [Karen Wetterhahn Memorial Award](#), Nicki Baker, a Ph.D. candidate at the University of Kentucky and the 15th SRP trainee to receive the award.

Baker presented findings from her dissertation project, “The role of PCBs in the development of diabetes,” which are reported in her new [paper](#) published in the journal *Environmental Health Perspectives*. In a series of experiments, Baker and her colleagues found that coplanar PCBs induce an inflammatory response in a dose-dependent manner that could be abolished through inhibition of aryl hydrocarbon receptor by an experimental compound and through dietary antioxidants in a mouse model.

Following Baker’s keynote presentation, Collman presented awards for the meeting’s poster session, which featured 143 posters — 128 of them from students. She then turned over the podium to [Timothy Phillips, Ph.D.](#), an SRP researcher at Texas A&M University (TAMU), to recognize the work of 2011 winners of the [K.C. Donnelly Externship Award Supplement](#), who presented ten-minute talks on their research.

- Celys Irizarry, a master’s student at the University of Puerto Rico, Mayagüez
- Alvine Mehinto, Ph.D., a postdoctoral researcher at the University of Florida
- Xianai Wu, Ph.D., a postdoctoral researcher at the University of Iowa

Phillips then presented the 2012 awards to three students who are just beginning their one-year externships.

- Sabine Vorrink, a graduate student at the University of Iowa
- Steven O’Connell, a graduate student at Oregon State University
- Vanessa De La Rosa, a graduate student at the University of California, Berkeley

Citation: Baker NA, Karounos M, English V, Fang J, Wei Y, Stromberg A, Sunkara M, Morris AJ, Swanson HI, Cassis LA. 2012. Coplanar Polychlorinated Biphenyls Impair Glucose Homeostasis in Lean C57BL/6 Mice and Mitigate Beneficial Effects of Weight Loss on Glucose Homeostasis in Obese Mice. *Environ Health Perspect*; doi:10.1289/ehp.1205421 [Online 24 October 2012].



The poster award winners in the non-biomedical category were, left to right, Timothy Jobe, University of California - San Diego (1st), Sahar Fathordoobadi, University of Arizona (2nd), and Daniel Brown, Duke University (Photo courtesy of Steve McCaw)



Phillips talked about the accomplishments of K.C. Donnelly, Ph.D., his associate and friend for many years at the TAMU SRP (see story). "Most importantly, he was a good guy," Phillips said. (Photo courtesy of Steve McCaw)



In the biomedical category, poster winners were, left to right, Erika Fritsch, UC Davis (3rd), Chase Williams, University of Washington (2nd), and Caitlin Howe, Columbia University (1st). (Photo courtesy of Steve McCaw)



Like her fellow 2011 Donnelly award winners, Mehinto presented the results of her work over the past year with the mentor from her home institution and a second mentor at her host school. (Photo courtesy of Steve McCaw)



Shown with Phillips are 2012 Wetterhahn winners, left to right, Vorrink, De La Rosa, and O'Connell. (Photo courtesy of Steve McCaw)



Shown above are 11 of the 15 Wetterhahn winners named since 1998. Seated, left to right, are Baker (2012), Monica Ramirez-Andreotta (2011), and Courtney Horath (2010). Standing, left to right, are Karrie Radloff (2009), Roxanne Karimi (2007), Laura Senier (2008), Elena Craft (2002), Alicia Timme-Laragy (2006), Tiffany Bredeldt (2005), Anne Spuches (2004), and Monica Mende (2003). (Photo courtesy of Steve McCaw)

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NIEHS welcomes Scholars Connect charter cohort

By Eddy Ball

A new internship program, aimed at getting minority scholars involved in the environmental health sciences, officially launched Sept. 17 at NIEHS. The charter cohort of nine undergraduates from universities in the Raleigh/Durham, N.C., area are part of the [NIEHS Scholars Connect Program \(NSCP\)](#), which is designed to foster the development of students who belong to groups traditionally underrepresented in science, technology, engineering, and math (STEM) careers.

The participants are highly motivated sophomores, juniors, and seniors at St. Augustine's University (SAU), North Carolina Central University (NCCU), and North Carolina State University (NCSSU) with STEM majors. They represent a diverse range of study concentrations in biology, chemistry, mathematics, and public health, and have at least a 3.0 grade point average overall and a 3.5 in their major field(s) of study.



Reid's office oversees a broad range of NIEHS outreach and diversity activities that include guided tours of the facilities, maintaining a speakers' bureau, and representing the Institute at national meetings of minority-focused scientific groups. (Photo courtesy of Steve McCaw)

“We ask the students to commit to two semesters, and a third semester is an option,” said NIEHS [Office of Science Education and Diversity](#) Director Ericka Reid, Ph.D., who organized the program as semester-long active learning experiences, or connections, for the scholars. “This is the fall connection, which runs Sept. 17 through Dec. 7.”

The scholars will spend up to 20 hours on research-related activities each week, during the 2012-2013 academic year, as paid interns, while they continue their academic programs at their home institutions. Research-related activities include laboratory work mentored by lead researchers, scientists, and postdoctoral fellows, along with literature reviews, participation in lab meetings, and attendance at research workshops and seminars.

The program requires interns to participate in weekly NSCP professional development seminars, where they engage in dynamic dialogues with NIEHS scientists on environmental health research topics. The seminars also aim to further the scholars’ scientific development, through opportunities to receive research-relevant software training, in preparation for presenting findings from their own scientific research at the end of each connection. The presentation represents the culmination of eight to 12 weeks of defining a research project, constructing an appropriate hypothesis, and conducting experiments to test that hypothesis.

NSCP operates under the supervision of part-time program coordinator Courtnea Rainey, a Ph.D. student in psychology at Duke University. The program is funded by the NIEHS Office of the Director, Division of Intramural Research, and Division of the National Toxicology Program.

Beginning in November, NSCP will begin accepting applications for the 2013 scholar selection.



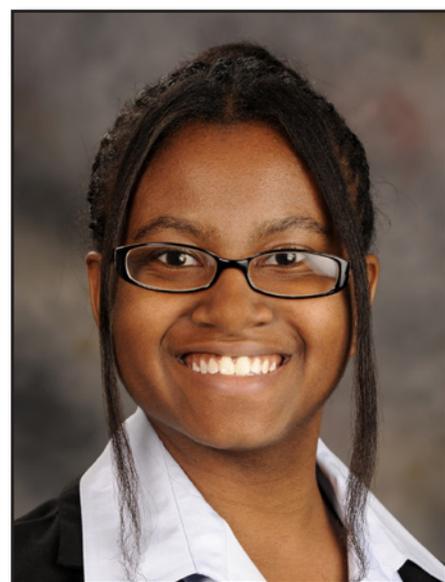
An important part of Rainey’s job is organizing the weekly NSCP seminar series. She is scheduled to be a presenter in three of the 12 seminars during the fall connection. (Photo courtesy of Steve McCaw)



NCCU student Robert Alston is working in the NIEHS [Developmental Neurobiology Group](#) with lead researcher Patricia Jensen, Ph.D., and postdoctoral fellow Jacqueline de Marchena, Ph.D. (Photo courtesy of Steve McCaw)



NCCU student Michael Lekwuwa is working with technical lab manager Kevin Gerrish, Ph.D., and biologist Laura Wharey in the NIEHS Microarray Group. (Photo courtesy of Steve McCaw)



NCCU student Lovie Matthews is being mentored by lead researcher David Miller, Ph.D., and staff scientist Ron Cannon, Ph.D., in the NIEHS [Intracellular Regulation Group](#). (Photo courtesy of Steve McCaw)



As part of the NIEHS [Environmental Cardiopulmonary Disease Group](#), SAU student Kacey McHoney is working with Scientific Director Darryl Zeldin, M.D., and postdoctoral fellow Matthew Edin, Ph.D. (Photo courtesy of Steve McCaw)



Assigned to NTP laboratories, NCCU student Charles Okechukwu works in the [Neurotoxicology Group](#) with lead researcher Jean Harry, Ph.D., and in the [Inorganic Toxicology Group](#) with postdoctoral fellow Ruben Orihuela Garcia, Ph.D. (Photo courtesy of Steve McCaw)



NCSU student Jaydave Patel is being mentored by lead researcher Anton Jetten, Ph.D., and staff scientist Hong Soon Kang, Ph.D., in the [Cell Biology Group](#). (Photo courtesy of Steve McCaw)



SAU student Jennifer Plair is working in the NTP [Molecular Pathogenesis Group](#) under the direction of lead researcher Darlene Dixon, D.V.M., Ph.D., and biologist Linda Yu. (Photo courtesy of Steve McCaw)



SAU student Malcolm Richbourg is being mentored by lead researcher Humphrey Yao, Ph.D., biologist Karina Rodriguez, Ph.D., and postdoctoral fellow Heather Franco, Ph.D., in the NIEHS [Reproductive Developmental Biology Group](#). (Photo courtesy of Steve McCaw)



As part of the NIEHS [Gamete Biology Group](#), NCSU student Brandon Williams conducts research under the direction of lead researcher Mitch Eddy, Ph.D., and postdoctoral fellow Tracy Clement, Ph.D. (Photo courtesy of Steve McCaw)

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Mobile technologies poised to aid training and emergency response

By Ed Kang

Several representatives of leading-edge organizations visited NIEHS Oct. 9 to demonstrate how mobile technologies are being used by responders, hazardous materials handlers, and other public health workers, to maintain safe operations and ensure that the most up-to-date information is deployed to the field when needed. The presentations and demonstrations by representatives from the U.S. National Library of Medicine, Cell Podium, and MetaMedia showed the potential of mobile computing to transform the delivery of education, training, and emergency response messages.

Each of the three organizations referred to the growth in the use of tablet computer and smart phones as a way to reach multiple demographics, including those who may not have access to other kinds of computing equipment such as desktop computers. The latest applications take advantage of shrinking device size, wireless communications, and multimedia capabilities.



Sharon Beard, who organized the session, described the capability of mobile technologies to deal with emerging environmental threats, one of the central themes of the new NIEHS *strategic plan*. Beard is an industrial hygienist in the NIEHS WETP. (Photo courtesy of Steve McCaw)



Attendees from across the Institute, including NIEHS Deputy Director Rick Woychik, Ph.D., second from left, and Charlie Tate, right, a member of the NIEHS Operations and Security Branch, got to see, firsthand, how tablet computers can be a vital tool for information delivery. They're pictured here with representatives from MetaMedia. (Photo courtesy of Steve McCaw)

Linked video:



Watch as Cesar Bandera, of Cell Podium, talks about using cell phones to deliver video content to a variety of users. One example of his company's success was delivering educational information about insulin treatment for diabetics (01:32)

(Launches in new window)

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“We want to bring science to the disaster and be proactive about looking at what the possible exposures could be before they actually happen,” said NIEHS Worker Education and Training Program (WETP) Analyst Jim Remington, who manages a portfolio of hazardous material training and oversees disaster response activities. “And when we have disasters, we want to get information to the folks out in the field, using mobile technologies, to help protect workers while they’re doing their jobs.”

The development of these technologies has been supported by WETP using small business research grants. Training for workers has traditionally required physical classrooms and educational materials, and recent technological advances have opened opportunities

Linked video:

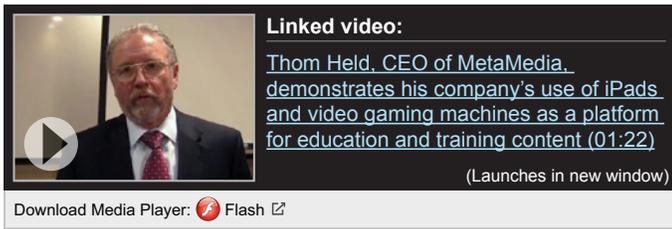


Join Bert Hakkinen, Ph.D., online as he describes a variety of tools NLM has developed to disseminate toxicological information about a variety of chemicals. This has been useful for hazardous material handlers, industrial workers, hobbyists, and many others (01:41)

(Launches in new window)

Download Media Player:  Flash 

for providing accessible, accurate, and interactive training through electronic channels. These new approaches help to rapidly and effectively equip workers with the skills and knowledge to protect themselves and their communities from hazards.



The seminar was sponsored by the NIEHS Division of Extramural Research and Training, as part of its ongoing Keystone Science Lecture Seminar Series.

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

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Reaching out to Hispanic, Native-American, and other minority students

Ericka Reid, Ph.D., director of the NIEHS [Office of Science Education and Diversity \(OSD\)](#), and postdoctoral fellow Anshul Pandya, Ph.D., represented NIEHS at the 2012 Society for Advancement of Chicanos and Native Americans in Science ([SACNAS](#)) National Conference Oct. 11-14. The [conference](#), titled “Science, Diversity, and Technology for a Healthy World,” was held in Seattle, Wash., and attracted talented students of Native American and minority backgrounds from around the country.

Connecting with young scientists

NIEHS, along with other NIH institutes and public and private universities, encourages Hispanic/Chicano and Native American students to pursue higher education and obtain advanced degrees. With more than 3,600 students in attendance, the NIEHS representatives focused on spreading awareness about NIEHS among the students. Along with Reid and Pandya, NIEHS Office of Communications and Public Liaison Director Christine Flowers was on hand at the NIEHS booth in the exhibition hall, where students looking for future opportunities in science research, including internships and fellowships, could ask questions and pick up information about the Institute and its research.

“It was a rewarding experience for me to talk to young students of minority backgrounds,” said Reid, who is working to enhance NIEHS’ education and diversity outreach. “The [NIH] Summer Internship Program was a popular topic, and I’m hopeful that interest will translate into an increase in the number of applicants from different states.”

Graduate students and Ph.D. candidates inquired about career opportunities available at NIEHS. “As an intramural postdoctoral fellow at the NIEHS, I was asked about my own experience of working at the NIEHS,” said Pandya, who is a member of the NIEHS [Ion Channel Physiology Group](#). “I was able to tell undergraduate and graduate students about the research training and career opportunities available at our Institute.”



For more than 30 years, SACNAS has been encouraging Hispanic/Chicano and Native American students to pursue science research, leadership, and teaching careers at all levels. SACNAS was named the National Science Board’s premier minority science organization promoting diversity in science careers, and was the winner of the 2004 Presidential Award for Excellence in Science, Mathematics, and Engineering Mentoring.

Pandya added, “This year I noticed some anxiety among students regarding their education and future careers. I thought it was a reflection of the economy and employment picture for fresh graduates out of college.” Pandya was attending his second SACNAS conference, as a part of NIEHS outreach and diversity efforts. Those who visited the NIEHS booth also learned about the exciting research being carried out in the intramural division of the NIEHS, and the funding opportunities and grants available,” he added.

“Meeting students face-to-face not only increases the public profile of the Institute, but it also spreads awareness about government-funded environmental and health research,” said Reid.

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Pandya, left, and Reid worked the NIEHS booth, in between sessions at the conference. (Photo courtesy of Christine Flowers)

Workshop addresses the millions who die yearly from household air pollution

By Cindy Loose

Cooking meals can be a deadly activity for the poorest three billion people in the world who burn wood, dung, and other biomass in their homes. Women and children, who usually spend the most time indoors breathing air polluted by cooking fires, are the most frequent victims. The pollutants are also a major contributor to global warming.

“Nearly two million women and children around the world die every year, and many more are made sick or disabled, as a result of exposure to smoke from biofuels,” said NIEHS/NTP Director Linda Birnbaum, Ph.D., in her keynote address at the [Household Air Pollution Research Training Institute](#) Meeting Oct. 9-12 at the Fogarty International Center on the National Institutes of Health Bethesda, Md., campus.

A critical problem

The extent of the problem was described to participants from multiple federal agencies and institutions around the world by NIEHS grantee [Kirk Smith, Ph.D.](#), a professor of global environmental health at the University of California, Berkeley. He noted that World Health Organization guidelines recommend particulate matter exposure at no more than 10-35 milligrams per cubic meter per year. “In India, the particulate matter exposure is 330 and that is every day,” said Smith. Exposures in homes in Guatemala have been measured at 8,670 milligrams per cubic meter, added speaker [Jacob Moss](#), director of the U.S. Cookstoves Initiatives at the U.S. Department of State.



Collins' presentation was a tangible expression of the interest NIH has in reducing indoor air pollution worldwide. (Photo courtesy of NIH)

Studies have shown clear evidence that household air pollution causes lung cancer and other respiratory diseases, chronic obstructive pulmonary disease, cataracts, and low birth weight. Further study is needed to confirm that it is implicated in a number of other diseases. Smith, who leads a project in Guatemala, said research shows that as exposures rise, childhood pneumonia soars. Birnbaum noted that pneumonia is the leading cause of death of children worldwide.

“We must have reduction in exposures and a little bit isn’t enough — it has to be a significant reduction,” said NIH Director Francis Collins, M.D., Ph.D., during the opening session the evening of Oct. 9, as he lauded the fact that numerous federal agencies participated, including three NIH institutes — NIEHS; the National Heart, Lung, and Blood Institute; and the Eunice Kennedy Shriver National Institute of Child Health and Human Development — that partnered with the U.S. Agency for International Development to organize the workshop.



Birnbaum observed that the NIEHS commitment to global health is an important component of the Institute’s 2012-2017 strategic plan, specifically theme 4 — health disparities and global environmental health. (Photo courtesy of Steve McCaw)

Solutions from science

Scientists and technicians have a twofold research mission — to quantify the health problems and identify interventions, including alternative cookstoves. Birnbaum noted that NIEHS is working on both fronts and providing \$3 million in cookstove research this year. Additionally, NIEHS, the Fogarty International Center, and the National Institute for Occupational Safety and Health jointly funded 16 applications for studies in five regions of the world.

Simple solutions for a major public health problem

Richard Grinnell, vice president and chief operating officer of HELPS International in Guatemala, demonstrated an inventive cookstove he brought, and said his organization first became alarmed about open cook fires because so many children came to the health clinic with severely burned hands, or with fingers fused or even missing. Later, his group realized the enormous risk of respiratory and other diseases.

U.S. Environmental Protection Agency Assistant Administrator for the Office of Air and Radiation [Gina McCarthy](#) said that solving the problem could resolve many existing issues — overall public health; women and children’s rights; safety in war zones where women and children risk their lives to collect fuel; environmental justice; and lack of education, because children who spend the day looking for fuel can’t go to school. Moss noted the potential benefit of cookstove alternatives on climate change, saying that 20 percent of black carbon — one of the most harmful climate changers — comes from burning biomass for cooking.

“Most times when it comes to environmental issues, the fat lady never sings because the problem is never over,” said McCarthy. “This is something we can get our arms around and solve. Every minute we put into this, we’ll be saving lives.”

Collins emphasized the point, while strumming his guitar and leading the group in a song with the refrain “If not now, if not now, tell me when.”



Along with many other honors, Smith received the Heinz Prize in the Environment and the Tyler Prize for Environmental Achievement, in recognition of his cookstove and household air pollution research. (Photo courtesy of the University of California, Berkeley)



NIEHS Senior Advisor for Public Health [John Balbus, M.D.](#), serves as the Institute's lead on the cookstove initiative. (Photo courtesy of Steve McCaw)

The three-day workshop exemplifies the training aspect of the effort. Numerous prototypes and alternative cookstoves were demonstrated and tested in workshops attended by both young and established researchers from the U.S., China, India, and a number of countries in Africa and South America. Other workshops discussed research designs for measuring exposures and health outcomes, and how to set standards so that cooking alternatives are sufficient to make a difference in public health.

Collins and others urged that alternatives be designed to consider cost, sustainability, ease of operation, and cultural differences. They noted that a stove perfect for cooking tortillas in Guatemala might not be good for cooking injera, a yeast-risen flatbread that is a staple in Ethiopia.

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

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Building bridges between risk assessment and environmental justice

By Eddy Ball

The Research Triangle Chapter of the Society for Risk Analysis sponsored a meeting Oct. 15 that may be one sign of a new working relationship between environmental justice (EJ) advocates and risk assessment scientists.

The meeting, hosted at the U.S. Environmental Protection Agency (EPA) at its Research Triangle Park, N.C., headquarters, brought together grass-roots advocates, NIEHS and EPA environmental health science researchers and risk assessment specialists, and others in the RTP scientific community. The daylong discussion gave participants an opportunity to discover a common ground for moving community engagement research forward, to eliminate environmental injustices that persist 18 years after President Bill Clinton signed his famous [Executive Order 12898](#) in 1994.

Welcoming remarks by Andrew Geller, Ph.D., deputy national program director of the EPA Sustainable and Healthy Communities Research Program, offered participants historical perspective on the issues involved and framed the discussion to follow with the directive by EPA Administrator Lisa Jackson to make EJ a priority at the agency.

Community perspectives on research

The first speaker on the agenda, NIEHS grantee [Steve Wing, Ph.D.](#), associate professor of epidemiology at the University of North Carolina at Chapel Hill (UNC) Gillings School of Global Public Health, set the tone for the meeting, by reflecting on the gap caused by the different socioeconomic backgrounds that scientists and community groups bring to EJ work. Despite his long relationship with such research in eastern North Carolina, Wing explained that he and other scientists need to approach the communities where they plan to conduct research without preconceptions.

“I don’t have the life experience of people who are facing environmental injustice,” Wing said. He also pointed to the high stakes involved. “Some people benefit because others are being denied benefits.”

The community representatives who followed Wing’s presentation offered concrete examples of those mixed benefits in their own communities. They also described their need for what they called community-engaged actionable research — scientific studies they can use to implement grass-roots change to improve environmental public health in their communities.

Activist Omega Wilson, director of the [West End Revitalization Association](#) in Mebane, N.C., opened the community perspective portion of the workshop with a keynote address on opposition to a proposed road project in his community, and efforts by his group to gain equal access to clean water and sanitation for residents. Criticizing researcher-initiated studies that support publications and tenure, but do little to advance community interests, Wilson called for more grant support for community-initiated investigations. “We need funding for ground-truthing research,” he said.

Five other speakers addressed the environmental injustices created by goods movement, landfills, and industrial hog production for residents and workers. “It [hog feces and the rendering of dead animals] may smell like money to the owners,” Devon Hall, of the [Rural Empowerment Association for Community Help \(REACH\)](#), told the audience, “but not to the worker making \$8 an hour.”



Working with the North Carolina Environmental Justice Network (NCEJN) and Concerned Citizens of Tillery, Wing has helped residents of eastern North Carolina oppose industrial farming practices that he said create environmental injustices. (Photo courtesy of Steve McCaw)



Wilson criticized what he called the guinea pig syndrome, when researchers come into a community, conduct their studies, and then fail to take the next step to protect public health. (Photo courtesy of Steve McCaw)

Science to address EJ

The afternoon keynote address by former NIEHS Director [Ken Olden, Ph.D.](#), helped transition the meeting from its community perspective to a consideration of how risk assessment scientists can strive to bridge the gap between the research and EJ communities. Olden, who is currently director of the EPA National Center for Environmental Assessment, is a pioneer in EJ, as well as a cancer biologist who has studied epigenetic profiles in the neighborhoods of New York City.

Although most of the work described by the scientists who followed Olden failed to strictly meet the definition of community-initiated actionable research, it was clear the risk assessment scientists had been listening to their community counterparts. As they discussed ongoing work on air quality and asthma, Martha Sue Caraway, M.D., of Duke University, and Kelly Duncan, Ph.D., from UNC, referred several times to the ideas Wilson and his colleagues had outlined that morning.

The final scientific talk of the day, by geophysicist [Timothy Barzyk, Ph.D.](#), explored community-initiated research applications for the broad range of risk assessment tools now available, or in development, by EPA. These include geographic information system programs that are capable of creating maps to integrate exposure data, potential environmental hazards, and health statistics at the community level, producing the kind of actionable research Wilson described.



Community speakers, right to left, Dothula Baron-Hall of REACH, Naeema Muhammad of NCEJN, and Hall shared stories of living conditions in communities where caged animal farming is widespread. (Photo courtesy of Steve McCaw)



As the meeting broke for lunch, Wing talked with SPHB Health Scientist Administrator Symma Finn, Ph.D., who was one of several observers from NIEHS attending the meeting. (Photo courtesy of Steve McCaw)

Looking ahead

Fittingly, the final speakers of the day were NIEHS Susceptibility and Population Health Branch (SPHB) Chief [Claudia Thompson, Ph.D.](#), and Geller, with presentations on “NIEHS and U.S. EPA: Science Planning to Address Environmental Justice.”

Geller described EPA’s role in cross-agency efforts to identify best practices for encouraging actionable research in EJ initiatives. He also noted that EPA and NIH are cofunding 10 [Centers of Excellence in health disparities](#) around the country, and he looked forward to the implementation of [EJ 2014](#), a roadmap that will help EPA integrate environmental justice into the agency’s programs.

Thompson described the long-standing NIEHS commitment to EJ that has resulted in nearly two decades of capacity building, outreach and training, policy change, and publications. She also outlined the NIEHS Partnership for Environmental Public Health program, a one-NIEHS umbrella initiative to foster extramural, Worker Education and Training, Program (WETP), and Superfund Research Programs, by promoting EJ through outreach, education, and community-driven research. She referred to the Institute’s deep-rooted commitment to EJ and equal access to a healthy environment through its [2012-2017 Strategic Plan](#).



Just before his presentation, Olden, left, sat with NIEHS WETP Director Chip Hughes. One theme in Olden's talk was that EJ is about health disparities. (Photo courtesy of Steve McCaw)



UNC researcher Duncan described work underway in her EPA-funded study, "The RTP-Area African American Children's Asthma Study." (Photo courtesy of Steve McCaw)



Barzyk titled his presentation, appropriately, "Bridging the Gap Between Cumulative Risk and Environmental Justice: Tools and Applications." (Photo courtesy of Steve McCaw)



Geller summed up a new direction in thinking about risk assessment and EJ. "Communities can identify their own problems," he said in his closing remarks. (Photo courtesy of Steve McCaw)

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GuLF STUDY makes final call for study participants

By Robin Mackar

During a series of media outreach efforts in October, NIEHS epidemiologist Dale Sandler, Ph.D., lead researcher for the [GuLF STUDY \(Gulf Long-term Follow-up Study\)](#), her team, and community partners throughout the Gulf region put a call out to encourage oil spill cleanup workers and volunteers to join the study before enrollment closes at the end of the year.

"Every worker and volunteer has a story to tell, and we would like to hear every story, to better understand the potential health effects of oil and dispersants," Sandler said during an Oct. 2 telephone press conference.



“With the help of more than 80 community and professional groups across the Gulf Coast, the GuLF STUDY has enrolled more than 29,000 people to date,” said Sandler, who is chief of the NIEHS Epidemiology Branch. “The cleanup response involved a wide range of tasks carried out by a large number of people who each experienced exposures to oil and dispersants under unique circumstances. We want to understand the experiences of all types of workers.”



Linked video:
Watch as U.S. Surgeon General Regina Benjamin, M.D., encourages cleanup workers and volunteers to become a part of the GuLF STUDY (01:00)
(Launches in new window)

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Community leaders

“The oil spill raised a lot of questions for people here who helped with the cleanup, and we hope the GuLF STUDY will provide answers,” said Paige Rucker, a community partner and the state director of [Project Rebound](#), an Alabama nonprofit organization assisting those impacted by the Deepwater Horizon oil spill.

Roberta Avila, executive director of the [Steps Coalition](#) in Mississippi, joined Rucker and Sandler for the teleconference with about 20 media outlets, encouraging workers to enroll in the study. “The information the GuLF STUDY provides could help inform public policy as it pertains to healthcare delivery in the area,” Avila told the attendees.

Calling all eligible workers and volunteers

NIEHS is seeking all eligible workers and volunteers — those who are healthy, as well as those who may have health challenges — to enroll in the study. NIEHS is also making a special request for anyone who worked near the source of the spill, such as oil rig workers and rig support personnel, to sign up. Because of their proximity to the spill, it will be important to understand how their exposure might affect their health.

Expected to last at least 10 years, the GuLF STUDY will generate important data that could help inform policy decisions on health care and health services in the Gulf Coast region. Findings could also influence responses to other oil spills in the future.

For more information, call the GuLF STUDY toll-free at 1-855-NIH-GULF (1-855-644-4853) or visit the GuLF STUDY website at <http://www.gulfstudy.nih.gov>.

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

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Sandler has led several recruitment tours in the Gulf region, forging partnerships with community groups and getting the word out to cleanup workers and volunteers. (Photo courtesy of Steve McCaw)



Rucker's background in advertising has helped Project Rebound craft a compelling message to Gulf residents. (Photo courtesy of Paige Rucker)



Avila has worked in nonprofit and social justice sectors on the Mississippi coast for 22 years. She was involved in Katrina relief efforts prior to the Gulf oil spill. (Photo courtesy of Roberta Avila)

Hardworking postdoc receives prestigious Pathway to Independence Award

By John House

If a trainee's goal is to successfully navigate the rocky highway of becoming a successful tenure-track lead researcher, the prestigious [NIH Pathway to Independence Award \(K99/R00\)](#) provides a paved on-ramp.

Ramendra Saha, Ph.D., a postdoc beginning his sixth year at NIEHS, became the latest beneficiary of this early-career support Oct. 1, when the National Institute of Mental Health announced his award. Because of action this year by the NIEHS Office of the Scientific Director, he will also become the first awardee to receive a merit increase of \$2,000 to his training stipend ([see text box](#)). Saha is a member of the NIEHS Synaptic and Developmental Plasticity Group, headed by [Serena Dudek, Ph.D.](#)

This highly sought-after award offers new investigators two years of additional mentored training, and also provides for an additional three years of grant support that awardees take along to the institution of their choice. While most new hires are scrambling to use their startup funds to get preliminary data before the money runs out, K99/R00 grantees hit the ground with additional funds to support their research plan already in place.

Expanding understanding of early gene transcription

Saha's work has focused on defining the mechanism involved in gene transcription induced by neuronal activity, building on findings that some genes, termed immediate early genes (IEGs), are transcribed extremely quickly after neuronal activity. After listening to a seminar by lead researcher [Karen Adelman, Ph.D.](#), another investigator at NIEHS working on chromatin signatures and Pol II poising on promoters for rapid transcription, Dudek and Saha hypothesized that IEG transcription downstream of neuronal signaling relied on Pol II poising on the promoters of these genes.

Saha's research demonstrated their hypothesis was correct. Transcripts of IEGs that came up in the two-minute to five-minute period after neuronal stimulation did, indeed, have Pol II poising that allowed for such a fast response, and this research netted him a Nature Neuroscience paper ([see story](#)). During his time at NIEHS, Saha has been first author on several publications, received an NIH Fellows Award for Research Excellence in 2010 and 2011, and been recognized with competitive Society for Neuroscience awards.

Dudek said of Saha, "Ramen has never been short on ideas for his research, which makes me think he will continue to succeed in grant writing. Importantly, Ramen is also good at designing and doing experiments to test these ideas, and I know he will make a good PI [principal investigator/lead researcher]."



Saha, left, earned his Ph.D. from the Nebraska Medical Center where he studied neurodegeneration. He considers it a privilege to be at the forefront of neuroscience discovery at NIEHS. Dudek said she is very excited about Saha's research work and looks forward to new discoveries stemming from this project. (Photo courtesy of Steve McCaw)

Two phases of early-career support

The NIH Pathway to Independence Award consists of two parts and is one of the few available to non-U.S. citizens, as well as U.S. citizens. The K99, or mentoring phase, lasts up to two years and ends when the awardee secures tenure-track employment. This portion of the award supports mentored training and provides for career development, to prepare grantees for success and independence. The R00, or research phase, begins when the awardee becomes a tenure-track investigator. This is a non-renewable grant of up to three years that allows the individual to continue work toward establishing his or her own independent research program.

Saha's K99 portion of the award starts immediately. NIEHS Scientific Director Darryl Zeldin, M.D., announced in September that successful grantees will also receive a monetary supplement to their training stipend during their K99 period, as a reward for their effort.

Saha's mentoring will continue under Dudek. He will also have a co-mentor, NIEHS lead researcher [Paul Wade, Ph.D.](#), as he studies the electrophysiology of neuronal cells. His research proposal focuses on the histone H2A.Z, which has several isoforms and can be epigenetically modified. H2A.Z is a variant of histone H2A, and studies have shown that H2A.Z localization in chromatin tends to be higher near gene promoters. Saha aims to determine the role each variant plays in synaptic plasticity and gene transcription and, in turn, how this interaction affects the long-term synaptic plasticity involved in memory formation.

(John House, Ph.D., is a postdoctoral fellow in the NIEHS Genetics, Environment, and Respiratory Disease Group.)

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HHS workshop aims to speed up public health emergency response

By *Cindy Loose*

Experts from NIEHS and nearly two dozen other federal agencies gathered Sept. 25 on the NIH campus in Bethesda, Md., to carry out a critical mission — to identify ways that research scientists can be deployed immediately in response to terrorist acts, natural disasters, accidents, and pandemics.

“We are not currently organized to do science in the moment,” said [Nicole Lurie, M.D.](#), assistant secretary for Preparedness and Response at the U.S. Department of Health and Human Services (HHS), which sponsored the workshop, “Scientific Preparedness and Response for Public Health Emergencies.” When a national disaster occurs, she explained, protocols are in place to send first responders rushing to the scene. Research scientists, however, too often must await approvals of data collection protocols, reviews of proposed studies, and funding, before rushing out the door to do critical work.

“The overriding question is, ‘What can we put in place to speed up the response, so that we save as many lives as we can?’” Lurie asked.



Linked video:

[Watch as Lurie discusses the importance of emergency-readiness with respect to natural disaster, terrorist attack, or biological epidemic at the City Club of Cleveland \(51:44\).](#) (Launches in new window)

Download Media Player: Flash

Getting scientists to work during emergency response

More than 70 experts from federal agencies, as diverse as HHS and the Government Accounting Office, the U.S. Department of Defense, and the Office of Management and Budget, came together to identify the best means of accomplishing that goal. Participants also included representatives from NIH, as well as 10 NIH institutes and centers (see text box).

“All the right people were in one place focusing on how to further scientific preparedness,” said NIEHS Senior Medical Advisor [Aubrey Miller, M.D.](#), who along with NIEHS Worker Education Training Program (WETP) Director Chip Hughes and program analyst Jim Remington, helped organize the conference.

Keynote speaker Harvey Fineberg, M.D., Ph.D., warned, “Catastrophes we know are coming.” He also quoted former President Dwight Eisenhower, saying, “Plans are useless, but planning is essential.” Fineberg, who is president of the Institute of Medicine, argued that, although research during a disaster is challenging, it is as essential as pre-disaster and post-disaster research.

“This is a very exciting time — we are tasked to make a difference,” said speaker Lewis Rubinson, M.D., Ph.D., deputy chief medical officer of the National Disaster Medical System. “Novel collaborations,” he added, “are required.”

“Science during crisis is difficult, but can be done,” said Gary Machlis, Ph.D., science advisor to the director of the U.S. National Park Service. He cited classic examples, including the development of radar during the Battle of Britain, the Manhattan Project in the midst of World War II, and the safe return of Apollo 13 after an explosion crippled the service module.

Areas of concern

In a series of six individual breakout sessions, participants focused on specific areas of concern and then summarized their ideas in a final forum.

Participants from one workshop suggested leveraging existing networks to create a roster of experts to be called upon for various contingencies. Addressing a recurrent theme about the nagging delays involved in getting independent reviews and approvals of research projects during an emergency, another panel suggested the development of a centralized independent human subject review panel at NIH.

Finding quicker funding mechanisms was also considered. Chip Hughes, who led two of the sessions, noted that this meeting dovetails nicely with new NIEHS strategic goals to promote involvement of staff and grantees in the underlying science of emergency responses and emerging threats. A summary of all the recommendations from the workshop are expected to be finished in coming months.



HHS created Lurie's office in the aftermath of Hurricane Katrina. (Photo by Chris Smith courtesy of HHS)



“This energy, coming in at a very high level, is very important to making needed progress,” Miller said of the meeting. (Photo courtesy of Steve McCaw)

NIEHS continues to be very involved in emergency response efforts through WETP, which has supported the responses to the 2001 World Trade Center attack and the 2010 Gulf oil spill. WETP has trained more than two million workers, nationwide, in emergency response and handling of hazardous materials. Additionally, NIH is involved in important national programs to develop new and improved medical countermeasures designed to prevent, diagnose, and treat biological, chemical, and radiological agents that can pose a public threat, such as anthrax (see text box).

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

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The NIH presence

Besides hosting the workshop, NIH representatives from NIEHS and nine other NIH institutes and centers (ICs) participated in the discussions.

- National Human Genome Research Institute
- National Center for Advancing Translational Sciences
- Center for Information Technology
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute of Neurological Disorders and Stroke (NINDS)
- National Heart, Lung, and Blood Institute
- *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)
- National Library of Medicine (NLM)
- National Institute of Mental Health

In addition to programs at NIEHS, [NINDS](#), [NICHD](#), and [NLM](#), programs for developing countermeasures are in place at other ICs, including the [National Institute of Allergy and Infectious Diseases](#), National Cancer Institute, National Eye Institute, National Institute of Arthritis and Musculoskeletal and Skin Diseases, and National Institute of General Medical Sciences.

Hispanic heritage month celebration promotes diversity united

By Ashley Godfrey

NIEHS observed Hispanic Heritage Month Oct. 3 with a program featuring keynote speaker Elizabeth Yeampierre, J.D., a civil rights attorney and the executive director of the [United Puerto Rican Organization of Sunset Park \(UPROSE\)](#). In her address, Yeampierre stressed facilitating leadership within communities, by encouraging a collective understanding of environmental issues and putting resources into the hands of community members.



Members of UPROSE took to the streets of Brooklyn with their call for empowerment. (Photo courtesy of Murad Awawdeh)

 **Linked video:**
[Watch a WNBC-TV video interview with Yeampierre discussing UPROSE and its public health and environmental justice initiatives \(02:45\)](#)
(Launches in new window)

Download Media Player:  Flash [↗](#)

“Her role and positive results organizing and inspiring community members to address environmental health hazards affecting the Brooklyn neighborhood of Sunset Park is very impressive,” said Gerard Román, NIH Hispanic Employment Program Manager and organizer of the event. “Her intergenerational model of advocacy and action seems to be very effective and quite fitting with the NIEHS strategies for securing environmental justice.”

Celebrating Diversity

This year’s celebration featured the theme “Diversity United, Building America’s Future Today.” The theme promotes the benefits of a united and diverse workforce, by encouraging a reflection of Hispanic-American contributions in the development of our nation, a message relevant to the mission of NIH and NIEHS.

As Joellen Austin, associate director for management at NIEHS, explained in her opening remarks, “We strive to be the nation’s model employer. Our goal is to recruit, develop, and retain a diverse and high-performing federal workforce.” Austin stressed that in the face of so many disparities in health, institutions must recruit people of varied perspectives to help make new discoveries in environmental health possible.

Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, introduced Yeampierre, by listing just a few of her many accomplishments. Yeampierre is a long-time advocate and trailblazer for community organizing, for sustainable and just development in Sunset Park, and she has been productive in delivering millions of dollars to her community for the creation of more green space. Yeampierre is the first Latina chair of the U.S. Environmental Protection Agency National Environmental Justice Advisory Council, and is also a new member of the NIEHS National Environmental Health Advisory Council.

“Environmental justice is important and there are lots of challenges,” acknowledged Yeampierre. She said that advocacy is about listening with all of her senses and, most importantly, about communication. The population is growing, particularly in urban areas, and there is now a demographic shift toward a mixed and diverse population. Yeampierre believes this growing diversity provides different perspectives and different approaches to solving problems, and needs to be celebrated.

Bringing science and math into communities

Yeampierre described her intergenerational model of bringing knowledge into the Latino community as an effort to invite everyone to sit at the table, regardless of age or education level. Her philosophy is about giving regular kids the power to own the language of science, which makes them feel empowered. Yeampierre challenged the audience to think about diversity and how we can level the playing field. Her organization is proof it is possible to transform kids other people have simply written off.



Collman described Yeampierre as a vibrant and active member of the advisory council and thanked her for providing her community-based perspective. (Photo courtesy of Steve McCaw)



Yeampierre’s passion was apparent throughout her talk. She began her address by stating how humbled she was to be asked to present the keynote, because of how hard she has worked to be transformative. (Photo courtesy of Steve McCaw)

Science can be exciting and inspirational for young people, Yeampierre told her audience. She explained that scientists are often isolated from the community, as they live in silos surrounded only by the information they know. Instead of retreating from the civic arena, she said, scientists need to make this knowledge accessible to communities at a grassroots level, allowing communities to own environmental justice and climate change in the same way they own civil rights.

Yeampierre encouraged putting power in the hands of community members, by actively engaging them. As an example of this transformation, she pointed to an UPROSE-initiated water-testing program where community members learned to test the water quality themselves.

“Local knowledge is power,” stated Yeampierre, “We need to incorporate culture into our work and come together to build community.”

NIEHS/NTP Director Linda Birnbaum, Ph.D., closed the presentation by stating environmental justice is ongoing. She said Yeampierre’s message goes beyond the Hispanic community and is valid for many different and diverse communities.



Birnbaum congratulated Yeampierre for her ability to empower communities to make better-informed decisions. “We need more people like you,” she said. (Photo courtesy of Steve McCaw)



The Diversity Council selected Yeampierre as the 2012 NIEHS Hispanic Heritage Month celebration keynote speaker, for her unique and exceptional background as a community environmental health leader. Yeampierre was presented with a copy of the poster announcing her seminar by members of the council. From left to right, Austin, Collman, NIEHS Diversity Council chair Brad Collins, Yeampierre, Birnbaum, Margaret Bennett from the NIH Office of Equal Opportunity and Diversity Management, and Román. (Photo courtesy of Steve McCaw)



NIEHS Office of Science Education and Diversity Director Ericka Reid, Ph.D., was one of several members of the NIEHS community on hand to hear Yeampierre’s inspirational keynote. (Photo courtesy of Steve McCaw)

Empowering Brooklyn's youth

Founded in 1966, UPROSE is Brooklyn's oldest Latino community-based organization. UPROSE is dedicated to the empowerment of Southwest Brooklyn residents, primarily through broad and converging environmental, sustainable development, and youth justice campaigns. The group's mission is to ensure and heighten community awareness and involvement, develop participatory community planning practices, and promote sustainable development with justice and governmental accountability. Led by Yeampierre, UPROSE gives the power of leadership directly to the community's youth. Many of the programs and campaigns are started and run by the participants, including a community coalition that defeated a 520 megawatt power plant application.

"We develop leadership at UPROSE — it is a continuum," stated Yeampierre. The participants range from 9 to 24, because UPROSE is intergenerational and no one ages out. According to Yeampierre, every student who has come through this program has been accepted by a tier one university.

Román said he hopes to stay connected with UPROSE for future outreach efforts. Students aspiring to become biomedical scientists and medical professionals need to know that they can also take advantage of the NIH summer internship program. In the future, his office will explore the possibility of having a group of students from UPROSE visit the NIH campus. "If this happens, we will ensure they get a rock-star welcome and first class, backstage access to the most amazing medical research place in the world," stated Román.

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

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Veterinary group recognizes animal welfare as specialty

By Eddy Ball

The [American Veterinary Medical Association \(AVMA\)](#) announced Sept. 19 its approval of animal welfare as a certification for veterinary specialists, to be conferred by the American College of Animal Welfare (ACAW). [ACAW](#) joins entities in the United Kingdom, Europe, and Australia-New Zealand as the only organizations in the world that certify animal welfare specialists.

ACAW is preparing to offer its first credentialing examination, which will be given in July 2013. The new diplomates will join the current group of 27 charter diplomates who gained certification based on their long experience as advocates of animal welfare and work as practitioners in the field.



Among the charter diplomates of the ACAW are [Rear Adm. William Stokes, D.V.M.](#), director of the [NTP Interagency Center for the Evaluation of Alternative Toxicological Methods \(NICEATM\)](#) and NIEHS principal representative on the [Interagency Coordinating Committee on the Validation of Alternative Methods \(ICCVAM\)](#), and the only federal veterinary doctor in the group; [Steven Hansen, D.V.M.](#), chief operating officer of the American Society for the Prevention of Cruelty to Animals (ASPCA) and a member of the [Scientific Advisory](#)

[Committee on Alternative Toxicological Methods \(SACATM\)](#); and former NTP pathologist and former SACATM member [Daniel Marsman, D.V.M., Ph.D.](#), who currently heads sections on product safety testing and animal welfare at Procter and Gamble.

“With their mission of replacing, reducing, and refining the use of animals in toxicity testing,” Stokes said of the announcement, “NICEATM, SACATM, ICCVAM, and its partners are a natural place for ACAW-certified veterinarians to be working.” Animal welfare is an integral part of veterinary practice, Stokes added, but to become a specialist in the field requires complementary training and experience.

A special skill set for practitioners

“As with all other disciplines within the veterinary profession, there are multiple levels of expertise, and it’s important for the profession to have individuals who are highly trained in the broad aspects of animal welfare and who understand the related science,” said [Bonnie Beaver, D.V.M.](#), in an [AVMA press release](#). Beaver is a professor at the Texas A&M University (TAMU) College of Veterinary Medicine and Biomedical Sciences, former AVMA president, and founding president of ACAW.

According to Beaver, the scientific study of animal welfare has grown exponentially in the past two decades, causing the field to evolve into a distinct discipline within veterinary medicine. ACAW diplomates will have received advanced training in all aspects of animal welfare science, including ethics, so they can offer the public, general veterinary practitioners, and other stakeholders accurate information and advice.

Much like other specialties, the field of animal welfare comes with its own scientific literature base. The college has identified more than ten peer-reviewed journals that publish animal welfare science exclusively, with an additional 90 plus journals publishing a substantial number of animal welfare-related scientific papers. In addition to the scientific journals, there are a number of ethical journals that devote considerable space to animal welfare concerns. And, there are multiple graduate programs around the world that are currently educating scientists in this field.

ACAW is one of 22 recognized [veterinary specialty organizations](#) comprising 40 distinct practice areas. More than 10,600 veterinarians have been awarded diplomate status in one or more of these recognized veterinary specialty organizations by completing rigorous postgraduate training, education, and examination requirements. These board-certified specialists are ready to serve the public, its animals, and the veterinary profession, by providing high quality service in disciplines as varied as internal medicine, surgery, preventive medicine, toxicology, dentistry, behavior, laboratory animal medicine, and pathology.



Stokes has been a tireless advocate for the development of alternative toxicology testing for product safety. In addition to his ACAW certification, he is a board-certified diplomate of the American College of Laboratory Animal Medicine and an American Academy of Environmental Engineers Board-Certified Environmental Scientist. (Photo courtesy of Steve McCaw)



Hansen, above, Marsman, and Stokes are part of the contingent of veterinarians who support SACATM, ICCVAM, and NICEATM efforts. In addition to his ACAW certification, Hansen is a diplomate of both the American Board of Toxicology and the American Board of Veterinary Toxicology. (Photo courtesy of ASPCA)



Marsman is the corporate veterinarian at Procter and Gamble and heads its product safety section, as well as its global product stewardship; health care and pet care; and welfare and animal alternatives programs. (Photo courtesy of Daniel Marsman)



Beaver was a lead advocate for the new animal welfare specialty, during its consideration by the AVMA executive board. From petition to approval, the process took nearly six years. (Photo courtesy of TAMU)

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NIEHS grantee meets with stakeholders to discuss aquatic toxicity project

By Sara Mishamandani

As part of a collaborative effort to understand the complexity of metal mixtures toxicity in the environment, researchers at the Colorado School of Mines (CSM) hosted a multimetallic project meeting and Superfund site visit Sept. 23-25 for stakeholders and NIEHS program administrator Heather Henry, Ph.D.

[James Ranville, Ph.D.](#), who leads the NIEHS-funded CSM Superfund Research Program (SRP), brought together industry, academic, and government stakeholders from around the country to discuss metal mixtures research. The meeting included two field trips to show the stakeholders, firsthand, an experimental stream facility in a Colorado State University (CSU) laboratory, and Superfund site on the North Fork of Clear Creek.



The CSM SRP Research Project Grant (R01) is a partnership involving Ranville; Joseph Meyer, Ph.D., from Arcadis; Will Clements, Ph.D., from CSU; and James Shine, Ph.D., from the Harvard School of Public Health (HSPH). The project leaders are working to improve bioavailability assessment tools, to gain insight into metal toxicity in aquatic ecosystems.

The primary objective of the research is to further develop a passive sampling device, named gellyfish, to provide data for a toxicity model of mixed metals on aquatic ecosystem health. The gellyfish sampler can simultaneously measure the free metal ion concentration of multiple metals to determine the amount of contaminants that can be taken up by aquatic organisms. Shine first developed the passive sampler in an NIEHS-funded SRP laboratory at HSPH.

Evaluating aquatic toxicity at a Superfund site

At the [Central City/Clear Creek Superfund site](#), stakeholders saw the damage being done from mining wastes. Two mine drainage tunnels in Black Hawk introduce metals and acidic water to the North Fork of Clear Creek. When dissolved iron enters the stream, it is oxidized and precipitated, staining the stream bed. On their visit to the site, stakeholders saw orange coating on rocks, turbid water, and a lifeless stream.

The U.S. Environmental Protection Agency (EPA) will begin building a treatment plant to treat the water coming from the tunnels. The SRP project is working to understand the current conditions of the stream and to measure the effectiveness of the remediation, as the EPA treatment plan is implemented. The scientists will use the gellyfish sampler to look at bioavailable metals and to examine how well the system recovers after the metals and acidity are removed.

Scientists involved in the project are also doing laboratory toxicity testing with real and simulated stream waters, to better understand the effects of mining waste on ecosystems and to optimize the sampler. During the meeting, stakeholders visited the laboratory at CSU where Clements has set up 18 artificial streams to study bacterial communities exposed to varying levels of metals and acidity.

Creating a collaborative effort with stakeholders

The metal industry stakeholders left the meeting with an improved understanding of the project. Nickel Producers Environmental Research Association scientists at the meeting felt that the combination of laboratory and field components are providing needed insight into the rate at which systems recover once contamination has been eliminated. The researchers are also adapting the gellyfish model to measure nickel. This is of interest to the nickel industry, because few methods exist to directly measure nickel speciation in the water column, an important step to understanding the toxicity of metals to aquatic organisms.



The CSU experimental stream facility has single simulated streams with trays and a drift net, to study bacterial communities and measure metal concentrations. (Photo courtesy of James Shine)



As part of the field trip, the group also visited an operating treatment plant located in Idaho Springs, to illustrate the planned EPA treatment system for the Central City/Clear Creek Superfund site. Meyer, left, listened as his colleague Ranville described the new facility. (Photo courtesy of Heather Henry)

“This project exemplifies the SRP R01 [research project] grant concept, because it achieves the integration between multiple disciplines, while also reaching out for stakeholder input,” said Henry. “Through effective coordination, this team is achieving the interdisciplinary goals of the SRP mandates, as well as the translational mission of our program.”

(Sara Mishamandani is a research and communication specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program, Worker Education and Training Program, and Division of Extramural Research and Training.)



Henry represented the NIEHS SRP at the meeting and tour. (Photo courtesy of Steve McCaw)



Shine, left, and Ranville at an outflow of acid mine drainage from the Superfund site. The team is setting up field sampling locations in the vicinity, to monitor metal concentrations in the water. (Photo courtesy of Heather Henry)

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Love of science and exemplary leadership define Mason’s tenure at NIEHS

By Jeffrey Stumpf

After a 34-year career at the bench, James “Jim” Mason, Ph.D., will step away from his role as leader of the *Drosophila* Chromosome Structure Group. Known for his industrious nature and collegiality, Mason plans to be active in science outreach in rural North Carolina.

NIEHS hired Mason in 1978 as a staff fellow in the Laboratory of Molecular Genetics (LMG) to test chemicals for mutagenicity using the fruitfly, *Drosophila melanogaster*. In addition, NIEHS wanted to research the basic biology of mutagenesis and turned to Mason to study the *mu2* mutant that exhibited increased mutations and sensitivity to irradiation.

“When Jim moved to NIEHS, he became our resident expert on the classical and molecular genetics of the mutation process in whole animals,” commented Jan Drake, Ph.D., founding chief of LMG.

What was particularly interesting about the *mu2* mutants was that DNA breaks were not repaired, as in normal cells, but rather were processed as if they were the end of the chromosomes, called telomeres. The characterization of *mu2* began a long-standing interest in regulation of telomeres and led to current studies on mutants with abnormally long telomeres. Mason's discoveries about *Drosophila* telomeres led to his election by his peers as a Fellow of the American Association for the Advancement of Science in 2010.

Of flies and men

While new technologies have emerged and attracted attention away from using model systems like *Drosophila*, Mason is unwavering about the importance of studying fruitfly genetics.

“How do you make the connection between human health and human genome?” Mason asked rhetorically. “You need an understanding to help bridge that gap and, in many cases, that understanding comes from the use of model organisms.”

Besides the scientific merit of studying *Drosophila*, Mason believes that the overwhelmingly collaborative culture of fruitfly geneticists models proper behavior for today's scientists. Sharing reagents and ideas freely is paramount to Mason's philosophy, which did not escape the notice of his trainees.

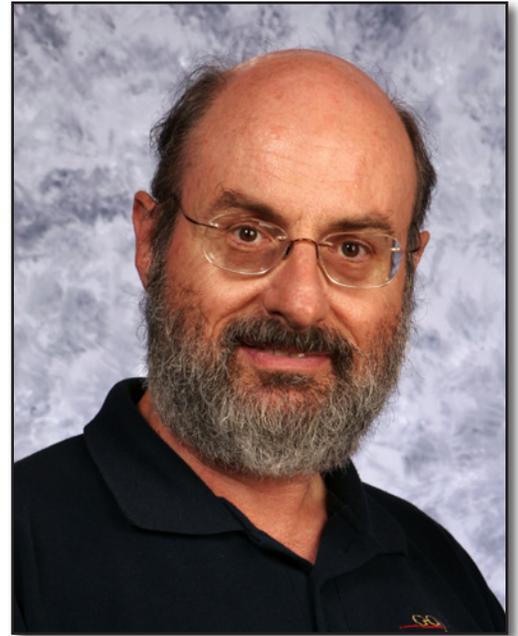
“Whether the request was from a graduate student or postdoctoral researcher, Jim goes out of his way to explain the correct way of doing fly genetics and using the right controls,” explained former trainee Raghuvardhan Dronamraju, Ph.D. “He is a true geneticist to the core.”

Inspired by his still active nonagenarian postdoctoral advisor, National Academy of Sciences member and fellow fly geneticist, Melvin Green, Ph.D., Mason works at the bench every day. “Being in the lab is why I became a scientist.” Mason remarked. “And I will continue to do science when there are no longer any postdocs or technicians around.”

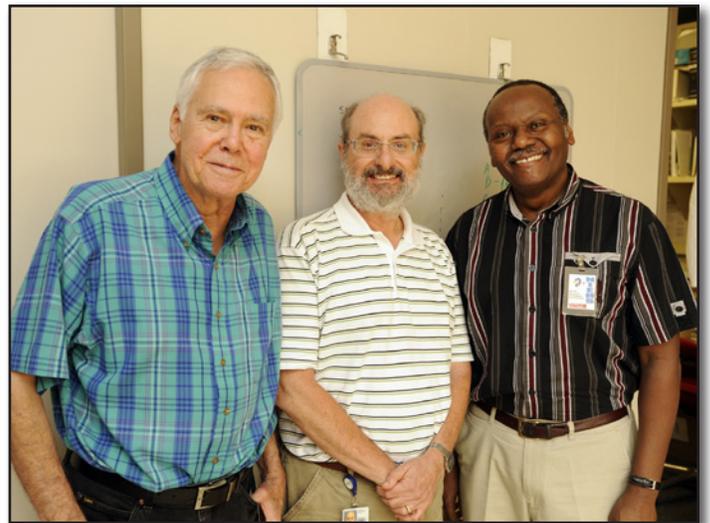
Leading promotions of biologists for two decades

What began as a three-year cycle, turned into an eighteen year commitment for Mason to lead the committee on promotion (COP3) for senior technical staff. Congruent with his nature of serving his co-workers, Mason transformed a promotions process with vague criteria into the present form with specific benchmarks. These important changes streamline promotions and clarify when promotions can be granted.

“I like the idea that I helped further people's careers by making a fairer process that is easier to understand,” Mason said.



Referring to the limitations of human genetics, Mason quipped, “You can't force breed them, which is what I do to flies all the time.”
(Photo courtesy of Steve McCaw)



Shown, left to right, Drake, Mason, and Champion, worked together for decades to study mutation rates. Drake commemorated his career with pea seeds from the abbey where Mendel made the first genetic observations from pea plants.
(Photo courtesy of Steve McCaw)

From next generation sequencing to next generation mentorship

From his years on, and leading, the Diversity Council, to his philosophy of sharing science, it is not surprising that Mason would be interested in passing his devotion to science on to the next generation. Mason plans to develop science projects for middle and high schools in rural, underserved communities, and to focus on the science process instead of just the facts.

“People learn by doing, not sitting in a chair listening to lectures. But most classrooms are the latter and not the former,” Mason discussed. “I want to get people out of their seats and let them do experiments, so that they can develop their own ideas and discuss them.”



Mason joined fellow LMG colleagues Michael Resnick, Ph.D., center, and Mercedes Arana, Ph.D., right, for a department-wide celebration of Mason's career. (Photo courtesy of Steve McCaw)

Former lab members share fond memories of Jim Mason

“He believes that ‘fly pushing’ can answer many questions where modern methodologies fail.”

— *Dronamraju, former visiting fellow*

“Jim was always available to discuss science. He encouraged me to attend meetings and present my work.”

— *Hemakumara Mutra, Ph.D., visiting fellow*

“His dedication and total commitment to science is impressive. Yet, outside of work, he has a normal family life with his children and grandchildren and other social activities. He has a very balanced life.”

— *Dave Brar, biologist*

“I learned a lot from him and will never forget working in the *Drosophila* Chromosome Structure Group under the direction of Jim Mason. He would always say, ‘It is important to do good research. You always want someone to be able to duplicate your results, just as you have presented them.’”

— *Larry Champion, former biologist*



Recent members of the *Drosophila* Chromosome Structure Group reunite in Mason's honor. Shown, left to right, are Mutra, Mason, Champion, Dronamraju, Essie Jones, and Brar. (Photo courtesy of Steve McCaw)

(Jeffrey Stumpf, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group and a regular contributor to the Environmental Factor.)

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With death of Arlen Specter, NIH loses a faithful supporter

By Eddy Ball

News of the death of former Sen. Arlen Specter (D-Pa.) Oct. 14 at his home in Philadelphia saddened many at NIH who had worked with him over the years to advance biomedical research. Specter, who died at age 82 of complications of non-Hodgkin's lymphoma, was eulogized at a memorial service Oct. 17 attended by many dignitaries, including NIH Director Francis Collins, M.D., Ph.D., and National Cancer Institute Director Harold Varmus, M.D.

A New York Times [article](#) on Specter's death described him as hard-edged and tenacious, yet ever the centrist. He was always known for his independence and bi-partisanship, especially when it came to his unwavering support for advancing science and medicine.

"There were many powerful testimonials delivered at the Har Zion Temple, including a very personal remembrance from the Vice President," Collins wrote afterwards. "Many of the comments from the eulogizers related to Arlen's support of medical research, and the NIH was repeatedly mentioned as a part of the federal government that the Senator cared deeply about. I was particularly moved by the final remembrance, delivered by his lawyer son Shanin."

In his [eulogy](#), Shanin Specter spoke to his father's abiding faith in the power of science. "He is survived by his will to fund and fight for a cure. From stem cells to medical research on Alzheimer's and Parkinson's and diabetes and, yes, to cancer, whose hateful mysteries he helped to try to unlock, he believed these wars were as important as our other wars."

"He knew that our battles for our health are waged on the ultimate battlefield, one where we are all the underdog. Cancer claimed him as it has too many. But one day it will be solved," Shanin Specter concluded. "And when it is, Arlen Specter will be counted among the righteous that made it happen."

Although NIEHS/NTP Director Linda Birnbaum, Ph.D., was unable to attend, she remarked about the depth of the loss to NIH and government-funded science. "For those many years, Sen. Specter stood by the value of biomedical research to the overall wellbeing of every American," she said. "We desperately more people with the foresight he brought to his work as a public servant — men and women who can understand the importance of maintaining our investment in the future of this country."

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Shown in the U.S. Senate before his defeat in the 2010 election, Specter was respected by legislators on both sides of the aisle for his principled stand on issues, ranging from Supreme Court nominees to funding for medicine, science, and public health.

NIH-funded program opens new doors for scientists with disabilities

By Ian Thomas

Staff and scientists from across NIEHS gathered in Rodbell Auditorium Oct. 15 for a unique presentation titled “Enhancing Access to Biomedical Laboratories for People with Disabilities: More Than Widening a Door.” Held in honor of National Disability Employment Awareness Month, the talk was led by [Susan Mendrysa Ph.D.](#), assistant director of the [Institute for Accessible Science \(IAS\)](#) at Purdue University, and offered attendees a brief glimpse of life behind the bench for aspiring scientists with disabilities.

“Research has shown that grade school students with disabilities have just as much interest in science as those without disabilities, yet very few of them ever make it through the educational pipeline to the field,” explained Mendrysa, an assistant professor in the Purdue University Department of Basic Medical Sciences. “At present, fewer than 2 percent of employed scientists and engineers under the age of 35 are people with disabilities.”

Funded by an NIH Director’s Pathfinder Award, the IAS mission is to promote the inclusion and retention of persons with disabilities in biomedical science careers, through practical laboratory experiences, assistive technology development, student and educator support services, and research.

Experiencing science

At present, IAS has two major initiatives to promote the involvement of persons with disabilities in science. The first is the Accessible Biomedical Immersion Laboratory (ABIL), a flexible wet-lab space, featuring ergonomically customized benches, movable work stations for wheelchairs, and an array of assistive computer technology, all designed to foster student independence in a laboratory setting.

“As scientists, we know how important it is to experience that aha moment of discovery in a lab,” said Mendrysa. “ABIL gives us the ability to put our students into an actual laboratory, with the tools they need to experience that moment for themselves.”

The second initiative is [IAShub](#), a cyberinfrastructure for global connectivity and information exchange, offering its users a wide range of interactive resources, ranging from computational and database services, to an ever-growing list of contacts in the field.



Mendrysa’s program has led to the development of assistive technology to ease the transition for people with handicaps into a lab space that does not contain unnecessary barriers. (Photo courtesy of Steve McCaw)



NIEHS/NTP Director Linda Birnbaum, Ph.D., right, was one of several in the audience with questions for Mendrysa. Seated in front of her was NIH Hispanic Employment Manager and NIEHS Equal Employment Opportunity Specialist Gerard Román. (Photo courtesy of Steve McCaw)

“One of the biggest problems that our students encounter when trying to break into the biomedical field is a lack of qualified role models,” Mendrysa noted. “The beauty of the IAShub is that it gives our students access to scientists and educators around the world, disabled and not, for everything from data to career advice.”

Changing the perception

While Mendrysa and her colleagues agree that student accommodations are a crucial component to leveling the career playing field for people with disabilities, they also agree that addressing the stigma of inequality surrounding them is every bit as important.

“Often times, it isn’t the disability itself that burdens someone, but rather the unnecessary sense of isolation that they feel as the result of that disability,” said Joellen Austin, NIEHS associate director for management, who welcomed several members of the NIEHS Bethesda, Md., campus to Mendrysa’s talk via webcast. “Today’s program is about ending that sense of isolation and opening the doors of the biomedical research field for everyone, including people with disabilities.”

Held each October, [National Disability Employment Awareness Month](#) is a national campaign that raises awareness about disability employment issues, and celebrates the many and varied contributions of America’s workers with disabilities. This year’s theme is “A Strong Workforce is an Inclusive Workforce: What Can YOU Do?”

(Ian Thomas is a public affairs specialist for the NIEHS Office of Communications and Public Liaison.)



NIEHS Diversity Council chair Brad Collins, right, sat by Austin during the presentation. (Photo courtesy of Steve McCaw)



Following the talk, Mendrysa joined NIEHS leaders. Shown, left to right, are Birnbaum, Mendrysa, Austin, Deputy Scientific Director Bill Schrader, Ph.D., Collins, Employee Services Manager Dona McNeill, and Román. (Photo courtesy of Steve McCaw)

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Science Notebook

Designing the next generation of sustainable chemicals

By Thaddeus Schug

Scientists committed to developing green solutions for replacing problem chemicals in the marketplace gathered Oct. 15-17 for a meeting on “Building the Path Forward for the Next Generation of Sustainable Chemicals,” held at the Rockefeller Brothers Fund Pocantico Center in Tarrytown, N.Y.



Linked video:

[Watch the 2011 Berkeley Big Ideas First Place winning video, The Sustainable Future, on the principles of green chemistry \(03:49\)](#)

(Launches in new window)

Download Media Player: Flash

The meeting, sponsored by the non-government organizations [Advancing Green Chemistry](#) and [Environmental Health Sciences](#), brought together a mixture of chemists, toxicologists, and biologists. Representatives from NIEHS and NTP included Division of Extramural Research and Training program administrators Jerry Heindel, Ph.D., and Thaddeus Schug, Ph.D.; Kristina Thayer, Ph.D., director of the newly named NTP Office of Health Assessment and Translation; and NTP Biomolecular Screening Branch Chief Ray Tice, Ph.D.

Designing safer chemicals

There are more than 83,000 chemicals in commerce today, many of which pose potential toxic hazards to human health and the environment. The challenge facing chemists designing replacement materials involves figuring out what kind of testing will need to be done to determine if the new chemical is safer than current ones to human health and the environment. One area of growing concern is how to ensure that the next generation of chemicals does not have the potential to act as endocrine disrupting compounds.

The meeting at Pocantico aimed to build upon a new set of testing tools — the Tiered Protocol for Endocrine Disruptors (TiPED) — developed by the



Heindel, center, goes to work creating a toxic pumpkin, while Tom Zoeller, Ph.D., left, and Wim Thielemans, Ph.D., take part in the fun. (Photo courtesy of Pete Myers)



Tice, left, and Thayer take part in a discussion of the endocrine disruptor screening protocol. (Photo courtesy of Pete Myers)



The meeting was held on the ground floor of the Coach Barn of the Pocantico Center, which is also known as the John D. Rockefeller Estate. Take a [video tour](#). (Photo courtesy of Ray Tice)

group over the past two years. The protocol, which will be published online Dec. 6 in the Royal Society of Chemistry journal [Green Chemistry](#), is not regulatory, but rather a tool to guide chemists as they develop a new chemical, to give them confidence as to whether the substance is or is not likely to be an endocrine disruptor.

The TiPED protocol offers a five-tiered approach, starting with what should be the fastest and cheapest assays, and working through increasingly specialized tests. The initial two phases rely on predictive computer modeling and high-throughput screening, to quickly weed out problem chemicals. These tests are followed by more specific *in vitro* cell-based screening assays with a goal of refining, reducing, and replacing animal testing as much as possible. The last two tiers are whole animal assays, to be used for looking for integrated endpoints and less understood systemic responses.

“The idea is that if chemists hit a positive early on, they would either go back to the drawing board or, if that positive was in a specific area, such as an estrogen receptor in a high throughput assay, they would follow that up with more comprehensive assays,” said Heindel. “A hit anywhere along the tiered system means chemists need to pull back, reanalyze, or throw the chemical out.”

The project emphasizes fundamental changes in the way that scientists design new chemicals, and in the process of bringing them into the marketplace. Chemists generally have little training in toxicology, so this plan offers guidelines they can follow early on in the product development process.

Moving forward with the plan

Following a team-building exercise on the evening of Oct. 15, involving pumpkins and toxicological design criteria, the first full day of the meeting was divided into discussion sessions aimed toward refining the specific testing strategies within each phase of the screening model. A good deal of time was dedicated to establishing criteria needed to assess the quality of assays within each tier of the protocol.

The meeting wrapped up with a discussion on strategies to conduct test runs of the protocol, using test chemicals synthesized by John Warner, Ph.D., president and founder of the [Warner Babcock Institute for Green Chemistry](#).

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

Disclaimer:

This report was written by members of the NIEHS staff based on materials prepared for this meeting and the discussions that took place there. It reflects the views of the authors and not necessarily those of the Rockefeller Brothers Fund, its trustees, or its staff.



The TiPED working group enjoyed the fall weather and the beautiful scenery at the Pocantico Center in Tarrytown, N.Y. (Photo courtesy of Ray Tice)

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NTP panel reviews outcomes of women treated for cancer while pregnant

By Robin Mackar

A stellar peer review panel convened by the National Toxicology Program (NTP) provided input and invaluable medical, pediatric, pharmaceutical, and other expertise on the [draft NTP Monograph on Developmental Effects and Pregnancy Outcomes Associated with Cancer Chemotherapy Use During Pregnancy](#).

“We know very little about pregnancy outcomes of women being treated for cancer. This is an extremely important topic that hasn’t been systematically looked at before,” said NIEHS/NTP Director Linda Birnbaum, Ph.D., as she welcomed the nine-member panel of external experts to the Oct. 1-2 meeting at NIEHS.

Under efficient chairmanship of Catherine Spong, M.D., associate director for Extramural Research at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, part of the National Institutes of Health, and a board-certified obstetrician and gynecologist, the panel was able to have in-depth discussions and concur by unanimous vote on each of the NTP’s five main findings.

Main findings

One of the first findings, presented by the lead scientist for the evaluation, Kembra Howdeshell, Ph.D., of the [NTP Office of Health Assessment and Translation \(OHAT\)](#), focused on congenital malformations.

Both NTP and the reviewers agreed that the evidence showed that chemotherapy for treatment of cancer in the first trimester represents a higher apparent risk of major malformations than treatment in the second or third trimesters only. This finding confirmed current medical opinion and predictions, based on the timing of fetal organ development during pregnancy. However, the lead reviewers for each of the findings presented by Howdeshell acknowledged the imprecision in the data available to NTP, and called on the NTP to point out the limitations.



The peer review meeting ran smoothly under the capable leadership of Spong, right. Birnbaum, left, and Bucher, center, listened closely to the discussions. (Photo courtesy of Steve McCaw)



Greene, chief of obstetrics at Massachusetts General Hospital, offered his perspective on the interpretation of published studies on pregnancy outcomes. (Photo courtesy of Steve McCaw)



Howdeshell showcased what she had learned over the past two years, as she analyzed more than 430 published studies, on 52 cancer drugs, that reported pregnancy outcomes of female cancer patients treated with the drugs during pregnancy. (Photo courtesy of Steve McCaw)

“I sympathize with those of you working on this topic. As someone who works in this area, I realize we all report things differently and our terminology is always changing. You can’t make the data better — you can simply point out limitations,” said Michael Greene, M.D., chief of obstetrics at Massachusetts General Hospital.

The panel also heard, and then voted on, additional health outcome findings, including the effects of chemotherapy on the risk of spontaneous abortion and stillbirth; pregnancy complications, such as reductions in amniotic fluid and fetal growth restriction; newborn weight and health; and growth development of the children. They again drew attention to data limitations and noted that some adverse effects, such as effects on the reproductive system and other organs, may not be apparent until later in life.

Research and outreach needs

The need for long-term follow-up studies of the gestationally exposed offspring was emphasized, as was the need for more easily accessible national registries for physicians to document cases. “There are so many research needs crying out for attention in this area,” Greene emphasized. “For one, we need to get our colleagues to do a better job of developing quality case reports.”

Other panelists, such as John Mulvihill, M.D., from the University of Oklahoma pediatrics department, a respected researcher on the topic of pregnancy outcomes following treatment with chemotherapy during pregnancy, suggested getting woman advocates, who have been successfully treated for cancer during pregnancy, to tell their stories. Panel member Janine Polifka, Ph.D., a developmental biologist in the department of pediatrics at the University of Washington, emphasized creating more awareness around resources already available for decision-making, such as [OTIS, the Organization of Teratology Information Specialists](#), a nonprofit organization that provides information to patients and health care professionals about exposures during pregnancy and lactation.

Mulvihill called on the NTP to make clear, bottom line messages in its conclusions. After one of Howdeshell’s presentations, he commented, “You are now the international expert on this topic. You will benefit the world with bottom line messages that can be understood by all. Be clear and spread your message widely.”



Panel member Polifka, center, suggested evaluating the reported data on pregnancy outcomes, to identify patterns of malformations possibly linked to a cancer drug or combination therapy, following exposure during the first trimester of pregnancy. Panel member Tina Rizack, M.D., right, from The Warren Alpert Medical School of Brown University, and OHAT staff member Abee Boyles, Ph.D., listened to the discussion. (Photo courtesy of Steve McCaw)



Mulvihill, a developmental geneticist who has authored many papers related to pregnancy outcomes of women receiving treatment with chemotherapy for cancer during pregnancy, referred to the NTP monograph as a landmark publication. (Photo courtesy of Steve McCaw)

Howdeshell, who has been working with her OHAT colleagues, including Vickie Walker and Mike Shelby, Ph.D., who recently retired, for nearly two years on this topic, gave a heartfelt thanks to all the panel members for their invaluable input. “This has been an incredible panel whose expert advice will surely make this document a state-of-the-science resource for both patients and physicians.”

In offering his thanks and appreciation to the chair, his staff, and the reviewers, NTP Associate Director John Bucher, Ph.D., joked that it was the first time that all the research needs identified by a panel did not fall on the NTP alone. The final NTP monograph should be available by summer 2013.

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

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Fellows and scientists stand out at NIH Research Festival

By Eddy Ball

NIEHS intramural scientists and trainees presented four talks and four posters at the annual [National Institutes of Health \(NIH\) Research Festival](#) Oct. 9-12 in the Natcher Conference Center at NIH in Bethesda, Md. In addition, NIEHS Laboratory of Reproductive and Developmental Toxicology (LRDT) head [Kenneth Korach, Ph.D.](#), co-chaired a concurrent symposium, [Here, there, everywhere: the journey of nuclear receptors](#), and NIH officially recognized 220 winners of the Fellows Award for Research Excellence (FARE), including 19 awardees from NIEHS ([see story](#)).

Along with a full slate of plenary talks, symposia, poster sessions, a biovisualization exhibit, and the annual meeting of the National Graduate Student Research Conference, NIH also took the opportunity to celebrate its 125th anniversary, tracing its roots to the one-room Hygienic Laboratory established in 1887 by [Joseph Kinyoun, M.D.](#) Kinyoun’s interest in bacteriology and his isolation of the cholera organism laid the groundwork for the present 27 institutes and centers of NIH.

Posters and talks reflect breadth of NIEHS research

- Talks at the “Here, there, everywhere: the journey of nuclear receptors” symposia session — “Whole-genome estrogen receptor binding in mouse uterine tissue revealed by ChIP-Seq,” by LRDT senior biologist [Sylvia Hewitt](#); and “Proteasome activity and glucocorticoid receptor transcriptional mechanisms in breast cancer cells,” by Laboratory of Molecular Carcinogenesis (LMC) staff scientist [Harriet Kinyamu, Ph.D.](#)



Environmental Genetics Group fellow Verhein won her second FARE this year. (Photo courtesy of Steve McCaw)



Shatz is a visiting fellow in the Chromosome Stability Group. (Photo courtesy of Steve McCaw)

- Talk at the “[Disease in a dish – modeling human diseases using induced pluripotent stem cells](#)” symposia session — “Differential susceptibility to ozone-induced lung inflammation maps to mouse chromosome 17: role of Notch receptors,” by Laboratory of Respiratory Biology fellow and FARE winner [Kirsten Verhein, Ph.D.](#)
- Talk at the “[Translational research of aging](#)” symposia session — “‘Premotor’ research on Parkinson’s disease,” by Epidemiology Branch lead researcher [Honglei Chen, M.D., Ph.D.](#)
- Virology section poster — “The three faces of riboviral spontaneous mutation: spectrum, mode of genome replication, and mutation rate,” by Laboratory of Molecular Genetics (LMG) visiting fellow [Maria Libertad García Villada, Ph.D.](#), and lead researcher [Jan Drake, Ph.D.](#)
- Cell Biology section poster — “Cytotoxic effects of cerium dioxide nanoparticles in primary human cells are mediated through apoptosis and autophagy,” by [Clinical Research Unit \(CRU\)](#) visiting fellow Salik Hussain, Ph.D., biologist Annette Rice, and biologist Jamie Marshburn; NTP Deputy Division Director for Science [Nigel Walker, Ph.D.](#); and CRU Medical Director [Stavros Garantziotis, M.D.](#)
- Signaling section poster — “p53 cooperates with MAP kinase and NFκB signal transduction pathways to potentiate human immune/inflammatory response,” by LMG fellow and FARE winner [Maria Shatz, Ph.D.](#), staff scientist [Daniel Menendez, Ph.D.](#), and lead researcher [Michael Resnick, Ph.D.](#)
- Stem Cell section poster — “Identification of a novel component of the self-renewal circuitry conserved in mouse and human ESCs,” by LMC visiting fellow and FARE winner [Xiaofeng Zheng, Ph.D.](#), former fellow Raluca Dumitru, M.D., Ph.D., and biologist [Brad Lackford](#); Biostatistics Branch (BB) former fellow Johannes Freudenberg, Ph.D.; LMC fellow [Ajeet Singh, Ph.D.](#), and LMC head [Trevor Archer, Ph.D.](#); BB lead researcher [Raja Jothi, Ph.D.](#); and LMC lead researcher [Guang Hu, Ph.D.](#)



Zheng is a visiting fellow in the Stem Cell Biology Group. (Photo courtesy of Steve McCaw)

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Kunkel steps away from administrative role as LSB lab chief

By Shannon Duncan

Lead researcher [Thomas Kunkel, Ph.D.](#), left his administrative leadership role as chief of the NIEHS Laboratory of Structural Biology (LSB) Oct. 1, a position he has held since the lab was established in 1996, to devote himself full time to research as head of the DNA Replication Fidelity Group. Darryl Zeldin, M.D., NIEHS scientific director, announced the news by thanking Kunkel for his leadership and service to the Division of Intramural Research, and congratulating lead researcher Traci Hall, Ph.D., on her selection as acting chief of LSB.

Of his appointed successor and colleague of 14 years, Kunkel said, “Traci is going to do a fabulous job.”

Expanding a network of support services for LSB scientists

During his 16-year tenure as lab chief, Kunkel has seen the lab grow to include resource facilities to help provide further insight into how environmental exposures impact human health. LSB uses an integrated approach to investigate macromolecular structures at the atomic level, by combining biochemical and genetic approaches in conjunction with the lab's core research facilities.

Kunkel came to NIEHS on May 3, 1982. Over his more than three decades of research on DNA replication, he has published more than 300 papers in peer-reviewed journals, mentored an impressive group of accomplished scientists, and received a number of prestigious awards for his research. He has also served on several committees, including the Tenure Track Advisory Committee.

In 2011, Kunkel was promoted to the rank of Distinguished Investigator, one of the highest honors the National Institutes of Health (NIH) awards to its scientists and one that only an estimated two to three percent of NIH scientists ever achieve during their careers. He has developed several novel experimental approaches for investigating DNA replication and is considered to be one of the world's leading experts in the field.

Under Kunkel's leadership, LSB became one of the first labs to enact the dual mentoring program, to help postdoctoral fellows network and seek advice from different scientists and professions, so they can become more competitive in a changing job market. Over the years, he has maintained an open door policy as a mentor and helped his postdocs transition into a variety of occupations, including teaching, scientific administration, and basic and clinical research.

Reflecting on his lab's many accomplishments and talented members, Kunkel singled out the outstanding administrative support provided by Amy Johnson over the years, which has helped everyone be more successful, by allowing lab members to focus solely on their science. He said that he considers her to be the most valuable employee in the lab.

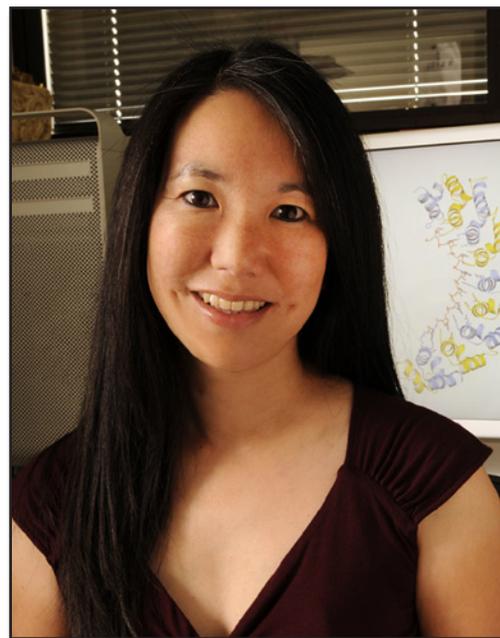
Looking to the future of LSB

Hall has been the head of the Macromolecular Structure Group since arriving at NIEHS in 1998. She came to NIEHS with a doctorate in pharmacology and molecular sciences from John Hopkins University, after completing a two-year fellowship at the American Association for the Advancement of Science (AAAS). In 2004, she achieved tenure and continues to lead her group in studying RNA pathways and the impact they have on environmental health, by understanding gene response and susceptibility to environmental stressors. She served as president of the NIEHS Assembly of Scientists in 2010 and has also served on the Scientific Director's Advisory Committee.

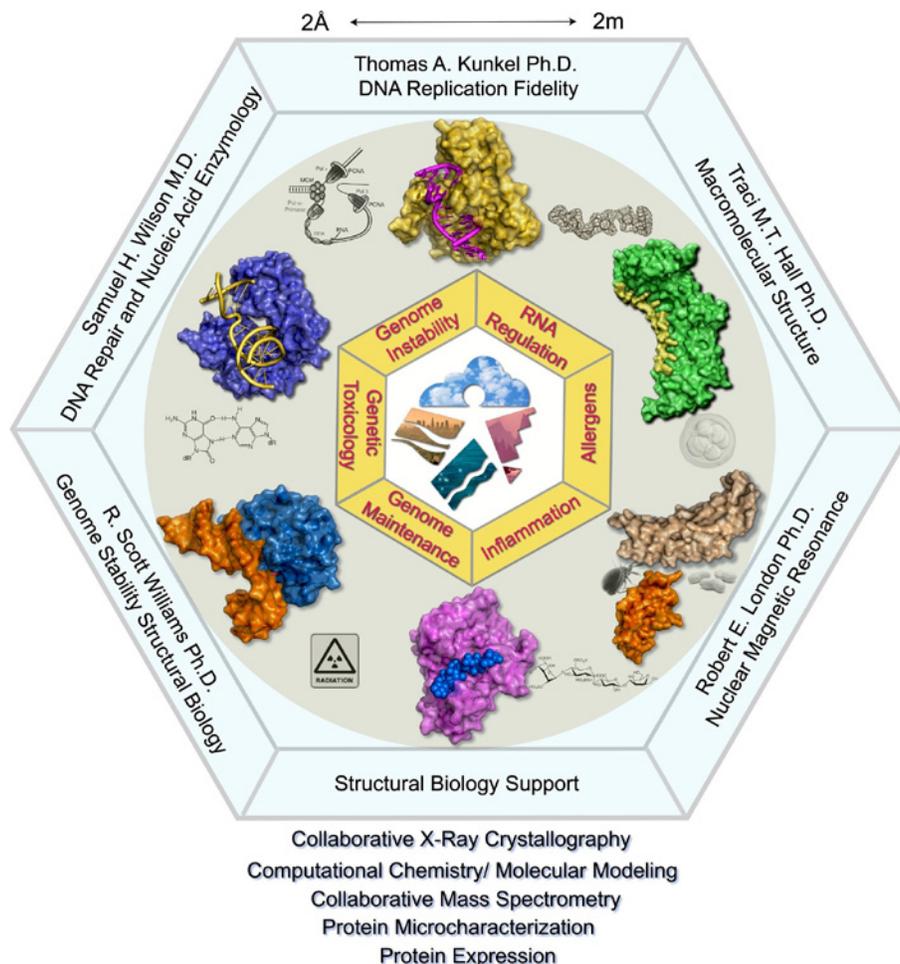
When asked about her upcoming role, Hall responded, "I am looking forward to helping NIEHS to continue our outstanding science and to grow in new directions."



Kunkel has been praised as one of the major intellectual drivers of LSB, who also possesses excellent managerial and leadership skills. (Photo courtesy of Steve McCaw)



LSB Acting Chief Hall (Photo courtesy of Steve McCaw)



(Shannon Duncan is an administrative technician in the NIEHS Laboratory of Structural Biology.)

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NIEHS researchers gather to combat obesity

By Thaddeus Schug

While dietary excess and lack of exercise are well-established factors fueling the obesity epidemic in the U.S., new research is emerging that suggests a class of environmental chemicals, termed obesogens, may also play a significant role in the risks associated with developing diabetes and obesity.

These connections were the focus of the “NIEHS Obesity/Diabetes/Metabolic Syndrome Grantee Meeting” Oct. 3-4 at the Ann Arbor Regent Hotel in Michigan. The meeting brought together NIEHS grantees and other scientists, representing fields ranging from molecular biology to epidemiology, to examine the science linking exposure to certain chemicals with the development of diabetes and obesity in humans.

DEPT program administrator Jerry Heindel, Ph.D., welcomed the attendees and opened the meeting with a push for scientists to provide input on potential testing strategies, options for identifying and filling data gaps, and future research needs to address the health problems associated with obesity. “Obesity is becoming a major health concern worldwide and a contributor to many diseases and dysfunctions over people’s lifetime,” he said. “I believe that what you have started here in this virtual consortium is an important step in determining how environmental exposures contribute to metabolic disease.”

New grantees take the spotlight

While the meeting contained a wide range of experts in the field of obesity, the focus was primarily on new NIEHS grantees funded through two recent initiatives — [Dietary Influence on the Human Health Effects of Environmental Exposures](#) and [Role of Environmental Chemical Exposures in the Development of Obesity, Type 2 Diabetes, and Metabolic Syndrome](#). Participants were given the opportunity to highlight their research proposal and preliminary data, and then engage in a question and answer session with the audience.

“As a hematologist, environmental and occupational chemical exposures to the liver keep me awake at night and present serious metabolic health concerns,” said Matthew Cave, M.D., assistant professor of medicine at the University of Louisville. Cave was recently awarded a grant for studies aimed at determining the impact of polychlorinated biphenyls exposure on obesity and metabolic syndrome through toxic metabolic endotoxemia.

Maria Bondesson, Ph.D., a research assistant professor of biology and biochemistry at the University of Houston, described a new project in which she uses zebrafish as a model system to detect chemical pollutants that perturb embryonic development which, in turn, leads to metabolic diseases later in life. NIEHS/NTP Director Linda Birnbaum, Ph.D., who attended the second day of the meeting, asked Bondesson and other grantees questions, and offered suggestions on how they could work to better coordinate their research with the new NIEHS strategic plan.

Birnbaum keynotes symposium

NIEHS/NTP Director Linda Birnbaum, Ph.D., delivered the keynote presentation, “NIEHS and a Vision for Environmental Health,” at the Developmental Origins of Metabolic Disease Symposium held Oct. 5 at the University of Michigan, sponsored by the Department of Pediatrics. Birnbaum highlighted NIEHS’ interest in addressing the contributory role of environmental pollutants to this growing epidemic and available research funding opportunities through the Institute. Obesity, she noted, has risen in prevalence along the same trajectory as several other diseases with known environmental components, suggesting that environmental factors, as well as lifestyle and diet, may be involved in its etiology.

The event was hosted by NIEHS grantee Vasantha Padmanabhan, Ph.D., a professor of pediatrics and director of pediatric endocrine research at the University of Michigan. Other speakers included researchers from throughout the U.S. and Great Britain.

- “Sex-Specific Inheritance and Transmission of Obesity-Related Phenotypes Following Exposure to a Maternal High Fat Diet,” Tracy Bale, Ph.D., University of Pennsylvania
- “You Are What Your Mother Ate: Developmental Patterning of Inflammation,” Jacob (Jed) Friedman, Ph.D., University of Colorado
- “DOHaD [Developmental Origins of Health and Disease]: Epigenetic Mechanisms,” Mark Hanson, D.Phil., University of Southampton
- “Mechanisms Underlying the Developmental Programming of Type 2 Diabetes,” Susan Ozanne, Ph.D., University of Cambridge
- “Intergenerational Effects of Developmental Nutritional Exposures,” Mary-Elizabeth Patti, M.D., Harvard Medical School
- “Improving Intrauterine Growth Restriction Through the Pancreatic Beta Cell,” Paul Rozance, M.D., University of Colorado
- “Nutritional Modification of Brain Development and Energy Balance,” Richard Simerly, Ph.D., University of Southern California
- “Interventions to Prevent the Development of Obesity in the Offspring of Obese Animals,” Rebecca Simmons, M.D., University of Pennsylvania

The meeting ended with a session led by Heindel and DERT program administrator Kimberly Gray, Ph.D., on data sharing, and how to improve communication between animal and human researchers. “I encourage you [researchers] to pool resources, share data, and to integrate endpoints on animal and human studies, so that we can more directly translate your findings to improve human health,” concluded Birnbaum, who also gave the keynote address at a symposium following the grantee meeting ([see text box](#)).

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



Participants from the NIEHS grantee meeting joined Heindel and Birnbaum, center front, outside the Ann Arbor Regent Conference Center. (Photo courtesy of Jerry Heindel)

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Getz uncovers exciting new trends in cancer genomes

By Jeffrey Stumpf

Gad Getz, Ph.D., provided a glimpse of the exciting new world of identifying and treating cancer, in his talk Oct. 5 at NIEHS. As director of Cancer Genome Computational Analysis at the Broad Institute of Harvard and the Massachusetts Institute of Technology, Getz discussed the difficulties and potential of analyzing genome and exon sequencing of around 6,000 tumor samples.

Getz’s research conducts an orchestra of scientists from various disciplines, including clinicians, computational biologists, software engineers, statisticians, data analysts, and project managers, all with the common goal that Getz stated clearly.



Getz mentioned that the amount of data sequencing generates is roughly equal to all of the YouTube website. (Photo courtesy of Steve McCaw).

“We want to kill cancer,” Getz boldly said.

Teaming up with [The Cancer Genome Atlas](#), Getz’s group wants to understand the genetics of tumor development. Using the vast array of DNA sequence data, Getz outlined a two-step approach.

- Characterize genes and pathways that are different between normal and tumor tissues.
- Interpret those differences in the context of a large population of cancer patients to find out if these mutations are occurring by chance.

Mutations along for the ride

Within a quagmire of mutations and genome rearrangements in cancer cells, it is important to know what mutations are necessary and sufficient for development of a tumor. Getz said that his dream would be to get the genome sequence of every cell in a tumor.

“It is kind of like archaeology, in that you have to take the status today and infer what was in the past,” Getz explained.

Mutations that drive cells to tumor formation, or drivers, need to be distinguished from so-called passenger mutations that coincide with the driver mutations during tumorigenesis. Getz searched for mutations that are common among tumors and identified mutations in 428 genes.

Some genes, such as those that encode olfactory receptors, are unlikely to be driver mutations. So, Getz used an algorithm to account for different mutation rates that occur at different regions of the genome. For instance, mutation rates increase in regions that replicate in the late part of the S-phase and are reduced in genes with higher gene expression. Accounting for heterogeneous mutation rates reduced the number of driver mutations to 13 and uncovered new pathways, such as RNA splicing, chromatin modeling, and ubiquitination, as possible pathways in driving tumor formation.

A flood of data

Getz explained that the cost of sequencing one million bases has declined from \$30,000 to 10 cents in a little over a decade, and this drop in cost has allowed sequencing of protein-coding regions to identify thousands of pairs of tumor and adjacent normal cells. The ambitious sequencing project has caused a problem that most scientists would love to have — too much data.



Postdoctoral researchers Scott Lujan, Ph.D., from the Laboratory of Structural Biology, left, and Kin Chan, Ph.D., from the Laboratory of Molecular Genetics, showed particular interest in whole genome sequencing for measuring mechanisms that affect genome stability. (Photo courtesy of Steve McCaw)



Drosophila Chromosome Structure Group lead researcher James Mason, Ph.D., studied the conclusions from Getz’s enormous consortium of data. (Photo courtesy of Steve McCaw)

Regardless, Getz envisions a future of personalized medicine where genome sequencing occurs routinely at birth as a reference point for later tumor formations. Providing a secure computational infrastructure will be the next challenge.

“Medicine, in general, is becoming an information-rich discipline. We need to build a system that integrates all this information for doctors to make the next choice in treatment,” said Getz.



NIEHS bioinformatics specialist David Fargo, Ph.D., co-hosted Getz's lecture with senior staff scientist Dmitri Gordenin, Ph.D. (Photo courtesy of Steve McCaw).



While introducing Getz, co-host Gordenin referred to the renowned scientist as a rock star, because of his numerous publications and citations on the systematic analysis of the cancer genome. (Photo courtesy of Steve McCaw)

(Jeffrey Stumpf, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group and a frequent contributor to the Environmental Factor.)

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Gabbay Foundation honors bisphenol researchers

By Eddy Ball

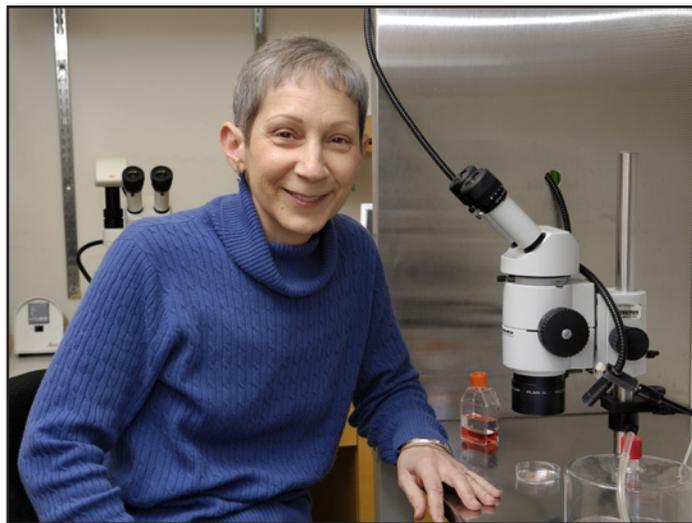
Three NIEHS grantees are this year's recipients of the [Jacob Heskell Gabbay Award in Biotechnology and Medicine](#) for their work on the health effects of bisphenol A (BPA). Along with their medallions, winners [Patricia Hunt, Ph.D.](#), [Carlos Sonnenschein, M.D.](#), and [Ana Soto, M.D.](#), will each receive a \$5,000 cash prize during a ceremony and dinner Oct. 22 at Brandeis University in Waltham, Mass., hosted by the Rosenstiel Basic Medical Sciences Research Center, which also administers the award for the foundation.

In 1998, the trustees of the Jacob and Louise Gabbay Foundation decided to establish a major new award in basic and applied biomedical sciences. “The Foundation, therefore, created the Jacob Heskell Gabbay Award in Biotechnology and Medicine to recognize... scientists in academia, medicine, or industry whose work had

outstanding scientific content and significant practical consequences in the biomedical sciences,” the award website explains. This year’s winners were honored specifically for identifying the cellular effects of bisphenol in plastics.

In addition to receiving their awards, the winners also presented invited talks at the ceremony.

- Hunt explored the effects of BPA exposure on reproduction, in her talk, “Making a perfect egg: how age and the environment affect our reproductive health.”
- Sonnenschein’s presentation examined “The social impact of scientific discoveries: the case of endocrine disruptors.”
- Soto placed endocrine disruption into the context of the tissue organization field theory of carcinogenesis, with her discussion of “Cancer as development gone awry: the case for bisphenol-A as a carcinogen.”



Award winner Hunt (Photo courtesy of Patricia Hunt)

 **Linked video:**
[Watch an interview with Sonnenschein and Soto about their thirty years of collaboration and their research on the estrogenic effects of BPA \(10:28\)](#)
(Launches in new window)
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NIEHS Health Scientist Administrator Jerry Heindel, Ph.D., oversees grants to Hunt, a professor in the School of Molecular Biosciences at Washington State University, as well as to Sonnenschein and Soto, who are professors in the department of anatomy and cellular biology in the Sackler School of Graduate Biomedical Sciences at Tufts University School of Medicine. The winners were among the 38 authors of the 2007 Chapel Hill bisphenol A expert panel consensus statement ([see story](#)).



Award winner Sonnenschein (Photo courtesy of Carlos Sonnenschein)

“Pat, Carlos, and Ana richly deserve this recognition,” Heindel said of the awards. “Their work has helped to dramatically change our understanding of endocrine toxicology and the very basis of carcinogenesis.”

Citations:

[Hunt PA, Lawson C, Gieske M, Murdoch B, Smith H, Marre A, Hassold T, Vandervoort CA.](#) 2012. Bisphenol A alters early oogenesis and follicle formation in the fetal ovary of the rhesus monkey. *Proc Natl Acad Sci U S A*; doi:10.1073/pnas.1207854109 [Online 24 September 2012].

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Award winner Soto (Photo courtesy of Ana Soto)

Genomics day highlights the new resources available to intramural researchers

By Sonika Patial

NIEHS celebrated Genomics Day Sept. 27, by showcasing new resources for high-throughput assessment and the advanced research these resources make possible. Scientists and trainees from NIEHS and the adjacent U.S. Environmental Protection Agency (EPA) gathered in Rodbell Auditorium for a series of talks followed by a stimulating poster session.

Kevin Gerrish, Ph.D., deputy director of the NIEHS Molecular Genomics Core, opened the event with a synopsis of the agenda for the day's activities and emphasized that the main goal of Genomics Day is to increase awareness and promote discussion about advances in genomic methods and software technology, as well as to inform researchers at NIEHS about the sophisticated bioinformatics resources available to them. Describing the array of genomic techniques scientists can access, Gerrish said, "I think we have a really robust program here at NIEHS."

In addition, Gerrish briefly described the restructuring that will combine the Microarray core, Molecular Genetics core, and Sequencing lab group into a consolidated core lab that will be called the Molecular Genomics Core.

NIEHS Sequencing Lab Group Manager Greg Solomon presented an overview of the new NextGen facilities available at NIEHS. Solomon proudly showcased the new MiSeq instrument, which is capable of a range of assays, from targeted resequencing, small genome sequencing, and RNA sequencing to methylated DNA sequencing.



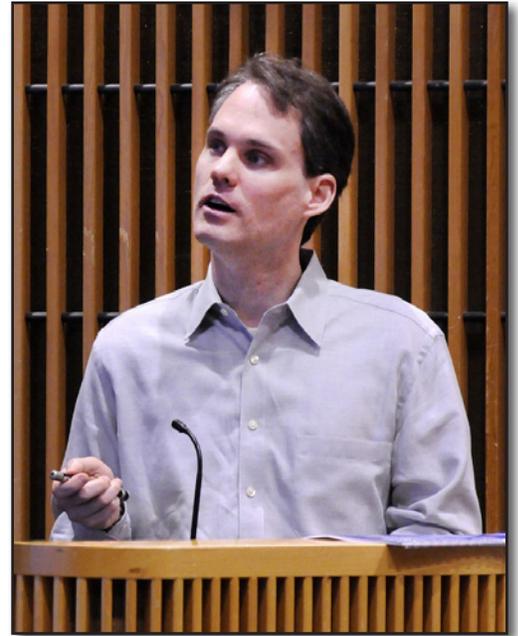
Gerrish, above, and his team keep themselves abreast of new developments in the rapidly advancing fields of genomic technologies and bioinformatics. (Photo courtesy of Steve McCaw)

Describing the new features of the versatile and virtually self-reliant little unit, Solomon said, “This technology is changing almost daily.”

A final resource presentation by David Fargo, Ph.D., director of the Integrative Bioinformatics Group in the NIEHS [Office of the Scientific Director](#), featured an overview of the bioinformatics support for the research programs at NIEHS, as well as the general and individually tailored bioinformatics training and mentoring. Fargo pointed to support available from his colleagues, Biostatistics Branch staff scientists [Pierre Bushel, Ph.D.](#), and [Grace Kissling, Ph.D.](#), as well as contractor Ruchir Shah, Ph.D.

Fellows took center stage with Genomics Day presentations

When it came time to show off the results of genomics support at NIEHS, fellows outnumbered senior researchers in sharing their work this year. Out of a total of seven presentations, five were made by fellows and two by group leaders (see text box). These oral presentations highlighted the wide range of different genomics technologies currently available to researchers and underscored the scope of these techniques, as well as how they are bound to revolutionize the field of biomedical research.



Fargo said he hopes to help empower researchers to work as independently as they want. (Photo courtesy of Steve McCaw)

Research highlights of the genomics day presentations

- “450K epigenome-wide scanning to identify DNA methylations in newborns related to maternal smoke during pregnancy,” by Bonnie Joubert, Ph.D., research fellow in the NIEHS [Genetics, Environment, and Respiratory Disease Group](#). Joubert and colleagues are the first at NIEHS to use **Infinium HumanMethylation450 BeadChip (450K) technology** ([see story](#)).
- “Dynamics of DNA methylation during B lymphocyte activation and differentiation using **methyl-binding domain enrichment, Nimblegen promoter arrays, and NextGen sequencing**,” by Anne Lai, Ph.D., postdoctoral fellow in the NIEHS [Eukaryotic Transcriptional Regulation Group](#).
- “Expression QTL (eQTL) analysis in lung development and hyperoxic lung injury in the neonatal inbred mouse using **Illumina gene expression microarrays**,” by Jennifer Nichols, Ph.D., EPA postdoctoral fellow and a former predoctoral fellow in the NIEHS [Environmental Genetics Group](#).
- “Artificial butter flavoring and a rat model of obliterans bronchiolitis (OB) using **laser capture micro-dissection and Affymetrix gene expression**,” by Dan Morgan, Ph.D., group leader in the NTP [Respiratory Toxicology Group](#).
- “Chromatin structure controls glucocorticoid receptor recruitment using **formaldehyde assisted isolation of regulatory elements (FAIRE) and NextGen sequencing**,” by Craig Burd, Ph.D., postdoctoral fellow in the NIEHS [Chromatin and Gene Expression Group](#).
- “The pervasive effects of Pol II pausing on stimulus-responsive gene networks using **ChIP-chip with Nimblegen promoter microarrays and NextGen sequencing**,” by Dan Gilchrist, Ph.D., postdoctoral fellow in the NIEHS [Transcriptional Responses to the Environment Group](#).
- “Meta-analysis identifies determinants of embryonic stem cell identity,” by Raja Jothi, Ph.D., lead researcher in the NIEHS [Systems Biology Group - Stem Cells, Epigenetics, and Gene Regulation](#).

Presenters were among the lead authors of the 41 posters that were displayed in the afternoon poster session. The poster session was structured so the researchers who were not selected for oral presentations would still be able to present their work. Organizers intermingled vendor posters with the NIEHS and EPA ones, to increase exposure and create dialogue with the companies that provide the reagents and platforms for performing genomic studies.

As Gerrish explained, the Genomics Day talks and poster session promote interaction between the NIEHS and EPA research communities.

(Sonika Patial, D.V.M., Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)



As part of her study, Lai assessed differences in DNA methylation during activation and differentiation of B cell subsets from inflamed tonsils. (Photo courtesy of Steve McCaw)



Using gene expression patterns, Nichols looked at windows of susceptibility for oxidative lung injury in infants. (Photo courtesy of Steve McCaw)



Kristin Lichti-Kaiser, Ph.D., a fellow in the NIEHS Cell Biology Group, right, discusses her work on thyroid hormone synthesis with lead researcher Carmen Williams, M.D., Ph.D. (Photo courtesy of Steve McCaw)



The poster session offered NIEHS scientists an opportunity to huddle in impromptu conversations. Shown, left to right, are lead researcher Steve Kleeberger, Ph.D., Solomon, and lead researcher Ken Korach, Ph.D. (Photo courtesy of Steve McCaw)

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Bacterial protein in house dust spurs asthma

By Robin Arnette

A bacterial protein in common house dust may worsen responses to indoor allergens, according to research conducted by scientists at NIEHS and Duke University Medical Center. The [finding](#), published online Oct. 14 in the journal *Nature Medicine*, is the first to document the presence of the protein flagellin in house dust, bolstering the link between allergic asthma and the environment.

“Most people with asthma have allergic asthma, resulting largely from allergic responses to inhaled substances,” said the paper’s corresponding author [Donald Cook, Ph.D.](#), an NIEHS lead researcher. His team began the study to identify environmental factors that amplify the allergic responses. “Although flagellin is not an allergen, it can boost allergic responses to true allergens.”

After inhaling house dust, mice that were able to respond to flagellin displayed all of the common symptoms of allergic asthma, including more mucous production, airway obstruction, and airway inflammation. However, mice lacking a gene that detects the presence of flagellin had reduced levels of these symptoms.

“More work will be required to confirm our conclusions, but it’s possible that cleaning can reduce the amount of house dust in general, and flagellated bacteria in particular, to reduce the incidence of allergic asthma,” Cook said.

In addition to the mouse study, the research team also determined that people with asthma have higher levels of antibodies against flagellin in their blood than do non-asthmatic subjects, which provides more evidence of a link between environmental factors and allergic asthma in humans.

“More than 20 million Americans have asthma, with 4,000 deaths from the disease occurring each year,” added [Darryl Zeldin, M.D.](#), NIEHS scientific director and paper co-author. “All of these data suggest that flagellin in common house dust can promote allergic asthma by priming allergic responses to common indoor allergens.”

Citation: [Wilson RH, Maruoka S, Whitehead GS, Foley JF, Flake GP, Sever ML, Zeldin DC, Kraft M, Garantzotis S, Nakano H, Cook DN](#). 2012. The Toll-like receptor 5 ligand flagellin promotes asthma by priming allergic responses to indoor allergens. *Nat Med*; doi:10.1038/nm.2920 [Online 14 October 2012].

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Cook heads the Immunogenetics Group in the NIEHS Laboratory of Respiratory Biology. (Photo courtesy of Steve McCaw)



In addition to being NIEHS scientific director, Zeldin also leads the [Environmental Cardiopulmonary Disease Group](#) in the Laboratory of Respiratory Biology. (Photo courtesy of Steve McCaw)

Dioxin exposure causes transgenerational health effects

By Brant Hamel

A new study, funded in part by NIEHS, found that dioxin affects not only the health of an exposed rat, but also unexposed descendants through a mechanism of epigenetic transgenerational inheritance.

The [study](#) was conducted in the laboratory of [Michael Skinner, Ph.D.](#), a professor in the Center for Reproductive Biology in the Department of Biological Sciences at Washington State University (WSU) who designed the [study](#). Co-authors included assistant research professor Mohan Manikkam, Ph.D., research technician Rebecca Tracey, and postdoctoral researcher Carlos Guerrero-Bosagna, Ph.D.

“Although not designed for risk assessment, these results have implications for the human populations that are exposed to dioxin and are experiencing declines in fertility and increases in adult onset disease, with a potential to transmit them to later generations,” the authors concluded.

Dangers of dioxin last for decades after initial exposure

Dioxin, 2,3,7,8-tetrachlorodibenzo[p]dioxin (TCDD), is a chemical compound that constitutes part of the Agent Orange herbicide used as a defoliant in the Vietnam War. According to research cited in the study, exposure is estimated to have caused 400,000 deaths and 500,000 birth defects. Dioxin has also been released from industrial accidents, leading to human exposures. Due to its extremely long half-life of up to 10 years in humans, dioxin may still affect pregnancies occurring even 20 years after exposure.

In the Skinner group’s experiments, exposure to dioxin caused changes in the DNA methylation patterns of sperm that were transmitted across generations, in an imprinted-like manner, to affect the health of multiple generations of descendants. The grandchildren of exposed rats showed dioxin-induced effects ranging from polycystic ovarian disease to kidney disease. The work raises the serious concern that even if toxic chemicals, such as dioxin, were completely removed from the environment, they could continue to cause disease for multiple generations.

Health effects of dioxin include early onset of puberty in females

Skinner’s group used low *in vivo* doses of dioxin, so that toxic effects were not expected. Female rats were exposed while pregnant, and both their direct progeny and descendants two generations removed were examined.

Although the most prominent phenotypes were kidney disease in males and polycystic ovarian disease in females, a number of other effects including abscesses, colon impaction, lung abnormalities, and missing testes were also observed in animals from the dioxin-treated lineage. Additionally, females from the dioxin-exposed lineage experienced the early onset of puberty. Conversely, males showed delayed puberty, suggesting sex-specific effects of exposure. Early puberty in humans has increased over recent decades and is believed to have an environmental link.



In a WSU [press release](#), Skinner said of his latest findings, “It is not just the individuals exposed, but potentially the great-grandchildren that may experience increased adult-onset disease susceptibility.” (Photo courtesy of Steve McCaw)

Dioxin alters methylation patterns in germ line DNA across generations

The researchers were able to identify 50 specific regions of DNA that were differentially methylated in the dioxin-treated animals. These regions were permanently reprogrammed and protected from DNA methylation, in a manner that allowed them to be passed down across generations. In the future, these regions may serve as biomarkers that would allow early detection of exposure and risk for disease.

Other chemical compounds, including bisphenol A, phthalates, the insecticide DEET, and the jet fuel JP8 have all been shown to promote disease across generations, through a similar mechanism of epigenetic transgenerational inheritance ([see story](#)). This pathway of disease propagation exists not only in rats, but also in humans, mice, worms, flies, and even plants. Thus, future research will be needed to see if other environmental compounds may also lead to health effects across generations.

In addition to NIEHS, NIH and the U.S. Department of Defense provided support for the study.

Citation: [Manikkam M, Tracey R, Guerrero-Bosagna C, Skinner MK](#). 2012. Dioxin (TCDD) induces epigenetic transgenerational inheritance of adult onset disease and sperm epimutations. *PLoS One* 7(9):e46249.

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

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Van Oijen visualizes DNA replication of single molecules

By Jeffrey Stumpf

University of Groningen professor Antoine van Oijen, Ph.D., showcased a variety of new imaging techniques that challenges basic beliefs about DNA replication and its response to nucleotide damaging agents. As part of the NIEHS Laboratory of Molecular Genetics (LMG) Fellows' Invited Series, van Oijen dazzled researchers Sept. 24 with images of DNA replication proteins altering single DNA molecules in real time.

Van Oijen used a variety of imaging techniques of fluorescently labeled proteins to show how simple *in vitro* replication systems coordinate various DNA modifying activities, such as the unwinding of DNA and priming DNA for replication. Single molecule imaging of DNA replication in *E. coli* and *Xenopus* cell extracts demonstrated important fundamental results about origins of replication and bypass of damage.

Trained as a physicist, van Oijen's research is a successful marriage of physics, microbiology, biochemistry, and virology. Jessica Williams, Ph.D., research fellow in the NIEHS DNA Replication Fidelity Group hosted the speaker's visit and noted the importance of the contributions from a variety of different fields. "By bringing these disciplines together, it has really provided novel answers to long-standing biological questions," Williams commented.



Van Oijen compared lagging strand synthesis to a phone cord, in that the distance from the phone to the base is shortened by the loops of the cord (Photo courtesy of Steve McCaw).

Visualizing DNA replication loops

Van Oijen described a technique that used modified viral DNA, with one end attached to a glass coverslip and the other end attached to a small bead, that can be visualized. When a force is applied to the DNA, the rate at which the DNA stretches to different lengths is different, depending on whether it is double-stranded (dsDNA) or single-stranded (ssDNA). Thus, van Oijen can determine the precise rates that polymerases create, and helicases unwind, double-stranded DNA.

For many NIEHS scientists in the audience, the possibilities, using van Oijen's technology, are endless. "This new imaging technique is really a breakthrough in the field," Williams stated. "It is one of the first demonstrations of single-molecule fluorescence techniques to study protein complexes at their physiologically relevant concentrations."

The single-molecule studies became more complex, when more replication proteins were added to the assay. Van Oijen recounted a particular moment of disappointment when adding the single-stranded binding protein gp 2.5 to the complex caused the length of the ssDNA-bound complex to be the same length as dsDNA.

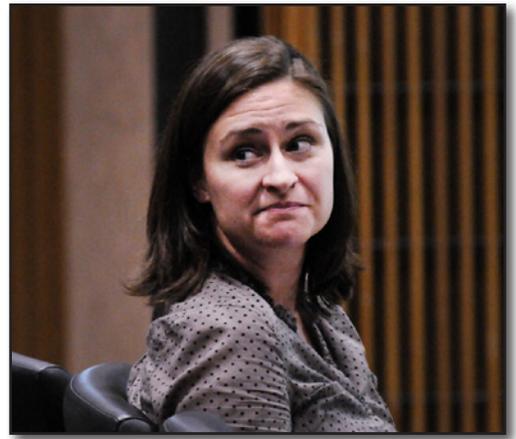
"This was two or three years after we established the assay that we realized that the assay doesn't work," lamented van Oijen.

The potential letdown of wasting years of research was short-lived, as van Oijen realized that his assay was actually the first to allow detection of replication loops that grow during lagging strand synthesis. Van Oijen showed that the replication of the previous fragment, and the priming of the next Okazaki fragment, signal the release of the loop.

Seeing polymerase degradation is believing

Van Oijen addressed the long-standing question of how specialized DNA polymerases, that function in DNA repair, gain access to the replication fork. By using fluorescently labeled proteins in *E. coli*, van Oijen imaged a striking response to UV damage. Pol III polymerase that is responsible for normal DNA replication disappeared, and the Pol V polymerase that bypasses UV-induced damage saturated the cell.

These results suggest that Pol V is eliminating the competition at the replication fork. In fact, van Oijen demonstrated the degradation of Pol III by a Pol V subunit, accounting for the disappearance of the Pol III signal. While previous genetic evidence suggested interplay between Pol III and Pol V at a UV-induced lesion (see [related story](#)), van Oijen's microscopy data, and the degradation of Pol III, changes the current thinking about the interplay among DNA polymerases.



Williams, a research fellow in the NIEHS DNA Replication Fidelity Group, listened intently, while moderating questions from the interested audience. (Photo courtesy of Steve McCaw)



Past and present members of LMG, including Director of the NIEHS Office of Fellows' Career Development Tammy Collins, Ph.D., center, took note of the powerful tools on display for studying their important questions in DNA replication. (Photo courtesy of Steve McCaw)



As head of the Genome Stability Structural Biology Group, Scott Williams, Ph.D., is no stranger to using complex biophysical techniques to study DNA repair. (Photo courtesy of Steve McCaw)

Mutations in the Pol V human homolog cause a variant of *xeroderma pigmentosa*, a rare genetic disease that causes extreme sensitivity to sunlight and predisposition to skin cancer. Microscopy approaches may also illuminate interactions among human polymerases, to help explain the mechanisms that occur to prevent disease.

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

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Bisphenol A linked to lower thyroid hormone levels in newborn boys

By Bono Sen

A new [study](#), funded in part by NIEHS, reports, for the first time, that exposure to bisphenol A (BPA) during pregnancy may affect thyroid hormone levels in pregnant women and newborn boys.

The study by researchers at the University of California (UC), Berkeley, published online Oct. 4 in the journal *Environmental Health Perspectives*, adds to the growing health concerns about BPA. In the background section of their study, the authors cited earlier research that found detectable levels of BPA in the urine of 95 percent of U.S. women of reproductive age in testing conducted as part of the National Health and Nutrition Examination Survey (NHANES) 2007-2008.

“Our data showed no evidence that there is a safe level of exposure,” said lead author Jonathan Chevrier, Ph.D., research epidemiologist at UC Berkeley’s Center for Environmental Research and Children’s Health (CERCH). “Studies suggest that small changes in thyroid hormone level, even if they’re within normal limits, may still have an effect on brain development.”



First author Jonathan Chevrier (Photo courtesy of Jonathan Chevrier)

BPA exposure affects thyroid hormone levels

The researchers analyzed BPA levels in the urine samples of 476 women during the second half of pregnancy. Also, blood samples to measure thyroid hormone levels were taken from 364 of moms and newborns during pregnancy and within a few days of birth, respectively. The study participants were residents of California’s Salinas Valley, a low-income community of mostly Mexican-American farm workers, who were part of the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study. BPA was detected in the urine of 82 percent of women.

For newborn boys, but not girls, a 9.9 percent decrease in thyroid stimulating hormone was observed with every doubling in BPA level. This association was strongest when the women’s BPA levels were measured during the third trimester, and the time between BPA and thyroid hormone measurements was shorter. According to the authors, this temporal pattern may be due to a specific developmental window of susceptibility to BPA, or may suggest a transient effect of BPA on thyroid hormones.

Clues as to why this response was not seen among newborn girls may be found in some animal studies that suggest that female rats have higher levels of a BPA metabolizing enzyme than their male counterparts.

The collaborative NIEHS approach to BPA research

Despite a proliferation of research over the past two decades, much about the potential health effects of BPA remains unknown, according to a new [paper](#) published Sept. 25 in *Environmental Health Perspectives* by NIEHS/NTP Director Linda Birnbaum, Ph.D., and leaders of the NTP, extramural, and intramural research branches of NIEHS.

“To address the uncertainties and concerns surrounding BPA research,” the authors wrote, “NIEHS developed an unprecedented, comprehensive research program that combines extramural grant funding with targeted intramural research efforts and overarching structures for collaboration to fill research gaps, solve controversies, and provide results that can inform regulatory decision-making.”

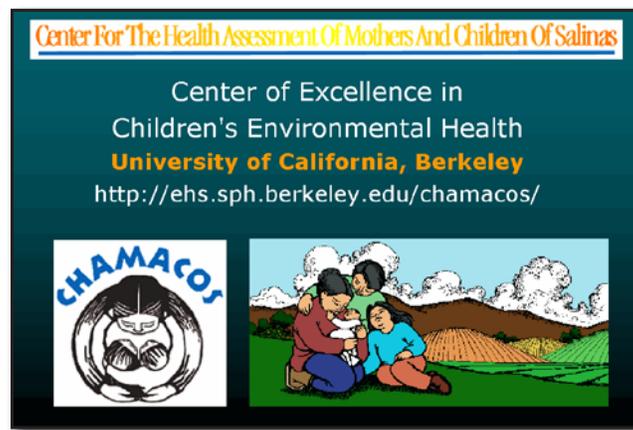
Looking ahead, the authors speculate that this kind of multipronged, collaborative approach may also prove useful in other areas of environmental health.

Citation: [Birnbaum LS, Bucher JR, Collman GW, Zeldin DC, Johnson AF, Schug TT, Heindel JJ.](#) 2012. Consortium-Based Science: The NIEHS’s Multipronged, Collaborative Approach to Assessing the Health Effects of Bisphenol A. *Environ Health Perspect*; doi.org/10.1289/ehp.1205330 (Online 25 September 2012).

BPA as a public health concern

BPA is a chemical widely used in making products such as baby and water bottles, tubing and medical devices, sports equipment, household electronics, plastic toys, lining of cans, and thermal receipts.

A previous NIEHS-funded [study](#) shows that BPA and phthalates are associated with a range of adverse health outcomes, many of which may be mediated through altered thyroid signaling. Thyroid hormones play an essential role in prenatal and postnatal growth and brain development in humans. Disruption of thyroid function may be responsible for potential effects of BPA on cognition and behavior.



Currently, 11 U.S. states have banned BPA in some products. In July, the U.S. Food and Drug Administration (FDA) banned the chemical from baby bottles and sippy cups. It has not banned BPA from food packaging yet, because research is still ongoing. NIEHS grantees are [collaborating](#) with the National Toxicology Program and FDA to help develop state-of-the-art rodent studies on BPA. Information gathered from these studies will be used to inform regulatory agencies tasked to determine the safety of BPA-containing consumer products.

In addition to NIEHS support for CHAMACOS and CERCH, the study was also supported by funding from the U.S. Environmental Protection Agency, UC Institute for Mexico and the United States, and the UC Berkeley Center for Latino Policy Research.

Citation: [Chevrier J, Gunier RB, Bradman A, Holland NT, Calafat AM, Eskenazi B, Harley KG.](#) 2012. Maternal Urinary Bisphenol A During Pregnancy and Maternal and Neonatal Thyroid Function in the CHAMACOS Study. *Environ Health Perspect*; doi:10.1289/ehp.1205092 [Online 4 October 2012].

(Bono Sen, Ph.D., is the program director for health literacy for the NIEHS journal *Environmental Health Perspectives*.)

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NIEHS researchers describe important cell signaling mechanism

By Ernie Hood

Scientists in the NIEHS Laboratory of Signal Transduction (LST) have discovered a mechanism by which glucocorticoids, stress hormones produced by the body to maintain homeostasis, act upon certain key cellular receptors. Since synthetic glucocorticoids are one of the most widely prescribed pharmaceuticals in the world — treating inflammatory diseases, autoimmune illnesses, organ transplant rejection, and lymphoid system cancers — understanding this signaling mechanism could lead to more precisely targeted therapeutic treatments that have increased efficacy and fewer side effects.

The research team, led by LST chief [John Cidlowski, Ph.D.](#), staff scientist Robert Oakley, Ph.D., and former research fellow Javier Revollo, Ph.D., published the [paper](#) online Oct. 8 in the Proceedings of the National Academy of Sciences (PNAS).

Cellular cross-talk

Using multiple cell types in its experiments, the Cidlowski group demonstrated that glucocorticoids act upon G protein-coupled receptors (GPCRs) by upregulating the gene expression of one signaling protein called beta-arrestin-1, while simultaneously downregulating expression of another, beta-arrestin-2. In other words, the researchers revealed that an important exchange of information was going on between receptors on the surface of a cell and those on the nucleus. This communication can either help or hinder how well GPCR-based treatments work.

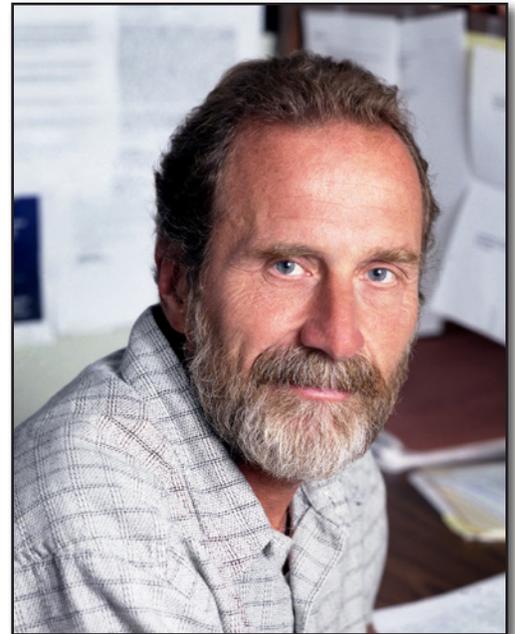
“Our work shows that glucocorticoid signaling pathways ultimately may determine the effect of pharmaceuticals in humans,” Cidlowski said.

Their findings may provide the molecular basis for the clinical synergism observed with glucocorticoid-GPCR agonist combination therapies currently used to treat asthma and chronic obstructive pulmonary disease (COPD). Understanding the mechanisms that make these combinations so powerful may allow the development of other regimens involving glucocorticoids and GPCR-targeted treatments that will be more safe and effective.

Interestingly, the person who edited Cidlowski’s PNAS paper, Duke University researcher Robert Lefkowitz, M.D., just shared the [2012 Nobel Prize in Chemistry](#) for his seminal discoveries related to GPCRs. Both Cidlowski and Lefkowitz have dedicated the majority of their careers to understanding these important receptors.

Citation: [Oakley RH, Revollo J, Cidlowski JA](#). 2012. Glucocorticoids regulate arrestin gene expression and redirect the signaling profile of G protein-coupled receptors. Proc Natl Acad Sci U S A 109(43):17591-17596.

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



Cidlowski heads the Molecular Endocrinology Group in LST. (Photo courtesy of Steve McCaw)



As lead author for the paper, most of the work and analysis was a result of Oakley’s expertise. (Photo courtesy of Steve McCaw)

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Household contaminants associated with childhood respiratory problems

By Nancy Lamontagne

Two NIEHS-funded studies from the Columbia Center for Children’s Environmental Health (CCCEH) at the Columbia University Mailman School of Public Health report new findings that link exposures to chemicals found in the home with childhood respiratory problems.

Rachel Miller, M.D., led the [study](#) showing that children exposed to piperonyl butoxide (PBO) in the womb had an increased risk of noninfectious cough at ages 5 and 6. PBO is used to bolster the effects of pyrethroid pesticides, the most commonly used pesticides for professional pest control and in-home application. The findings provide evidence that children’s respiratory systems are susceptible to damage from contaminants during the prenatal period.

The researchers studied 224 mother-child pairs who lived in upper Manhattan and the south Bronx for at least one year. They examined levels of PBO and permethrin — a pyrethroid insecticide — by having mothers wear personal air monitors during pregnancy. They also collected air samples from the home when children were between 5 and 6 years old.

The researchers found that children with higher prenatal exposure to PBO were more likely to have a cough, unrelated to a cold or the flu, when they were between 5 and 6 years old. Exposures to PBO at ages 5 and 6 were not a factor, and the study results did not indicate that PBO or permethrin exposures were associated with other respiratory outcomes, such as wheeze or asthma. The researchers also did not find any association between prenatal or childhood permethrin exposure and cough, perhaps because PBO is much easier to measure in air samples than permethrin.

“While it is unclear whether the effect is due mainly to PBO itself or residential pyrethroids, of which PBO is an indicator, it is important to remember that cough is a very common complaint for which children and adults seek medical attention,” said Miller. “The results suggest that avoidance of exposure to PBO may be most important during pregnancy.”

Phthalates and airway inflammation

In another [study](#) from CCCEH, researchers report that children exposed to diethyl phthalate (DEP) and butylbenzyl phthalate (BBzP) have a greater risk of asthma-related airway inflammation. Phthalates are used widely in consumer products, including plastics, vinyl flooring, and personal care products. Phthalate exposure can occur through ingestion, inhalation, and absorption through the skin.

The researchers led by [Matthew Perzanowski, Ph.D.](#), studied children ages 5 to 9 who were part of the same Manhattan-Bronx cohort used in Miller’s study. Urine tests revealed detectable, although varied, levels of phthalates in all 244 study participants. To quantify airway inflammation, the researchers measured the nitric



Shown above during a grantee meeting at NIEHS, Miller said her latest study found that prenatal exposure to PBO increased the odds of noninfectious childhood cough. Cough is a common reason for doctor visits in children younger than 5 years old. (Photo courtesy of Steve McCaw)

oxide in the child's exhaled breath. Nitric oxide is a biological marker of airway inflammation and was previously shown to increase in response to known asthma triggers, such as vehicle emission. The study is the first to use this biomarker to investigate airway responses to phthalate exposure in children.

The team found that higher levels of both DEP and BBzP were associated with higher levels of nitric oxide in exhaled breath. "We found that exposure to two phthalates, believed to have substantial inhalational exposure, was associated with greater airway inflammation and that this association was strongest among the children with recent asthma symptoms," Perzanowski said. "Increases in airway inflammation, especially among these children with recent symptoms, could increase the likelihood of future asthma exacerbations."

In addition to the NIEHS funding, Miller's study received support from the Thrasher Research Fund and the U.S. Environmental Protection Agency (EPA). Perzanowski's research also received funding from the U.S. EPA, the John and Wendy Neu Family Foundation, Blanchette Hooker Rockefeller Fund, New York Community Trust, Educational Foundation of America, and Millstream Fund.

Citations: Liu B, Jung KH, Horton MK, Camann DE, Liu X, Reardon AM, Perzanowski MS, Zhang H, Perera FP, Whyatt RM, Miller RL. 2012. Prenatal exposure to pesticide ingredient piperonyl butoxide and childhood cough in an urban cohort. *Environ Int* 48:156-161.

Just AC, Whyatt RM, Miller RL, Rundle AG, Chen Q, Calafat AM, Divjan A, Rosa MJ, Zhang H, Perera FP, Goldstein IF, Perzanowski MS. 2012. Children's urinary phthalate metabolites and fractional exhaled nitric oxide in an urban cohort. *Am J Respir Crit Care Med*; doi:10.1164/rccm.201203-0398OC [Online 23 August 2012].

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

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Exploring regulatory mechanisms in the fruit fly genome

By Sheila Yong

"People generally view the nucleosomes as static structures of histone core proteins in the center with DNA wrapped around them," said Kami Ahmad, Ph.D., at the beginning of his talk at NIEHS Oct. 2. Nucleosomes are the fundamental units of the chromatin in a eukaryotic cell that facilitate the packing of large genomes into the nucleus while still allowing ample access to the DNA. "However, nucleosomes are in fact dynamic structures and their histone core proteins are frequently replaced," he explained.

Ahmad, an assistant professor at Harvard Medical School, uses the fruit fly, *Drosophila melanogaster*, as a model system for his research on histone variants and the biological properties of chromatin. During his talk, he discussed his group's findings on the mechanism of histone replacement and efforts to identify regulatory elements in the *Drosophila* genome.



By using fractional exhaled nitric oxide as a biological marker of airway inflammation, Perzanowski's research team could discern short-term associations between environmental measures and airway inflammation. Making these connections is important, because airway inflammation is associated with subsequent worsening of asthma. (Photo courtesy of Columbia University)

Histone H3.3 variant participates in replication-independent histone replacement

The first part of Ahmad's talk focused on histone H3.3, a histone H3 variant that differs from histone H3 by only four amino acids. This histone variant is evolutionarily conserved in many species, highlighting its importance in chromatin structure maintenance. Ahmad pointed out that, unlike canonical histones, which are mainly used for nucleosome assembly during different cell cycle phases, histone H3.3 participates in DNA replication-independent histone replacement, which occurs outside of S-phase of the cell cycle. In particular, histone H3.3 plays a role in facilitating nucleosome assembly at sites of transcription where DNA has to unwind to allow RNA polymerase II access.

Ahmad and his team employ a temperature-controlled heat shock protein *Hsp70* expression system that enables them to activate transcription of the *Hsp70* gene and observe histone H3.3 replacement. Their studies revealed that chromatin remodeler Xnp, which is normally dispersed throughout the genome, colocalized with histone H3.3 during transcription activation.

Besides Xnp, several histone chaperones such as Hira and ASF1 were also localized at the transcription bulbs. Upon recovery, these factors were released and the nucleosomes were repackaged. However, when they knocked down *H3.3* expression, the nucleosome repackaging efficiency was markedly reduced. Moreover, while most of the proteins involved in *Hsp70* transcription were released upon recovery, Xnp and Hira remained at the transcription sites.

One interesting question that was raised during the presentation was if histone H3 can rescue the phenotype observed in *H3.3*-deficient flies. "Yes, it can," Ahmad responded. "Therefore, it remains to be determined why the cells choose to use H3.3 instead of H3 for histone replacement during transcription."



Shown with his host, visiting fellow Hemakumara Mutra, Ph.D., left, Ahmad said the goal of his research is to identify new regulatory elements and dissect the epigenomic changes that occur throughout the genome during development. "We are excited about these observations, because they imply that our purification technique can isolate proteins bound to the DNA fragments, based on proximity, even if they do not make direct contact with one another," he told the audience. (Photo courtesy of Steve McCaw)

Identifying regulatory elements in the *Drosophila* genome

In the second part of his talk, Ahmad discussed his group's involvement with the *Drosophila* model organism ENCYClopedia of DNA Elements (**modENCODE**), which aims to unravel the transcriptome, as well as various properties of the chromatin and nucleosomes. Ahmad's group uses a modified micrococcal nuclease digestion and salt fractionation protocol to detect and measure nucleosome and chromatin dynamics.

To illustrate this point, Ahmad used the fruit fly *Hsp26* promoter as an example. Ahmad pointed out that the purification method not only confirmed that the heat shock factor (HSF) was bound to the promoter, but also revealed that the *Drosophila* GAGA factor (GAF) was also present at the site. "In this case, we discovered that GAF and HSF form a complex, although they bind to adjacent sites on the promoter," Ahmad noted.

Ahmad concluded that this isolation method can potentially be used to identify clusters of small chromatin particles, and subsequently lead to the discovery of novel regulatory elements in the genome and proteins that bind to them. Data obtained from these studies can then be analyzed using a systems biology approach, to illustrate the architecture of regulatory elements in the eukaryotic genome and the relationship between different protein factors that regulate gene expression.

(Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)

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Study offers insight into HIV metal and ligand binding

By Cindy Loose

A discovery by scientists in the NIEHS Laboratory of Structural Biology (LSB) opens the door for developing new treatments for human immunodeficiency virus (HIV). Members of the LSB Nuclear Magnetic Resonance (NMR) Group, headed by [Robert London, Ph.D.](#), identified a new, highly sensitive probe that can monitor the binding of compounds to a viral enzyme that allows HIV to infect humans. The finding is particularly critical, as some patients become resistant to existing antivirals for HIV.

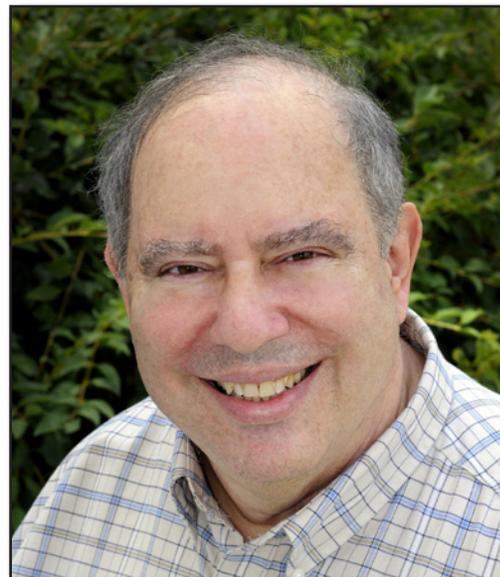
“The HIV virus is a moving target, due to its exceptionally high ability to mutate,” London said. “This allows it to escape existing drug therapies. Hence, additional strategies are needed to interfere with the virus.”

London and three members of his group published their [findings](#) online Aug. 31 in the publication *Nucleic Acids Research*.

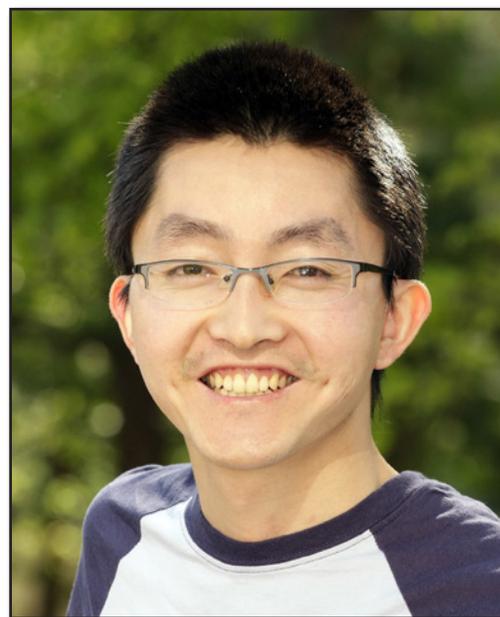
The critical role of the RNase H domain

Understanding the breakthrough requires information about how the virus and current treatments work. HIV is a retrovirus, meaning it stores its genome as RNA instead of DNA, explained staff scientist and paper co-author Geoffrey Mueller, Ph.D. The virus has to convert the single-stranded RNA into double-stranded DNA to infect the host cell. It does so in a three-step process. First, it copies the RNA into DNA creating an RNA:DNA hybrid molecule. Second, it destroys the RNA part of the RNA:DNA hybrid. Third, it copies the remaining single strand of DNA to make double-stranded DNA that eventually infects the host.

According to Mueller, most treatments currently available target steps one and three. They do so by interrupting, or inhibiting, the process by which the viral genome is copied. So far, none of the drugs inhibit step two, which is the destruction of the old RNA genome. Mueller believes the new discovery could allow scientists to target this activity, which is carried out by the RNase H domain of the reverse transcriptase enzyme. The RNase H domain is considered equally essential to the replication of the HIV virus as the polymerase domain that is currently targeted by existing treatments.



London's NMR Group studies the molecular mechanisms that underlie problems of environmental concern. (Photo courtesy of Steve McCaw)



Research Fellow Xunhai Zheng, Ph.D., is first author on the paper. (Photo courtesy of Steve McCaw)

NMR

The new probe identified by London and colleagues can monitor the binding of compounds to the RNase H domain. They found that one of the residues of the protein had a characteristic signature when compounds bound, despite the residue being very distant from the active site. Using Nuclear Magnetic Resonance (NMR) spectroscopy, they realized that the residue is a good probe of what's in the active site. Their results will allow scientists who are testing a treatment intended to inhibit the HIV virus to see whether or not the potential drug is binding to the RNase H domain and having an effect.

NMR is a research technique that exploits the magnetic properties of atomic nuclei to study molecules. It can provide detailed information about the structure, dynamics, chemical environment, and even the reactions of molecules.

“There had been attempts to identify inhibitors of RNase H activity, but because it has such a strange active site, the work has been difficult,” said Mueller. “This finding advances the goal of finding an antiviral that works on this domain.”

The group plans to continue work on understanding the RNase H domain and its promise as a drug target.

Citation: [Zheng X, Mueller GA, DeRose EF, London RE](#). 2012. Metal and ligand binding to the HIV-RNase H active site are remotely monitored by Ile556. *Nucleic Acids Res*; doi:10.1093/nar/gks791 [Online 31 August 2012].

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

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Mueller was instrumental in explaining the science for this Environmental Factor article. (Photo courtesy of Steve McCaw)



Eugene DeRose, Ph.D., is a co-author and serves as NMR Center Manager. (Photo courtesy of Steve McCaw)

Committee recommends using fewer animals in eye hazard testing

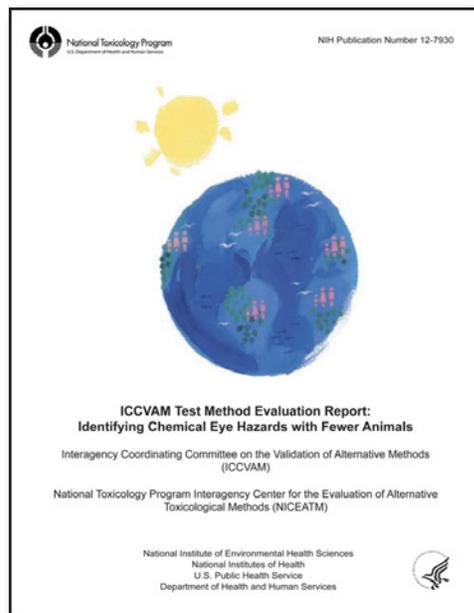
By Debbie McCarley and Cathy Sprankle

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) has transmitted recommendations to federal agencies on reducing animal use for identifying chemical eye hazards, according to an Oct. 10 [announcement](#) in the Federal Register.

When it is necessary to use animals for eye safety testing, the recommendations maintain hazard classification equivalent to current testing procedures outlined in U.S. Code of Federal Regulations (CFR) [16 CFR 1500.42](#), while using as many as 50 to 83 percent fewer animals than current testing procedures. The recommendations harmonize the number of animals used for identifying chemical eye hazards across U.S. regulatory agencies and international test guidelines.

NIEHS/NTP Director Linda Birnbaum, Ph.D., forwarded the recommendations, on behalf of Secretary of the U.S. Department of Health and Human Services Kathleen Sebelius. ICCVAM, an interagency committee of the federal government, is administered by the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), a center within the Division of the National Toxicology Program (NTP) at NIEHS.

“Non-animal methods should always be considered before using animals for this type of testing, and they should be used only when determined appropriate,” commented NICEATM Director Rear Adm. William Stokes, D.V.M. “However, in those situations where it is determined necessary to use animals to meet regulatory safety testing requirements, these recommendations will help ensure that only the minimum number of animals is used.”



Safety testing prevents eye injuries

An estimated 2 million eye injuries occur every year in the U.S. More than 40,000 of these eye injuries cause permanent visual impairment. Chemical products are the third most common cause of eye injuries, many associated with the use of household cleaning products by consumers.

To warn consumers and workers of the potential for chemicals and products to cause eye injuries, eye safety testing is performed to determine if substances may cause temporary or permanent eye damage. Test results are then used for hazard classification of chemicals and products, and appropriate warning labeling.

Recommendations reduce variation among testing agencies

Eye safety testing procedures currently vary among U.S. agencies. CFR procedures require as many as 18 animals per test substance to reach a hazard decision. Other U.S. and international test guidelines for eye safety testing use a maximum of three animals per test. However, the testing procedures described in 16 CFR 1500.42 do not provide criteria to classify results from three-animal tests.

NICEATM and ICCVAM scientists conducted an [analysis](#), which they published in the journal *Regulatory Toxicology and Pharmacology*, to determine how results from a three-animal test could be used to maintain eye hazard classification equivalent to current testing procedures. The ICCVAM recommendations are based on this analysis.

ICCVAM concluded that using a classification criterion of one or more positive animals in a three-animal test to identify eye hazards will maintain hazard classification equivalent to current testing procedures. When eye safety testing using animals is necessary, testing should be conducted using the minimum number of animals, in the most humane manner possible, consistent with testing objectives. This protocol includes the routine use of medications to avoid or reduce any discomfort that might otherwise occur.

The ICCVAM recommendations are detailed in NIH Publication No. 12-7930, “[ICCVAM Test Method Evaluation Report: Identifying Chemical Eye Hazards with Fewer Animals](#).” Federal agencies have 180 days to respond to the recommendations, and agency responses will be posted on the [NICEATM-ICCVAM website](#) as they are received.

Citation: [Haseman JK, Allen DG, Lipscomb EA, Truax JF, Stokes WS](#). 2011. Using fewer animals to identify chemical eye hazards: revised criteria necessary to maintain equivalent hazard classification. *Regul Toxicol Pharmacol* 61(1):98-104.

(Debbie McCarley is a special assistant to Stokes. Cathy Sprankle is a communications specialist with ILS, Inc., support contractor for NICEATM.)

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New study describes mechanism of anticancer drug resistance

By Robin Arnette

In general, cancer drugs kill cancer cells, but some tumors continue to grow even during aggressive pharmaceutical treatment. An NIEHS group led by researcher [Scott Williams, Ph.D.](#), reports it has visualized how malignant cells help evade annihilation, in a cellular process involving interaction between two important proteins, tyrosyl-DNA phosphodiesterase 2 (Tdp2) and topoisomerase II (topo II).

Using X-ray crystallography and biochemical analyses, Williams and his team determined how Tdp2 dictates a repair pathway that is critical for cells dealing with bulky topo II-DNA adducts, which are structures that develop when topo II forms a chemical bond with DNA. They published their [results](#) online Oct. 28 in the journal *Nature Structural and Molecular Biology*. In the paper, they described how Tdp2 acts as one of the agents responsible for chemotherapy drug resistance.

Molecular tango

Williams said that topoisomerases play pivotal roles in life by enabling DNA replication and transcription. Topo II binds to DNA and untangles it by catalyzing a biochemical reaction. While critical for life, topoisomerases are also sensitive to environmental stressors and constitute an Achilles' heel for cancer cells.

Environmental toxicants, compounds in the diet, and existing DNA damage, present in the cell, can influence the topo II reaction, causing topo II to stop its biochemical reaction prematurely and become chemically bonded to DNA. As a result, topo II can block the replication and transcription machinery from doing their jobs. When a cell can't copy its DNA, it can't divide and eventually dies. Williams said the ability to arrest topo II on DNA is also how some of the most successful cancer therapeutic strategies work, by promoting genome instability and cell death in cancer cells.

The other partner in this cellular dance is Tdp2. Its job is to remove topo II–DNA adducts, by recognizing topo II-DNA conjugates and reversing the linkage between the two. Tdp2 is a key player in a major pathway in human cells for this action. By examining the protein at the atomic level, Williams' group was able to trap Tdp2 in a number of conformations bound to DNA and a mimic of the topo II-DNA lesion. These X-ray crystallography studies mapped out a molecular mechanism for the removal of topo II.



Williams is head of the Genome Stability Structural Biology Group in the NIEHS Laboratory of Structural Biology. (Photo courtesy of Steve McCaw)

“Using this information, we may be able to interfere with how Tdp2 repairs these topo II-DNA cross-links, to prevent cancer cells from overriding and combating the action of chemotherapeutic agents,” Williams said.

Cancer and cold interventions?

Matthew Schellenberg, Ph.D., a visiting fellow in the Williams’ group and lead author on the paper, said that the work may also lead to advances in preventing the replication of picornaviruses, including the virus responsible for the common cold. During the picornavirus life cycle, analogous protein-nucleic acid cross-links occur, except they form with RNA rather than DNA. Recent research from other groups suggests that Tdp2 reverses these protein-RNA conjugates as well. This RNA processing function suggests TDP2 also plays an important role in the life cycle of these viruses.

“Our Tdp2 studies will also contribute to the understanding of viruses that hijack the host cell’s DNA repair machinery as part of their normal life cycle,” Schellenberg said.

Citation: Schellenberg MJ, Appel CD, Adhikari S, Robertson PD, Ramsden DA, Williams RS. 2012. Mechanism of repair of 5’-topoisomerase II-DNA adducts by mammalian tyrosyl-DNA phosphodiesterase 2. Nat Struct Mol Biol; doi:10.1038/nsmb.2418 [Online 28 October 2012].

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This month in EHP

The November issue of [Environmental Health Perspectives \(EHP\)](#) highlights mercury exposures from mining, and the immediate and long-term effects of dam removal.

Quicksilver and Gold: Mercury Pollution from Artisanal and Small-Scale Gold Mining

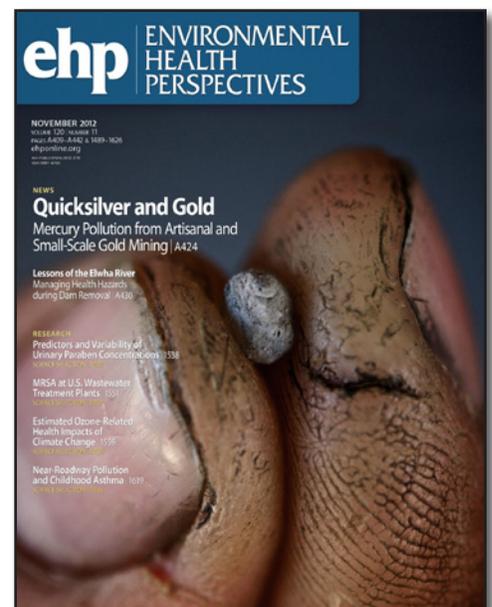
Mercury amalgamation has been used for centuries to process precious metals. Today, artisanal and small-scale gold mining is the world’s second greatest source of atmospheric mercury pollution, after coal combustion. Other mercury waste ends up in soils and waterways. With gold prices now exceeding \$1,600 per ounce, artisanal and small-scale gold mining is on the rise, along with its mercury problem.



Schellenberg gave a brief synopsis of the research, saying, “We are learning, at atomic resolution, how these protein-adducted DNA breaks are repaired when topoisomerases go awry.” (Photo courtesy of Steve McCaw)



<http://twitter.com/ehponline>



Lessons of the Elwha River: Managing Health Hazards During Dam Removal

The Elwha River's two hydroelectric dams have become stars of a four-decade-long saga, culminating in the complete removal of the lower Elwha Dam this past summer, and the planned removal of the taller Glines Canyon Dam by summer 2013. Tearing down dams releases mass quantities of sediment and, in some cases, contaminants in the short term, but restores ecosystems in the long term. As the Elwha River ecosystem begins a dramatic transformation, the biggest dam removal in history is being touted as a model for future dam breaches.

Podcast — Exploring Links Between Arsenic and Diabetes, with Ana Navas-Acien

Arsenic is a problem in communities around the world, from Bangladesh to New Hampshire. It's one of the environmental chemicals the National Toxicology Program explored at a recent workshop as possibly contributing to the worldwide rise in diabetes. In this [podcast](#), Ana Navas-Acien, M.D., Ph.D., talks about a new review by investigators at that workshop, who summarize the evidence for a link between arsenic exposure and diabetes.

Featured commentaries, reviews, and research this month include:

- Variation in Estimated Ozone-Related Health Impacts of Climate Change Due to Modeling Choices and Assumptions
- Near-Roadway Pollution and Childhood Asthma: Implications for Developing “Win-Win” Compact Urban Development and Clean Vehicle Strategies
- Methicillin-Resistant *Staphylococcus aureus* (MRSA) Detected at Four U.S. Wastewater Treatment Plants
- Predictors and Variability of Urinary Paraben Concentrations in Men and Women, Including Before and During Pregnancy

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Extramural papers of the month

By Nancy Lamontagne

- Non-coding DNA variants may link early exposures with later health problems
- Reversible epigenetic changes associated with bee behavior
- Fetal BPA exposure harms reproductive health in primates
- Assay quantifies effects of DNA damage on transcription



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

Non-coding DNA variants may link early exposures with later health problems

Researchers, supported in part by NIEHS, report that genetic differences linked to a variety of diseases are activated during fetal development. These findings could help explain why some early environmental exposures increase disease risk years or even decades later.

The researchers investigated whether variants in noncoding regions of DNA regulate gene expression, by looking at thousands of these variants identified in genome-wide association studies (GWAS). They mapped regions that are sensitive to DNase I cleavage, because these hypersensitivity sites mark regions that actively regulate gene expression.

They found that more than 76 percent of noncoding GWAS variants were in, or very near, DNase I hypersensitivity sites, indicating that most of the noncoding variants in these samples regulate genes. In addition, 88 percent of the variants in regulatory DNA regions are active in fetal development, including variants associated with adult-onset disease. This suggests that environmental exposures during this period could influence risk for a large number of diseases.

The researchers also identified the genes regulated by hundreds of GWAS variants, including genes associated with blood platelet counts, amyotrophic lateral sclerosis (ALS), Crohn's disease, breast and ovarian cancer, and schizophrenia. Almost 80 percent of GWAS variants in regulatory DNA were connected to genes that were not the closest ones to the variant, which is probably why previous attempts to link GWAS variants with target genes have been so difficult.

Citation: Maurano MT, Humbert R, Rynes E, Thurman RE, Haugen E, Wang H, Reynolds AP, Sandstrom R, Qu H, Brody J, Shafer A, Neri F, Lee K, Kutayavin T, Stehling-Sun S, Johnson AK, Canfield TK, Giste E, Diegel M, Bates D, Hansen RS, Neph S, Sabo PJ, Heimfeld S, Raubitschek A, Ziegler S, Cotsapas C, Sotoodehnia N, Glass I, Sunyaev SR, Kaul R, Stamatoyannopoulos JA. 2012. Systematic localization of common disease-associated variation in regulatory DNA. *Science* 337(6099):1190-1195.

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Reversible epigenetic changes associated with bee behavior

Researchers studying honeybees report what could be the first evidence of reversible epigenetic changes associated with behavior. The research may shed light on problems that people have with learning, memory, stress response, and mood disorders, which all involve interactions between genetic and epigenetic components. The work was supported by an NIH Director's Pioneer Award.

Although all worker honeybees are genetically identical within the same hive, they carry out different roles. For example, some bees nurse larvae, while others forage for food. Since genetics isn't responsible for the differing behaviors, epigenetic changes are likely involved. Epigenetic changes, such as DNA methylation, modify gene expression without changing the genetic code.

To study the role of epigenetic changes in bee behavior, the researchers used a method known as comprehensive high-throughput arrays for relative methylation (CHARM) to locate methylated DNA in the brains of bees. They found no differences in DNA methylation between worker and queen bees, roles that are irreversible. However, they saw substantial differences between nurses and forager bees. Reverting foragers back to nurses reestablished methylation levels for a majority of genes, providing evidence of reversible epigenetic changes that are associated with behavior.

Citation: Herb BR, Wolschin F, Hansen KD, Aryee MJ, Langmead B, Irizarry R, Amdam GV, Feinberg AP. 2012. Reversible switching between epigenetic states in honeybee behavioral subcastes. *Nat Neurosci* 15(10):1371-1373.

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Fetal BPA exposure harms reproductive health in primates

A new primate study from NIEHS grantees adds more evidence that exposure to bisphenol A (BPA) can be disruptive to female reproductive systems. Although the study involved only a small group of animals, the findings support those from rodent studies and raise concerns about current levels of human exposure to BPA.

BPA is found in polycarbonate plastics and epoxy resins, and exposure can occur through consuming foods or beverages kept in packaging made with BPA. The researchers looked at how maternal levels of BPA, similar to those reported in humans, would affect the fetal ovary of rhesus monkeys. They assessed various durations and routes of exposure to BPA, including single daily doses of BPA and sustained low-level exposure.

The study's findings suggest that, like mice, the fetal primate ovary is sensitive to BPA. Specifically, the researchers found that when second trimester monkeys were exposed to BPA at the beginning of fetal egg cell meiosis, the egg cells failed to divide properly during the earliest stage of development. In monkeys exposed continuously, the researchers also observed complications in the third trimester, noting that the eggs in the fetus were not packaged appropriately in follicles. The problems with fetal egg development could potentially affect later reproductive success and longevity.

Citation: [Hunt PA, Lawson C, Gieske M, Murdoch B, Smith H, Marre A, Hassold T, Vandervoort CA. 2012. Bisphenol A alters early oogenesis and follicle formation in the fetal ovary of the rhesus monkey. Proc Natl Acad Sci U S A 109\(43\):17525-17530.](#)

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Assay quantifies effects of DNA damage on transcription

A new assay, developed by NIEHS grantees, could help explain how DNA damage from environmental chemicals leads to development of cancer and other diseases. The competitive transcription and adduct bypass (CTAB) assay quantifies how DNA damage effects the rate and fidelity of transcription, the process that converts DNA's genetic information into proteins. Using this information, investigators can assess how DNA damage hinders protein synthesis, leading to mutant proteins.

The researchers demonstrated the assay by showing how oxidative-induced DNA damage affected transcription *in vitro* and in mammalian cells. They say that the CTAB assay should be applicable for studying other types of DNA damage. It can also be used to examine proteins involved in DNA repair.

Citation: [You C, Dai X, Yuan B, Wang J, Wang J, Brooks PJ, Niedernhofer LJ, Wang Y. 2012. A quantitative assay for assessing the effects of DNA lesions on transcription. Nat Chem Biol; doi:10.1038/nchembio.1046. \[Online 19 August 2012\]. \[Story\]\(#\)](#)

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

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Intramural papers of the month

By Nisha Cavanaugh, Anshul Pandya, and Darshini Trivedi

- New treatment allows medicines to cross blood-brain barrier
- Neuromodulators may affect learning and memory
- Inverse relationship between allergy and heart attack
- Low-level p53 expression reveals supertransactivating response element sequences

New treatment allows medicines to cross blood-brain barrier

A new study by NIEHS researchers has identified a signaling pathway that reduces the transport activity of P-glycoprotein, an ATP-driven drug efflux pump in rat brain capillaries known to be a major obstacle to delivering medicines to the brain. The work may lead to new treatments for brain and spinal cord injury, brain cancer, and epilepsy in humans.

The research team used a confocal microscopy-based assay to identify a signaling pathway that abolished P-glycoprotein transport activity without changing transporter protein expression. In brain capillaries, this pathway uses sphingosine-1-phosphate (S1P) and its receptor, sphingosine-1-phosphate receptor 1 (S1PR1), to rapidly and reversibly reduce P-glycoprotein activity. The investigators used fingolimod, a drug used clinically to treat multiple sclerosis, to stimulate the S1PR1 signaling pathway in the blood-brain barrier, which turned off P-glycoprotein.

These findings were validated *in vivo* and led the researchers to conclude that signaling through S1PR1 can reduce P-glycoprotein activity and allow small molecule pharmaceuticals to safely cross the blood-brain barrier. (AP)

Citation: Cannon RE, Peart JC, Hawkins BT, Campos CR, Miller DS. 2012. Targeting blood-brain barrier sphingolipid signaling reduces basal P-glycoprotein activity and improves drug delivery to the brain. *Proc Natl Acad Sci U S A* 109(39):15930-15935.

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Neuromodulators may affect learning and memory

Scientists at NIEHS may have found a novel mechanism by which neuromodulators, such as acetylcholine (ACh), could enhance synaptic plasticity. Synaptic plasticity is the strengthening or weakening of synapses, and is a fundamental neurological mechanism that is thought to underlie learning and memory. This work helps scientists better understand how the brain processes and integrates higher brain functions.

Previous studies by the research group demonstrated that stimulation of the alpha7 nicotinic ACh receptors (nAChRs) can induce two forms of synaptic plasticity, long-term potentiation (LTP) and short-term depression (STD). In the current study, team members utilized a novel coculture, system comprised of septal tissue and hippocampus, to specifically express alpha7 nAChRs to either presynaptic or postsynaptic sites, or both, in alpha7 nAChR-deficient tissue, and dissect out the different roles of the alpha7 nAChRs in inducing LTP and STD.

The investigators found that coordination between both presynaptic and postsynaptic activities is required for the induction of alpha7 nAChR-dependent synaptic plasticity. Furthermore, the use of dual-colored genetically encoded calcium indicators indicated that the time course of presynaptic and postsynaptic changes during LTP or STD were different, suggesting that there are independent presynaptic and postsynaptic modulations during plasticity. **(DT)**

Citation: [Gu Z](#), [Lamb PW](#), [Yakel JL](#). 2012. Cholinergic coordination of presynaptic and postsynaptic activity induces timing-dependent hippocampal synaptic plasticity. *J Neurosci* 32(36):12337-12348.

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Inverse relationship between allergy and heart attack

In a recently published article, NIEHS researchers reported that people who have allergies, also known as atopy, are less likely to have experienced a heart attack. The study was based on laboratory data and questionnaires from the National Health and Nutrition Examination Survey (NHANES) 2005-2006, a cross-sectional analysis of the U.S. population. It is the first analysis of the relation between atopy, as indicated by serum allergen-specific IgE (sIgE) antibody, and previous myocardial infarction (MI).

Previous work in mice found that those born with a Th1-biased immune program developed atherosclerosis and other inflammatory diseases, while mice displaying a Th2 bias generally developed allergies and were protected from atherosclerosis. To determine what was happening in humans, the researchers measured sIgEs that were specific to 19 allergens, and found that individuals with a history of MI also had lower sIgE antibody levels and were less likely to have a positive sIgE test or hay fever. Detailed statistical analysis found that house dust mite was the only allergen for which sIgE was associated with a reduced chance of suffering an MI. These results, if confirmed in prospective studies, may have important clinical implications for how allergen sensitization affects people's risk for heart attack. **(AP)**

Citation: [Jaramillo R](#), [Cohn RD](#), [Crockett PW](#), [Gowdy KM](#), [Zeldin DC](#), [Fessler MB](#). 2012. Relation between objective measures of atopy and myocardial infarction in the United States. *J Allergy Clin Immunol*; doi:10.1016/j.jaci.2012.06.033 [Online 23 August 2012].

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Low-level p53 expression reveals supertransactivating response element sequences

Published in a recent issue of *Proceedings of the National Academy of Sciences*, NIEHS researchers provide a new understanding of how the transcription factor p53, a highly relevant tumor suppressor, interacts with its target sequences over a wide range of cellular p53 levels. In addition, they reveal new supertransactivating DNA sequences that are highly responsive at very low amounts of p53.

The researchers employed their previously developed yeast-based model system to examine cellular transcriptional activation from various target sequences in a constant chromatin environment in response to level of p53. These features were then compared to *in vitro* characteristics and interactions with p53.

Transactivation at higher levels of p53 follows thermodynamic binding properties. However, transactivation at low levels correlates with the torsional flexibility of the targets.

Surprisingly, they identified two supertransactivating sequences, Con-A and GGG, that supported high transactivation at very low p53 expression. These had the kinetic properties of high flexibility and also low off rate for p53. They found that Con-A could potentially serve as a diagnostic tool for functionality of p53 mutations, including those associated with breast cancer that they identified in an earlier study. (NC)

Citation: [Jordan JJ, Menendez D, Sharav J, Bono I, Rosenthal K, Resnick MA, Haran TE](#). 2012. Low-level p53 expression changes transactivation rules and reveals superactivating sequences. *Proc Natl Acad Sci U S A* 109(36):14387-14392.

(Nisha Cavanaugh, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Structural Biology. Anshul Pandya, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Laboratory of Neurobiology. Darshini Trivedi, Ph.D., is an IRTA fellow in the NIEHS Laboratory of Toxicology and Pharmacology.)

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Inside the Institute

CFC races toward \$115K goal

By Eddy Ball

With proceeds from a bake sale Oct. 2, the Combined Federal Campaign (CFC) at NIEHS had raised nearly \$32,200, as of Oct. 29, toward its 2012 goal. CFC brought in an additional \$700 from its book sale in late October.



This year's co-chairs, Office of Management employees [Claire Long](#), a member of Associate Director for Management Joellen Austin's staff, and [Scott Redman](#), from the Financial Management Branch, called for employees to keep on making pledges.

"We're 26.7% of the way toward our ambitious goal of \$115,000," said Long. She and Redman praised the generosity of employees so far in the campaign, but also emphasized that the community still needs help from pledges during the final six weeks of the campaign, which will end Dec. 15.

To make giving as satisfying and easy as possible, the drive has a website accessible through the NIEHS intranet, where employees can link to the Greater North Carolina Area CFC pledge [site](#) and watch videos about the charity of the week.

Following the Halloween Fun Run/Walk with employees of the U.S. Environmental Protection Agency Oct. 31, the CFC will hold its Ice Cream Social Nov. 20, from 2:30-3:15 p.m., in the NIEHS cafeteria.



During the CFC bake sale, Voldness, right, sang the praises of baked goods to shoppers, left to right, Debra Cherry, Spencer Bridges, and Katrina Loper. (Photo courtesy of Steve McCaw)

Pledging is easy

Online — Visit the official website of the [Greater North Carolina Area CFC](#) to pledge, authorize payroll deductions, and find out more about participating charities.

Contact NIEHS division chairs — More information about CFC, pledging, and participating charities is available just an email or phone call away by contacting these volunteers:

[Elizabeth Ruben](#), Division of Extramural Research and Training

[Bob Petrovich](#), Division of Intramural Research

[Eli Ney](#) and [Pat Stockton](#), Division of the National Toxicology Program

[Debbie Wales](#), Office of the Director

[Dona McNeill](#), Office of Management

[Leigh Voldness](#), Office of Research Facilities

[Delise Mahoney](#), Office of Human Resources



NIEHS contractor Michelle Heacock, Ph.D., took advantage of the book sale in Keystone, to shop for things for her family. (Photo courtesy of Steve McCaw)



The bake sale also showcased local charities. Kenneth Newkirk of Durham Rescue Mission, left, explained his organization's mission to NIEHS postdoctoral fellow Sheila Yong, Ph.D. (Photo courtesy of Steve McCaw)

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Memorial to Frank Kari dedicated at University of Illinois

By Eddy Ball

Following the untimely death in 2007 of NIEHS/NTP toxicologist Frank Kari, Ph.D., at age 55, friends at NIEHS planted a red bud tree in his honor in the Institute's lakeside memorial gardens ([see story](#)) and later installed a plaque in his memory. Today, that tree thrives in Research Triangle Park, N.C., and, farther north, visitors are enjoying more of the University of Illinois (UI) Arboretum, thanks to his family's support of the [Dr. Frank W. Kari Walkway and Ponds Restoration Project](#).

In an Oct. 1 message to several of Kari's longtime friends, including NTP research physiologist Jef French, Ph.D., Steven Clinton, M.D., Ph.D., a professor at The Ohio State University Comprehensive Cancer Center announced the dedication Sept. 27 of a walkway around the once neglected Arboretum ponds, which were restored with funds from the project.

"The Frank W. Kari Walkway and Ponds Restoration project provides a look at various types of native plant communities found in Illinois," Clinton wrote. "Work on the ponds involved removing invasive plants and cattails, grading and mulching the banks, planting new beds along the banks, and installing over 26,000 plantings.

In addition to the walkway, native plants and trees were planted adjacent to the ponds, and benches and educational signs were placed along the walkway. An endowment provides ongoing care for the plants, signs and walkway."



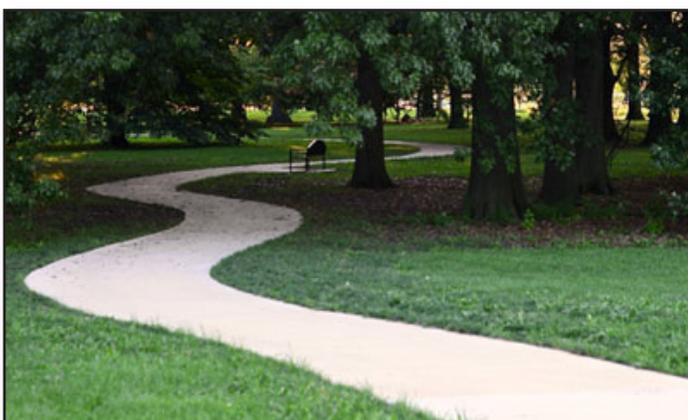
A robust Kari before his illness (Photo courtesy of Steve McCaw)

When he died March 26, 2007, Kari had worked for NIEHS and NTP for 21 years. His final two years were spent in declining health, as he struggled with a rare variant of multiple myeloma known as plasma cell leukemia. During this period, he participated as a volunteer in clinical research trials and underwent multiple courses of chemotherapy, as well as a stem cell transplant.

As he concluded his message, Clinton described Kari as a gifted researcher with a unique ability to dissect and interpret scientific data. “As a mentor, he impacted many in training, serving as an extraordinary role model, maintaining a youthful and inquisitive approach to research, while always embracing new concepts or technology,” Clinton wrote. “His life was also enriched by numerous and diverse interests, ranging from traditional and bluegrass music, stained glass artistry, and woodworking. Most notably, Dr. Kari’s lasting legacy is the devotion to his family and the treasured friendship he provided to so many, which profoundly defined the character of the man.”



Kari is remembered at waterside gardens in Illinois, above, and North Carolina. (Photo courtesy of Steven Clinton)



The new walkway takes visitors around the ponds and through the forests surrounding them. (Photo courtesy of Steven Clinton)

A rich life in science and a dedication to public health

By Steven Clinton

Frank Kari was born in Evanston, Ill., and attended the University of Illinois (UI), where he received his B.S. and later completed his Ph.D. in the Division of Nutritional Sciences in 1981. After finishing his undergraduate work in 1974, he worked as a chemist for the Illinois Environmental Protection Agency, prior to returning to UI for his graduate training in 1977.

Kari conducted his thesis work under the mentorship of Willard Visek, Ph.D., currently a professor emeritus in the UI department of food science and human nutrition. Kari established a research program focusing upon the role of diet and nutrition in modulating the host response to environmental toxins and carcinogens, a theme that would resonate throughout his research career.

Following his training at UI, Kari pursued postdoctoral studies at the University of North Carolina at Chapel Hill (UNC-CH) as a recipient of a National Cancer Institute Fellowship in the laboratory of the late [Ron Thurmond, Ph.D.](#)

In 1985, Kari was recruited to NIEHS as a research toxicologist in the National Toxicology Program. He later also became an adjunct assistant professor in the UNC-CH department of nutrition. During his career, Kari contributed to over 60 peer-reviewed journal publications, reviews, book chapters, and NTP Technical Reports.

Kari enthusiastically reviewed scientific manuscripts for leading journals and gave numerous invited lectures and seminars. For his accomplishments, he received recognition and a number of awards from the U.S. Public Health Service, National Institutes of Health, and NIEHS.



NIEHS volunteer biologist Betsy Kennington, center, and French placed the first few shovelfuls of dirt, as they planted Kari's tree in 2007. (Photo by Eddy Ball)



Along with the tree planted in tribute to Kari, his friends at NIEHS and NTP later placed a plaque on the wall of memory in the garden on campus. (Photo courtesy of Steve McCaw)

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Durham Magazine highlights NIEHS/EPA early learning center

By Eddy Ball

This summer, Durham Magazine writer Mark Griffin profiled the [First Environments Early Learning Center](#) in a story titled “[Eat \(And Grow\) Your Veggies.](#)”



Linked video:

[Watch Mark Griffin's video of young gardeners in action at the First Environments Early Learning Center on the NIEHS/EPA campus \(01:10\)](#)

(Launches in new window)

Download Media Player: Flash [⌵](#)

The five-star childcare center, established in 1986 and located on the U.S. Environmental Protection Agency (EPA) Research Triangle Park campus since 2005, serves children of employees and contractors at NIEHS and the EPA. Each year, students and teachers grow more than 600 pounds of pesticide-free produce in the center's garden, and use the fresh vegetables for meals during the growing season.

Sustainability is an important part of the First Environments learning experience, for its nearly 200 infants, toddlers, and preschool children. In addition to its gardening program, the center features recycling and conservation activities, and uses rooftop solar panels to produce electricity for its facility and for resale to the grid.

NIEHS Employee Services Manager Dona McNeill is the NIEHS daycare liaison.



The big people gathered the gardening team together. McNeill, left, is a frequent visitor to First Environments. Outdoor Learning Environment Specialist Sue Esperson, right, supervises the tending. (Photo courtesy of Mark Griffin)



First Environments teaches important lessons about the natural world. This young gardener turned out in a color-coordinated outfit and watering can. (Photo courtesy of Mark Griffin)



Esperson led the children in hands-on learning about helping plants grow. (Photo courtesy of Mark Griffin)



The rewards are tangible and immediate, as children prepare to eat the produce they have just helped to nurture. (Photo courtesy of Mark Griffin)

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