

June 2011

## NIEHS Spotlight



### [NIEHS leaders set the tone at Health Affairs briefing](#)

NIEHS/NTP Director Linda Birnbaum, Ph.D., and Director Emeritus Ken Olden, Ph.D., led off an impressive list of speakers May 4 in Washington, D.C.



### [Council updated on several NIEHS research initiatives](#)

At its meeting May 19-20, the National Advisory Environmental Health Sciences Council was briefed on the progress of a number of NIEHS initiatives.



### [NTP achieves division status at NIEHS](#)

In an April 28 Federal Register announcement, NIH Director Francis Collins, M.D., Ph.D., officially established the Division of the National Toxicology Program.



### [WETP workshop explores lessons learned from the Gulf oil spill](#)

The workshop “Deepwater Horizon Lessons Learned: Improving Safety and Health Training for Disaster Cleanup Workers” convened May 3-5 in Mobile, Ala.



### [Breast cancer advisory panel making good progress](#)

The committee is charged with delivering a comprehensive report on federal research in breast cancer and the environment.

## Science Notebook



### [Liu discusses a systems biology approach to breast cancer](#)

Edison Liu, M.D., outlined a novel integrative genomics and systems biology approach to breast cancer during his 2010-2011 NIEHS Distinguished Lecture Series presentation.



### [Taking the pulse of toxicogenomics at GEMS](#)

The Genetics and Environmental Mutagenesis Society (GEMS) welcomed a series of speakers with ties to NIEHS and EPA working in the emerging field of toxicogenomics.



### [NIEHS holds symposium on the proteins of aging](#)

The event, “Sirtuins in Aging and Age-associated Diseases,” focused on a genetic pathway controlled by a group of proteins called sirtuins.



### [Williams discusses the effects of neonatal phytoestrogen exposure](#)

Members of the National Advisory Environmental Health Sciences Council enjoyed a scientific talk May 19 by NIEHS Principal Investigator Carmen Williams, M.D., Ph.D.



### [Health Affairs highlights environmental health science and policy](#)

The peer-reviewed journal Health Affairs made history in May with its first thematic issue ever devoted exclusively to environmental health research.

## NIEHS Spotlight



### [2011 Biomedical Career Fair draws capacity audience](#)

NIEHS held its 14th annual Biomedical Career Fair April 29 at the U.S. Environmental Protection Agency conference center in Research Triangle Park.



### [International workshop deliberates on indoor air pollution, cook stoves](#)

An international workshop convened May 9-11 to discuss current evidence on adverse health effects of indoor air pollution and exchange views on improving human health.



### [Kissling to be honored by American Statistical Society](#)

Grace Kissling, Ph.D., will receive the highest honor in her field for what the ASA described as “outstanding contributions to the statistical profession.”



### [Postdoc to head computational biology group at Indian institute](#)

For NIEHS Visiting Fellow Sailu Yellaboina, Ph.D., June brings a trip home, a family reunited, and a position as an associate professor on the campus of his alma mater.



### [NIH grantee receives Wisconsin Regents Teaching Excellence Award](#)

The University of Wisconsin announced May 4 that Craig Berg, Ph.D., is one of two individual winners of the 2011 Regents Teaching Excellence Award.

## Science Notebook



### [NIEHS study explains rapid transcription of immediate early genes in the brain](#)

The team of NIEHS researchers demonstrated that RNA Polymerase II stalling renders a kinetic advantage to transcription of rapidly induced immediate early genes in brain.



### [Failed experiment leads to big discovery](#)

NIEHS grantee Michael Skinner, Ph.D., spoke May 10 on his discovery and how it has shifted the field of genetics, as part of the Keystone Science Lecture Seminar Series.



### [LMG speaker explores BRCA signaling network](#)

Understanding genomic instability early on may offer insight into the many factors involved in cancer, according to biologist Roger Greenberg, M.D., Ph.D.



### [Early prenatal vitamins may decrease incidence of autism](#)

A study finds that mothers of children with autism were less likely to report having taken prenatal vitamins during the three months before and the first month of pregnancy.



### [Arsenic and smoking synergistic. Superfund study shows](#)

Researchers find that arsenic exposure increases a person's risk of dying from cardiovascular disease, and that the effect is magnified up to sixfold in smokers.

## NIEHS Spotlight



### [NIEHS receives five plain language awards](#)

NIEHS was among the NIH centers and institutes recognized at the 2010-2011 NIH Plain Language/Clear Communication Awards Ceremony May 17 in Bethesda, Md.

## Inside the Institute



### [NIEHS celebrates Earth Day](#) Video

NIEHS celebrated Earth Day 2011 on May 4 in the Rall Building on the main campus and May 5 at its Keystone satellite facility.



### [Laughter lecture kicks off Health and Fitness Week](#) Video

Henry Lesesne, M.D., gave a lecture on the power of laughter as medicine May 9 in Rodbell Auditorium, followed by a round of "laughter yoga."



### [Employees enjoy rites of spring during Health and Fitness Week](#)

NIEHS offered a slate of activities encouraging employees to practice a healthy lifestyle through exercise, balanced nutrition, and weight management.



### [Kids enjoy mostly indoor activities on Take Your Family to Work Day](#)

The threat of rain canceled the outdoor activities planned for Take Your Family to Work Day May 16, but there was still plenty left to do.

## Science Notebook



### [New study estimates heat wave mortality from climate change](#)

Researchers used climate change models and local historical data to predict the potential impact of warming on human mortality in the Chicago metropolitan area.



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

The lead news story in Environmental Health Perspectives this month explores the current state of the science on autoimmune disease and its connection to the environment.



### [Upcoming Rodbell lecturer Brigid Hogan](#) Video

Noted developmental biologist Brigid Hogan, Ph.D., will deliver the 2011 Martin Rodbell Lecture on stem cells and lung disorders June 14 at NIEHS.



### [Upcoming bioinformatics conference to be held at UNC Friday Center](#)

The third Toxicogenomics Integrated with Environmental Sciences Conference will take place Sept. 15-16 at the William and Ida Friday Center in Chapel Hill, N.C.

## Calendar of Upcoming Events

- **June 2**, Webinar, Partnerships in Environmental Public Health, 3:30-4:30 p.m. — ECO Youth: Education and Community Advocacy by Providence High School Students, [register](#)
- **June 3**, in Keystone 1003AB, 10:00 a.m.-11:00 p.m. — Keystone Science Lecture Seminar Series presentation on “Biomarkers for Parkinson Disease - The Quest for the Holy Grail?” featuring Jing Zhang, M.D., Ph.D.
- **June 4-8 (offsite event)**, at the Raleigh Convention Center, Raleigh, N.C. — Society for In Vitro Biology Annual Meeting, [register](#)
- **June 9**, in Rodbell Auditorium, 9:00 a.m.-5:00 p.m. — Conference: “Emerging Concepts in T Cell Activation and Disease”
- **June 14**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Rodbell Lecture with Brigid Hogan, Ph.D., exploring “New Perspectives on Stem Cells and Lung Disorders”
- **June 15**, in Rall F-193, 11:00 a.m.-12:00 p.m. — Laboratory of Neurobiology Seminar Series with Malgorzata Dukat, Ph.D., topic TBA
- **June 16-17 (offsite event)**, at the Hilton Arlington in Arlington, Va., 8:30 a.m.-5:00 p.m. — Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) Meeting
- **June 27**, in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — Engineered Tissue Models for Environmental Health Sciences Research
- **June 30**, in Keystone 1003AB, 1:00-2:00 p.m. — Keystone Science Lecture Seminar Series, featuring Greg Diette, M.D., topic TBA
- View More Events: [NIEHS Public Calendar](#)

## Extramural Research

### [Extramural papers of the month](#)

- [Water purifier harnesses nanotechnology](#)
- [Elevated blood levels of flame retardants in Mexican-American children](#)
- [Ah receptor activation delays development of chemical-induced mammary tumors](#)
- [Risk of bladder cancer higher in diabetics](#)

## Intramural Research

### [Intramural papers of the month](#)

- [Innate immunity linked to DNA damage response](#)
- [Human PUMILIO proteins adopt multiple RNA binding modes](#)
- [Separation of function mutations identified in estrogen receptor alpha](#)
- [Estimating relative risk in epidemiological studies using imputed data sets](#)

# NIEHS Spotlight

## NIEHS leaders set the tone at Health Affairs briefing

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., and Director Emeritus Ken Olden, Ph.D., led off an impressive list of speakers at a briefing May 4 in Washington, D.C. The groundbreaking event, hosted by the journal Health Affairs made possible by a grant from the Kresge Foundation ([see related story](#)), launched the first thematic issue devoted exclusively to environmental health during the publication's 30-year history.

Moderated by Editor-in-Chief Susan Dentzer, the [briefing](#) was designed to educate Health Affairs readers and supporters about an area of health that Dentzer described as long-neglected, underappreciated, and incompletely understood by many people. "There's plenty that we already know," she told the audience, "but there's a lot more to know, as this issue makes clear." Dentzer pointed to estimates that the environment is involved in as much as 85 percent of disease at a cost of nearly \$77 billion per year, to underscore the magnitude of the public health challenge ahead.



*"Efforts to protect health by stimulating health behaviors and improving environmental conditions represent the best and perhaps only strategy for slowing the growth of disease prevalence," Dentzer maintained in her opening remarks. "[Otherwise] the direct and indirect cost of [chronic disease] could easily overwhelm any other efforts to bend the cost curve of health care." (Photo courtesy of Health Affairs)*

**Linked video:**  
[See Birnbaum and others at the Health Affairs briefing](#)  
(Launches in new window)

Download Media Player: Flash [↗](#)

### Getting basic about the challenges of environmental health

Following her introductory remarks and comments from David Fukuzawa, director of [The Kresge Foundation's Health Program](#), Dentzer turned to the overview panel, featuring Birnbaum, Olden, and [Rachel Morrello-Frosh, Ph.D.](#) The keynote speakers introduced important concepts in environmental health and proposed changes in policy to better safeguard the public from environmental



*Birnbaum's introduction to the wide range of factors that constitute the environment set the tone for overview panel presentations and introduced themes that the daylong program of speakers would explore in their talks. (Photo courtesy of Health Affairs)*

factors that cause disease, such as reforming the Toxic Substances Control Act and striving to achieve environmental justice for all.

As the first panelist to speak, Birnbaum opened her presentation by describing the broad and complex range of factors that constitute the environment and introduced an important conceptual shift now driving health research through the paradigm of “many genes, many diseases, many exposures.” Describing factors such as industrial chemicals, diet, drugs, the microbiome, psychosocial stress, and climate change, as well as their interactions and their effects on gene expression, she argued, “We’ve got to move beyond looking at one exposure at a time and think cumulatively.”

“Chronic diseases in general have extremely complex etiologies and we need to remember that,” Birnbaum continued. She also discussed the concept of windows of susceptibility and why timing makes a major difference in the effects of exposures.

### **Epigenetic changes that lead to disease**

Olden followed Birnbaum with his talk on epigenetic changes that impose another layer of control superimposed on the genetic code. “Genetics is not the only risk factor,” Olden said. “Enough emphasis has not been placed on identifying the risk factors in the other areas.”

As Olden explained, “The epigenome is all the chemical tags that are added to chromatin or to histones, creating a physical structure that influences translation of genes.” He compared the epigenome to the punch cards once used in computer programming, and to the role of a choreographer of a ballet troupe who decides which of the many routines in its repertoire is performed at a given venue. Olden predicted that understanding the collaboration of the genome and epigenome will be the central challenge in medical research over the next fifteen years.

### **The quest for environmental justice**

Toward the end of his talk, Olden made a statement about the epigenetic effects of social exposures that served as a transition to the final speaker of the day, toxicologist and environmental justice advocate Morello-Frosch, who outlined the role of psychosocial stress in amplifying the effects of other exposures to trigger disease.



*“The environment plays a major role in reprogramming the epigenome,” Olden explained, seated with Morello-Frosch. “We believe there will be neighborhood-specific epigenetic signatures and possibly disease-specific epigenetic signatures.” (Photo courtesy of Health Affairs)*



*“We cannot just regulate one chemical at a time,” Morello-Frosch insisted, as she called for regulatory reform, a better understanding of cumulative impacts, and environmental parity. “Place matters. Our neighborhoods matter.” (Photo courtesy of Health Affairs)*



*A diverse audience engaged the speakers, following the panel presentation. (Photo courtesy of Health Affairs)*

“[The] cumulative impacts [approach] really talks about a triple jeopardy,” Morello-Frosch said, “of the ways in which social inequalities create health disparities through environmental exposures and social stressors .... We know enough now to start screening and to take precautionary action to reduce exposures and to ameliorate some of these social factors that are definitely fixable.”

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## Council updated on several NIEHS research initiatives

*By Ernie Hood*

At its meeting May 19-20 at NIEHS, the [National Advisory Environmental Health Sciences Council](#) was briefed on the progress of a number of NIEHS initiatives. In its only voting action, the panel approved a sweeping concept clearance (see [text box](#)) designed to provide for continuation of the research work conducted by the [NIH Genes, Environment and Health Initiative \(GEI\)](#) through NIEHS funding.

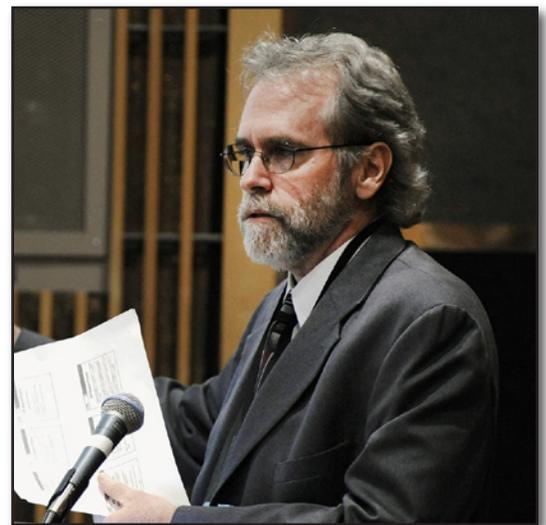
### Advancing clinical research

Joan Packenham, Ph.D., director of the [NIEHS Office of Human Research Compliance \(OHRC\)](#), updated Council on NIEHS efforts to protect human research subjects. She noted that to provide an integrated approach to human research subjects’ protection as the institute was beginning its clinical research program, in 2008 the institute established the OHRC, which manages the NIEHS Human Research Protection Program (HRPP). Packenham mentioned that NIH is preparing for accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). The accreditation process is under the leadership of the NIH Office of Human Subjects Research Protections, under the direction of Michael Gottesman, M.D., NIH Deputy Director for Intramural Research.

As Packenham explained, the NIEHS role is to make sure that NIEHS has a high quality HRPP that meets the goals, principles, and standards outlined by AAHRPP and is in compliance with NIH HRPP regulations. NIEHS serves as a leader in this process and has been invited to participate on several trans-NIH committees as NIH refines its HRPP policies and procedures. NIH will submit the application for accreditation sometime in 2011. The Association for the Accreditation of Human Research Protection Programs, the gold seal for human research protection programs, “gives assurance to research participants, research organizations, researchers, sponsors, and the general public that an organization’s HRPP is focused first and foremost on excellence, safety, and ethically sound research.”



*Balshaw had good reason for elation, as the Council approved the concept clearance to extend development work on research pioneered in the GEI. (Photo courtesy of Steve McCaw)*



*DETR Deputy Director Pat Mastin, Ph.D., briefed the Council on the new NIH appeals process, which applies to grant applications submitted for the January 25, 2011 due date and*

## Exploring the epigenome

NIEHS extramural investments in research on environmental epigenetics and epigenomics were the subject of a presentation by Fred Tyson, Ph.D., of the Cellular, Organ, and Systems Pathobiology Branch of the Division of Extramural Research and Training (DERT). He explained that research investments are growing rapidly because of increasing recognition that “the epigenome serves as the interface between the genome and environment in common complex human diseases.” Extramural investments have expanded exponentially since 1998, he said, and have included several targeted solicitations, including two still in development; many investigator-initiated grants; grants within the NIH Roadmap Epigenomics Program, specifically funding Epigenome Mapping Centers; and a variety of well-attended international meetings and workshops.



*Birnbaum alerted Council to the latest edition of the journal Health Affairs (see related story ), which for the first time was devoted entirely to articles on environmental health science, including contributions by Birnbaum and her Chief of Staff, Paul Jung, M.D., former NIEHS Director Kenneth Olden, Ph.D., and several NIEHS grantees. (Photo courtesy of Steve McCaw)*

## Confronting the epidemic of autism

Autism is another relatively new frontier for environmental health research, and DERT Health Science Administrator Cindy Lawler, Ph.D., who specializes in autism research, provided Council with a guided tour of the investments that NIEHS has made in addressing this very urgent public health concern. She pointed to the many significant developments in recent years, such as establishment of the [Interagency Autism Coordinating Committee](#), which is comprised of both public members and federal officials, including NIEHS/NTP Director Linda Birnbaum, Ph.D., and NIH Director Francis Collins, M.D., Ph.D. The NIEHS autism portfolio now includes large-scale human studies such as [CHARGE](#) and [EARLI](#), which will enable reliable identification of environmental risk factors and gene-environment interplay involved in the development of autism.



*The 133rd meeting of the Council was held May 19-20 at NIEHS. (Photo courtesy of Steve McCaw)*

## Addressing climate change and health issues

Senior Advisor for Public Health John Balbus, M.D., briefed Council on NIEHS efforts to integrate human health with research endeavors on global climate change and sustainability. He noted that it had been precisely one year since Council had approved the [NIEHS Human Health Impacts of Climate Change \(HHICC\) program](#), the first within NIH. “Through our research grant-making, we are taking a major step to build [a] community of climate change researchers who will ultimately be informing policy both in this country and around the world,” said Balbus.



*According to Packerham, NIEHS currently has 61 active clinical protocols subject to Institutional Review Board oversight. (Photo courtesy of Steve McCaw)*

## Shaping a vision for NIEHS

NIEHS Deputy Director Richard Woychik, Ph.D., reported on recent developments in the Institute's strategic planning process. With its first phase aimed at gathering broad-based stakeholder input, the first mechanism to do so was the opportunity to submit visionary ideas to the [New Strategic Plan Web site](#). Woychik called the response "wildly successful."

Woychik also noted that nearly 600 nominations had been received for the stakeholder community workshop in July. The process of selecting, inviting, and securing attendance commitments from 200 individuals representing a cross-section of the global environmental health sciences community should be completed by the end of May, he said.

The panel was also briefed on recent NIEHS and DERT activities and accomplishments by NIEHS/NTP Director Linda Birnbaum, Ph.D. and DERT Director Gwen Collman, Ph.D., and met in closed session to consider grant applications. The members also enjoyed a scientific presentation by NIEHS Principal Investigator Carmen Williams, M.D., Ph.D. ([see related story](#)).

The Council will meet again September 1-2.



*Council member Mary Lee, M.D., from the University of Massachusetts Medical School, made a point about strategic planning during Council discussion. (Photo courtesy of Steve McCaw)*



*Frederick Tyson updated Council on NIEHS/DERT investment in environmental epigenetics and epigenomics, a hot area of scientific activity. (Photo courtesy of Steve McCaw)*

## Council approves next steps for gene-environment efforts

David Balshaw, Ph.D., a program administrator in the DERT Center for Risks and Integrated Sciences who has been one of the administrators of the Exposure Biology Program — the environmental side of the GEI led by NIEHS — told Council that, although the GEI has had tremendous successes, its four-year timeline was not sufficient to accomplish its lofty goal of comprehensively integrating genetics and environmental exposures ([see related story](#)). He said there is more work to be done before the integration can truly be accomplished. As fellow DERT Health Science Administrator and co-presenter Kimberly McAllister, Ph.D., put it, "The ultimate goal of the new proposed activities is to try to demonstrate the value of putting together the genetics and the environmental factors for disease risk."

The team proposed six initiatives, all to be conducted and funded in partnership with sister NIH institutes that were also involved with the GEI. The projects address three identified gaps in the research: continued development of tools for exposure biology (such as sensors and biomarkers), proof of principle studies designed to integrate genetics with environmental studies and vice versa, and functional analysis of gene-environment interactions. Collman pointed out that the projects would probably span five to ten years, so that the activities would build upon each other and establish continued momentum.

Oregon Health and Science University professor and Council member Stephen Lloyd, Ph.D., left no doubt about how he felt about the proposal. "This is a long-term but extremely important commitment by this institute... It's so integral and germane to the NIEHS mission [that] it's something we can't possibly punt on." His Council colleagues agreed, voting unanimously to approve the concept.

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

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# NTP achieves division status at NIEHS

By Eddy Ball

In an April 28 Federal Register [announcement](#), NIH Director Francis Collins, M.D., Ph.D., officially announced establishment of the Division of the National Toxicology Program (NTP), which was formerly a program within the NIEHS Division of Intramural Research (DIR). The announcement is the final step in NTP officially becoming a division at NIEHS, and it marks the achievement of an important goal for NIEHS/NTP Director Linda Birnbaum, Ph.D., the first board-certified toxicologist to serve as the Institute's leader.

In addition to NIH approval, the reorganization was approved by HHS Secretary Kathleen Sebelius. Congress was also notified, since this was one of the first reorganizations that occurred under the [NIH Reform Act of 2006](#), requiring a number of additional steps for Institute reorganizations.

In her email message to employees, Birnbaum outlined the benefits of the reorganization. "The new structure will promote greater efficiency at NIEHS, by making a clear staffing and budgetary demarcation between those components of the NIEHS carrying out work dedicated solely to the pursuit of the goals and initiatives of the NTP, and those principal investigator-initiated efforts carried out by staff in the DIR," she wrote.

The new organizational structure, which became effective Feb. 22, retains four of the previous branches — Biomolecular Screening, Cellular and Molecular Pathology, Program Operations, and Toxicology. Newly established is the NTP Laboratory reflecting the important role of targeted in-house research in achieving NTP objectives.

In addition to holding the position of associate director of NTP, John Bucher, Ph.D. will now serve as the director of the Division of the National Toxicology Program.

"I am very pleased to be overseeing the day-to-day activities of this new division," said Bucher. "Having divisional status provides recognition of the unique mission and goals of the NTP within NIH, and the unique capabilities and talents of our staff."

Learn more about the new division by visiting the organizational chart [online](#).

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*Shown above at the January meeting of the NTP Board of Scientific Counselors, Birnbaum has taken an active role in board and technical review peer review meetings. She generally attends the entire meeting, makes a presentation as director of NTP — now the Division of NTP — and participates in board discussions and question-and-answer sessions. (Photo courtesy of Steve McCaw)*



*NTP gathered for a recent group photo at NIEHS with Birnbaum, first row center, in burgundy sweater and print skirt. (Photo courtesy of Steve McCaw)*

# WETP workshop explores lessons learned from the Gulf oil spill

By Ryan Campbell

The NIEHS Worker Education and Training Program (WETP) workshop “Deepwater Horizon Lessons Learned: Improving Safety and Health Training for Disaster Cleanup Workers” convened May 3-5 in Mobile, Ala.

The intensive [workshop](#) brought together many people involved in responding to the Deepwater Horizon oil spill, including NIEHS WETP awardees, federal agency staff, and community leaders, as well as British Petroleum (BP) personnel and contractors. Approximately 120 people attended the three-day event.

## The federal perspective

In opening remarks, WETP Director Joseph “Chip” Hughes spoke about the decisions made during the oil spill. He highlighted a recent U.S. Coast Guard report that set, as a future goal, a more ideal safety culture, including comprehensive training for both platform workers and cleanup workers. He acknowledged the value of input from the U.S. Department of Labor Occupational Safety and Health Administration (OSHA) on the right to understand for training those whose first language is not English. As part of the Unified Command Team, NIEHS developed training materials in English, Spanish, and Vietnamese during the initial response.

John Ferris, of the [OSHA Directorate of Technical Support and Emergency Management](#), highlighted the differences between the Deepwater Horizon response effort and more typical natural disaster responses. Ferris said that for an oil spill response, the responsible party for the disaster, in this case BP, plays the central role, although the U.S. Coast Guard, U.S. Environmental Protection Agency, and OSHA still have major responsibilities. Ferris also emphasized the importance of partnerships with local officials.

In her keynote address, [Linda Birnbaum, Ph.D.](#), NIEHS/NTP director, highlighted NTP efforts to research the effects of the crude oil and dispersants. She noted that there are eight other U.S. Department of Health and Human Services components researching the health impacts of the oil spill, that NIEHS quickly issued a number of time-sensitive grants related to the spill, and that webinars and meetings have been held in the Gulf region to promote stakeholder involvement and awareness. Birnbaum closed by describing the recently launched GuLF STUDY (Gulf Long-term Follow-up Study), an NIEHS health study specifically for workers and volunteers who helped clean up the Deepwater Horizon oil spill ([see story](#)).



*Hughes, standing, made his opening remarks as WETP Program Analyst Jim Remington watched. Hughes described the worker training WETP facilitated for the Deepwater Horizon oil spill response, compared to previous disasters, especially considering the size of the workforce involved. (Photo courtesy of MDB)*



*Ferris said that in the future, agencies must work closer with responsible parties to protect workers and commit to obtaining a greater number of skilled and trained workers. (Photo courtesy of MDB)*

## The community perspective

The first plenary panel of the workshop gave voice to the diverse perspectives of communities affected by the Deepwater Horizon oil spill. Grace Scire, area director of [Boat People SOS-Gulf Coast](#), a non-profit Vietnamese support organization, discussed the language barriers associated with training Vietnamese populations in the Gulf region. She advocated that community groups be integrated into the response process as early as possible.

Lizzie Grossman, an independent journalist in the Gulf region, said that at times she experienced delays in obtaining information, and suggested that both government agencies and the responsible party need to provide more information sooner to reporters and residents.

## Lessons learned on the front lines

The second plenary panel, “On-Site Lessons Learned,” consisted of a fishing boat captain, a worker safety advisor, and a representative from BP. Captain Bob Zales, president of the [National Association of Charterboat Operators](#), who was hired by BP for cleanup operations at sea, emphasized the importance of locally obtained knowledge and skills when working in the often-tricky currents and tides of the Gulf of Mexico. Zales said local crewmen know Gulf navigation best and can assist with logistical coordination during a disaster.

David Coffey, lead for the NIEHS-funded [The New England Consortium](#) at the University of Massachusetts Lowell, was a worker safety advisor and performed on-site evaluations in the Gulf region. He observed a need for more educational materials, training provided in additional foreign languages, and a better understanding by trainers of conditions at the disaster site itself.

Tamara Joslin, incident training lead for BP, described the partnerships and contractors utilized by BP, while highlighting the company’s training matrix used to identify the various modules of training required.

## Workshop summary in production

A report on the entire workshop including the recommendations focused on best practices, training and community resources and tools, and additional steps for improving response efforts during a disaster, is currently in preparation.

(Ryan Campbell is on the staff of MDB, a contractor for the WETP and NIEHS Superfund Research Program.)



*Grossman emphasized the need for real-time communication during a disaster, as well as the need for better communication and trust between all the parties involved. (Photo courtesy of MDB)*



*Mary Williams, program manager for community outreach at the NIEHS-funded Deep South Center for Environmental Justice at Dillard University, offered insight into the spill’s impact on the people of the region. (Photo courtesy of MDB)*

## For the record, looking ahead

On the final day of the workshop, attendees divided into three structured breakout sessions: community involvement during disasters, site-specific training, and pre-deployment training. These sessions focused on best practices, training and community involvement resources and tools, and additional steps for improving response efforts during a disaster.

NIEHS WETP sincerely thanked all of the participants for their candor and thoughtfulness during this extensive workshop evaluation of response efforts in the aftermath of the April 20, 2010 explosion and subsequent months-long oil spill.

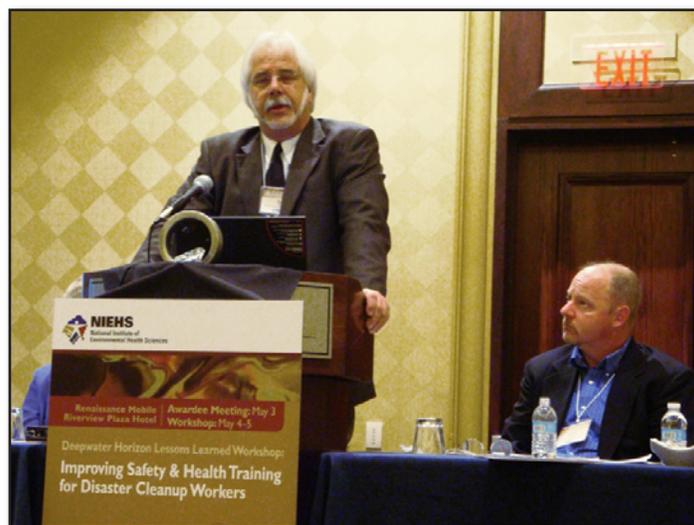
Created in 1986 under the Superfund Amendments and Reauthorization Act, WETP funds non-profit organizations with a demonstrated track record in developing and delivering hazardous waste operation and emergency responder training under the standards implemented by OSHA.



*NIEHS Senior Medical Advisor Aubrey Miller, M.D., moderated a panel on medical monitoring and surveillance efforts in the aftermath of the oil spill. (Photo courtesy of MDB)*



*Joslin offered the perspective of the systems implementation team at BP on lessons learned from the historic oil spill. (Photo courtesy of MDB)*



*Zales, standing, advocated for having workers trained prior to the next disaster occurrence. Seated beside him, Coffey prepared to speak about training gaps. (Photo courtesy of MDB)*

# Breast cancer advisory panel making good progress

By Ernie Hood

It was only the second face-to-face meeting of the 19-voting-member Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC) since it was formed in 2010 ([see story](#)), but the group's conference May 12-13 at NIEHS in Research Triangle Park, N.C., marked a significant step forward in its appointed tasks.

The committee, which was created by congressional mandate in 2008 and is led by NIEHS in collaboration with the National Cancer Institute (NCI), is charged with delivering a comprehensive report on federal research in breast cancer and the environment to the Secretary of the Department of Health and Human Services. The panel and its three subcommittees have met frequently by teleconference in recent months, but Gwen Collman, Ph.D., NIEHS director of the Division of Extramural Research and Training and co-executive Secretary of the IBCERCC noted, "As people get to know each other better through their interactions on the phone, there's nothing that replaces face-to-face conferencing and discussing the issues. It's really great to see all of the progress we were able to make, and it was very gratifying to see that everybody had their sleeves rolled up and were ready to go," she said. "I think we accomplished a lot."



*NIEHS/NTP Director Linda Birnbaum, Ph.D., was obviously delighted with the substantial progress made by the IBCERCC at its May 12-13 meeting. (Photo courtesy of Steve McCaw)*

## Subcommittee updates

The three subcommittees—State-of-the-Science, Research Process, and Research Translation, Dissemination and Policy Implications—are each responsible for drafting a section of the report. "The legislation asks for us to identify a comprehensive strategy for research across the federal agencies in breast cancer and the environment," said committee chair Michele Forman, Ph.D., a professor of epidemiology at the University of Texas M.D. Anderson Cancer Center. "The three subcommittees are derived from efforts to complete the tasks delineated in the legislation."

Forman stressed that the diversity of the panel will be a vital element of its success as the project moves forward. "We have a very strong interest in garnering the forces of the advocates, the stakeholders, and others to be engaged in this process on breast cancer and the environment, from the research development stage, to the request for proposal stage to the peer review stage and all the way through to the conduct of the research, so that we keep our eyes on the target," she said. "The target is the individual and her risk (or his risk, for that matter) for breast cancer, and how we can identify environmental exposures that have some influence. The membership itself has a tremendously energizing effect. Without the advocates, the non-profits, the academics, and the government all joining forces, none of this would happen."



*The 19-member panel met both in full committee sessions, as seen above, and in working breakout sessions of its three subcommittees. (Photo courtesy of Steve McCaw)*

Although the report does not have a set due date, Forman said she is pushing toward completion “as soon as possible, because breast cancer and the environment has been an area that has not had the attention that it deserves.” With that incentive, the subcommittees will now be working on writing and then circulating first drafts of their sections in advance of the next full committee meeting, which is scheduled for September.

## Needed – common language for talking about breast cancer research

The subcommittees worked to flesh out the initial outlines of the chapters to be included in their sections of the report, while the entire group arrived at consensus on global themes and issues to be discussed in the report, including agreement on definitions of important but tricky terms such as “environment,” “innovation,” and “research translation.” With a diverse panel made up of federal agency scientists, academic researchers, members of the breast cancer advocacy community, and representatives of non-profit groups such as the American Cancer Society, the adoption of common nomenclature is critical.

“It became apparent that people use the same words to mean very different things, and sometimes we were talking at multiple levels and there wasn’t a shared understanding. This often happens when you get a group of people working together who come from different disciplines,” said Collman. “It certainly has been true in our breast cancer and the environment field, when you have advocates and members of the general public, survivors, at the table. They are learning about the research process, and the researchers are learning about the issues they feel are very important. So it’s always best to define everything up front.”



*Forman, who also chairs the State-of-the-Science Subcommittee, updated the panel on the subcommittee’s recent activities. (Photo courtesy of Steve McCaw)*



*Deborah Winn, Ph.D., deputy director of the National Cancer Institute’s Division of Cancer Control and Population Sciences, serves as co-executive secretary of the IBCERCC. (Photo courtesy of Steve McCaw)*



*Collman serves as co-executive secretary of the IBCERCC, representing the NIEHS portion of the collaboration with NCI. (Photo courtesy of Steve McCaw)*



*Michael Gould, Ph.D., a professor of oncology at the University of Wisconsin–Madison, chairs the IBCERCC's Research Process subcommittee. (Photo courtesy of Steve McCaw)*

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



*Jeanne Rizzo, R.N., is president and CEO of the San Francisco-based Breast Cancer Fund, a non-profit group devoted to exposing and eliminating the environmental causes of breast cancer. She chairs the IBCERCC's Research Translation, Dissemination and Policy Implications subcommittee, and provided healthy snacks to all of the meeting's attendees. (Photo courtesy of Steve McCaw)*

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## 2011 Biomedical Career Fair draws capacity audience

*By Emily Zhou*

NIEHS held its 14th annual [Biomedical Career Fair](#) April 29 at the U.S. Environmental Protection Agency (EPA) conference center in Research Triangle Park, N.C. The event was organized by postdoctoral fellows in the [NIEHS Trainees Assembly \(NTA\)](#) and in training at EPA, with financial and in-kind support from the NIEHS Office of the Scientific Director and EPA.

This year, the gathering drew 382 students and trainees from throughout North Carolina for an opportunity to explore a range of job choices in the biomedical sciences and create a professional contact network as they plan for their future careers. The daylong career fair featured a keynote talk on career development strategies, workshops, panel discussions, and vendor displays.

### **A sharper focus on practical skills and the how of landing a job**

Most students and trainees have dream jobs in mind, but, as keynote speaker Richard Weibl reminded the audience, “Luck strikes when preparation meets opportunity.” Weibl, who is director of the AAAS Center for Careers in Science and Technology, strongly encouraged young scientists to prepare themselves well to reach their goals.



*Zeller-Knuth reflected on her own postdoctoral experience when introducing keynote speaker Weibl to deliver his talk, titled “The Postdoctoral Experience: Preparing to Lead.” (Photo courtesy of Steve McCaw)*

“Master academic, occupational, and general employability skills,” he said, particularly communications and leadership, to be able to discuss science with different audiences and inspire others through networking and productive collaboration.

“In past career fairs, we learned about career choices available to Ph.D.s,” said Corinne Zeller-Knuth, Ph.D., NIEHS postdoc and co-chair of the planning committee, “but not as much emphasis was placed on how to get them.” This year’s event, by contrast, offered more interactive panel discussions on navigating through the hiring process for different career tracks, with panelists bringing different perspectives from diverse scientific and business backgrounds to share with attendees.

The planning committee sought out panelists who work in human resources or who have recently landed their jobs to share their experiences. Describing her impressions of the panel discussion on “Navigating the Process: Industry and Biotech,” NIEHS postdoc and planning committee member Cynthia Holley, Ph.D., noted afterwards, “There really was a ton of information in the session.” Holley said she had taken four pages of notes.



*Lori Conlan, Ph.D., director of Office of Postdoctoral Services at NIH, addressed a large crowd of interested attendees there to learn important aspects of job search. (Photo courtesy of Steve McCaw)*

### **From networking through interviewing for the job**

The career fair also highlighted 12 non-traditional off-the-bench career options available to better prepare students and trainees for their career transition.

These were offered in a short session format with only one speaker each session to provide tips on how they successfully transitioned into a specific career track and what tools and skills are needed to do so. Among many inspired participants, Anirudh Ullal, Ph.D., of Duke University, said, “It is one of the best career fairs in the area that I’ve ever been to.”

Due to time and space constraints, many of the sessions were offered concurrently. To inform interested participants who might have missed a session, moderators of each session wrote summaries of the key points and tips covered by speakers that are available online at the NIEHS Biomedical Career Fair Web site.

Along with formal sessions, the career fair provided a range of opportunities for networking with speakers and company exhibitors, as well as a chance to take advantage of one-on-one consultation with career development experts to revamp resumes and CVs.

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

### **A network of supporters**

The career fair owes an acknowledgement to many behind-the-scene contributors for making possible what has become a grand tradition at NIEHS. Diane Klotz, Ph.D., director at the [Office of Fellows’ Career Development](#) at NIEHS, was instrumental in guiding the long process of preparing for the career fair. She said she is very satisfied and considers this year’s fair one of the best ever. NIEHS Deputy Scientific Director Bill Schrader, Ph.D., and the NIEHS [Office of the Scientific Director](#) have given this event generous support.

Organizers also offer sincere thanks to the many [panelists and workshop instructors](#), as well as exhibitors, who volunteered their time to help their young colleagues better understand how to make the job search a successful one. Finally, an event of this size would never have been possible without the work of the many volunteers from NIEHS and EPA who helped out with the career fair.



Government panelists John Vandenberg, Ph.D., of EPA, left, and Scott Williams, Ph.D., of NIEHS, engaged in an interactive discussion with a room full of interested audience members. (Photo courtesy of Steve McCaw)



Andy Seipel, Ph.D., took notes while listening to NIEHS Program Administrator Mike Humble, Ph.D., at the Program Management short session, pondering the difficulties and rewards in this career option. (Photo courtesy of Steve McCaw)



One of several employees from NIEHS, Humble gestured as he shared his own distinctive career odyssey that took him from teaching science in high school, through participating in the NIEHS summer internship program and completing his Ph.D., to his current position in program management. (Photo courtesy of Steve McCaw)



Weibl inspires audiences to take a lead in their career. He said, "Shaping a career in science is not a solitary experience." He urged the audience to strengthen communication skills. (Photo courtesy of Steve McCaw)



Active members of the NTA Steering Committee listened intently to the keynote address. Left to right: Tammy Collins, Ph.D., Jana Stone, Ph.D., Sarah Swerdlow, Ph.D., and Allison Schorzman, Ph.D. (Photo courtesy of Steve McCaw)



Schorzman, right, talked with Conlan at the networking dessert reception. (Photo courtesy of Steve McCaw)



*The career fair's planning committee included fellows from NIEHS and EPA. Shown, left to right, standing, are Sabrina Robertson, Ph.D., Tina Stevens, Ph.D. (EPA), Sindura Ganapathi, Ph.D., Zeller-Knuth, Ph.D., Ashley Godfrey, Ph.D., and Xiaoqing Chang, Ph.D. Seated, left to right, are Patricia Gillespie, Ph.D. (EPA), Holley, Swerdlow, co-chair Yixing (Emily) Zhou, Ph.D., Qing Cheng, Ph.D., John Jack, Ph.D. (EPA), and Andrew Seipel. Valerie Davis, Ph.D., not pictured, commented afterwards, "I had a great time serving on the committee." (Photo courtesy of Steve McCaw)*

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## International workshop deliberates on indoor air pollution, cook stoves

*By Ed Kang*

An international workshop convened May 9-11 in Arlington, Va., to discuss current evidence on adverse health effects of indoor air pollution and to exchange views on improving human health. Spearheaded by NIEHS, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the Fogarty International Center (FIC), the meeting of more than 150 scientists and policy makers from multiple countries focused on research gaps, exposure assessment, and the burgeoning global initiative that aims to deliver clean, affordable cook stoves to the developing world.

Global leaders in public health took the opportunity to emphasize their commitment to support further efforts. Among the speakers were NIEHS/NTP Director [Linda Birnbaum, Ph.D.](#); Francis Collins, M.D., Ph.D., director of the National Institutes of Health; Kris Balderston, representative for global partnerships in the Office of the U.S. Secretary of State; Gina McCarthy, assistant administrator for the U.S. Environmental Protection Agency Office of Air and



*Balbus leads NIEHS efforts on [climate change](#) and human health. In this capacity he serves as HHS principal to the U.S. Global Change Research Program, for which he also co-chairs the Interagency Working Group on Climate Change and Health. (Photo courtesy of Michael Spencer)*

Radiation; and Pilar Nores de Garcia, president of the Peruvian Instituto Trabajo y Familia (Institute for Labor and Family), who spoke about the successes of the Peruvian National Stove Program.

Also playing major roles in the workshop were officials from partner NIH institutes and centers, including FIC Director Roger Glass, M.D., Ph.D.; NICHD Director Alan Guttmacher, M.D.; and NICHD Associate Director for Prevention Research and Health Promotion William Martin, M.D.

According to conference organizer, NIEHS Senior Advisor for Public Health [John Balbus, M.D.](#), the workshop presented a first-ever opportunity to hear the state-of-the-science on the health impacts of indoor air pollution and to identify critical research needs. The need for such a meeting is considerable since the poorer half of the world's population uses biomass — wood, crop residue, or dung — or coal as fuel to cook and heat, contributing to a variety of health conditions including pneumonia, lung cancer, cardiovascular disease, low birth weight, and cognitive impairment. The World Health Organization states that indoor air pollution in developing countries is the fourth leading cause of morbidity and mortality, and the second leading environmental contributor to ill health affecting primarily women and children.

### Exposure assessment critical to progress

In his opening remarks to the assembly, Balbus spotlighted the need to improve exposure assessment to quantify the relationship between specific levels of emissions reduction and improvements in population health status. Not all scenarios in developing countries are identical — differences in behavior, fuel characteristics, and stove construction are confounded with weather factors, overall health condition, nutrition, and other pollution sources contributing to the complexity of assessing human exposure.

[Kirk Smith, Ph.D.](#), a longtime NIEHS grantee from the University of California, Berkeley, further set the tone for the meeting by defining the scope of the global problem. In a presentation titled, “Household air pollution in lower and middle income countries,” he described his decades of exposure studies in places such as Guatemala, India, Nepal, and China.

Smith and Balbus described the importance of biomarkers and the development of inexpensive, portable electronic monitors as a means to gather exposure assessment data. “Unless researchers can determine with precision how dirty is unhealthy, it will not be possible to inform cook stove designers and program managers of the essential answer to the question how clean is clean,” said Balbus.



*Led by the United Nations Foundation, the Global Alliance for Clean Cookstoves is a public-private partnership with the ultimate goal of making cleaner, healthier cook stoves universally accessible. In videotaped remarks, U.S. Secretary of State Hillary Rodham Clinton proudly [spoke](#) of the U.S. government's commitment of more than \$50 million — nearly half from NIH — to help promote this technology throughout the developing world.*



*Smith, standing left, and Birnbaum took the opportunity to pursue dialogue with other global health leaders during one of the question and answer sessions. (Photo courtesy of Michael Spencer)*

Organizers intend to issue a full report of the workshop proceedings by mid-summer, identifying areas of research gaps and opportunities to reduce global health disparities.

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



*Collins and de Garcia share a lighter moment during the popular networking session. (Photo courtesy of Michael Spencer)*



*Gwen Collman, Ph.D., right, director of the NIEHS Division of Extramural Research and Training, was on hand to discuss the possibilities of grant funding for related projects. She's pictured above with Deborah Winn, Ph.D., of the National Cancer Institute. (Photo courtesy of Michael Spencer)*

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## Kissling to be honored by American Statistical Society

*By Eddy Ball*

NIEHS/NTP Staff Scientist [Grace Kissling, Ph.D.](#), will join a handful of her colleagues when she is officially inducted as a fellow of the [American Statistical Association \(ASA\)](#) Aug. 2 at a Joint Statistical Meetings awards ceremony in Miami Beach, Fla. Kissling will receive the highest honor in her field for what the ASA described as “outstanding contributions to the statistical profession.”

Kissling is a member of the NIEHS Biostatistics Branch (BB) headed by Chief [Clare Weinberg, Ph.D.](#) Working with scientists across the Institute, Kissling provides statistical advice and assistance for the toxicology and carcinogenicity studies carried out by the NTP and experimental studies carried out by NIEHS researchers. She collaborates on research at all stages — study design, statistical analysis, and interpretation — and has co-authored more than 125 peer-reviewed studies.



*During her induction at the awards ceremony, Kissling will be presented with a marble Fellows paperweight. (Photo courtesy of Steve McCaw)*

Weinberg, who nominated Kissling and has been an [ASA Fellow](#) herself since 1995, described election to the ASA Fellows as “an extremely high honor — one achieved by only a tiny fraction of statisticians in their lifetime of work.” Commenting on Kissling’s work, Weinberg added, “As the person tasked with maintaining the statistical integrity of studies related to the National Toxicology Program, Grace has displayed an outstanding level of creative productivity. It’s gratifying to see our ‘unsung hero’ get this well-deserved recognition!”

According to ASA rules, no more than one-third of one percent of the ASA membership may be elected each year to become new ASA Fellows. Fewer than 3,000 members have been so honored since the society began electing fellows in 1914. In addition to Kissling and Weinberg, NIEHS BB Principal Investigator [Shyamal Peddada, Ph.D.](#), who was elected in 2005, and BB Staff Scientist [David Umbach, Ph.D.](#), named in 2009, are also ASA Fellows.

ASA, which was founded in Boston in 1839, is the second oldest, continuously operating professional society in the United States. The organization serves statisticians, quantitative scientists, and users of statistics across a wealth of academic areas and applications. With an international membership of 16,000, ASA applies its expertise to many diverse tasks — from assessing environmental risk factors and assuring quality measures in industry, to examining social issues and establishing statistical standards used at all government levels.

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## Postdoc to head computational biology group at Indian institute

*By Eddy Ball*

For NIEHS Biostatistics Branch Visiting Fellow Sailu Yellaboina, Ph.D., June brings a trip home, a family reunited, and a position as an associate professor on the campus of his alma mater.

Along with his research duties as a member of the Centre for Excellence in Computational Genomics at the [C.R. Rao Advanced Institute of Mathematics, Statistics and Computer Science \(AIMSCS\)](#), Yellaboina will serve as head of the institute’s Bioinformatics and Computational Genomics Group. Founded in 2007 as a leading institute in basic research with grants from the Indian government and individual donors, AIMSCS is located on the campus of the University of Hyderabad in India.

### For Yellaboina, NIEHS stands out

Prior to coming to NIEHS, Yellaboina held fellowships at the University of Tennessee Health Science Center and the National Institute of Aging, where he worked after completion of his doctorate in bioinformatics at the University of Hyderabad. Looking back on his experiences as a trainee at three institutions, Yellaboina said, “NIEHS is the place where I received the training I needed to become an independent investigator.”

Although his successful transition from trainee to professor and principal investigator owes a great deal to his own talent and hard



*Yellaboina enjoyed his time at work with Jothi, describing him as an “excellent mentor and a exceptional scientist.” He also said he visited the NIEHS Fitness Center regularly to unwind and relax as he exercised, and he is proud of the bronze medals he won in fitness and table tennis competition during NIEHS Health and Fitness Week 2011. (Photo courtesy of Steve McCaw)*

work, Yellaboina also credits quality mentoring from NIEHS Principal Investigator [Raja Jothi, Ph.D.](#) (see text box), as well as the resources offered by the [NIEHS Office of Fellows Career Development \(OFCD\)](#), as important factors in tipping the job search scales in his favor.

### Advice for other trainees

Yellaboina said the grant writing workshop and workshops for improving his English were especially helpful and, in retrospect, wishes he'd been able to work more on his presentation skills, all of which he recommends for other fellows at NIEHS. He noted that his ability to write research proposals landed him four interviews and job offers in India, including the one he decided promised the best scientific environment and professional opportunity.

India has a robust economy, and government support of scientific research and training is strong, Yellaboina said. And he had advice for others who want to pursue careers there. "I highly recommend that Indian postdocs who want to return to India attend the [[IndiaBioscience.org](#)] [Young Investigator Meeting](#) to learn about opportunities in India."



*Jothi came to NIEHS from another NIH Institute, the National Heart, Lung, and Blood Institute, where he was a research fellow. (Photo courtesy of Steve McCaw)*

## Yellaboina and the Systems Biology Group

Yellaboina joined the Systems Biology Group in the NIEHS Biostatistics Branch as a postdoctoral fellow in August 2009, working with Jothi, who said of his protégé, "Sailu is an outstanding scientist with a strong character. He has a very positive attitude and truly embraces learning all there is know about molecular and computational biology. He never hesitated to reach out to other scientists at NIEHS, whose expertise, he thought, would help improve the scope of his projects. This work ethic and the career development skills he gained as a trainee have served him well in his job search."

Yellaboina worked with Jothi towards identifying novel regulators required for mouse embryonic stem (ES) cell maintenance. He used Bioinformatics and Genomics approaches to discover several novel regulators of ES cell identity including a gene with an unknown function and a few genes with roles in epigenetic modifications. The NIEHS Systems Biology Group uses interdisciplinary approaches, both experimental and computational, to understand how transcription factors and epigenetic modifications regulate gene expression programs during cellular development and differentiation.

In 2010, Yellaboina won a Fellows Award for Research Excellence (FARE), for his research with Jothi into "Computational Prediction and Experimental Validation of Novel Genes Essential for Embryonic Stem Cell Maintenance and Self-renewal" and gave an invited talk, "Identification of Novel Regulators Required for Embryonic Stem Cell Maintenance," at the NIH Research Festival in October 2010 ([see story](#)).

In February 2011, Yellaboina was awarded a travel grant to attend and present his stem cell poster at the [IndiaBioscience.org Young Investigators Meeting](#) in what is known as the "temple city of India," Bhubaneswar, capital of the state of Orissa. He will present his final talk as a postdoc on "Integrating Genomic Datasets to Understand Mechanisms of Embryonic Stem Cell Maintenance," during a plenary symposium June 7 convened by NIEHS biostatisticians Pierre Bushel, Ph.D., and Leping Li, Ph.D., at the [2011 In Vitro Biology Meeting in Raleigh](#).

## From farm boy to computational biologist

When he gets established in Hyderabad, Yellaboina will be just 50 miles away from where he was born in the village of Cheetakodur in the town of Jangaon Mandal in the Warangal district of the Indian state of Andhra Pradesh. Remembering his childhood there, he said, “It [Cheetakodur] has a population around 2000, and 99 percent of the families depend on agriculture for a living. Most of the time when I wasn’t in school, I also used to work at farming the land.”

He could easily have followed tradition and stayed in agriculture in Cheetakodur, but Yellaboina had dreams. He worked hard at Kaktiya University, where he earned his bachelor’s degree, and at the University of Hyderabad, where he became the first person from his village to earn a master’s degree and a Ph.D.

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## NIH grantee receives Wisconsin Regents Teaching Excellence Award

*By Eddy Ball*

In a May 4 [press release](#), the University of Wisconsin (UW) announced that NIH grantee Craig Berg, Ph.D., is one of two individual winners of the 2011 [Regents Teaching Excellence Award](#). In addition to the honor conveyed by the UW system’s highest recognition for members of its faculty and academic staff, when he accepts his award at the Board of Regents meeting June 10 in Milwaukee, it will include a \$5,000 stipend for professional development.

[Berg](#) is a professor in the Department of Curriculum and Instruction in the School of Education at the UW Milwaukee (UWM) and director of the Milwaukee Collaborative Science and Mathematics Teacher Education Program (MACSTEP), an innovative approach to producing exemplary science teachers. He is a co-principal investigator with NIEHS Children’s Environmental Health Sciences Core Center [grantee](#) David Petering, Ph.D., on a Science Education Partnership Award (SEPA) [program](#). The award is funded by NIEHS in conjunction with the [NIH National Center for Research Resources](#), which oversees the large science, technology, engineering, and mathematics (STEM) program.

Commenting on this year’s winners, Regent Betty Womack, chair of the selection committee, said, “My fellow committee members and I were deeply inspired by the creative energy and passion for their craft that these gifted teachers share with their students, their colleagues, the campus community, and beyond.”

### A collaborative program to shape the STEM education

Much of Berg’s teaching is focused on the MACSTEP program at UWM. MACSTEP is a cutting-edge science and mathematics teacher-preparation program that has been extensively shaped through the collaborative efforts of faculty, practicing teachers in the Milwaukee Public Schools (MPS), former students, and other strategic



*“Students everywhere really need the best teachers and programs we can provide for them — especially those students in urban settings who have many other challenges in their lives,” Berg said of the work that earned him this prestigious award. (Photo courtesy of Kyle Stevens)*

players who work to incorporate best practice into coursework and field experiences. Students benefit from highly coordinated courses and fieldwork experiences delivered through the synergy of instructors from UWM and MPS.

The program is tailored to train undergraduate students, those who already have B.S./B.A., master's, or Ph.D. in a science or mathematics field, and those who also want to start working towards a master's degree while becoming certified to teach. One of Berg's areas of interest is the effective use of technology in instruction, with programs designed to implement collaboration between science, mathematics, and social studies teachers by using the Internet.

Berg was quoted in a [UWM press release](#) as saying, "Student's attitudes toward science, their interest in taking more science, almost always depend on the quality of the teachers teaching science. One excellent science teacher can make a huge difference in student attitudes and their desire to continue working toward a STEM career." Berg adds that they are constantly striving to develop highly effective science and mathematics teachers who will then have maximum positive impact on their students.

Berg and Petering's SEPA program, "Biology-Environmental Health Science Nexus: Inquiry, Content, and Communication," focuses on the high school general science and biology teachers and students in metropolitan Milwaukee, particularly minority students in the Milwaukee Public School District. The program's general objective is to develop the skills of inquiry in teachers and students as the basis for doing and understanding science, particularly in relation to life science and environmental health.

"I am thrilled to be working with scientists who are doing cutting-edge research and who have a passion for translating their work into classroom experiences for children," Berg explained. "In this project I also work with dedicated teachers who help hone these materials into exciting activities for their classroom. SEPA is a program that helps keep me grounded in the real world of doing science and science teaching."

Along with Berg, the Regents honored UW-Green Bay Professor Regan Gurung, Ph.D., with an individual award, and the UW-Green Bay Professional Program in Education for exceptional commitment to and effectiveness in teaching by an academic unit.

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## **NIEHS receives five plain language awards**

*By Eddy Ball*

NIEHS was among the NIH centers and institutes recognized at the 2010-2011 [NIH Plain Language/Clear Communication Awards Ceremony](#) May 17 in Bethesda, Md. Plain language and clear writing have been official goals at NIH for at least a [decade](#) and are now a government-wide requirement of the Plain Writing Act of 2010, signed into law by President Obama in October of last year.

In a message to employees, NIEHS/NTP Director Linda Birnbaum, Ph.D., congratulated this year's NIEHS recipients and said she was delighted by the news.

- [The National Children's Study Web site](#) and [The Global Alliance for Clean Cookstoves Web site](#) by NIEHS Office of Communications and Public Liaison (OCPL) Science Editor Robin Arnette, Ph.D.

- [Let's Talk About SELF: Study of Environment, Lifestyle and Fibroids](#), by NIEHS Women's Health Group Principal Investigator Donna Baird, Ph.D., along with four contractors with Social Scientific and Systems, Inc. — Christie Barker-Cummings, Dr.P.H., Milele Bynum, Christina Makarushka, and Carrissa Dixon
- [What's in a Color? The Unique Human Health Effects of Blue Light](#), by Environmental Health Perspectives News Editor Susan Booker, freelance writer David Holzman, and two Brogan and Partners contractors — Matthew Ray and Joseph Tart
- [The NIEHS Overview Fact Sheet](#) by NIEHS OCPL Director Christine Flowers, NIEHS OCPL News Director Robin Mackar, NIEHS OCPL Program Specialist Anne Thompson, and Image Associates contractor Donna Jeanne Corcoran

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# Science Notebook

## Liu discusses a systems biology approach to breast cancer

By Archana Dhasarathy

Edison Liu, M.D., outlined a novel integrative genomics and systems biology approach to breast cancer during his 2010-2011 NIEHS Distinguished Lecture Series presentation April 22, titled “Systems reconstruction of the ER-alpha network: From bench to the clinic.” NIEHS Environmental Stress and Cancer Group Principal Investigator Rick Paules, Ph.D., hosted the talk by Liu, who is currently executive director of the [Genome Institute of Singapore](#) and president of the [Human Genome Organisation \(HUGO\)](#).

“One thing that the genome has taught us is that it is really complex,” said Liu. He stressed the need to embrace this complexity and resolve biological mechanisms by a deeper understanding of each component and its nodes of interaction.

**Linked video:**



[Liu describes the power of a systems biology approach to studying cancer during an interview at the National Cancer Research Institute Cancer Conference in November 2010 \(07:59\)](#)  
(Launches in new window)

Download Media Player:  Flash 



*Liu describes his work as spanning cancer biology, genomics, human genetics, and molecular epidemiology. (Photo courtesy of Steve McCaw)*

### Mapping estrogen receptor DNA binding sites in the genome

Estrogen receptor alpha (ER-alpha) is a key molecule in breast cancer, and loss of ER-alpha is associated with poor prognosis. In the presence of estrogenic compounds like estradiol, ER-alpha binds to distinct regions of DNA called estrogen response elements (EREs) and helps to turn genes on or off. Using genome-wide techniques with the MCF-7 breast cancer cell line enabled Liu's group to identify the locations of EREs, and map them to genes that are regulated by estrogen. The researchers determined that many of these EREs are located near genes that are significantly associated with breast cancer biology. Further, they determined that approximately 98 percent of these EREs have sequences that energetically favor ER-alpha binding.

When Liu and his colleagues examined the motifs adjacent to the ER-alpha binding sites, they found the presence of two other transcription factors, GATA3 and FOXA1, which can co-occupy some of the same binding sites as ER-alpha. The best induction of cell growth and gene activation results when all three factors are present around the same binding site. Thus, the presence of these co-factors helped to organize the genome for optimal binding.

### The importance of DNA loops in gene regulation

The mapping results revealed that while many EREs were located as expected near the start sites of genes, approximately 40 percent were actually in intragenic regions, suggesting different mechanisms of action.

The researchers also found that even when an ERE was located away from the start of a gene, it was still associated with RNA polymerase, which is necessary for genes to be actively transcribed. This association suggested to them that an alternative mechanism could help bring both the ER-alpha and RNA polymerase that are bound to a distal site in close proximity to the start site of the gene, and allow transcription. Hence, a major finding of their research was that ER-alpha could influence gene expression across distances of up to 100 kilobases or more.

Liu's group hypothesized that the formation of a DNA loop provides a sort of DNA cage for factors, such as ER-alpha and RNA polymerase, to bring them all together and allow gene transcription. DNA acts as a catalyst to bring different factors together, maximizing transcription factor usage. Many sites could consequently be covered by the limited number of transcription factors in a cell, which maximizes efficiency of gene regulation.

### **ER-alpha and breast cancer susceptibility**

Liu then asked whether variations in ER-alpha signaling could influence breast cancer susceptibility. Global tests of genetic association between SNPs in the ER-alpha pathway and breast or endometrial cancer identified the aromatase SNP as significant, pointing to the potential of using aromatase inhibitors in therapy.

As Liu ended his talk, he told the audience, "God made ER-alpha signaling for reproduction, not for oncologists to understand breast cancer susceptibility." The regulation of ER-alpha is highly controlled, so that even slight perturbations can lead to evolutionary demise, while individual variations can enhance survival of the species, he concluded.

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

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## **Taking the pulse of toxicogenomics at GEMS**

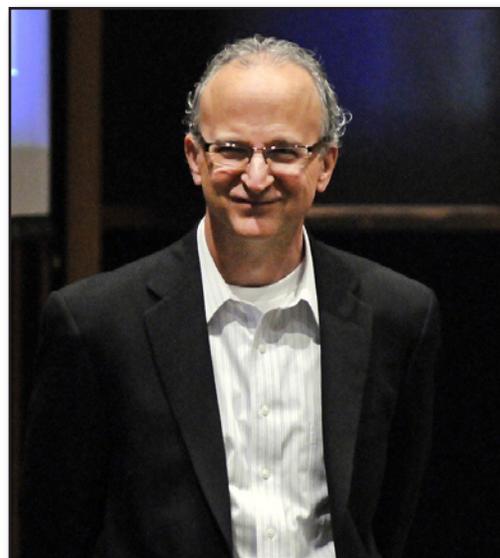
*By Ernie Hood*

At its annual spring meeting held May 2 at the U.S. Environmental Protection Agency (EPA) campus in Research Triangle Park, the Genetics and Environmental Mutagenesis Society (GEMS) welcomed a series of speakers with ties to NIEHS and EPA working in the emerging field of toxicogenomics in recent years.

The meeting was organized by GEMS President-elect Nagu Keshava, Ph.D., and President Stephen Little, both of the EPA, around the theme of "Application of Genomics Data to Understand Chemical Mechanisms



*NIEHS Laboratory of Molecular Genetics Principal Investigator Mike Resnick, Ph.D., was one of several scientists who asked questions following the talk. (Photo courtesy of Steve McCaw)*



*Paules watched and often smiled as Liu joked as he answered queries from the audience. (Photo courtesy of Steve McCaw)*

of Action.” As Keshava explained, “The original idea was to see how far we have come in terms of toxicogenomics or any genomics or systems biology data for using in risk assessment.”

Little agreed, and noted that the program emphasized the importance of new tools for gaining knowledge about chemicals’ mechanisms of action. “They can help you assess the likelihood that a chemical is going to contribute to a toxicological endpoint,” he said.

### Resources linked to NIEHS

In the initial presentation, [Michael Waters, Ph.D.](#), chief scientific officer of ILS, Inc., and a longtime researcher at both EPA and NIEHS, set the tone for the day’s proceedings, with his talk on “Utilizing Available Toxicogenomics Datasets to Understand Chemical Mode of Action.” He showed that recent advances in the field allow more robust queries of existing toxicogenomics datasets ([see text box](#)).

NIEHS grantee [Ivan Rusyn, M.D., Ph.D.](#), of the University of North Carolina at Chapel Hill Gillings School of Public Health briefed GEMS attendees on his group’s work in population-based discovery of toxicogenomic biomarkers for hepatotoxicity. Using dozens of thoroughly genotyped inbred mouse strains as models for human genetic diversity, Rusyn and his team have made important strides in understanding the genotoxic and epigenotoxic effects of toxicants.

Following the scientific presentations, NIEHS/ NTP Director [Linda Birnbaum, Ph.D.](#), provided the GEMS members a comprehensive overview of NIEHS and NTP genetics, epigenetics, genomics and epigenomics-related research. She delineated both intramural and extramural activities, as well as multi-agency and trans-NIH programs such as the Genes, Environment and Health Initiative and the Environmental Genome Project, outlining the Institute’s extensive endeavors in the field, both currently and over the past 45 years.

### EPA initiatives

Vincent Coglianò, Ph.D., head of the [EPA Integrated Risk Information System \(IRIS\)](#), reported on “The Use of Mechanistic Data to Classify Carcinogens — An IARC [International Agency for Research on Cancer] Classification.” He noted that mechanistic studies had been pivotal in more than 60 of IARC’s cancer classifications — assessments in which the mechanistic data had actually changed the classifications from what they would have been based upon epidemiological or animal bioassay data alone. Moving forward, he said, IARC guidelines now recognize that chemicals can be classified as carcinogenic based solely on mechanistic data.



*GEMS President-elect Keshava introduced the day’s proceedings, titled “Application of Genomics Data to Understand Chemical Mechanisms of Action.” (Photo courtesy of Steve McCaw)*



*Little pointed to the potential impact of toxicogenomics on public health — “speeding up getting information about the large number of chemicals that are out there that the public is worried about and we don’t have a lot of information on.” (Photo courtesy of Steve McCaw)*

EPA scientist Stephen Edwards, Ph.D., of the National Health and Environmental Effects Research Laboratory (NHEERL), described a systems biology-based approach to understanding gene-environment interactions and developing disease-centric predictive toxicology, in conjunction with working with the EPA National Center for Computational Toxicology. The idea of the disease-centric approach is to treat chemical exposures as one of many potential perturbations to a system, and to seek better comprehension of how the system responds and adapts to such perturbations as it seeks to maintain homeostasis.

EPA researcher Lyle Burgoon, Ph.D., also of NHEERL, provided an update on “Use of Genomics and Systems Biology Data in Risk Assessment — [The NexGen Project](#).” Burgoon discussed the need for EPA to begin to incorporate so-called next generation data being spawned by toxicogenomics, metabolomics and similar approaches from molecular systems biology into its risk assessment decision-making processes in the interagency Advancing the Next Generation of Risk Assessment (NexGen) program.

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



*Birnbaum found herself back on familiar turf, as she revisited EPA, where she worked for many years, to present to the GEMS attendees. (Photo courtesy of Steve McCaw)*



*Waters illustrated a point in his GEMS presentation on the use of existing toxicogenomics databases to understand chemical modes of action and pre-disease genomic signatures. (Photo courtesy of Steve McCaw)*



*Edwards described the potential to improve risk assessment through systems biology by developing a predictive model incorporating a wide variety of factors to generate useful risk estimates. (Photo courtesy of Steve McCaw)*



*Burgoon updated GEMS attendees on the NexGen program, EPA’s collaborative initiative with other Federal and state partners, including NIEHS/NTP, to incorporate systems biology and omics data into risk assessment decision-making. (Photo courtesy of Steve McCaw)*

## Waters running deep

In his GEMS presentation on the use of available toxicogenomics databases to understand chemical modes of action, Waters reported that he was particularly excited about the NTP's 2010 acquisition of the commercial DrugMatrix database and the recent public release of a Japanese toxicogenomics database called TG-GATEs. "These two databases actually have about 82 chemicals in common that could be looked at to verify that the technology is giving you the same information in two different parts of the world," Waters said. He also noted the largely untapped resource represented by the NTP's extensive archive of formalin-fixed, paraffin-embedded (FFPE) two-year carcinogenicity bioassay materials.

By applying the new tools such as microarray technology and NexGen sequencing to early, acute-phase toxicity studies such as those found in DrugMatrix and TG-GATEs and to longer-term studies, such as the NTP 2-year bioassays, it should be possible to characterize both chemicals' modes of actions and associated gene expression signatures pertinent to the disease process. "We would use that 'pre-disease' signature to describe what we think are the markers that would indicate the disease that is going to occur in two years, or sometimes between 90 days and two years," Waters explained. "The technologies and the data are now available to do this," he added. "We have an opportunity that we didn't have before, and I think we really should exercise that opportunity."



*A significant number of NIEHS/NTP scientists are members of GEMS. Shown above, left to right, are former NIEHS scientist Errol Zeiger, Ph.D., J.D., NTP scientist Ruth Lunn, Ph.D., and former NTP scientist Barbara Shane, Ph.D. (Photo courtesy of Steve McCaw)*



*Among the many EPA scientists at the meeting was biochemist Jeff Ross, Ph.D., above, who served as GEMS president-elect in 2008 and president in 2009. (Photo courtesy of Steve McCaw)*

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# NIEHS holds symposium on the proteins of aging

By Robin Arnette

NIEHS hosted an all-day symposium April 27 that dealt with the genetic factors and environmental influences that contribute to aging. The event, “Sirtuins in Aging and Age-associated Diseases,” focused on a genetic pathway controlled by a group of proteins called sirtuins. Sirtuins regulate the body’s metabolism and are believed to play a role in a number of cellular processes, including metabolism, stress response, DNA repair, genome stability, and aging.

[Xiaoling Li, Ph.D.](#), a tenure-track investigator in the NIEHS Laboratory of Signal Transduction and head of the Mammalian Aging Group where she studies sirtuins, invited an all-star lineup of sirtuin researchers to talk about their work ([see text box](#)). Acting Scientific Director David Miller, Ph.D., provided opening remarks for the seminar and noted the importance of sirtuins to NIEHS and the National Institutes of Health.

“Sirtuins have also been implicated in a number of diseases, for example Alzheimer’s disease and diabetes,” said Miller. “These proteins seem to be expressed in a wide variety of organisms, and there are a large number of them.”

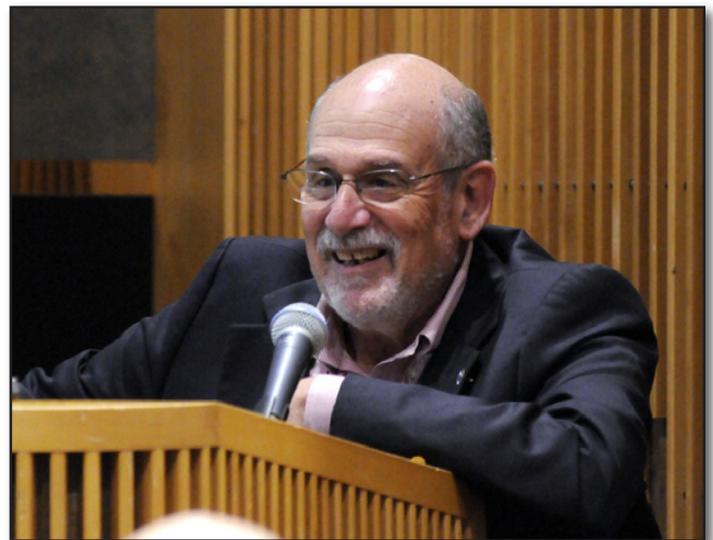


*Symposium organizer Li was excited to have so many sirtuin researchers together in one place. (Photo courtesy of John Maruca)*

## The keynote address

[Leonard Guarente, Ph.D.](#), a Novartis Professor of Biology at the Massachusetts Institute of Technology, was the first lecturer of the morning session. He said that he and his lab started working on yeast sirtuins more than 20 years ago. They wanted to identify the yeast genes that affected the lifespan of mother cells — yeast that give rise to progeny by budding off daughter cells. It took almost a decade and several people conducting a series of genetic screens to find what they were looking for.

“We determined that in normal, wild-type yeast, a mother cell divided 20-25 times before it underwent senescence, but knocking out the Sir2 gene shortened that lifespan, and adding an extra copy increased the lifespan,” Guarente explained. “We carried out similar experiments in the roundworm, *Caenorhabditis elegans*, and found that the worm version of the gene, Sir2.1, functioned the same way.”



*“Understanding the mechanism behind some of the sirtuin-associated diseases might be important to us who are aging,” Miller quipped. (Photo courtesy of John Maruca)*

Guarente said that the Sir2 genes later came to be known as sirtuins and generally counteract the aging process.

Raluca Dumitru, M.D., Ph.D., an Intramural Research Training Award (IRTA) fellow in the Laboratory of Molecular Carcinogenesis, thoroughly enjoyed Guarente's presentation. She said afterwards, "Dr. Guarente gave us a broad overview of sirtuins and his research has provided enough evidence to link sirtuins to diabetes and cancer, as well as neurodegenerative diseases."

### **Covering all aspects of sirtuins**

Following Guarente's talk, Chuxia Deng, Ph.D., chief of the Mammalian Genetics Section at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), discussed the role sirtuins play in cancer. Deng said that the closest mammalian homolog of Sir2 is called SIRT1, and that mammals have seven sirtuin genes. His work with BRCA1, a gene that is involved in the development of hereditary breast and ovarian cancer in humans, demonstrated that BRCA1 forms a complex with another protein and binds to the SIRT1 promoter. Deletion of SIRT1 increases the incidence of cancer in mice.

After a short break, several other investigators talked about various aspects of sirtuins, including function, structure, and disease models. NIEHS postdoctoral fellows relished the opportunity to engage the speakers one-on-one during the lunch hour in the cafeteria.

Li presented the last seminar of the day, which debated the role of phosphorylation in the regulation of SIRT1. Although the function of SIRT1 has been extensively studied in the past decade, researchers still don't know how environmental signals regulate SIRT1 activity. Li and her lab have recently shown that SIRT1 can be activated by phosphorylation modification in response to environmental stresses. Their new data indicate that this modification probably modulates SIRT1 protein's oligomeric status.

At the end of the day, speakers and members of the audience left the symposium with a better understanding of sirtuins and their capacity to regulate key cellular mechanisms.

## **Presenters for "Sirtuins in Aging and Age-associated Diseases"**

### **SIRT1 and SIRT3 in Aging and Diseases**

**Leonard Guarente, Ph.D. (Keynote Speaker)**

Novartis Professor of Biology  
Massachusetts Institute of Technology

### **Knockout Mouse Models for Sirtuins: Metabolism, Cancer, and Aging**

**Chuxia Deng, Ph.D.**

Chief, Mammalian Genetics Section  
National Institute of Diabetes and Digestive and Kidney Diseases

### **Metabolic Switches**

**Marcia Haigis, Ph.D.**

Assistant Professor of Pathology  
Harvard Medical School

### **Nutrient Signaling for the SIRT1/PGC1 Chromatin Complex: Implication for Metabolic Diseases**

**Pere Puigserver, Ph.D.**

Associate Professor of Cell Biology  
Dana-Farber Cancer Institute

### **Advances in Metabolic Regulation by SIRT1**

**Domenico Accili, M.D.**

Professor of Medicine  
Columbia University

### **Chromatin Regulation and Genome Maintenance by Mammalian Sirtuins**

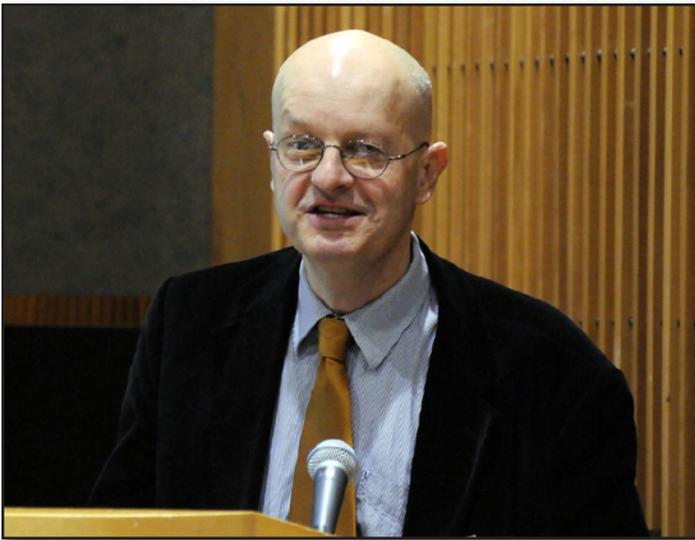
**Katrin Chua, M.D., Ph.D.**

Assistant Professor of Medicine  
Stanford University

### **Regulation of the Regulator**

**Xiaoling Li, Ph.D.**

Principal Investigator  
National Institute of Environmental Health Sciences



*Guarente said that early on he wondered why a gene that counteracted aging existed evolutionarily. Answering this question made him want to study the biochemistry of Sir2 genes. (Photo courtesy of John Maruca)*



*Deng mentioned that although SIRT1 has been shown to inhibit the tumor suppressor gene p53 and is over expressed in certain kinds of cancers, deletion of SIRT1 in mice leads to genomic instability and increased incidence of cancer. (Photo courtesy of John Maruca)*



*Laboratory of Toxicology and Pharmacology principal investigator Jau-Shyong Hong, Ph.D., was interested in more detail about work in the areas of neurodegenerative diseases. (Photo courtesy of John Maruca)*



*Symposium speakers, left to right are Puigserver, Accili, Haigis, Li, Guarente, Chua, and Deng. (Photo courtesy of John Maruca)*

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# Williams discusses the effects of neonatal phytoestrogen exposure

By Eddy Ball

Members of the [National Advisory Environmental Health Sciences Council](#) enjoyed a scientific talk by NIEHS Principal Investigator [Carmen Williams, M.D., Ph.D.](#), during their spring meeting May 19 at NIEHS.

Williams, who heads the [Reproductive Medicine Group](#), outlined results of her group's most recent investigations using a mouse model. Her presentation was titled "Permanent Reprogramming of Gene Expression in Response to Neonatal Phytoestrogen Exposure: Implications for Female Reproductive Tract Function and Pathology." The work, as Williams explained, addresses important public health issues — unexplained infertility and difficulty of conception, reproductive tract abnormalities, and premature birth — linked to widespread environmental exposures that could be mitigated by primary preventive measures.



*Williams said adult vegetarians consume about one milligram per kilogram daily. "Babies who only drink soy formula as their source of nutrition take in five- to ten-fold that amount," she said. (Photo courtesy of Steve McCaw)*

In his introduction of Williams, NIEHS Acting Scientific Director David Miller, Ph.D., praised her accomplishments as a physician-scientist capable of integrating basic, clinical, and translational research. "She adds quite a bit to our Laboratory of Reproductive and Developmental Toxicology," he said.

## From bedside to bench

Following her M.D. and advanced clinical training in reproductive endocrinology and infertility, Williams completed her Ph.D. in cell and molecular biology and then served as an attending physician in the University of Pennsylvania Health System. As she said at the beginning of her talk, her interest in endocrine disrupting compounds in the environment actually began in the hospital, where one of her first gynecological cancer patients was an 18 year old who died from vaginal cancer triggered by prenatal exposure to diethylstilbestrol (DES), a synthetic form of estrogen.

Her current work in gene expression reprogramming initiated by exposure to phytoestrogens, she said, involved taking, to the next stage, a dormant project that was actually initiated here at NIEHS more than ten years ago to study the effect of estrogens on female reproductive tract development. Williams has advanced the original project, which studied DES exposure in a rodent model, to focus on neonatal exposure to plant-based phytoestrogens at levels comparable to those in formula-fed infants, specifically genistein, the most abundant isoflavone in these formulas.

## Elegantly designed experiments

In previous work on the project by NIEHS investigators Retha Newbold and Wendy Jefferson, Ph.D., neonatally exposed animals were mated at two months, four months, and six months of age. Animals receiving the higher dose of genistein, 50 milligrams per kilogram daily, were unable to carry their embryos to term. There was evidence to suggest that they did conceive at lower rates, but with smaller implantation sites than controls and loss of embryos soon afterwards. Animals exposed to a lower dose could conceive but tended to have a smaller average number of pups. Testing determined that hormone levels in exposed animals were normal.

After Williams picked up the project, further testing *in vitro* and in nonexposed foster dams indicated that there was also no problem with egg quality, suggesting that something in the oviduct or uterus was the cause of infertility. After flushing embryos from the oviducts of exposed animals, Williams was able to determine that the loss of embryos was taking place somewhere between day two and day three.

Although there was evidence of problems in both oviduct and uterus, which failed to support the embryos, Williams decided to focus her follow-up experiments on the oviduct on day two of pregnancy. At that point, the group removed the oviducts from controls and treated animals to look at morphology and gene expression.

### Pinpointing gene expression

Through histology and microarray analysis of the adult oviducts of neonatally exposed and control animals, Williams' group determined that genistein-exposed mice showed abnormal oviduct morphology attributable to changes in expression of genes that modulate neonatal oviduct morphogenesis, including *Hoxa*, *Wnt*, and hedgehog signaling genes. There was also permanent upregulation of homeobox genes normally expressed only in the cervix and vagina, including *Six1*, *Pitx1*, and *Nkx3-1*.

According to Williams, numerous immune response genes were significantly altered in the adult oviduct before and during early pregnancy, suggesting that the abnormal oviduct responded inappropriately to hormone-mediated modulation of mucosal immunity that is required for survival of the embryos.

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## Health Affairs highlights environmental health science and policy

By Eddy Ball

The peer-reviewed journal [Health Affairs](#) made history in May with its first [thematic issue](#) ever devoted exclusively to environmental health research. Founded in 1981 under the aegis of Project HOPE, a nonprofit international health education organization, Health Affairs describes itself as “the leading journal of health policy thought and research... explor[ing] health policy issues of current concern in both domestic and international spheres.”

The journal held a briefing, “Environmental Challenges for Health,” May 4 in Washington, D.C., where it released the issue ([see related story](#)). The briefing featured talks by NIEHS/NTP Director [Linda Birnbaum, Ph.D.](#), NIEHS Director Emeritus [Kenneth Olden, Ph.D.](#), and 14 other leading figures in the environmental health sciences. The briefing and the themed issue, with contributions from many of the speakers, were supported by a grant from the Kresge Foundation.

With help of authorities in the field, Health Affairs Editor-in Chief [Susan Dentzer](#) brought a review of what scientists know and don't know about environmental health, as well as explanations of key concepts in the



*Miller selects a principal investigator to speak at each Council meeting, highlighting the leading-edge research happening in the Institute's intramural program. (Photo courtesy of Steve McCaw)*



(Image courtesy of Health Affairs)

field, to the journal’s 10,000 domestic and international subscribers and online readers, who make an average of 1.9 million page views each month.

Dentzer opens her editorial by observing, “We’ve long ignored the obvious: The environment plays a role in nearly 85 percent of all disease.” Still, she continues, “What we know about that subject — as opposed to what we need to know or do to protect health — is at best an inch deep.”

Environmental health science, as a whole, and the NIH’s sole environmental institute, NIEHS, in particular, have gained a potentially influential advocate in Dentzer, who is also a regular commentator on health issues for the PBS NewsHour. The Health Affairs briefing and themed issue promise to raise awareness of environmental health and could help make it more of a household term than ever before.

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## A peek inside the special issue of Health Affairs

The lineup in the May issue of Health Affairs includes articles written by NIEHS scientists, grantees, and collaborators, as well as papers by some of the leading authorities in the field of environmental health science and policy:

- **Birnbaum and NIEHS Chief of Staff Paul Jung, M.D.**, address costs, issues, and controversies in [“From Endocrine Disruptors To Nanomaterials: Advancing Our Understanding Of Environmental Health To Protect Public Health”](#)
- **Olden, Nicholas Freudenberg, Dr.PH., Jennifer Dowd, Ph.D., and Alexandra Shields, Ph.D.**, contribute an analysis and commentary piece on [“Discovering How Environmental Exposures Alter Genes Could Lead To New Treatments For Chronic Illnesses.”](#) Currently the founding dean of the City University of New York (CUNY) School of Urban Public Health, [Olden](#) was NIEHS director for 14 years. Freudenberg and Dowd are colleagues at CUNY. Shields is a professor at Harvard University.
- **Philip Landrigan, M.D., and Lynn Goldman, M.D.**, author a study highlighted on the journal’s home page, [“Children’s Vulnerability To Toxic Chemicals: A Challenge And Opportunity To Strengthen Health And Environmental Policy.”](#) University deans and board-certified pediatricians, [Landrigan](#) and [Goldman](#) are former grantees and longtime partners with NIEHS.
- **Phil Brown, Ph.D., and Alissa Cordner**, explore regulating chemical use in [“Lessons Learned From Flame Retardant Use And Regulation Could Enhance Future Control Of Potentially Hazardous Chemicals.”](#) A veteran NIEHS Superfund grantee, [Brown](#) and [Cordner](#), one of his doctoral students, conduct their studies through the Brown University Department of Sociology.

# NIEHS study explains rapid transcription of immediate early genes in the brain

By Emily Zhou

In a new [study](#) published in Nature Neuroscience, NIEHS Visiting Fellow Ramendra Saha, Ph.D., lead author, and his colleagues detail the mechanism underlying rapid transcription of immediate early genes (IEGs) in neurons.

The team of researchers demonstrated that RNA Polymerase II (Pol II) stalling renders a kinetic advantage to transcription of rapidly induced IEGs in brain. These genes already possess active chromatin marks and come preloaded with transcription factors with Pol II, awaiting only an activity-induced signal, such as what might occur with learning or any of a number of processes, such as development and drug addiction.

As Saha pointed out, “The findings open up lots of research directions [in the field].” For example, using Pol II stalling as a signature, researchers can determine whether expression of a gene of interest might be regulated by chemical signals from synapses or whether action potentials, through calcium, might be sufficient. “The importance of this study is that we have shown two biological classes of IEGs in neurons,” Saha added.

Saha is part of the Synaptic and Development Plasticity Group headed by [Serena Dudek, Ph.D.](#), a principal investigator in the NIEHS Laboratory of Neurobiology and corresponding author and principal investigator on the study.

## Pol II stalling at the promoter of *arc* gene

Recruitment of RNA Polymerase II (Pol II) is typically the rate-limiting step in transcription initiation. A general phenomenon that Pol II pauses at the promoter-proximal region of some genes has recently been observed in diverse species from bacteria and virus to *Drosophila* and human, and is referred to as promoter proximal Pol II stalling.

When Saha began his research project to tackle the mechanism of rapid transcription of IEGs in response to neuronal activity, he had a long list of the usual suspects for possible regulators, but the key inspiration for the study came from a seminar given by [Karen Adelman, Ph.D.](#), head of the Transcriptional Responses to the Environment Group at NIEHS and a co-author of the paper. Her seminar led Saha and Dudek to the idea that Pol II stalling might be the mechanism. They chose the widely studied *arc* gene as the model IEG because it was well known to be induced by neuronal activity within five minutes of stimulation, so Saha knew its rapid transcription would require an out-of-the-ordinary mechanism for speedy induction.

Using Chromatin ImmunoPrecipitation assays on neuron cultures, Saha and colleagues saw Pol II was poised in proximity of the *arc* transcription start site. Similar to what has been observed in non-neuronal cells, the Negative Elongation Factor (NELF) was found enriched with Pol II in the promoter region of *arc*.



*Saha obtained his Ph.D. from Nebraska Medical Center where he studied neurodegeneration. He considers it a privilege to be at the forefront of neuroscience discovery here at NIEHS. The new study is the culmination of research that Saha presented, in its early stage, at the 2009 NIH Research Festival and that won him a Fellows Award for Research Excellence for 2009 and, in 2010, a travel award from the Society for Neuroscience. (Photo courtesy of Steve McCaw)*

Upon the neurons' firing, NELF enrichment was lost from the activated *arc* gene, but not globally. Knocking down of NELF significantly reduced promoter-proximal Pol II enrichment at the *arc* promoter and the fast response.

### Identification of other IEGs

Using microarrays to identify IEGs upregulated by neuronal activity, Saha found 22 that responded within 15 minutes — rapid IEGs — with the other “delayed IEGs” taking much longer. A genome-wide analysis using ChIP-seq, with help from NIEHS Bioinformatics Information Specialist David Fargo, Ph.D., revealed that nearly all of the rapid IEGs have stalled Pol II, but, in contrast, most of the delayed IEGs lacked the poised Pol II.

Saha was reassured to find that the promoter proximal Pol II enrichment was also detected in brain tissue and that the kinetic difference between these gene classes was observed in response to the animals' exposure to a novel environment, suggesting a real biological role for this mechanism. He said he has exciting experiments underway to follow up on this provocative research project, which he hopes to complete before looking to start his own group.

*Citation:* Saha RN, Wissink EM, Bailey ER, Zhao M, Fargo DC, Hwang JY, Daigle KR, Fenn JD, Adelman K, Dudek SM. 2011. Rapid activity-induced transcription of Arc and other IEGs relies on poised RNA polymerase II. *Nature Neurosci*; doi:10.1038/nn.2839: [Online 29 May 2011].

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

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## Failed experiment leads to big discovery

*By Thaddeus Schug*

A failed laboratory experiment led to an accidental discovery that is helping to change the way we understand genetics. It happened in the lab of NIEHS grantee Michael Skinner, Ph.D., at Washington State University. Skinner was studying genetic mutations, when he found, by chance, that, under the right conditions, environmental factors can change the way our genes work for generations far into the future, without damaging DNA. Skinner, who is a professor of biological sciences, spoke May 10 on his discovery and how it has shifted the field of genetics, as part of the Keystone Science Lecture Seminar Series.

Skinner's findings have contributed to a paradigm shift in the field of genetics. “Instead of relying solely on DNA and inheritance, the field of epigenetics now demonstrates how environmental factors can also determine diseases in our future, and in our children and grandchildren's future,” Skinner said. “It's called transgenerational inheritance, the process by which something in the environment alters the health not only of the individual exposed to it, but also of that individual's descendants.”



*Dudek said she is very excited about this research work and is gratified to have it published in Nature Neuroscience. She looks forward to new discoveries stemming from this provocative project. (Photo courtesy of Steve McCaw)*

Skinner explained that the term epigenetics refers to the things around DNA that regulate its activity but are independent of the DNA sequence. His lab focuses on chemical modifications of DNA called methylation. When methyl groups are added or removed from certain sections of DNA, they can change the way genes are regulated. Environmental factors, such as chemical exposures and nutrients, can influence the DNA methylation status and, according to Skinner, these changes can be passed on for multiple generations.

### Experiment gone wrong

A few years ago, Skinner was studying sexual determination in rats during early stages of development. His lab exposed embryos to endocrine disrupting chemicals (EDCs), believing they would alter sexual development. To his disappointment, the EDCs did not change sexual determination. However, he did observe that embryos exposed to vinclozolin, a common fungicide, developed a high rate of disease as they became adults.

“This is when things got interesting,” explained Skinner. “Mistakenly, a lab member continued to breed the rats to the next generation, which would be the grandchildren of the mother that was exposed during gestation. We continued to see high levels of disease in the animals, even after four generations. The only way we could explain this event is through an epigenetic-type process,” said Skinner.

Skinner noted that his discovery is not limited to rats or the fungicide he fed them. “Other labs are reporting that environmental stimuli — nutrients, chemicals, or even smoking — are capable of altering the methylation status of genes and affect not only those individuals, but also their children and grandchildren.

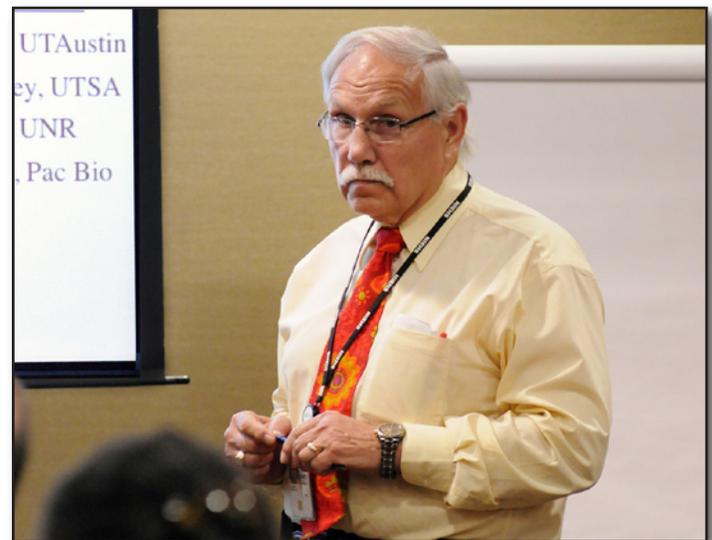
### Mapping the epigenetic changes

Skinner proposes that DNA methylation status is defined during a critical developmental period of the germ line. Therefore, chemicals capable of permanently altering the male germ line epigenome during this time frame of DNA methylation programming can cause effects that persist for generations.

Skinner has identified several promoter regions that have altered DNA methylation three generations after the initial exposure and pinpointed common genomic features present in these regions. He has also identified a potential common consensus DNA motif among the regions that presented a transgenerational change in methylation.



*Skinner is a pioneer in the field of epigenetic transgenerational inheritance, and for that reason he has met his share of resistance. “The notion that your genes, the environment, and your epigenetic programming, all play a role in your health, as well as your children’s and grandchildren’s, is a difficult concept for many people to handle,” said Skinner. (Photo courtesy of Steve McCaw)*



*Division of Extramural Research and Training (DERT) Program Administrator Jerry Heindel, Ph.D., hosted Skinner’s lecture. Heindel oversees much of the endocrine disruptor grant portfolio and has interests in how chemical exposure impacts human development. (Photo courtesy of Steve McCaw)*

These alterations appeared in the sons of the mothers exposed to the fungicide when they were pregnant, in the grandsons, and in the great-grandsons. The result is that because some genes in the mother that were supposed to be dormant were instead active, and some genes that were supposed to be active were not, males in succeeding generations developed abnormalities later in life.

Skinner is hopeful that advances in technology will allow for more cost-effective and accurate mapping of the epigenome in the near future. This will enable him to decipher, more precisely, which DNA elements are modified by exposures, and for how many generations those changes persist.

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

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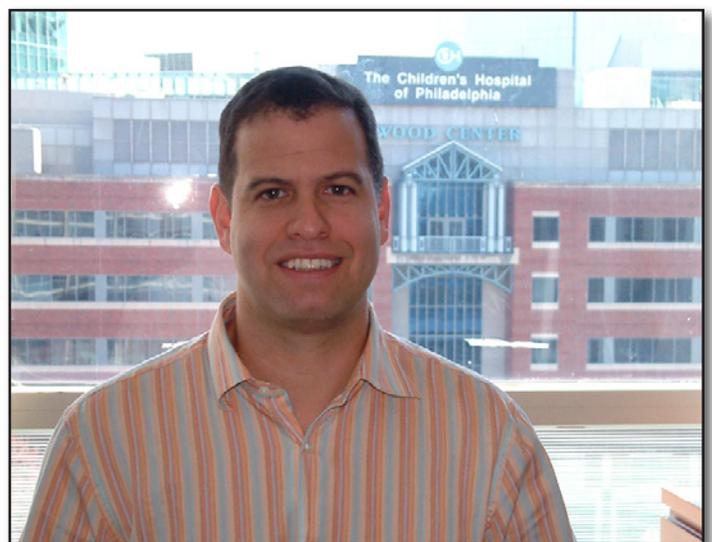
*NTP Toxicologist, Chad Blystone, PhD., listens in on Skinner's seminar. The talk drew a capacity audience from across the Institute's labs and branches. (Photo courtesy of Steve McCaw)*

## LMG speaker explores BRCA signaling network

*By Eddy Ball*

Understanding genomic instability early on may offer insight into the many factors involved in cancer, according to biologist Roger Greenberg, M.D., Ph.D. Greenberg's talk May 2 at NIEHS, "Relationship of Chromatin Responses to DNA Repair and Tumor Suppression," was hosted by Intramural Research Training Award Fellow [Steven Roberts, Ph.D.](#), as part of the NIEHS Laboratory of Molecular Genetics (LMG) Fellows Invited Lecture Series.

[Greenberg](#) is an assistant professor of cancer biology and assistant investigator in the Abramson Family Cancer Research Institute at the University of Pennsylvania (Penn) School of Medicine Institute for Translational Medicine and Therapeutics. He and his group at Penn investigate the molecular events that contribute to inherited breast and ovarian cancer predisposition, particularly the role of the breast and ovarian cancer suppressor protein BRCA1 in biochemical pathways involved in DNA double strand break (DSB) repair.



*Genome instability is a hallmark of cancer, Greenberg explained, leading "to the hypothesis that genome integrity through DNA damage responses was necessary for tumor suppression." (Photo courtesy of Roger Greenberg)*

## **A family of factors involved in familial cancers**

Single nucleotide polymorphisms (SNPs) of BRCA1 and BRCA2, first identified in the 1990s by groups that included NIEHS scientists, explain some cases of breast cancer. But Greenberg is convinced that the causes of more than half of familial breast cancers involve anomalies in at least 13 different tumor repressors that interact with BRCA1 and constitute a BRCA1-centered breast and ovarian tumor suppressor network. Individuals harboring these SNPs presumably have compromised DNA repair capabilities leading to further gene mutations and epigenetic alterations that contribute to tumor development in response to endogenous metabolic events and environmental exposures, including oncogenic viruses and ionizing radiation. Better understanding what goes awry in the BRCA1-centered tumor suppressor network, Greenberg maintains, could lead to interventions to prevent or reverse processes that allow tumor formation and proliferation.

Under normal conditions, Greenberg explained, the breast cancer gene BRCA1 helps orchestrate the repair of damaged DNA. When the BRCA1 gene is mutated or the network goes haywire with mutations of genes encoding BRCA1-interacting proteins, a woman's vulnerability to breast or ovarian cancer rises because the rate at which genes are altered increases. These errors in the BRCA1-center tumor suppressor network inhibit the recruitment of repair complexes to DNA damage sites.

Greenberg has found interactions among BRCA1 and a number of proteins in the recognition of DNA damage. Most are familiar to scientists in the field of molecular genetics, such as ubiquitin, which is instrumental in post-translational modification, RAD51, Abraxas, BRCC36, RNF8, and MDC1. Two relatively new players, both ubiquitin-interacting proteins — RAP80, which was discovered by the group headed by NIEHS Principal Investigator Anton Jetten, Ph.D., and the Greenberg group's own discovery, MERIT40 — have also been shown to strongly influence BRCA1 function.

## **From DSBs to epigenetic modification of chromatin**

Mutations and genetic alterations, such as translocations, are often thought of as the main drivers of cancer. However, Greenberg believes other cellular changes may be important as well. “Not only are there genetic changes in the early stages of cancer,” Greenberg said, “but there are chromatin changes as well here, as seen in the phosphorylation of the histone H2A variant, gamma-H2aX.”

In recent experiments, the Greenberg lab has demonstrated a further link between the generation of DSBs and alterations in chromatin structure. His group has recently published evidence that DSBs induce an ATM kinase-dependent transcriptional silencing that spans multiple kilobases of chromatin in cis to the site of DNA damage. He explained that the interplay between chromatin structure and DNA repair influences diverse biological phenomena, including cellular senescence and viral latency, that are part of the molecular basis underlying epigenetic changes that occur during carcinogenesis.

Not surprisingly, given the complexity of the BRCA1 signaling network, Greenberg remains cautious about progress. However, as his experiments have demonstrated, DSB-induced silencing can be reversed, pointing the way to other potential interventions to manipulate DNA damage response and restore DSB repair efficiency and balance. One intriguing development in new work from the Greenberg group is the potential of the protein ICP0, which promotes transcription of latent herpes simplex virus, to effectively reverse DSB-induced silencing when expressed.

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# Early prenatal vitamins may decrease incidence of autism

By Ed Kang

A new study by NIEHS-funded researchers indicates that mothers of children with autism were less likely than those of typically developing children to report having taken prenatal vitamins during the three months before and the first month of pregnancy. There was, however, no observed change in associated risk for autism when prenatal vitamins were taken after the first month of pregnancy or when multivitamins were taken at any time.

In the first [study](#) to link maternal intake of vitamins to autism risk, researchers at the University of California (UC), Davis [Medical Investigation of Neurodevelopmental Disorders \(MIND\)](#) Institute examined prenatal vitamin intake between mothers of children with autism and those of typically developing children. Mothers were asked about their vitamin use during the three months prior to pregnancy through the breastfeeding period.

“Women who did not take daily prenatal vitamins early were nearly twice as likely to have a child with an autism spectrum disorder as women who did take the supplements,” said Rebecca Schmidt, Ph.D., assistant professor in the Department of Public Health Sciences in the UC Davis School of Medicine and the study’s lead author. “The associated risk rose to seven times as great when combined with a high-risk genetic make-up.”

## Folic acid, B vitamins critical to neurodevelopment

“While the cause of autism is still unknown, this study provides more clues in our search for answers,” said Linda Birnbaum, Ph.D., director of NIEHS, which provided a majority of the funding for the study.

Prenatal vitamins generally have higher levels of iron, vitamins B6 and B12, and twice as much folic acid (folate) as multivitamins. These nutrients are known to be critical to neurodevelopment, and the study’s authors suggest a protective effect against deficits in early fetal brain development.

Approximately 700 participants, who included children with autism and typically developing children, were recruited from the larger Childhood Autism Risks from Genetics and the Environment (CHARGE) study, a population-based, case-control study of Northern California families.

Autism, according to the U.S. Centers for Disease Control and Prevention, affects about one in 110 children in the United States and is a pervasive developmental disorder marked by poor verbal and communication skills, repetitive behaviors, and difficulties in forming social connections.



*Schmidt discovered associations that suggest the time around conception might be particularly sensitive to environmental risk factors for autism. (Photo courtesy UC Regents)*



*“The good news is that if this finding is replicated, it will provide an inexpensive, relatively simple action that women can take to reduce risks for their child, which is to take prenatal vitamins as early as possible in a pregnancy and even when planning for pregnancy,” said Hertz-Picciotto, the study’s senior author and a researcher affiliated with the UC Davis MIND Institute. (Photo courtesy UC Davis)*

The study was supported by grants from NIEHS, including funding provided by the American Recovery and Reinvestment Act of 2009. Additional funding was also provided by the U.S. Environmental Protection Agency and the UC Davis MIND Institute.

*Citation:* Schmidt RJ, Hansen RL, Hartiala J, Allayee H, Schmidt LC, Tancredi DJ, Tassone F, Hertz-Picciotto I. 2011. Prenatal vitamins, functional one-carbon metabolism gene variants, and risk for autism in the CHARGE study. *Epidemiology*; doi: 10.1097/EDE.0b013e31821d0e30 [Online 23 May 2011].

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

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## Public television showcases challenges and new developments in the field of autism

Irva Hertz-Picciotto, Ph.D. and several colleagues from the MIND Institute were among the national experts featured on the six-part Public Broadcasting System series “Autism Now,” which aired beginning April 18. The six-part series was produced and narrated by Robert McNeil.

The series also features an [extended interview](#) with Hertz-Picciotto on what may be behind the rising incidence of autism.

## Arsenic and smoking synergistic, Superfund study shows

By Anne Johnson

Arsenic exposure and cigarette smoking both pose enormous global health challenges. The two are even more deadly in combination, according to a recent study from the University of Chicago Medical Center, funded in part by an NIEHS Superfund Research Program (SRP) [grant](#). The research findings underscore the urgent public health need to prevent arsenic exposure and reduce smoking rates worldwide.

The [study](#), led by [Habibul Ahsan, M.D.](#), professor of epidemiology and director of the Center for Cancer Epidemiology and Prevention at the University of Chicago, tracked nearly 12,000 Bangladeshi men and women for more than 6 years. It found that arsenic exposure increases a person’s risk of dying from cardiovascular disease, and that the effect is magnified up to sixfold in smokers over non-smokers. The findings appeared online May 6 in the *British Medical Journal*.

Arsenic, an element found naturally in rocks and soils, is known to be toxic. Its role in causing skin lesions, respiratory disease, and several types of cancer has been extensively studied, but its association with cardiovascular disease has only recently drawn attention from the scientific community. This large prospective cohort study sheds new light on the relationships among arsenic exposure, heart disease, and smoking.



*The study builds on ongoing work by Ahsan and Columbia University SRP grant Principal Investigator Joe Graziano, Ph.D. ([see story](#)), that includes a 2010 study on all-cause mortality and arsenic exposure. (Photo courtesy of Habibul Ahsan and the Columbia University SRP)*

## Arsenic increases risk for heart disease

An estimated 57 million people in Bangladesh are chronically exposed to arsenic through contaminated well water. Arsenic also poses a threat in many other areas of the globe, including the United States, where about 13 million people are at risk from elevated levels of arsenic in groundwater. People can be exposed to arsenic through drinking water, food, or air.

The researchers recruited 11,746 Bangladeshis starting in 2000 and tracked each individual's exposure to arsenic, smoking behavior, and other factors for an average of 6.6 years. Study participants received a personal visit every two years, which included a physical examination and a structured interview. The researchers measured arsenic exposure by testing drinking water sources and taking urine samples from study participants. The results were adjusted to take into account potential confounders such as age, sex, and body mass index.

During the study period, a total of 460 study participants died, 198 of them from cardiovascular disease. The researchers attributed nearly 30 percent of the deaths from cardiovascular disease to elevated arsenic levels in drinking water.

Those who drank water with high levels of arsenic — above 148 parts per million (ppm) — were nearly 50 percent more likely to die of cardiovascular disease than those drinking water below 12 ppm. The maximum arsenic concentration considered safe by the World Health Organization is 10 ppm.

The association between arsenic exposure and cardiovascular disease death was strongest at the highest levels of arsenic exposure, but even exposure to moderate levels of arsenic — 12ppm to 148 ppm — significantly increased a person's risk of dying from heart disease. The mechanism through which arsenic contributes to cardiovascular disease is not known.

## A dangerous interaction

The researchers also studied how cigarette smoking influences the risk of heart disease in those exposed to arsenic. They found that smoking exacerbates the effects of arsenic exposure — the heart disease risk for those who smoke and are exposed to arsenic was greater than the sum of the two risk factors taken separately.

Non-smokers exposed to high levels of arsenic faced a 50 percent greater chance of dying of heart disease than those exposed to safer levels of arsenic. By comparison, current smokers exposed to high levels of arsenic were 300 percent more likely to die of heart disease than smokers exposed to lower levels of arsenic.

*Citation:* [Chen Y, Graziano JH, Parvez F, Liu M, Slavkovich V, Kalra T, Argos M, Islam T, Ahmed A, Rakibuz-Zaman M, Hasan R, Sarwar G, Levy D, van Geen A, Ahsan H. 2011. Arsenic exposure from drinking water and mortality from cardiovascular disease in Bangladesh: prospective cohort study. \*BMJ\* 342:d2431.](#)

## Bolstering the argument for primary preventive efforts

The increased risk associated with smoking and arsenic in combination was also seen in former smokers and among those exposed to only moderate levels of arsenic exposure. The findings suggest that smoking influences arsenic toxicity, making even moderate levels of arsenic exposure particularly dangerous for smokers.

The results offer important insights for public health efforts to combat the health effects of both smoking and arsenic exposure. The synergistic effects of smoking and arsenic exposure mean that each factor is even more dangerous in the presence of the other — but the interaction also means that, where both factors exist, a reduction in one factor can have a greater-than-expected impact on improving health and reducing cardiovascular disease.

(Anne Johnson is on the staff of MDB, a contractor for the NIEHS Superfund Research Program and Worker Education Training Program.)

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## New study estimates heat wave mortality from climate change

By *Melissa Kerr*

Heat waves have always posed a threat to human health. With global climate change models continuing to predict rising temperatures, the specific implications of rising temperatures compounded by more frequent heat waves are a growing public health concern.

In a new study funded by [NIEHS](#) and the U.S. Environmental Protection Agency (EPA), researchers used climate change models and local historical data to predict the potential impact of warming on human mortality in the Chicago metropolitan area. One of the first efforts of its kind, the study, “[Toward a Quantitative Estimate of Future Heat Wave Mortality under Global Climate Change,](#)” appeared in the May issue of *Environmental Health Perspectives*.

“Our study looks to quantify the impact of increased heat waves on human mortality. For a major U.S. city like Chicago, the impact will likely be profound and potentially devastating,” said lead author [Roger Peng, Ph.D.](#), in a Johns Hopkins University press release. Peng is an associate professor in the Department of Biostatistics at the Bloomberg School of Public Health at Johns Hopkins University. His former colleague at Hopkins, NIEHS grantee [Francesca Dominici, Ph.D.](#), now a professor in the Department of Biostatistics and associate dean for information technology in the Harvard University School of Public Health, was principal investigator on the study.



*In several earlier studies, Peng, above, and Dominici have collaborated with NIEHS Outstanding Young Environmental Scientist (ONES) awardee Michelle Bell, Ph.D., an associate professor in the Yale University School of Forestry and Environmental Studies, who was also an author on this study. (Photo courtesy of Christopher Hartlove)*

### Heat waves of the past

According to the researchers, heat waves have a taxing affect on the human body. Prolonged exposure to heat stresses the heart and other aspects of the human body’s regulation system. If the temperature remains elevated overnight, the body becomes overwhelmed because it doesn’t get the respite that it needs.

Because there is no universally accepted definition of a heat wave currently available, the researchers applied one that uses two threshold temperatures and duration as criteria. To qualify as a heat wave, they said, the high temperature must reach or exceed the 97.5th percentile of daily maximum temperatures recorded in Chicago from 1987 to 2005 for at least three days, with temperatures remaining above the 81st percentile for the entire period.

According to the researchers, Chicago was selected for the study because of its significance nationally and the frequency of heat waves there. During the 19-year period studied, there were 14 heat waves lasting an average of 9.2 days each. A total of 1,007 excess deaths, approximately 53 per year, could be attributed to heat waves.

## Heat waves of the future

The research team used seven climate model simulations of temperature from the Program for Climate Model Diagnosis and Intercomparison (PCMDI) as part of the Coupled Model Intercomparison Project (CMIP3) to estimate future heat waves. The analysis examined data from the National Morbidity, Mortality, and Air Pollution Study, the National Center for Health Statistics, and the National Climatic Data Center, as well as the EPA Air Quality System, integrating historical mortality, weather, and air pollution data with climate model output.

“A key advantage of our approach is that it can be easily modified with respect to the various inputs and assumptions about the future to obtain predictions from a wide range of plausible scenarios,” the authors explained.

Based on estimates for 2081-2100, the study predicts that Chicago could expect from 166 to as many as 2,217 deaths per year from heat waves, depending on the climate change model used.

“Even in the presence of [these] large intermodel variations,” the researchers explain, “the results of our analysis suggest that annual heat wave mortality will increase in the future.”

While the researchers concede the limitations of their study, including uncertainty about future trends of human adaptation to extreme temperatures, they remain hopeful that the results of this study can be used to stimulate further research on this important topic and spur efforts to mitigate the effects of climate change.

“The impact of future heat waves on human health will likely be profound, and significant gains can be expected by lowering future carbon dioxide emissions,” they concluded.

*Citation:* Peng RD, Bobb JF, Tebaldi C, McDaniel L, Bell ML, Dominici F. 2011. Toward a Quantitative Estimate of Future Heat Wave Mortality under Global Climate Change. *Environ Health Perspect* 119(5):701-706.

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

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*Dominici gave a talk about her research in June 2010 at NIEHS. She is developing novel models to help solve one of the persistent mysteries of public health — the effects of environmental exposures to complex mixtures. (Photo courtesy of Steve McCaw)*

## This month in EHP

By Eddy Ball

The lead news story in [Environmental Health Perspectives \(EHP\)](#) this month explores the current state of the science on autoimmune disease and its connection to the environment, addressing questions about whether autoimmune disease is on the rise and whether there are specific — and potentially avoidable — environmental triggers involved. A second news feature examines the fourth National-Scale Air Toxics Assessment released by the U.S Environmental Protection Agency in March and discusses toxicity implications of the data.

This June [Researchers' Perspective](#) podcast marks the tenth anniversary of EHP Chinese Edition, with host Ashley Ahearn discussing air pollution in China with [Junfeng Zhang, Ph.D.](#)

Featured review and research studies this month include the following:

- Enhancing Credibility of Chemical Safety Studies
- Pollution Control Measures and Inhalation Cancer Risk
- Estimating the Global Public Health Implications of Electricity and Coal Consumption
- Rotenone, Paraquat, and Parkinson's Disease
- Chemicals in Pregnant Women (NHANES)

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## Upcoming Rodbell lecturer Brigid Hogan

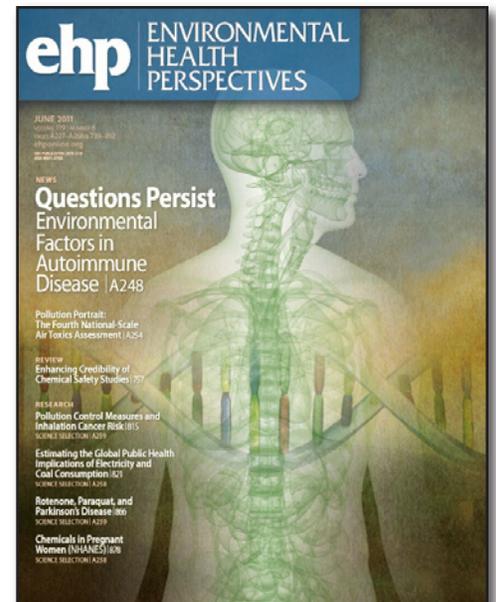
By Eddy Ball

Noted developmental biologist Brigid Hogan, Ph.D., will deliver the 2011 Martin Rodbell Lecture June 14 at NIEHS. Hosted by NIEHS Reproductive Medicine Group Principal Investigator [Carmen Williams, M.D., Ph.D.](#), Hogan will explore the topic “New perspectives on stem cells and lung disorders,” in talk that begins at 11:00 a.m. in the Rodbell Auditorium.

[Hogan](#) is a professor and chair of the Department of Cell Biology at Duke University. Educated at Cambridge University in her native England, she was head of the Laboratory of Molecular Embryology at the National Institute for Medical Research in London before joining the faculty at the Vanderbilt University Medical Center, where she was a Howard Hughes Medical Institute investigator. Among her many honors, Hogan has been selected as a member of the National Academy of Sciences and the Institute of Medicine, as well as a fellow of the American Academy of Arts and Sciences and the Royal Society of London.



<http://twitter.com/ehponline>



Linked video:

[Watch an interview of Hogan during a 2009 symposium at Cold Spring Harbor, as she discusses science and the role of women in scientific leadership \(24:23\).](#)

(Launches in new window)

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In her work with the human lung, Hogan and her [lab](#) have focused on the biology of embryonic stem cells and primordial germ cells, and the process of organogenesis, the development of a complex and specialized organ from a small population of undifferentiated stem cells. According to Hogan, potential applications of her research could include accelerating lung development in premature babies, better understanding the lung's response to environmental toxins, irradiation, and disorders such as asthma, and discovering how to generate endodermal cells from undifferentiated embryonic stem cells.

The Rodbell Lecture, now in its 13th year, is one of two named talks in the annual NIEHS Distinguished Lecture Series. It honors former NIEHS Scientific Director and Nobel Laureate [Martin Rodbell, Ph.D.](#), who presented the first talk in the series shortly before his death in 1998. Rodbell shared the 1994 Nobel Prize in Physiology or Medicine with [Alfred Gilman, Ph.D.](#), for the discovery of G-proteins, signal transducers that transmit and modulate signals in cells to control fundamental life processes.

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*Hogan holds the distinction of being the first woman to chair a basic science department at the Duke University Medical Center. She is the second woman to be honored with an invitation to present a Rodbell Lecture at NIEHS, joining an impressive group of scientists that includes three Nobel Prize winners. (Photo courtesy of Brigid Hogan)*

## Upcoming bioinformatics conference to be held at UNC Friday Center

*By Robin Arnette*

The third Toxicogenomics Integrated with Environmental Sciences (TIES) Conference will take place Sept. 15-16 at the University of North Carolina at Chapel Hill (UNC) William and Ida Friday Center for Continuing Education in Chapel Hill, N.C. The two-day event is sponsored by the National Institute of Environmental Health Sciences (NIEHS), the U.S. Food and Drug Administration National Center for Toxicological Research (NCTR), the SAS Institute, and UNC. The international meeting will focus on how bioinformatics and emerging technologies help researchers better understand the environmental influences behind the development and progression of human disease.

The conference theme is “The Biology and Bioinformatics behind Environmental and Toxicologic Influences,” and will feature oral presentations and a poster session. Keynote speakers include John Quackenbush, Ph.D., professor of computational biology and bioinformatics at the Harvard School of Public Health Dana-Farber Cancer Institute; William Slikker Jr., Ph.D., director of NCTR; Rebecca Fry, Ph.D., assistant professor of environmental sciences and engineering at UNC Gillings School of Global Public Health; and Xihong Li, Ph.D., professor of biostatistics at the Harvard School of Public Health.

For more information and to register, visit <http://eseconf.sph.unc.edu/TIES2011>. Registration for NIEHS and NCTR staff is free.

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# Extramural papers of the month

By Jerry Phelps

- [Water purifier harnesses nanotechnology](#)
- [Elevated blood levels of flame retardants in Mexican-American children](#)
- [Ah receptor activation delays development of chemical-induced mammary tumors](#)
- [Risk of bladder cancer higher in diabetics](#)



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

## Water purifier harnesses nanotechnology

Scientists at the University of Kentucky, with support from the NIEHS Superfund Research Program, have invented a water purifier that degrades chemical toxins without the addition of acids or other harmful chemicals. The device employs nanotechnology to generate hydroxyl radicals and could be used to provide safe, clean drinking water for the developing world and the U.S.

Two-thirds of all hazardous waste sites in the U.S. are contaminated with trichloroethylene (TCE). Along with trichlorophenol, TCE is responsible for drinking water contamination in much of the world. To remove these chemicals from drinking water is costly and requires the use of acids and other hazardous chemicals in large amounts. The Kentucky investigators first mix glucose with contaminated water and then let it pass through a nanostructured membrane embedded with glucose oxidase, an enzyme that produces hydrogen peroxide from glucose. A second membrane containing iron trapped in an acidic matrix converts the peroxide into hydroxyl radicals, which interact with and destroy the organic pollutants.

The investigators are currently filing for patents for the technology. The device could represent a major step forward in providing clean drinking water inexpensively in areas of the world where chemical contamination is prevalent.

*Citation:* Lewis SR, Datta S, Gui M, Coker EL, Huggins FE, Daunert S, Bachas L, Bhattacharyya D. 2011. Reactive nanostructured membranes for water purification. *Proc Natl Acad Sci U S A* 108(21):8577-8582.

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## Elevated blood levels of flame retardants in Mexican-American children

NIEHS-funded epidemiologists at the University of California Berkeley report that levels of flame retardants are seven times higher in Mexican-American children living in California than children in Mexico. They report that levels of the flame retardant chemicals, polybrominated diphenyl ethers or PBDEs, are higher in these children than almost all other groups of children ever studied.

PBDEs are used in a variety of products, including padding in upholstered furniture, carpet pads, child car seats, mattresses, and clothing. Some of these products have been reported to contain as much as fifty percent of the

chemicals by weight and they tend to have long lifespans. PBDEs do not bind chemically to the products they are used in. As the products age and degrade, the chemicals are released in the form of dusts. California has very high anti-flammability standards; these could have inadvertently led to high levels of PBDE-laden dusts in homes.

Prior research suggests that exposure to PBDEs is linked to infertility problems and thyroid hormone imbalances. The levels reported in this study represent a major challenge for California public health officials.

*Citation:* Eskenazi B, Fenster L, Castorina R, Marks AR, Sjödin A, Rosas LG, Holland N, Guerra AG, López-Carrillo L, Bradman A. 2011. A comparison of PBDE serum concentrations in Mexican and Mexican-American children living in California. *Environ Health Perspect*; doi:10.1289/ehp.1002874; [Online 15 April 2011].

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## Ah receptor activation delays development of chemical-induced mammary tumors

In a somewhat surprising finding, NIEHS-supported investigators report that exposure to tetrachlorodibenzo-*p*-dioxin (TCDD) prior to exposure to the known mammary tumor promoter dimethylbenz[*a*]anthracene (DMBA), delays the development of breast cancer in mice and produces a lower overall incidence of breast tumors. The researchers conclude that the effect is caused by activation of the Ah receptor by TCDD.

The Ah receptor has been studied extensively because of its role in the toxic effects of dioxin-like compounds. However, recently there have been numerous reports that the receptor is involved in normal development, carcinogenesis, and cell cycle regulation.

Previous work has suggested that exposure to TCDD during pregnancy causes impaired mammary gland growth and development. Normal pregnancy-induced mammary differentiation has been shown to be protective against breast cancer. The investigators' initial hypothesis was that TCDD exposure would make the mice more susceptible to DMBA-induced tumor development.

In both pregnant and non-pregnant mice, TCDD treatment prior to exposure to DMBA caused a four-week delay in tumor formation and a lower tumor incidence throughout the six month study. No markers for tumor initiation differed between TCDD-treated and control mice. These findings suggest that Ah receptor activation causes the delay in tumor formation and could provide an opportunity for possible therapeutic interventions.

*Citation:* Wang T, Gavin HM, Arlt VM, Lawrence BP, Fenton SE, Medina D, Vorderstrasse BA. 2011. Aryl hydrocarbon receptor activation during pregnancy, and in adult nulliparous mice, delays the subsequent development of DMBA-induced mammary tumors. *Int J Cancer* 128(7):1509-1523.

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## Risk of bladder cancer higher in diabetics

NIEHS Superfund Research Program grantees at Dartmouth Medical School report that a history of diabetes and taking oral medications for diabetes significantly increase a person's risk for developing bladder cancer. These findings are based on a case-control study in New Hampshire including nearly 600 people.

Recent research has demonstrated a link between diabetes and bladder cancer. However, these studies did not consider type or duration of diabetic therapy. The current study found that diabetics were more than twice as likely to develop bladder cancer as matched controls. The association was even stronger in diabetics with a history of the disease of more than 16 years. Their risk was more than 3½ times higher. Diabetics with a history of taking oral hypoglycemic medications were at more than three times greater risk for bladder cancer.

The researchers point out that their study was limited by their inability to differentiate between Type 1 and Type 2 diabetics. They conclude that more research is needed to determine the weighted effects of duration of diabetes and medication type on the risk of bladder cancer.

*Citation:* MacKenzie T, Zens MS, Ferrara A, Schned A, Karagas MR. 2011. Diabetes and risk of bladder cancer: Evidence from a case-control study in New England. *Cancer* 117(7):1552-1556.

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

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## Intramural papers of the month

*By Erin Hopper and Jeffrey Stumpf*

- [Innate immunity linked to DNA damage response](#)
- [Human PUMILIO proteins adopt multiple RNA binding modes](#)
- [Separation of function mutations identified in estrogen receptor alpha](#)
- [Estimating relative risk in epidemiological studies using imputed data sets](#)

### Innate immunity linked to DNA damage response

Tumor suppressor p53 is a transcription factor that binds to response elements of greater than 200 genes, allowing cells to cope with DNA damage. NIEHS researchers have found that the innate immune system is yet another important target of the p53 network in a manner that is specific to primates.

Previous work at NIEHS showcased sequence motifs that predicted the location of p53 binding and the degree of activation of the downstream gene. These initial studies suggested that some Toll-like receptors (TLRs), proteins that recognize various molecules and trigger the inflammatory immune response, may be activated by p53.

This recent study reveals that in primary human lymphocytes and alveolar macrophages, expression of nearly all TLRs is altered by DNA damage, and most of the changes are dependent on p53. For example, TLR8 expression is controlled by p53, and a natural single nucleotide polymorphism (SNP) in the TLR8 response element changed p53 activation, suggesting the exact location of p53 binding.

The study also shows variability of p53 responsiveness among individuals. Because p53 is important in tumor suppression, this variability may help explain different genetic predispositions to cancer. These findings on individual differences in TLR induction by p53 activation and DNA damage should prove useful in the development of TLR-targeted vaccines and TLR-based cancer treatments.

*Citation:* [Menendez D\\*](#), [Shatz M\\*](#), [Azzam K](#), [Garantziotis S](#), [Fessler MB](#), [Resnick MA](#). 2011. The Toll-like receptor gene family is integrated into human DNA damage and p53 networks. *PLoS Genet* 7(3):e1001360. (\*co-first authors) [Story](#)

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## Human PUMILIO proteins adopt multiple RNA binding modes

Investigators at NIEHS have demonstrated that human PUMILIO proteins can adopt multiple binding modes to interact with a variety of RNAs. PUMILIO proteins are members of the PUMILIO/FBF (PUF) family of proteins, which is a group of RNA-binding proteins that is responsible for post-transcriptional regulation of gene expression.

All PUF proteins contain an RNA-binding domain called the Pumilio homology domain (PUM-HD), in which eight PUM repeats and two pseudo-repeats come together to form a crescent-shaped structure. In a 1:1 binding mode, each PUM repeat recognizes and binds a single RNA base. However, recent studies have suggested that PUF proteins bind a wider variety of RNAs than would be predicted from a 1:1 binding mode.

In this study, the investigators crystallized the PUM-HD of human PUMILIO1 and PUMILIO2 in complex with four RNAs that varied in sequence. They found that these proteins exhibit three different binding modes around the fifth RNA base, including two 1:1 modes and one base-omission mode. These multiple binding modes allow for the recognition of a larger variety of RNA sequences. While these binding modes do not appear to vary the binding affinity of RNA, they may serve to expose alternate binding surfaces for various protein interaction partners.

*Citation:* [Lu G](#), [Hall TM](#). 2011. Alternate modes of cognate RNA recognition by human PUMILIO proteins. *Structure* 19(3):361-367.

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## Separation of function mutations identified in estrogen receptor alpha

NIEHS researchers have identified critical sequences for each function of estrogen receptor alpha (ERalpha) by mutating the gene that encodes it. Because estrogen receptors (ERs) mostly determine the effects of estrogen, mapping receptor functions is important for understanding hormone regulation.

Ligands that bind to ERs have the ability to activate three distinct functions of this receptor: binding directly to DNA to regulate gene expression; binding to other transcription factors that bind DNA and alter gene expression; and facilitating rapid action signaling cascades in response to various ion exchange pathways. Of the three functions, crucial amino acids were only described for the direct DNA binding activity. The researchers focused on the D-domain of ERalpha and found sequences within this domain critical for interaction with other transcription factors. They also blocked nuclear localization of the receptor to block genomic responses to focus on the rapid action signaling events.

This study reported three distinct mutants that separately block recruitment of transcription factors, nuclear localization, and all ligand-mediated actions in the nucleus, but all three mutants maintained the ability to promote rapid action responses.

Separation of function mutants are critical for understanding the role of each function in vivo. Because targeting estrogen and its receptors is important in many therapeutic strategies, these studies promote the possibility of precisely changing a specific activity involved in estrogen regulation.

*Citation:* Burns KA, Li Y, Arao Y, Petrovich RM, Korach KS. 2011. Selective mutations in estrogen receptor alpha D-domain alters nuclear translocation and non-estrogen response element gene regulatory mechanisms. J Biol Chem 286(14):12640-12649.

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## Estimating relative risk in epidemiological studies using imputed data sets

Researchers from the Biostatistics Branch and Epidemiology Branch at NIEHS recently developed a new method to estimate relative risk using imputed single nucleotide polymorphism (SNP) data from cases and their parents. Data imputation allows for the exploration of untyped SNPs and is required for meta-analyses of multiple studies that used different platforms for genotyping. SNP imputation involves using software to substitute in SNP data when gaps in the data are present. Before the development of this method, no technique for meta-analysis of imputed SNP data involving both family-based studies and case-control studies existed.

The researchers used a log-additive model to estimate the relative risk for a disease-related variant and ran a simulation to test the model. The simulation confirmed that the method was accurate at estimating risk using genotyped SNP data. Next, the researchers applied the method to a real data set using the Mexico City Childhood Asthma Study (1998-2003). This data set allowed for the comparison of relative risks calculated using genotyped SNP data and data imputed using the software package MACH.

The estimated relative risks calculated using the imputed data correlated very well with those calculated using the actual genotypes, confirming the effectiveness of this method for the analysis of imputed SNP data. This method will allow researchers to conduct meta-analyses using a mix of case-parent triad and case-control studies.

*Citation:* Shi M, London SJ, Chiu GY, Hancock DB, Zaykin D, Weinberg CR. 2011. Using imputed genotypes for relative risk estimation in case-parent studies. Am J Epidemiol 173(5):553-559.

(Erin Hopper, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Structural Biology Mass Spectrometry Group. Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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# Inside the Institute

## NIEHS celebrates Earth Day

By Eddy Ball

NIEHS celebrated Earth Day 2011 May 4 in the Rall Building on the main campus and May 5 at its Keystone satellite facility. At both venues, visitors could learn about ways to help the environment, enjoy fellowship and organic, chemical-free coffee, and make a pledge to “Be the Change” by taking specific action to promote sustainability.

Volunteers and members of the NIEHS Environmental Awareness Advisory Committee (EAAC), which organized the event, were on-hand to talk about hybrid, electric, and standard vehicle comparisons; encourage employees to consider reducing energy by using public transportation, cycling, and teleworking; and demonstrate recycling and composting.

 **Linked video:**  
[See how to make a worm composting bin for the home \(04:37\)](#)  
(Launches in new window)

Download Media Player:  Flash 



Volunteers Dick Sloane, left, and Beth Anderson wait for the next pot of organic coffee. Sloane tried to recruit people to share vehicles, ride the bus, cycle, and telecommute to save energy and reduce stress. (Photo courtesy of Steve McCaw)



Paul Johnson, left, and volunteer Betsy Kennington discussed the products of vermiculture — and the worms responsible for the highly successful NIEHS composting program, which has dramatically reduced landfill waste from the NIEHS cafeteria. (Photo courtesy of Steve McCaw)

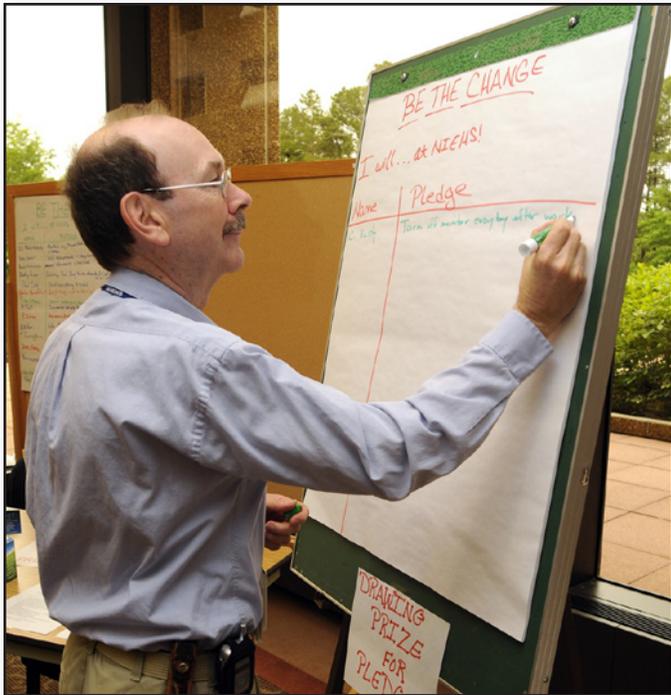


Kennington shows off the humble hero of the NIEHS composting program, the red wiggler worm. WikiHow has posted easy to follow directions [online](#). (Photo courtesy of Steve McCaw)

People who took the “Be the Change” challenge were entered into a drawing for a gift basket. It included a pound of coffee, a mug, a glass, and a book titled “Javatrekker.” A total of 34 people at the NIEHS pledged to make a change while at work. Some examples of the pledges people made were to print double-sided, telework, start paperless meetings, give up personal printers, and to turn off the computer monitor when leaving the desk. The winner of the gift basket was Benny Encarnacion — Congratulations!



Volunteers J.J. Bell-Nichols, left, and Jenn Evans have reason to smile as they show off the first group of pledges to “Be the Change.” (Photo courtesy of Steve McCaw)



Clyde Hasty, above, witnessed for sustainability by entering his pledge into the “Be the Change” signup sheet on display for all to see. (Photo courtesy of Steve McCaw)



And the proud winner of the “Be the Change” drawing was Benny Encarnacion. EAAC co-chair Paul Johnson and member Jenn Evans, who coordinated the “Be the Change” event, presented Encarnacion with his prize basket. (Photo courtesy of Paul Johnson)

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## Laughter lecture kicks off Health and Fitness Week

By Matt Goad

Henry Lesesne, M.D., kicked off Health and Fitness Week at NIEHS with a lecture on the power of laughter as medicine May 9 in Rodbell Auditorium, followed by a round of “laughter yoga.”

Lesesne, a gastroenterologist with UNC Health Care, set as the topic for his talk “Was Patch Adams Right?” referring to the hit movie – filmed partly Chapel Hill – about a medical student who espouses techniques of treatment that emphasize personal connection with a patient, instead of treating the patient like an object. The film was based on the true-life story of Hunter “Patch” Adams, M.D.

Lesesne showed about ten minutes of the film, including a portion in which Adams, then a first-year medical student impatient to begin healing, sneaks into the hospital to make rounds with more advanced medical students. As the students gather around a diabetic patient and discuss her condition and treatment, including the possibility of amputation, Adams asks what her name is, a question that raises the eyebrows of the other students. As the group walks on, he gives her hand a little touch.

### Health benefits of laughter

The point, Lesesne argued, is that doctors don't have to be comedians, but that showing a personal, humane touch can make treatment more effective. And there are proven health benefits to outright laughter, he said.

For example, the arteries, Lesesne pointed out, dilate during laughter. He advised that anyone having a heart attack take two chewable aspirin, call 911, cough, and then try to laugh while waiting for help to arrive.

Also, Lesesne discussed a study in which participants first were shown horror movies for a week, then checked for the antibody Immunoglobulin A (IgA). Then, they watched comedies for a week and were checked again. Their IgA levels plummeted after the first week, and skyrocketed after the second, suggesting positive effects on immune system balance.

And, ten minutes of laughing, Lesesne said, burns 45 calories, what he calls "internal jogging."

### Laughter yoga

To continue the laughter as healing theme, after the lecture, the group participated in laughter yoga, led by certified laughter yoga instructor Kyle Turner.

The body doesn't even need to know why it is laughing to reap the benefits, Turner instructed the group, so the key is to not wait for a funny joke but to just start laughing. Also important is eye contact.



*Lesesne discussed the benefits of laughter on human health and the ways humor can ease patients' anxiety in the clinical setting. (Photo courtesy of Steve McCaw)*



*Betty Lewis, NIEHS on-site coordinator for Kelly Government Solutions, reacts with a smile to Lesesne's comedic efforts. (Photo courtesy of Steve McCaw)*

So he had the members of the group perform exercises such as “the lion,” where they roamed around the room and roared at each other and lifted their arms up and “the milkshake,” where they acted like they were pouring a milkshake from one cup to another.

One move anyone can use when they need a break at the office, Turner explained, is “the cell phone,” which simply involves holding up a cell phone to the ear and laughing, as if there was a hilarious conversation going on.

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

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*And NTP contractor Xiaohong Gu, Ph.D., right, could barely contain herself as the jokes kept coming. (Photo courtesy of Steve McCaw)*

## Employees enjoy rites of spring during Health and Fitness Week

*By Eddy Ball and Matt Goad*

NIEHS held its annual Health and Fitness Week May 9-13 with a slate of activities encouraging employees to practice a healthy lifestyle through exercise, balanced nutrition, and weight management. Events included a lecture on laughter and medicine ([see story](#)), health and fitness demonstrations, Bike to Work Day, and many fun activities, such as Wii games, a golf outing, a 2-mile walk, and line dancing, that promote active participation geared to an individual’s own pace.

Many of the highlights of Health and Fitness Week involve good-natured and often longstanding rivalry among very talented amateur athletes in competitive events, such as the Rogathon 5K marathon, basketball contests, and the fast-paced table tennis tournament that made the F-module entry hall sound like a firing range, as opponents sent balls rapidly back and forth across the net.



*The walkers started out on the 2-mile walking course in front of the Rall building. (Photo courtesy of Steve McCaw)*



Number 57, Liam O'Fallon, led the pack to start the Rogathon 5K. (Photo courtesy of Steve McCaw)



Jeff Stumpf took his 13-month-old son, Cameron, along during the Rogathon 5K. Stumpf finished ninth overall. (Photo courtesy of Steve McCaw)



O'Fallon, left, and Bonnie Joubert were the men's and women's winners of the Rogathon 5K, which was named in honor of retired race director Walter Rogan. (Photo courtesy of Steve McCaw)



Elena Braithwaite won the women's basketball triple-threat challenge, edging out defending champion Stephanie Bullock-Allen and Claudine Cates by one point. Bullock-Allen captured second place in the playoff. D. A. Leathers won in the men's division, finishing ahead of six-time champion A. G. Carrington. (Photo courtesy of Steve McCaw)



The three-on-three tournament drew about 40 spectators to the basketball court across from F Module, to cheer, jeer, hoot, and holler their champions on. (Photo courtesy of Steve McCaw)



*Gordon Caviness put up a shot over Ron Altiery in the three-on-three round robin tournament. Caviness and team members Eric Potts and Carrington overcame the best efforts of Altiery, Antonio Gatling, and Sha-Mel Riggins in the final game to win first place, avenging a loss from last year. (Photo courtesy of Steve McCaw)*



*Altiery fights to get a shot off over Potts. (Photo courtesy of Steve McCaw)*



*And the bragging rights — at least until next spring, that is — go to the winners, shown left to right, Caviness, Carrington, and Potts. (Photo courtesy of Steve McCaw)*



*Participants, some, like Jerry Phelps, right, in full cyclist attire, ride in loose formation May 12 on Bike to Work Day, another cherished tradition during Health and Fitness Week at NIEHS. (Photo courtesy of Steve McCaw)*

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

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# Kids enjoy mostly indoor activities on Take Your Family to Work Day

*By Matt Goad*

The threat of rain canceled the outdoor activities planned for Take Your Family to Work Day May 16, but there was still plenty left to do.

“It’s really, really great to have you all here, so have fun,” NIEHS Director Linda Birnbaum, Ph.D., said in her welcoming remarks to the families in the cafeteria.

Lunchtime activities included a cakewalk and sing-along into a real microphone. Natalie, 7, daughter of Lt. Cmdr. Lindia Engram of the Commissioned Corps of the U.S. Public Health Services and senior nurse manager for NIEHS, was especially enthusiastic about the sing-along. “I like singing because it’s all about when you share your expressed feelings,” Natalie said.

For the cakewalk, contestants circled a ring of numbered chairs while music played. The contestant whose chair matched the number that Richard Woychik, Ph.D., deputy director of NIEHS and NTP, pulled out won a cake or other sweet treat.

After lunch, activities for the children included face painting, Wii games, bingo, and making party hats in Rodbell Auditorium. A TV in the corner showed cartoons, but it went unwatched as the children opted for more active entertainment.

A planned intramural softball tournament was postponed until a yet-to-be-determined date, because of the ominous forecast.

Despite a few drops of rain, though, the weather was nice enough for many employees to take their families for walks around the NIEHS lake. “Somehow we arranged to have a beautiful day, even with all the rain we’ve had lately,” Birnbaum noted.

Shirley Wang, Ph.D., of the Laboratory of Toxicology and Pharmacology, pushed her 9-month-old son Jason in a stroller toward the lake as her mother, Guiying Jin accompanied them. Wang’s father, Guohong Wang practiced catch-and-release fishing in the lake nearby. Wang’s parents were visiting from China for six months, returning in June. “That’s why I’m taking them to see my workplace,” Wang said. “They’ve never seen such a nice workplace with a lake and everything. It’s such a beautiful campus.”



*One participant showed off her face painting during NIEHS Take Your Family to Work Day. (Photo courtesy of Steve McCaw)*



*Beaming with pride at her handiwork, another crafted a party hat after lunch. (Photo courtesy of Steve McCaw)*



*Birnbaum was on hand to welcome family members to NIEHS. (Photo courtesy of Steve McCaw)*



*Woychik, right, and his wife, Janice, led the Take Your Family to Work Day cakewalk in the cafeteria. (Photo courtesy of Steve McCaw)*



*This eager contestant could hardly wait for the music to restart at the cakewalk. (Photo courtesy of Steve McCaw)*



*The kids sing along to "All-Star" by Smashmouth during the sing-along. (Photo courtesy of Steve McCaw)*



*A young winner selected a cake after her number was called in the cakewalk. (Photo courtesy of Steve McCaw)*



*It's easy to understand this young man's fatigue at the end of a busy stay visiting labs and having fun at NIEHS, but some of the kids were still eager for more. (Photo courtesy of Dona McNeill)*

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

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