



Environmental Factor

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May 2009

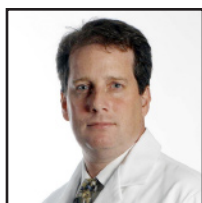
NIEHS Spotlight



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Former NIEHS Scientist to Direct Gynecologic Oncology Research at Michigan State

John Risinger, Ph.D., who began his career as a biologist at NIEHS in 1989, is the new director of

Gynecologic Oncology Research at the Michigan State University (MSU) College of Human Medicine community-based program in Grand Rapids, Mich. ...[read more](#)



SBRP Alum Named Environmental Health Science Communication Fellow

Superfund Basic Research Program (SBRP) Alumna Kathleen McCarty, Sc.D., was named to the 2009

Science Communication Fellows program sponsored by Environmental Health Sciences, the publisher of *Environmental Health News* and *The Daily Climate*.[read more](#)

Science Notebook



Nobel Laureate Oliver Smithies Gives Rodbell Lecture

The 2009 Dr. Martin Rodbell Lecture Series speaker, Oliver Smithies, D. Phil., is truly a giant in the field of science. His lecture, "Turning Pages:

From Gels to Genes," took place on April 14 and provided an overview of his impressive 61 years of research. ...[read more](#)



Colwell Presents 8th Annual Spirit Lecture on Global Health

People from NIEHS and the Triangle scientific community turned out on March 27 to hear distinguished scientific leader and microbiologist

Rita Colwell, Ph.D., discuss her life in science and her career-long quest to understand the *Vibrio cholerae* bacterium. ...[read more](#)



GEMS Meeting Focuses on Genome Variability

The Genetics and Environmental Mutagenesis Society (GEMS) held its Spring Meeting April 13 at the U.S. Environmental Protection Agency (EPA)

Auditorium in Research Triangle Park.[read more](#)



NIEHS Speakers Offer Caveats During NIH NanoWeek

The NIH Nanotechnology Task Force and the NIH Nanomedicine Roadmap hosted a series of symposia and other events in Natcher Auditorium on the

NIH campus April 7– 10, celebrating "The Promise of Nanotechnology for Medicine."[read more](#)

NIEHS Spotlight



NIEHS Recognized for Excellence in Animal Care

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EHP Partners with Mexican Public Health Journal

Scientists in Mexico and other Spanish-speaking countries can now enjoy the benefits of a new partnership announced in March between the NIEHS-funded journal *Environmental Health Perspectives (EHP)* and the interdisciplinary Mexican journal *Salud Pública de México*, according to *EHP* Editor-in-Chief Hugh Tilson, Ph.D. ...[read more](#)



Understanding Parkinson's as a Disability

The NIEHS Diversity Council Disability Advocacy Committee (DAC) presented the latest in its series of specialized seminars on health topics April 7.

The program, titled “Parkinson's Disease [PD]: Etiology, Clinical and Disability Management,” addressed medical, social and personal dimensions of a condition that affects approximately one million Americans at an estimated cost of \$27 billion annually. ...[read more](#)



NIEHS Remains #1 IC in Postdoc Satisfaction

For the fourth straight year, NIEHS ranked first among NIH institutes and centers (ICs) on the annual

survey of “Best Places to Work” for postdocs conducted by *The Scientist* magazine.[read more](#)

Science Notebook



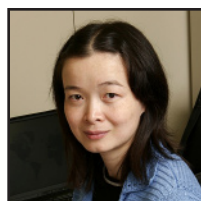
Bogenhagen Discusses Nucleoid Replication in Mitochondria

The NIEHS Laboratory of Molecular Genetics (LMG) Fellows Invited Guest Lecture series welcomed its latest speaker on March 30 with a talk on “Biogenesis and Heredity” by Dan Bogenhagen, M.D.[read more](#)



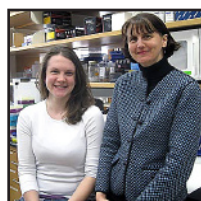
Birnbaumer To Lead NIH Directors Challenge Award Project

On April 3, NIEHS Senior Investigator Lutz Birnbaumer, Ph.D., was notified that his ambitious project to better understand the mechanisms involved in epigenetic modifications was selected for support by the NIH Director's Challenge Award Program. ...[read more](#)



Intramural Researchers Find a Key Regulator of Fat Metabolism in Liver

A new study conducted by researchers at NIEHS suggests that nuclear protein SIRT1 regulates fat metabolism in liver. ...[read more](#)



Researcher Presents Strategy for Studying Environmental AhR Modulation

In the wake of her 2008 study of dioxin's effects on the ligand-activated transcription factor aryl hydrocarbon receptor (AhR) and influenza A infection in mice, NIEHS grantee B. Paige Lawrence, Ph.D., has published a review of research on AhR modulation of anti-viral immunity... ..[read more](#)



Nobel Winner Andrew Fire to Give Distinguished Lecture

On May 19, Nobel Laureate Andrew Fire will explore “Cellular Responses to Foreign Nucleic Acids” in the latest seminar of the 2008-2009 NIEHS Distinguished Lecture Series. ...[read more](#)

NIEHS Spotlight



DOD and NIEHS Discuss Environmental Sensors

During a daylong discussion on April 21, representatives from NIEHS and Department of Defense (DOD) found that they had more in common than they thought, especially when it comes to a mutual interest in developing sensors that detect chemicals and other potentially harmful agents in the environment. ...[read more](#)



Countries Unite to Reduce Animal Use in Product Toxicity Testing

Representatives from four international agencies, including the director of the U.S. National Toxicology Program (NTP), signed a memorandum of cooperation on April 27 that could reduce the number of animals required for consumer product safety testing worldwide.[read more](#)



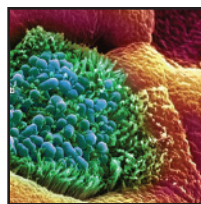
Friends and Colleagues Honor Wilson

Friends and colleagues from NIEHS and beyond gathered on April 6 to honor NIEHS Principal Investigator (PI) Samuel Wilson, M.D., for his scientific and leadership contributions to the Institute.[read more](#)

Comments Invited on Stem Cell Guidelines

In the April 23 issue of the *Federal Register*, NIH announced that it is accepting public comments on its new draft National Institutes of Health Guidelines for Human Stem Cell Research through May 26, 2009. ...[read more](#)

Science Notebook



This Month in EHP

The May 2009 issue of *Environmental Health Perspectives* is now available on-line, with a feature story on environmental effects on the microbiota — the vast population of bacteria and other microbes that regulate health in the gut. ...[read more](#)

Extramural Research

Extramural Update

The NIEHS Division of Extramural Research and Training (DERT) recently recognized three additional NIH Pathway to Independence Award (K99/R00) recipients for their successful transition to tenure track or equivalent status and officially welcomed them as members of the NIEHS grantee community. ...[read more](#)

Extramural Papers of the Month

- [Pesticide Exposure Raises Risk of Parkinson's Disease](#)
- [Solution Found to Increase Nanotube Luminescence](#)
- [Nasal Injury in Rats Exposed to Diacetyl May Be Predictive of Lung Injury in Humans](#)
- [Increased Immunoglobulin in Children with Autism](#)

Intramural Research

Intramural Papers of the Month

- [Telomere Length Is Associated with Obesity and Weight Gain](#)
- [Mouse Allergens Associated with Asthma Symptoms](#)
- [Female Mice Neonatally-Treated with Genistein Exhibit Reproductive Abnormalities](#)
- [Novel Role for Estrogen Receptor Beta in Granulosa Cells](#)

Inside the Institute



Assembly of Laboratory Staff Elects Officers and Councilors

On April 14, the NIEHS Assembly of Laboratory Staff (AoLS) announced the results

of its online election of officers and councilors, paving the way for the first organization of its type at NIEHS to serve as an officially sanctioned advocate for the interests of laboratory technical staff — much as the Assembly of Scientists performs that role for the Institute's staff scientists and principal investigators. ...[read more](#)



Earth Week 2009 Kick Off

NIEHS kicked off its annual celebration of Earth Week on April 21 with remarks by Director Linda Birnbaum, Ph.D., who addressed a group of staffers gathered on the patio outside the

Institute's main building. ...[read more](#)



NTP Staffer Writes of Inspiration, Faith and Encouragement

National Toxicology Program (NTP) Administrative Specialist Carolyn Hall doesn't advertise her extracurricular

talents, but the word is getting around on campus about her new book, *Intimate Journey: A Guide to Your Spiritual Path*.[read more](#)

Calendar of Upcoming Events

- **May 7**, in Rodbell Auditorium, 1:00–2:00
— Laboratory of Structural Biology Seminar Series with Angela Gronenborn, Ph.D., speaking on “The CVNH family of lectins — structure, folding and sugar binding”
- **May 13**, in Rall F-193, 11:00–1:00
— Laboratory of Neurobiology Seminar Series featuring a talk by Miriam H. Meisler, Ph.D., on “Neurogenetic mutants in the mouse reveal human disease genes: epilepsy and ALS”
- **May 18**, in Rodbell Auditorium, 10:00–11:00
— Laboratory of Molecular Genetics Fellows Invited Guest Lecture Series featuring Christophe Herman, Ph.D., speaking on “Beyond Mutation: Transcription and Protein Folding Errors Generate Heritable Epigenetic Change”
- **May 19**, in Rodbell Auditorium, 11:00–12:00
— Lecture on “Cellular Responses to Foreign Nucleic Acids” by Nobel Laureate Andrew Fire, Ph.D.
- **May 20**, in Rodbell Auditorium, 11:00–12:00
— Summers of Discovery Seminar Series, Speaker TBA
- **May 21–22**, in Rodbell Auditorium, 8:30–5:00
— NIEHS National Advisory Environmental Health Sciences Council Meeting
- **May 26**, in Rodbell Auditorium, 11:00–12:00
— Frontiers of Environmental Sciences Lecture, Speaker TBA
- **May 26**, in Rall D-350, 11:00–12:00
— Biostatistics Branch Seminar by Ruth Pfeiffer, Ph.D., topic TBA
- **May 27**, in Rodbell Auditorium, 11:00–12:00
— Summers of Discovery Seminar Series, Speaker TBA
- View More Events: [NIEHS Public Calendar](#)

Birnbaum Addresses Children's Health at Policy Translation Conference

By Eddy Ball

During her keynote address at a children's environmental health meeting March 30 at Columbia University, NIEHS Director [Linda Birnbaum, Ph.D.](#), took advantage of her time at the podium to reinforce the Institute's commitment to the [Children's Centers](#) program and highlight the range of other NIEHS research related to promoting children's environmental health. She followed a keynote talk in the morning session by Lisa Jackson, newly appointed head of the U.S. Environmental Protection Agency (EPA), co-sponsor with NIEHS of the Children's Centers.

Birnbaum spoke to an audience that included a number of NIEHS grantees and partners at the meeting, which was organized around the theme of "[Translating Science to Policy: Protecting Children's Environmental Health.](#)" The daylong event focused on three major environmental health concerns affecting children in urban areas — air pollution from fossil fuel combustion, residential pesticides, and endocrine-disrupting chemicals found in common consumer products. The meeting was co-hosted by two NIEHS grantees — the [Columbia Center for Children's Environmental Health \(CCCEH\)](#) and [WE ACT for Environmental Justice](#).

Birnbaum's talk, "The Promise of Children's Health," began with what she described as "a children's success story" in the battle to reduce lead exposures. As a consequence of legislation in the 1970s and volumes of research since — much of it supported by NIEHS — blood lead levels in children have dropped dramatically, she said, from a median level of 25 micrograms per deciliter in 1976–1980 to one-tenth that amount in 1999–2000. Birnbaum cautioned, however, that "there is no safe level of lead" and that efforts to protect children completely from exposure must continue.

As a veteran EPA scientist and NIEHS director, Birnbaum spoke adamantly about the contributions of the federal partnership-supported Centers for Children's Environmental Health and Disease Prevention Research. Researchers in this program, she explained, have raised public awareness of the hazards posed by asthma,



Birnbaum reminded her audience that mixtures pose dangers that may not be completely understood. "Some chemicals may act in an additive fashion," she said, "When we look one compound at a time, we may miss the boat." (Photo by Streetfly Studio/J.R. Carvey and courtesy of the CCCEH)



Jackson, above, told attendees, "We are guardians of the things we all value." Like Birnbaum, she was adamant about the importance of federal partnerships in children's environmental health. "EPA is an advocate for the people, and we are back on the job." (Photo by Streetfly Studio/J.R. Carvey and courtesy of the CCCEH)

indoor pollution and vehicle exhaust on the respiratory health of children, both directly and, in recent [work](#), indirectly through intrauterine exposures to air pollution that trigger epigenetic alterations in infants' gene expression.

This recent work by the CCCEH researchers provided a transition for Birnbaum as she moved into related research exploring the “Barker hypothesis” on the latent effects of early exposures *in utero* or during infancy. This research includes studies at four [Breast Cancer and the Environment Research Centers](#), supported by another federal partnership between NIEHS and the National Cancer Institute.

In addition to investigations of children's neurodegenerative disorders ongoing at the Children's Centers, Birnbaum continued, NIEHS partners with other funding sources to support an aggressive research agenda into autism spectrum disorders (ASD). The Institute serves on the Department of Health and Human Services Interagency Autism Coordinating Committee, which has set the direction for American Recovery and Reinvestment Act stimulus funding for ASD research.

Birnbaum, who has research interests herself in endocrine disruption, discussed several highlights of NIEHS-sponsored investigations into bisphenol A and other estrogen-mimicking compounds suspected of interfering with normal development and reproductive function. Along with the National Toxicology Program, which oversees the [Center for the Evaluation of Risks to Human Reproduction](#), NIEHS has been at the leading edge of strengthening the science base of toxicology and risk assessment.

Throughout her talk, Birnbaum underscored the accomplishments and potential of work supported by NIEHS, while emphasizing how much work lies ahead. She called children's health “a report card on adults.” She closed by admonishing the audience to join NIEHS in striving to make sure “our report cards give us, increasingly, A's.”



Frederica Perera, Dr.P.H., director of the CCCEH, was both a host and presenter. Birnbaum referred to her recent study of gene expression and asthma in the children of mothers exposed to diesel exhaust during their pregnancies. (Photo by Streetfly Studio/J.R. Carvey and courtesy of the CCCEH)



Panelists listened as NIEHS grantee Phil Landrigan, M.D., second from right, spoke during Roundtable 2: “Healthy Homes — Regulating Residential Pesticides and Consumer Products.” (Photo by Streetfly Studio/J.R. Carvey and courtesy of the CCCEH)



Alfred Lerner Hall at Columbia, where the meeting took place, was filled to capacity with an estimated 400 scientists, community members, policymakers and advocates for effective science-based policy on children's environmental health. (Photo by Streetfly Studio/J.R. Carvey and courtesy of the CCCEH)

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Former NIEHS Scientist to Direct Gynecologic Oncology Research at Michigan State

By Eddy Ball

John Risinger, Ph.D., who began his career as a biologist at NIEHS in 1989, is the new director of Gynecologic Oncology Research at the Michigan State University (MSU) College of Human Medicine community-based program in Grand Rapids, Mich. The MSU program works in conjunction with Spectrum Health and the Van Andel Institute. Risinger will begin his work building a laboratory research team that will eventually move to facilities at the Van Andel Institute.

Spectrum Health Executive Vice President Matt Van Vranken described the appointments of “highly acclaimed senior investigators” Risinger and colleague Jack Lipton, Ph.D., as “the latest step in building a research and health care hub in West Michigan.” Risinger said of his new position, “We really want to take my program to another level, where we will try to integrate things we see in the lab with problems we see in patients and then try to find some solutions.”

Risinger joined [MSU](#) following two-and-one-half years as director of the women’s cancer program at the Curtis and Elizabeth Anderson Cancer Institute at Memorial University Medical Center (MUMC) in Savannah, Ga. — a two-state healthcare organization serving a 35-county area in southeast Georgia and southern South Carolina. While he was at MUMC, Risinger was principal investigator on the Obesity and Cancer Program project, which was funded by a \$3 million grant from the U.S. Department of Defense.

During his ten years at NIEHS, Risinger worked with former Scientific Director J. Carl Barrett, Ph.D., as a biologist and later as a staff scientist. In 1997, he completed his doctorate at the University of North Carolina at Chapel Hill in Molecular Biology and Genetics while working full time at the Institute. When Barrett left NIEHS to work in the Laboratory of Biosystems in the Cancer Center for Cancer Research at the National Cancer Institute (NCI), Risinger turned down an offer from Duke University and followed his mentor to NCI.

Risinger described his time at NIEHS as “far and away my best experience in science” and a “truly unbelievable experience.” He was working within the Laboratory of Molecular Carcinogenesis led by Barrett in the mid-nineties when discovery of the *BRCA1* gene linked to breast cancer brought NIEHS Principal Investigator Roger Wiseman, Ph.D., and Andrew Futreal, Ph.D. — and the young Institute — national fame.



Risinger followed an alternative career path that bypassed the customary postdoctoral fellowship and found himself with Barrett, he said, “the beneficiary of a very forward-thinking guy.” (Photo courtesy of Geri Kelly and the MSU College of Human Medicine)



Former NIEHS Scientific Director Carl Barrett (Archive photo courtesy of Steve McCaw)

Risinger was also on hand when another Barrett-led team identified, isolated and cloned the *KAI1* gene that was able to suppress the spread of prostate cancer in animals. At the same time, Risinger and colleagues Tom Kunkel, Ph.D., and Asad Umar, Ph.D., were working on identification and understanding the role of mismatch repair genes in cancers. All of this together created an exciting atmosphere.

Risinger is a modest man, who attributes much of his meteoric rise in the field of gynecologic oncology to serendipity. Working with Barrett and other mentors, such as Principal Investigators Kunkel and Wiseman, the young scientist juggled a full-time job and a rigorous Ph.D. program. Choosing to stay with Barrett instead of pursuing the usual postdoctoral fellowship track, Risinger immersed himself in cancer research and developed a network with leading figures in the field, including gynecologic oncologists at Walter Reed Medical Center, which he credits with helping him combine bench science with clinical research in primary care settings.

Looking back, Risinger is amazed by the way his career has unfolded. “I could easily have gotten stuck in a non-productive postdoctoral experience,” he said, “but I was able to take advantage of the latitude Carl enjoyed as scientific director.” When he was at NIEHS in the mid-nineties, he recalled, “I would never have guessed where I would be today.”

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SBRP Alum Named Environmental Health Science Communication Fellow

By Rebecca Wilson

Superfund Basic Research Program (SBRP) Alumna [Kathleen McCarty, Sc.D.](#), was named to the 2009 Science Communication Fellows program sponsored by Environmental Health Sciences, the publisher of *Environmental Health News* and *The Daily Climate*. She is among nine other junior scientists named to the yearlong program, which seeks to train scientists in the communication of scientific research and close the gap between environmental health research and the public understanding of research results.

[McCarty](#) has extensive experience in interdisciplinary scientific work. She is an assistant professor at Yale University, holding a joint appointment with the Graduate School of Arts and Sciences and Yale Medical School Division of Environmental Health Sciences. She conducted her doctoral research on “Arsenic and Health in Taiwan and Bangladesh” at the Harvard School of Public Health, where she worked with the [SBRP-funded group](#) headed by [David Christiani, M.D.](#) This was followed by a postdoctoral position at the University of North Carolina at Chapel Hill in the Epidemiology department, investigating environmental and genetic factors that influence biomarker response and susceptibility to breast cancer.



Kathleen McCarty, above, was an SBRP trainee from 2002-2005. Her most recent [synopsis](#) is currently online. (Photo courtesy of NIEHS SBRP)

[Environmental Health Sciences](#) is a non-profit organization dedicated to advancing public knowledge of environmental health sciences by providing access to worldwide news on a variety of subjects.

Its [Science Communication Fellows](#) program is unique in that it specifically seeks out scientists to communicate research findings, rather than environmental journalists or other science reporters. Each yearlong fellowship carries with it a stipend of \$5,000.

The Fellows will work at the intersection of science and journalism. Each month, they will identify important research results and summarize them in order to make the conclusions more accessible to science reporters and the general public. In addition to these articles, the Fellows will write commentaries on the science behind current environmental health issues.

McCarty credits SBRP with her training in multidisciplinary science and her approach to science communication. Says McCarty, “Participating in this fellowship is just one of the many valuable contributions that the Superfund Basic Research Program has made to my career. Through this fellowship I am learning firsthand the value of being able to communicate the complexities of science in a manner that is meaningful to the audience — from the lay public to the veteran academic.”

Other 2009 Science Communication Fellows with NIEHS ties include NIEHS Postdoctoral Fellow [Negin Martin, Ph.D.](#), and NIEHS [Outstanding New Environmental Scientist \(ONES\)](#) grantee and North Carolina State University Assistant Professor [Heather Patisaul, Ph.D.](#)

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Basic Research Program and Worker Education and Training Program.)

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NIEHS Recognized for Excellence in Animal Care

By Eddy Ball

Reviewers described the NIEHS animal care program as “exemplary” during a recent site visit by the Council on Accreditation of the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International). In a March 17 letter, the group officially notified NIEHS Comparative Medicine Branch (CMB) Chief Diane Forsythe, D.V.M., of the NIEHS program’s full accreditation.

The decision by [AAALAC](#) was based on the Institute’s complete compliance with the very detailed [Guide for the Care and Use of Laboratory Animals](#) (Guide), which covers every aspect of animal care. Prepared by the National Research Council in 1996, the Guide represents the gold standard of best practices for more than 750 AAALAC-affiliated government, university, hospital and private laboratories engaged in research using animals.

“This is what’s called a ‘clean’ letter,” Forsythe said of the notification, “because there are no suggestions for improvement,



“AAALAC accreditation is voluntary and is a symbol of quality,” Forsythe said. “It shows that we’re willing to go above and beyond what the regulations and requirements are, that we’re very committed to having an outstanding animal care program.” NIEHS research proposals undergo a detailed review by the Animal Use and Care Committee before any experiment using animals can begin. (Photo courtesy of Steve McCaw)

[which is] very unusual” in this rigorous review process. “The use of the word ‘exemplary’ is also very rare,” she added, “and we’re very happy about that.”

Mice make up the vast majority of the NIEHS animal population. “We have a small number of rats, a very small number of frogs and an even smaller number of fish,” Forsythe said. “We also use invertebrates such as nematodes and fruit flies.”

In his letter to Forsythe, Council on Accreditation President John Bradfield, D.V.M, Ph.D., wrote that reviewers were especially impressed by the Institute’s knowledgeable and committed staff, well equipped and maintained facilities, inclusive occupational health and safety program, and comprehensive training. Forsythe shares praise for the high quality and outstanding efforts with her 22-member staff and 60 contractors who support the animal care and use program. She also readily acknowledges the significant contributions of many others in the Institute, including personnel in the National Toxicology Program (NTP), Health and Safety Branch, Facilities Management Branch, Operations and Security Branch, and Office of the Scientific Director for their “tremendous support of the program.”

Forsythe mentioned that in 1972 NIEHS became the first NIH institute to be accredited by AAALAC. The AAALAC organization was formed in 1965. The main NIH campus in Bethesda, Md. received full accreditation in 1993.

“We have a strong commitment to reducing the number of animals used in research,” Forsythe concluded, pointing to the strong support by NIEHS and NTP for developing alternative testing. “However, there are studies where animal models are the only appropriate tools to investigate mechanisms of disease. In these studies it is critical to be sure that research is conducted appropriately and humanely. AAALAC accreditation confirms that we are continually striving to have the best animal care program possible.”

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Maintaining Optimal Animal Health and Wellbeing

As Forsythe explained, meeting the strict standards outlined in the Guide is not only humane—the most important consideration by far — but also practical. “Healthy, disease-free animals are going to give you the best research data,” she observed.

To that end, the living conditions of the animals at NIEHS are “monitored much, much more closely than we would monitor our own.” Room temperature, humidity, light cycles and air exchange rates are carefully controlled. The Comparative Medicine Branch lab analyzes all feed and bedding that is used in animal cages, including testing feed for pellet hardness and bedding for dust content. Feed and bedding are autoclaved to eliminate pathogens and analyzed to check for contaminants.

“The water is purified and quality is also closely monitored,” she said. The animals are kept free of a long list of specific pathogens, and the facility is secured to protect laboratory animals from diseases and parasites that may be carried by animals outside the walls of the building.

The constant effort to protect the animals from disease includes strict rules about protective clothing requirements for staff and visitors and about the acceptance of animals from elsewhere. “We don’t bring in animals directly from unapproved sources,” Forsythe continued. “We re-derive them in using embryo transfer” — a time-consuming, but necessary process to make certain that new animals, including transgenic mouse models, meet the health standards of the facility.

“We’re very careful to maintain our barrier,” Forsythe added, “and we’re routinely testing our animals for the presence of pathogens. We transport animals in climate-controlled trucks and in shipping containers that are sanitized before entry into the animal facility.”

“By incorporating all these procedures into our animal care program and maintaining the high standards noted in our AAALAC site visit report,” she added, “we can assure our scientists and the public that animal welfare and animal health at NIEHS are of the highest caliber.”

***EHP* Partners with Mexican Public Health Journal**

By Eddy Ball

Scientists in Mexico and other Spanish-speaking countries can now enjoy the benefits of a new partnership announced in March between the NIEHS-funded journal *Environmental Health Perspectives (EHP)* and the interdisciplinary Mexican journal *Salud Pública de México*, according to *EHP* Editor-in-Chief Hugh Tilson, Ph.D. Issues of the Mexican journal now feature 10 to 12 pages of *EHP* environmental health news articles translated into Spanish to help Latin American readers stay up-to-date on advances in the environmental health sciences.

In the *EHP* announcement of the partnership, Tilson said, “We are happy to share *EHP* with our Spanish-speaking neighbors, to increase the reach of these important environmental health studies, and to increase overall awareness of environmental issues worldwide.”

Carlos Oropeza Abúndez, executive editor of *Salud Pública de México*, pointed to the importance of such binational cooperation. “It is our desire that the collaboration between *EHP* and *Salud Pública de México* will strengthen the scientific communication in Spanish of key environmental health issues, and that it will be the first of future efforts to promote public health,” he said.

EHP is an open-access journal published monthly, available free online and by subscription. It is number one of 160 environmental science journals, with an impact factor of 5.64. The partnership with *Salud Pública de México* is the latest of the journal’s **international outreach efforts**, which include a Chinese-language edition, as well as partnerships with *Mali Médical*, *Ciencia y Trabajo*, and *Ciência & Saúde Coletiva*. The journal also has established collaborations with foreign public and environmental health organizations.

The Instituto Nacional de Salud Pública (INSP), an independent entity supported by Mexican federal funds, has published the bimonthly *Salud Pública de México* since 1959. The journal, with articles in English and Spanish, is indexed by MEDLINE and other major indexing organizations.

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EHP Editor-in-Chief Hugh Tilson
(Photo courtesy of Steve McCaw)



Salud Pública de México Executive Editor Carlos Oropeza Abúndez
(photo courtesy of *Salud Pública de México*)

Understanding Parkinson's as a Disability

By Eddy Ball

The NIEHS Diversity Council Disability Advocacy Committee (DAC) presented the latest in its series of specialized seminars on health topics April 7. The program, titled “Parkinson’s Disease [PD]: Etiology, Clinical and Disability Management,” addressed medical, social and personal dimensions of a condition that affects approximately one million Americans at an estimated cost of \$27 billion annually.

The seminar was conducted by members of the NIEHS Epidemiology Branch — Principal Investigator and Chief [Dale Sandler, Ph.D.](#), program facilitator, and Tenure-track Investigator and co-presenter [Honglei Chen, M.D., Ph.D.](#) — along with a guest clinical lecturer, neurologist [Xuemei Huang, M.D., Ph.D.](#) Chen is currently involved with two large cohort studies of PD patients, and Huang treats PD patients in the movement disorders clinic at the Milton S. Hershey Medical Center at Pennsylvania State University.

DAC member Alyce Bradbury opened the program by welcoming the audience, and Sandler then introduced the speakers. Huang began her segment of the program with an outline of the characteristics of PD used in diagnosis, such as the classic tremor at rest and rigidity of movement. She progressed to possible early signs of the disease, ranging from loss of the sense of smell and curling toes to drooling, constipation and decreased arm movement when walking.

Huang surveyed the current array of treatment options, which are largely limited to increasing dopamine through drugs such as levodopa to control motor symptoms and addressing such related symptoms as sleep disturbance, depression and sexual dysfunction with adjunctive treatments and medications. She said that with the drugs currently available, physicians can reduce the impact of PD for decades after onset, but that preventive treatment remains elusive and restorative interventions are still in the experimental stage.

Chen explored the epidemiology of PD, outlining well-established and preliminary associations observed between PD and genetic and environmental factors. He explained that monogenic early-onset and familial PD, manifest in five to ten percent of people with the disease, have been linked to nine PARK genes and 15 loci, while the role of genetics remains unclear in late-onset PD.



Huang, with microphone, shared insights from her work with patients as Sandler, who moderated the seminar, rested on the podium beside her. (Photo courtesy of Steve McCaw)



As an epidemiologist, Chen was careful to distinguish between association and cause. He said that among PD patients in their 80's, men outnumber women two to one. (Photo courtesy of Steve McCaw)

Late-onset PD, which manifests in middle age or later and accounts for more than 90 percent of disease incidence, Chen explained, is thought to be more closely related to environmental factors. Research thus far has found well-established associations of risk for PD with age and gender and strong protective associations with caffeine consumption and smoking — which he was quick to warn against because of the serious pulmonary and cardiovascular health risks linked to tobacco use.

Pesticide exposure, especially to rotenone and paraquat, and head injury are highly suspected of increasing risk. Chen noted that recent studies have found higher risk with consumption of milk and dairy foods and reduced risk in people with higher levels of uric acid, physical activity and use of non-steroidal anti-inflammatory drugs (NSAIDs).

With so much left to learn about the causes and prevention of PD, Chen looks forward to more in-depth epidemiological research. Huang recommended that people become aware of the early signs of disease to get treatment started as soon as possible and adopt an holistic approach combining medical treatment with social support, a wellness orientation, and physical and speech therapy. As the boomer generation ages, Sandler observed, expanding training of specialists will become more important than ever before.

The seminar concluded with the presentation of tokens of appreciation to Chen and Huang by NIEHS Biologist and DAC Chair Alicia Moore.

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Bradbury followed the questions the audience had for Huang from her front-row seat beside Moore, left, and Chen. (Photo courtesy of Steve McCaw)



NIEHS Principal Investigator Dan Morgan, Ph.D., of the Respiratory Toxicology Group, foreground, and NTP Biologist Stan Stasiewicz were part of a diverse audience with a variety of scientific and practical interests in learning more about PD. (Photo courtesy of Steve McCaw)

NIEHS Remains #1 IC in Postdoc Satisfaction

By Eddy Ball

For the fourth straight year, NIEHS ranked first among NIH institutes and centers (ICs) on the annual survey of “Best Places to Work” for postdocs conducted by *The Scientist* magazine. The Institute retained its 2008 place as number 16 in the survey of trainee satisfaction for 2009, ahead of both the National Cancer Institute (NCI), which rose to place 19th, and NIH, which dropped to number 32.

The [survey](#) accompanied a [lead story](#) in the March issue of *The Scientist* on the special challenges faced by international postdocs working at U.S. institutions. The report included supplementary charts with data on career expectations, satisfaction with the postdoc experience and the length of respondents’ postdoctoral training.

Responses analyzed in the survey credited NIEHS for its strengths in the areas of facilities and infrastructure and training and mentoring. The responses also indicated that more than 78 percent of survey participants described their postdoc experience as excellent, very good or good.

Acting Director of the [NIEHS Office of Fellows’ Career Development \(OFCD\)](#) Diane Klotz, Ph.D., offered her perspective on the survey itself and the ranking of NIEHS. “Based on all of the caveats of this survey, some of which are acknowledged by *The Scientist* itself, I’m not too concerned about exactly where the NIEHS ranks from year to year,” she said. “What is of value to those of us involved in scientific training and career development is learning where our postdocs would like to see improvement and what they think we are doing well.”

As chair of the [NIEHS Trainees Assembly \(NTA\)](#) Steering Committee, Postdoctoral Fellow [Stephanie Nick McElhinny, Ph.D.](#), felt that the survey results point to several things NIEHS is doing well. “The consistency with which NIEHS receives strong marks in training and career development is in part due to the phenomenal efforts of the OFCD, to provide NIEHS fellows with a wealth of diverse training and career development opportunities.”

[NIEHS Postdoctoral Fellow Allison Schorzman, Ph.D.](#), who is chair of the planning committee for the 2009 NIEHS Biomedical Career Fair, also underscored the value of the career-development opportunities available to trainees. “The Biomedical Career Fair highlights careers in academia as well as non-traditional careers, with interactive panel discussions on such fields as science policy, industry, communications and technology transfer,” she explained. “The networking opportunities, career development workshops and résumé consultations available there also help trainees develop skills necessary for a successful job search.”



(Logo courtesy of *The Scientist*)



Klotz, above, was an NIEHS postdoc herself. “I’m pleased to see that our postdocs are happy with their training and mentoring, since that is an aspect of the postdoctoral experience that we here at the NIEHS can directly influence,” she said. (Photo courtesy of Steve McCaw)



In her various roles with the NTA, Nick McElhinny has worked closely with Klotz and others in the NIEHS Office of the Scientific Director to help trainees become flexible enough to cope with a changing job market. (Photo courtesy of Steve McCaw)



After serving on the planning committee in 2008, Schorzman assumed the chair for the 12th annual Biomedical Career Fair. The survey indicated that 38 percent of participants think they will enter non-tenure career tracks, where career development skills will be especially important. (Photo courtesy of Steve McCaw)

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DOD and NIEHS Discuss Environmental Sensors

By Robin Mackar

During a daylong discussion on April 21, representatives from NIEHS and Department of Defense (DOD) found that they had more in common than they thought, especially when it comes to a mutual interest in developing sensors that detect chemicals and other potentially harmful agents in the environment.

Program administrators from the Division of Extramural Research and Training Program (DERT) including David Balshaw, Ph.D., Daniel Shaughnessy, Ph.D., Jerry Heindel, Ph.D., Elizabeth Maull, Ph.D., and Interim DERT Director Gwen Collman, Ph.D., as well as NIEHS Director Linda Birnbaum, Ph.D., informally shared information with DOD science staff about different research areas within the NIEHS portfolio. Representing DOD were Craig Postlewaite, D.V.M., M.P.H, from the Office of the Assistant



Balshaw's Council report may have set the stage for a creative interchange among researchers with different scientific backgrounds and different funding sources. (Photo courtesy of Steve McCaw)

Secretary of Defense for Health Affairs, Reed Hoyt Ph.D., from the US Army Research Institute of Environmental Medicine and Dave Jackson, Ph.D., from the US Army Center for Environmental Health Research.

NIEHS staff gave presentations about the progress being made in the Genes, Environment and Health Initiative (GEI), the Small Business and Innovation Research (SBIR) program, and the NIH Countermeasures Against Chemical Threats (CounterACT) Research Network. In turn, the guests presented their own organizations' efforts in the environmental sensor arena including the role of DOD in protecting the health of its forces, updates on exposure biomarker discoveries and some real examples of promising detector technologies such as nanoscale sensors.

“Clearly, you are all doing a lot of things we are interested in, and we are very glad to be starting this dialogue with you,” said Postlewaite. He also stressed the breadth of the DOD organization and acknowledged what was being presented was a small sampling of the DOD portfolio in this area.

A number of factors brought the agencies together, including a comment made by a council member at the recent National Advisory Environmental Health Sciences Council meeting. Ex-officio member, CPT Michael J. Macinski, Director of Public Health, MSC, USN Navy and Marine Corps Public Health Center, who serves as the DOD representative on the Council, was impressed with the Exposure Biology update provided by Balshaw at the February meeting and suggested NIEHS get together with DOD to exchange information. Another key factor was the message articulated by Birnbaum to promote new and renewed relationships with other government agencies, universities, advocates, sister institutes and centers at NIH, and the general public. A third contributing factor was a recent [SBIR announcement](#) that highlighted the special topics of interest to NIEHS.

“We couldn't have written that SBIR better ourselves,” said Postlewaite “It's like it was written by and for us. Reading that announcement made me realize we both want the same thing — tools and biomarkers that will let us know what people are being exposed to, so we can find ways to prevent or protect them the best way we can.”

In his presentation, Postlewaite emphasized the comprehensive health surveillance system that has been put in place since the Gulf War to capture a wide array of health information on each soldier from pre- to post-discharge. Shaughnessy asked about the wealth of data in the DOD system for NIEHS grantees. “If researchers have a good hypothesis and want to access our samples, we can work with you to accomplish that,” Postlewaite added. He noted that there were more than 46 million samples in the system and over 11,000 air, water and soil samples from Iraq and Afghanistan.

He stressed that the Department is genuinely interested in protecting military personnel and knowing more about environmental exposure. “Ideally, we'd like to work toward the gold standard of being able to put a small lapel pin on each soldier that can detect exposure to all chemicals.”

Balshaw said there are a wide range of technologies out there, but none yet that can detect more than a few chemicals or chemical classes at one time.



Macinski's military perspective on exposure biology may lead to expanded partnerships between NIEHS and DOD that have the potential to save money for both agencies while improving both of their programs. (Photo courtesy of Steve McCaw)

During their remarks, both Birnbaum and Collman thanked the DOD representatives for taking the time to come to North Carolina and share what DOD is doing in the biomarker and sensor development arena. “We see opportunities for collaboration,” Birnbaum noted.

Collman and others remarked that there is a long way to go before these devices are readily used in population settings. “We need to identify markets and venues for these products so companies will continue to invest in their development. It’s not enough for them to just be used in NIH-funded studies.”

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

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Countries Unite to Reduce Animal Use in Product Toxicity Testing

By Robin Mackar

Representatives from four international agencies, including the director of the U.S. National Toxicology Program (NTP), signed a [memorandum of cooperation](#) on April 27 that could reduce the number of animals required for consumer product safety testing worldwide. The agreement between the United States, Canada, Japan and the European Union will yield globally coordinated scientific recommendations on alternative toxicity testing methods that should speed their adoption in each of these countries, thus reducing the number of animals needed for product safety testing.

“Signing this international agreement demonstrates our commitment to finding and advancing alternatives to animal testing,” said Linda Birnbaum, Ph.D., director of the NTP and NIEHS. “This agreement will help us achieve greater efficiency by avoiding duplication of effort and allowing us to leverage limited resources.”

Birnbaum signed as the U.S. representative on behalf of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), one of the national validation organizations participating in the agreement. Others who signed include Elke Anklam, Ph.D., for the [European Centre for the Validation of Alternative Methods \(ECVAM\)](#), David Blakey, D.Phil., for the [Environmental Health Science and Research Bureau within Health Canada](#), and Masahiro Nishijima, Ph.D. for the [Japanese Centre for the Validation of Alternative Methods \(JaCVAM\)](#).

The agreement promotes enhanced international cooperation and coordination on the scientific validation of non- and reduced-animal toxicity testing methods. If the toxicity testing methods are shown to be reproducible based on strong scientific information, and able to accurately identify product related health hazards, the tests are more readily accepted by regulatory agencies.



Participants gathered for a group photo. Shown left to right are Hajime Kojima, Birnbaum, Anklam, Stokes, in uniform, Wind and Blakey. (Photo courtesy of NIH)

“The memorandum covers three critical areas of test method evaluation: validation studies, independent scientific peer review meetings and reports, and development of test method recommendations for regulatory consideration,” said Marilyn Wind, Ph.D., chair of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and a scientist at the Consumer Product Safety Commission (CPSC).

“This international cooperation will benefit both people and animals,” said William Stokes, D.V.M., director of NICEATM and executive director of ICCVAM. Stokes is also an assistant surgeon general in the U.S. Public Health Service. “The cooperation will serve an important role in translating research advances into more effective public health prevention tools. It will speed the adoption of new test methods based on advances in science and technology that will provide more accurate predictions of safety or hazard. Animal welfare will also be improved by the national and international acceptance of alternative test methods that reduce, refine, and replace the use of animals.”

Federal agencies are committed to the welfare of animals used in research. All animals used in federally-funded research are protected by laws, regulations and policies to ensure they are used in the smallest number possible and with the greatest commitment to their comfort. ICCVAM is working to promote the development and validation of alternative test methods. Alternative test methods are those that accomplish one or more of the 3Rs - reducing the number of animals used in testing, or refining procedures so animals experience less pain and distress, or replacing animals with non-animal systems.

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

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Friends and Colleagues Honor Wilson

By Eddy Ball

Friends and colleagues from NIEHS and beyond gathered on April 6 to honor NIEHS Principal Investigator (PI) [Samuel Wilson, M.D.](#), for his scientific and leadership contributions to the Institute. They came together for a program of tributes by colleagues that ranged from heart-felt expressions of respect and appreciation to light-hearted jest and parody. Afterwards, they joined their former leader, colleague and collaborator for refreshments and conversation.

The event was hosted by NIEHS and National Toxicology Program (NTP) Director [Linda Birnbaum, Ph.D.](#), who succeeded Wilson at the helm of NIEHS in January 2009. At that time, Wilson, who had served as NIEHS acting director since August 2007, decided to step away from his role as deputy director, a position he had held since joining NIEHS in 1996, to devote more time to his work as head of the NIEHS DNA Repair and Nucleic Acid Enzymology Group.



Wilson enjoyed the spirit of the occasion as he donned the “top cop” hat Kunkel had borrowed for his routine from one of the Institute’s security officers. (Photo courtesy of Steve McCaw)

Birnbaum set the tone for the homage to Wilson by citing his many accomplishments, such as developing the genetic susceptibility initiative at NIEHS, boosting children's and minority health programs, and promoting community outreach by grantees. She thanked her predecessor for his dedication to the integrity of NIEHS and described him as an "unbelievably gracious" colleague who helped her make a smooth transition to her new position.

Former NIEHS Division of Extramural Research and Training Director Anne Sassaman, Ph.D., returned from her semi-retirement to add her notes of appreciation and praise to the chorus of voices paying homage to Wilson. She also read comments from NIEHS Director Emeritus Ken Olden, Ph.D., whose current duties as head of the new school of urban public health at the City University of New York prevented him from attending in person. She quoted Olden, who recruited Wilson to NIEHS, as writing of his colleague, "I've never known anyone as devoted to NIH and NIEHS... a completely unselfish nature."

Even before he joined NIEHS, Wilson had touched the lives and careers of NIEHS PI [Tom Kunkel, Ph.D.](#), former PI Ben Van Houten, Ph.D., now at the University of Pittsburgh, and Bill Suk, Ph.D. the acting deputy director under Wilson and currently director of the NIEHS Center for Risk and Integrated Sciences. Each of the three punctuated their praises for Wilson as investigator and visionary leader with gentle jabs about his style and fashion preferences.

Representing the Division of Intramural Research (DIR), Kunkel took the humor of the event to another level with a routine that kept Wilson and the audience laughing nearly non-stop for ten minutes. After praising his long-time friend as "one of the best scientists I've ever known," Kunkel wore a series of silly hats in a slap-stick running commentary on the many roles Wilson played during his career at NIEHS.

Standing in for absent associates, were NIEHS Office of Human Research Compliance Director Joan Packenham, Ph.D., and NTP Deputy Program Director for Policy Mary Wolfe, Ph.D. Packenham read a letter from former NIEHS Director of Education and Biomedical Research Marian Johnson-Thompson, Ph.D., who combined her words of praise and gratitude with a quip about



An exuberant Birnbaum was the first — but certainly not the last — speaker to comment on Wilson's energy and dedication to his multiple roles at NIEHS. (Photo courtesy of Steve McCaw)



Sassaman, who retired in 2006, joked about being the representative of the "old guard" at NIEHS — the visionaries who led the Institute with former Directors David Rall, M.D., Ph.D., and Ken Olden. (Photo courtesy of Steve McCaw)



Kunkel, dressed in lab coat and one of the many "hats" Wilson has worn in his career, played his friend as physician. He quipped, however, that Wilson may need to brush up on his skills before sticking needles into patients again. (Photo courtesy of Steve McCaw)

Wilson's "poker face." Wolfe presented the man of the hour with a plaque of appreciation on behalf of NTP and conveyed best wishes from her colleagues and NTP Associate Director John Bucher, Ph.D.

Before turning the program over to Wilson, Birnbaum presented him with a plaque of appreciation from NIEHS. Wilson ended the event with remarks about the importance of the NIEHS, which he described as "way beyond any other institute at NIH." He concluded, "It has been an honor to serve the American people by working here at NIEHS," promoting the Institute's mission "to protect human health and prevent disease."



Suk joined in the spirit of the roast as he goaded Wilson about the latter's formal dress. Suk was Wilson's loyal colleague during the Institute's challenging transition. (Photo courtesy of Steve McCaw)



Packenhams, center, conveyed Johnson-Thompson's assessment of Wilson as "a real genuine human being." Both women expressed their appreciation for Wilson's support of their efforts to expand opportunities in science education. (Photo courtesy of Steve McCaw)



During the reception, Van Houten, center, talked with former NIEHS colleagues, PIs Perry Blackshear, M.D., D.Phil., left, and Traci Hall, Ph.D., right. (Photo courtesy of Steve McCaw)



The man of the hour, center, enjoyed quality reception time with Suk, left, and Blackshear. NTP Geneticist Jack Bishop, Ph.D., and Packenhams talked in the background, left. (Photo courtesy of Steve McCaw)

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Comments Invited on Stem Cell Guidelines

By Eddy Ball

In the April 23 issue of the *Federal Register*, NIH announced that it is accepting public comments on its new draft [National Institutes of Health Guidelines for Human Stem Cell Research](#) through May 26, 2009. The guidelines were prepared in response to the Executive Order 13505: Removing Barriers to Responsible Scientific Research Involving Human Stem Cells issued by President Barack Obama on March 9.

According to the [announcement](#), the Guidelines describe the circumstances under which [human embryonic stem cells](#) are eligible for use in NIH-funded research. They also include a section on uses of human embryonic stem cells and induced pluripotent stem cells that are ineligible for NIH funding.

The announcement includes a [web site](#) where comments may be submitted electronically. Comments can also be submitted by mail at the following address:

NIH Stem Cell Guidelines
MSC 7997
9000 Rockville Pike
Bethesda, MD 20892-7997

NIH will also receive inquiries about the guidelines by mail, telephone or e-mail at the following addresses:

Division of Grants Policy
Office of Policy for Extramural Research Administration
National Institutes of Health
6705 Rockledge Drive, Suite 350
Bethesda, MD 20892
Telephone: (301) 435-0938
FAX: (301) 435-3059
Email: GrantsPolicy@od.nih.gov

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Science Notebook

Nobel Laureate Smithies Gives Rodbell Lecture

By Robin Arnette

The 2009 [Dr. Martin Rodbell](#) Lecture Series speaker, Oliver Smithies, D. Phil., is truly a giant in the field of science. His lecture, “Turning Pages: From Gels to Genes,” took place on April 14 and provided an overview of his impressive 61 years of research. Smithies is responsible for developing the gel electrophoresis technique that scientists routinely use today, and he shared the [2007 Nobel Prize in Physiology or Medicine](#) for work on the introduction of specific gene modifications in mice using embryonic stem cells.

Smithies thrilled the audience with a presentation that included photocopies of entries from his research notebooks. Pages from his early days showed incredibly detailed writings and hand-drawn lab results. Smithies remarked, “You might wonder why there aren’t any photographs. My lab didn’t have a camera, so everything had to be sketched.”

Smithies credited his undergraduate tutor at Oxford, [Alexander “Sandy” Ogston, D.Phil.](#), with teaching him how to do good science. One of Ogston’s assignments was to have Smithies write an essay on metabolic processes involving energy-rich phosphates. The forward-thinking Smithies generated a diagram that illustrated these phosphates in a continuous cycle. Although Smithies’ scheme was incorrect, he and Ogston found the biochemical error and jointly published the findings in *Physiological Review* in 1948. It was Smithies’ first journal article and a portent of many ground-breaking discoveries.

Smithies’ childhood dream was to become an inventor, and as he matured as a scientist, he found a way to merge both of his passions. During his postdoctoral fellowship at the University of Wisconsin, he published a paper that used data generated from simple calibrated pipettes. However, he found that the accuracy of the results



Smithies, Excellence Professor and the Weatherspoon Eminent Distinguished Professor of Pathology and Laboratory Medicine at the University of North Carolina at Chapel Hill (UNC-CH) School of Medicine, enthralled the standing-room-only audience. After all the seats were filled, employees and visitors lined the walls and sat in the aisle, willing to sacrifice comfort for the opportunity to hear the story of his life in science. (Photo courtesy of Steve McCaw)



NIEHS Principal Investigator Ken Korach, Ph.D., stood in for his colleague Principal Investigator Perry Blackshear, M.D., D.Phil., as host of the lecture. Blackshear was delayed by weather from catching his flight back to NIEHS. (Photo courtesy of Steve McCaw)

was greatly improved with the use of an automatic pipette that he built himself. The tool was good to within a quarter of a percent, but Smithies never published work about his invention.

As a result, he missed an opportunity to revolutionize the manipulation of small volume samples when the adjustable [micropipette](#) was patented in 1957. Smithies said, “In science, sometimes you advance because of a chance happening and sometimes you have an opportunity, and very occasionally you do something that you’ve planned.”

Another chance advancement occurred during his first job at the University of Toronto. Smithies was looking for the precursor of insulin and utilized an electrophoresis technique using starch grains to separate proteins. This laborious method required that he cut the starch frames into 40 slices and do protein estimations for every slice — until he remembered something from his childhood.

“When my mother starched my father’s shirt collars, she would cook the starch until it turned into a gooey liquid,” Smithies recalled. “I thought if I make this starch into a gel, I could stain the gel instead of having to do 40 protein determinations.” The improved starch gel electrophoresis separated molecules based on size and charge and is the basis for polyacrylamide and agarose gel electrophoresis.

Out of curiosity, Smithies used his new electrophoresis system to separate human serum. When he did, he saw 11 components rather than the 5 proteins known at that time to make up serum. More work on this project determined that some people had extra components in their blood, and that this difference was due to an inheritance of a single gene. When Smithies investigated further, he stumbled upon the predictable “crossing-over” or homologous recombination (HR) of genetic sequences. To demonstrate HR, Smithies built his own electroporation apparatus — using a baby bath tub, a test tube rack and off-the-shelf components — and transformed mammalian cells with an HR construct. He found one colony that had been altered, and it was the first demonstration of gene targeting.

Smithies said that many of his scientific successes occurred while working on Saturdays, a tradition he still continues. He said, “If a Saturday is a particularly good one, three things will happen: I’ll do an experiment, take my wife to lunch and fly my glider.”



Rodbell’s widow, Barbara, right, and family friend David Klein, M.D., professor of Neurosurgery at UNC-CH School of Medicine, clearly enjoyed Smithies’ humor as much as the rest of the audience did. (Photo courtesy of Steve McCaw)



The talk appealed to people across the Institute, such as Bioethicist David Resnik, J.D., Ph.D. (Photo courtesy of Steve McCaw)



Many in the audience, such as Principal Investigator Bob Langenbach, Ph.D., smiling above, could relate to Smithies' acknowledgement that scientific progress is often built on lessons learned from failed experiments. (Photo courtesy of Steve McCaw)



Korach, left, presents the Rodbell statue to Smithies as he poses with Barbara Rodbell. Smithies is the eleventh speaker in the series, the first of which featured Rodbell himself shortly before his death in 1998. (Photo courtesy of Steve McCaw)

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Colwell Presents 8th Annual Spirit Lecture on Global Health

By Eddy Ball

People from NIEHS and the Triangle scientific community turned out on March 27 to hear distinguished scientific leader and microbiologist Rita Colwell, Ph.D., discuss her life in science and her career-long quest to understand the *Vibrio cholerae* bacterium. Colwell's talk was sponsored by the NIEHS Diversity Council, which honors women in science each year with the Spirit Lecture, and the NIEHS Frontiers of Environmental Sciences Lecture Series, which has featured several recent talks on the impact of climate change on global health.

NIEHS Biologist Molly Vallant, chair of the Spirit Lecture Committee, opened the program. NIEHS Director Linda Birnbaum, Ph.D., then introduced Colwell, calling her a "shining light" for women in science. Birnbaum described the speaker as "a woman who has managed to do it all" by successfully combining an outstanding career in microbiology, environmental public health and scientific leadership with a rewarding family life.

In the course of her Spirit Lecture on "Climate, Oceans, Infectious Disease and Human Health: The Saga of Cholera," Colwell engaged her audience with stories of her childhood and anecdotes of her struggles with male domination in science. Colwell, who was once told by her department chairman at Purdue University



Colwell urged that "it's important to integrate the information that we gain" at every level of research "in order to understand how this wonderful planet operates.... Whether we like it or not," She added, "we are a global village." (Photo courtesy of Steve McCaw)

that “we don’t waste fellowships on women,” opened the global health portion of her talk with an overview of such climate-change triggered health risks as the spread of malaria into newly warmer and wetter environments and the hantavirus outbreak in the Southwestern U.S. following the 1991–1992 El Niño.

Colwell then related the story of her groundbreaking research into the lifecycle of the cholera bacterium and novel ways for predicting outbreaks. She also described an elegantly simple and inexpensive filtration method to help people in developing nations protect themselves against the preventable misery, disease and death caused by exposure to cholera in their drinking water. According to Colwell, cholera is grossly underreported, causing many more than the hundreds of thousands of cases and many thousands of deaths documented each year by governments and public health organizations.

Vibrio, Colwell explained, is a “home grown” organism present in the waters of virtually every estuary in the world’s temperate and tropical regions. The bacterium is responsible, she said, for the majority of deaths among children under five years old in developing countries. She predicted that climate change has the potential to modify the environment in ways that will make outbreaks of bacterial disease even more common and trigger “evolution at a breakneck pace” among vector organisms and their hosts.

Her groundbreaking discoveries of the dormant, non-culturable stage in the lifecycle of cholera and the roles of phytoplankton and zooplankton in cholera outbreaks laid the foundation for research on ways to predict when the conditions are right for outbreaks in specific areas and how intense the outbreaks will be. Colwell continues her work developing a model driven by satellite-remote sensing capable of tracking the spatial and temporal development of plankton plumes, as they emanate from major rivers where cholera is known to be endemic to coastal areas where people can be exposed to large numbers of the bacteria.

Toward the end of her talk, Colwell showcased the results of translational research into preventing cholera infection in Bangladesh by filtering untreated surface water to remove the zooplankton, particularly copepods, that carry *V. cholerae*. She and her colleagues demonstrated that residents can effectively remove more than 99 percent of *V. cholerae* cells attached to plankton from their water — using the inexpensive sari cloth that even the poorest women in Bangladesh wear, folded four to eight times, as a filter to capture plankton as small as 20 microns in diameter.

Following her talk, NIEHS Chemist and Chair of the Diversity Council Brad Collins presented Colwell with a certificate of appreciation from NIEHS.



Vallant, above, noted that the Spirit Lecture series honors women “who have made significant achievements in their fields, while balancing the multiple roles women have to play in their everyday lives.” (Photo courtesy of Steve McCaw)



Birnbaum said that Colwell “sends a message to everyone that there are ways to work together to have a great career... and to have the family life that’s so important to so many of us.” (Photo courtesy of Steve McCaw)



As she talked about women in Bangladesh filtering their water, shown above, Colwell noted with a smile, “What’s especially nice is that the old sari cloth they were using for rags served as a very nice filter.” Colwell said there was excellent compliance among the subjects, well after the end of the three-year study. (Photo courtesy of Rita Colwell)



Early in the talk, Colwell showed an illustration based on the Hindu mandala — an ancient symbol of wholeness — to represent her vision of the integration of science into a unified ethos of understanding and responsibility to further the well-being of the planet and its occupants. The theme of integration ran throughout her lecture. (Photo courtesy of Steve McCaw)



National Toxicology Health Scientist Diane Spencer, above, was part of the near capacity audience at the talk. Spencer is a member of the Spirit Lecture Committee. (Photo courtesy of Steve McCaw)

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GEMS Meeting Focuses on Genome Variability

By Eddy Ball

The Genetics and Environmental Mutagenesis Society (GEMS) held its Spring Meeting April 13 at the U.S. Environmental Protection Agency (EPA) Auditorium in Research Triangle Park. The program, organized and facilitated by GEMS President-elect and NIEHS scientist [Jef French, Ph.D.](#), who is acting chief of the National Toxicology Program Host Susceptibility Branch, involved an afternoon of invited lectures on the evolution of genome architecture and the inheritance of complex chromosome structural variations that impact behavior and disease susceptibility.

[GEMS](#) President and EPA molecular biologist Jeff Ross, Ph.D., welcomed the approximately 150 attendees before turning the program over to French, who introduced the speakers.

The speakers followed biological changes in genomic architecture from double-strand break repair in yeast, through genetic variation in mice strains and their utility in predicting cellular response to toxicity, to the implications of structural genomic variation in humans. French told the audience that the talks would all tie into a growing body of “intense research on understanding the role of copy number variation (CNV) in genetic susceptibility” to chronic diseases.

The program began with a discussion by NIEHS Principal Investigator [Mike Resnick, Ph.D.](#), on “Double-Strand Breaks and Repair: Reconfiguring the Genome.” The central premise of Resnick’s research in the yeast model is that, along with their role in protecting the organism, “double strand breaks may [also] be places of remarkable potential for mutability” — leading to aberration, amplification and changes in CNV. Understanding the molecular events involved in breaks and their repair through recombination, Resnick explained, could provide a key to “how these breaks can open up the genome to reconfiguration.”

Moving on to the mouse model, University of North Carolina at Chapel Hill (UNC-CH) Associate Professor [Fernando Pardo-Manuel de Villena, Ph.D.](#), addressed strain variation in his talk on “The Mouse Genome: It Takes Three to Make a Mouse.” Working with data from the NIEHS mouse genome sequencing project of 15 inbred and wild-derived mice strains, de Villena has uncovered genomic variations that developed over an estimated 15 million generations of reproduction and breeding. His work involves both understanding those



French said that understanding copy-number variation can help scientists better explain how genetic variability influences the gene-environment interactions linked to disease. (Photo courtesy of Steve McCaw)



Resnick joked about being overdressed for the occasion. “For those of you who don’t recognize me, I’ll take off my jacket,” he quipped. He also got laughs when he explained the “shift happens” concept of mismatch repair. (Photo courtesy of Steve McCaw)

variations, including CNV and epigenetic alterations, and the development of a better mouse model for researchers studying complex diseases linked to multiple genes at different locations in DNA.

David Threadgill, Ph.D., chair of the Department of Genetics at North Carolina State University (NCSU) and a professor at NCSU and UNC-CH, outlined work that converges at several points with de Villena's lines of research. Threadgill is involved in the Collaborative Cross project that is working to produce a thousand highly diverse, highly randomized mouse strains as a reference population. In his talk on "Systems Biology and Functional Genomics Approaches for the Identification of Cellular Responses to Toxicity," Threadgill discussed his use of new mice strains and molecular and proteomic tools for identifying genes involved in responses to drugs and other toxic compounds that can vary significantly from individual to individual. Threadgill has explored sporadic colorectal cancer and the link between genetic variation and resistance against and susceptibility to the more invasive forms. These cancers are characterized by flat and depressed polyps that are much more difficult to identify with standard colonoscopy.

Rounding out the theme of the program with a focus on humans was Harvard Medical School Associate Professor and Principal Investigator **Charles Lee, Ph.D.**, who spoke on "Our Incomplete Understanding of the Human Genome: The Impact of Structural Genomic Variation." Lee explained that structural genomic variations "are not single



Threadgill argued that the standard paradigm used in toxicology and drug development is not adequate for identifying individual variation in response to environmental exposures. (Photo courtesy of Steve McCaw)

Transitioning to the GEMS Fall Meeting

Twice each year, GEMS offers an affordable way to introduce students, postdoctoral fellows and area scientists to leading-edge research in genetics and mutagenesis and learn more about new trends in biomedical research. Dues for the group are an affordable \$5.00 per year for students and \$10.00 per year for others. For students, registration fees for the meetings are less than the value of the food and refreshments served.

In 2009, the program of the Spring Meeting will be continued at the full-day GEMS Fall Meeting on October 5 at the William and Ida Friday Center in Chapel Hill. As in previous years, the program will be divided between presentations by outstanding senior scientists and poster and oral presentations by students and trainees.

In their part of the program, young scientists compete with their peers for cash prizes ranging from \$250 for the best posters to \$1500 for best oral presentation. Winners typically use their grants for attending professional meetings they might otherwise have been unable to afford. The GEMS competition gives students and trainees from colleges in North Carolina, NIEHS and EPA an affordable opportunity to fine-tune their presentation skills and network with senior investigators and peers.

Serving senior investigators, postdoctoral fellows and students from NIEHS, EPA and several universities in North Carolina since 1982, GEMS has been an important part of the scientific experience for hundreds of researchers and students. Over the years, NIEHS and EPA have been generous with their financial and in-kind support, and both agencies have been well represented in the membership and governance of the organization.

base-pair changes, but a gain of specific DNA sequences, deletions, insertions or translocations, and, of course, conversions.... all contributing to [CNVs and] our uniqueness from one another.” He said that a map of CNV in the human genome developed by his group shows humans are genetically far more diverse than previously expected. It should even be possible, he noted, to distinguish between individual twins by mapping their individual genomic architecture.



National Toxicology Program Staff Scientist Barbara Shane, Ph.D., left, joined Biostatistics Branch (BB) Research Fellow Min Shi, Ph.D., center, and BB Computational Biologist Liwen Liu, right. (Photo courtesy of Steve McCaw)



Veteran GEMS member Carl Blackman, Ph.D., is a research scientist in the EPA Environmental Carcinogenesis Division with research interests in the influence of DNA methylation on the expression of tumor suppressor genes. (Photo courtesy of Steve McCaw)



The speakers joined French for a group photo. Shown, left to right, are Lee, Resnick, French, Threadgill and de Villena. (Photo courtesy of Steve McCaw)

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NIEHS Speakers Offer Caveats During NIH NanoWeek

By Eddy Ball

The NIH Nanotechnology Task Force and the NIH Nanomedicine Roadmap hosted a series of symposia and other events in Natcher Auditorium on the NIH campus April 7– 10, celebrating “The Promise of Nanotechnology for Medicine.” While the general tone of [NanoWeek](#) was upbeat and optimistic, talks by NIEHS Senior Science Advisor Sally Tinkle, Ph.D., and [grantee](#) Martin Philbert, Ph.D., on April 7 struck more cautious notes, as they addressed concerns about the impact of this promising technology on public health and the environment.

Tinkle serves as a lead representative of NIEHS on trans-NIH, interagency and international nanotechnology and Nano-Health working groups. [Philbert](#) is a professor of Environmental Health Sciences and the senior associate dean at the University of Michigan School of Public Health. He is a former member of the [NIEHS National Advisory Environmental Health Sciences Council \(NAEHSC\)](#) and a toxicological pathologist whose nanomaterial research is supported in part by NIEHS.

Tinkle spoke briefly on “Harnessing the Power of Nanotechnology for Human Health at the NIH.” She established common ground with her audience, which had spent the day hearing enthusiastic reports on the many advancements in imaging and targeted drug delivery of medications possible through nanotechnology, by underscoring the “shared research questions” and “same research goals” at the intersection of basic and clinical research and exposure prevention research.

Tinkle encouraged scientists to keep in mind the ambiguity inherent in the term “harnessing.” While most of the day’s speakers had talked of harnessing in the sense of “mastering” nanotechnology for innovative applications, Tinkle said that the word also can signify “holding back” — progressing more cautiously in a responsible manner with a new technology whose nanobiointeractions remain inadequately understood.

Philbert’s talk developed the themes of Tinkle’s message with an impressive catalogue of reasons to be concerned about the long-term effects of exposure to nanomaterials, supported by extensive data from his recent research. Toxicological testing conducted thus far has led him to conclude that nanomaterials have “[patterns of] pharmacokinetics that are much more complex than in a single molecule” and a marked susceptibility to contamination and “nuisance-surface chemistry” during manufacture and use.



Although Tinkle criticized researchers for using “a very narrow light” in their work with nanotechnology, she was also busy building bridges. “We’re asking the same questions that you’re asking,” she reassured the audience. “We are one research community with one research focus.” (Photo courtesy of Steve McCaw)



Philbert, shown at a 2007 meeting at NIEHS, began his talk by warning the audience that “I’m the ugly fly in the punchbowl.” He reminded listeners of the unanticipated long-term health effects of nanoparticles in asbestos, air pollution and cigarette smoke. (Photo courtesy of Steve McCaw)

The talk began with an overview of the various methods employed in the synthesis and manufacture of nanomaterials — producing a heterogeneous range of particles with a high surface-to-volume ratio whose impacts on health and the environment can be highly unpredictable. He noted that some cells will accumulate and aggregate nanomaterials in ways that could lead to unexpected super concentration and that carbon nanotubes, under the right conditions, can stiffen and behave like asbestos.

Accurately assessing of risk is also fraught with problems, he said, including coming up with a well-characterized material for testing and determining just what part of the material might have caused the effects observed in experiments. “One [also] has to be very careful in transition from *in vitro* to *in vivo* models,” Philbert argued. “We need to be more vigilant in following these cases out in time” — noting that it can take two to three decades to develop frank symptoms of disease triggered by asbestos exposure.

In closing, Philbert urged the scientists to broaden their perspectives to consider the entire lifecycle of nanomaterials from manufacture to disposal. “As we move into this era of what Mauro [Ferrari, a previous speaker] called ‘second- and third-generation nanomedicine,’” he argued, “we need to be very mindful of the manufacturing processes.”

There should be more attention paid to using “green” manufacturing and producing more biodegradable materials that won’t persist in the environment. However great the immediate potential of nanotechnology for improving diagnosis and treatment, Philbert insisted, scientists and regulators also need to see this wonder technology framed by the possible long-range unintended impacts on human health and the ecosystem.

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Bogenhagen Discusses Nucleoid Replication in Mitochondria

By Eddy Ball

The NIEHS Laboratory of Molecular Genetics (LMG) Fellows Invited Guest Lecture series welcomed its latest speaker on March 30 with a talk on “Biogenesis and Heredity” by Dan Bogenhagen, M.D. The talk was hosted by LMG Visiting Fellow Rajesh Kasiviswanathan, Ph.D., a member of the [Mitochondrial DNA \(mtDNA\) Replication Group](#).

[Bogenhagen](#) is a professor in the Department of Pharmacological Sciences at the State University of New York at Stony Brook. His talk outlined what he called “the slightly different direction” of research in his lab at Stony Brook, with protein-sequencing techniques, and at the Howard Hughes Medical Institute (HHMI) Janelia Farm Research Campus, using super-resolution imaging techniques, to study the mechanisms of nucleoid replication in mitochondria.



Bogenhagen enjoyed a receptive audience that included longtime friend and colleague Bill Copeland, Ph.D., seated at right, principal investigator in the NIEHS Mitochondrial DNA Replication Group. (Photo courtesy of Steve McCaw)

Pointing to the “intimate involvement” of mitochondria in the life and death of the cell, Bogenhagen launched his discussion by noting that it is also the only organelle apart from the nucleus that is known to contain DNA.

This “compact circular mtDNA genome,” he said, is an excellent “complete genetic system” for studying the repair and encoding processes related to mtDNA dysfunction that impacts neurodegeneration, cancer and many other diseases.

As Bogenhagen explained, his central research interests are “how mtDNA is packaged and what the actual molecular environment is for the mitochondrial genome.” He said that the mitochondria genome encodes only 13 protein subunits of enzyme complexes — “probably only about one percent of the proteins that work in mitochondria.” According to Bogenhagen, the mechanisms involved in mtDNA packaging are not well understood.

“There are probably 200 proteins in the nuclear genome just to support the luxury of having 13 genes controlled in mtDNA,” Bogenhagen continued. “In many ways, this may not be a very sensible design.... Despite a large investment of resources, it doesn’t really work very well — kind of like our banking system.” He said that “on a per base-pair basis, mtDNA is one of the most disease-rich DNA regions in our bodies.” The inefficiency of repair proteins may make mtDNA especially susceptible to oxidative stress and contribute to polymorphism and human disease, he added.

Bogenhagen discussed studies of animal models — mutated mice and aging non-human primates — that have shown that mitochondrial dysfunction increases with age, accompanied by a loss of muscle mass and an increase in electron-chain abnormalities. He then described unbiased searches for accessory proteins involved in organizing and packaging mtDNA and metabolic proteins that revealed metabolic proteins associated with mtDNA.

This work suggested a model in which mtDNA nucleoids function as centers for mitochondrial biogenesis. In collaboration with researchers at the HHMI, he has also tested high-resolution microscopy methods, such as photoactivated localization microscopy (PALM), to produce higher resolution images to help localize nucleoids.

Using the model his lab has developed, Bogenhagen devoted the final part of the lecture to what he conceded was “speculation about what would be the implications ... on how mtDNA is managed in the cell.” One overriding theme was that “mitochondrial biogenesis is local,” leading to the hypothesis that genetic complementation is limited and that nucleoids are stable and remain segregated as they “service their own neighborhoods” to ensure adequate energy production in the mitochondria.

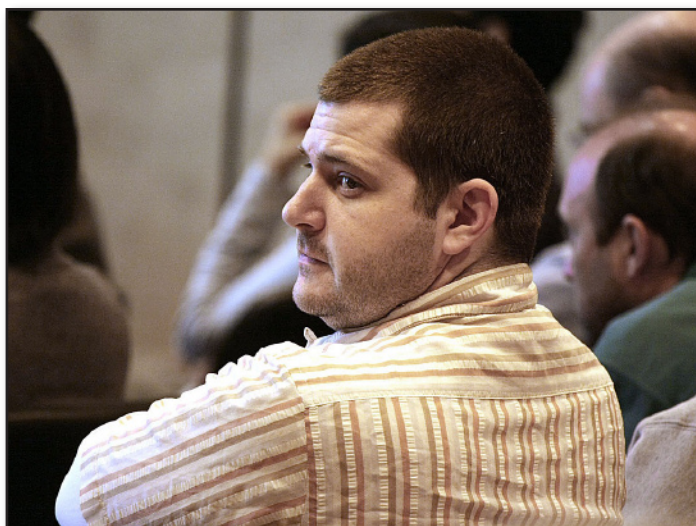


Research Fellow Daniel Menendez, Ph.D., seemed to ponder the ways Bogenhagen’s work intersects with his own in the NIEHS Chromosome Stability Group. (Photo courtesy of Steve McCaw)



NIEHS DNA Replication Fidelity Group Postdoctoral Fellow Amy Abdulovic, Ph.D., is a member of the LMG Trainee Action Committee, the group that sponsors the speakers’ program and the annual LMG retreat. (Photo courtesy of Steve McCaw)

Understanding of the replication, repair and expression of mtDNA, according to Bogenhagen, is important due to the association of mtDNA polymorphism in a growing list of diseases. Mitochondrial DNA mutations have been implicated both in rare genetic diseases and, increasingly, in more common conditions such as Parkinson's disease and type 2 diabetes — diseases that worsen with age, possibly both as a direct cause and as a contributing factor because of the progressive mitochondrial dysfunction observed with advanced aging.



NIEHS Postdoctoral Fellow Rich Gradman, Ph.D., turned as an audience member asked Bogenhagen about his recent data. Gradman recently joined the LMG Spontaneous Mutation and DNA Repair Group. (Photo courtesy of Steve McCaw)



Kasiviswanathan, above, introduced the speaker and monitored the question-and-answer session following the talk. (Photo courtesy of Steve McCaw)

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Birnbaumer To Lead NIH Directors Challenge Award Project

By Eddy Ball

On April 3, NIEHS Senior Investigator [Lutz Birnbaumer, Ph.D.](#), was notified that his ambitious project to better understand the mechanisms involved in epigenetic modifications was selected for support by the NIH Director's Challenge Award Program. One of eight such awards made this year, Birnbaumer's two-year project is a trans-NIH effort involving NIEHS Biostatistics Branch Principal Investigator [Leping Li, Ph.D.](#), and three senior investigators with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) as collaborators — [Ann Dean, Ph.D.](#), [Gary Felsenfeld, Ph.D.](#), and [Karen Usdin, Ph.D.](#)

The goal of the project, titled "The Methylome in Health and Disease: Survey of Unmethylated CpGs," is to define tissue- and cell-specific DNA methylation patterns that vary in health and disease. "Methylome" refers to the totality of DNA sites affected by methylation.

During normal development, the methylation of these dinucleotides — C and G linked by a phosphate group — triggers epigenetic alterations in gene expression that are involved in cell differentiation. Later in life, abnormal deposition and removal of methylation marks have been linked to a range of diseases such as cancer, obesity and metabolic syndrome.

According to Birnbaumer's proposal, the group has performed proof-of-principle experiments that lead them to believe they can be successful in mapping the methylome. Using methods developed in Birnbaumer's lab,

the team prepared and sequenced chemical libraries of CpG tags derived from ends created by digestion of mouse liver DNA. The experiment returned 32 million sequences that mapped approximately one-third of the CpGs in the mouse genome back to unique sites. The researchers were able to map to 22,000 high-confidence unmethylated regions (HC UMRs) where CpGs are unmarked.

The team's proposal lists specific aims in regard to methodology, data collection and evaluation of outcome that promise to significantly advance research on the methylome. These advances include the following:

- Methodology — improving the tag recovery from DNA ends and automation used to map tags back to databases containing sequences of interest and developing a web-based mapping tool
- Data Collection — preparing CpG tag libraries from a variety of tissues, which will enable the team to test the hypothesis that HC UMRs vary from tissue to tissue
- Evaluation of Outcome — refining a high-resolution, digital approach for use in an unbiased, genome-wide search to map unmethylated CpGs back to single CpG sites

The NIH Director's Challenge Award will provide the project two years of support for personnel, equipment and supplies in FY 2009 and FY 2010, with second-year funding contingent upon review of the group's progress at the end of the first year of funding. At a mini-symposium in 2010, Birnbaumer and his colleagues will join the other awardees to present the results of their projects.

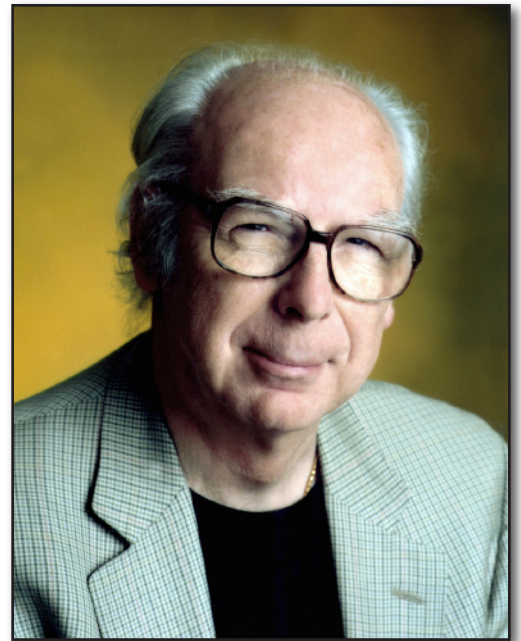
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Intramural Researchers Find a Key Regulator of Fat Metabolism in Liver

By Negin Martin

A new study conducted by researchers at NIEHS suggests that nuclear protein SIRT1 regulates fat metabolism in liver. SIRT1 belongs to the family of proteins named sirtuins that extend the life span of yeast, *C. elegans*, and *Drosophila* in response to caloric restriction. As worldwide epidemics of obesity and diabetes threaten metabolic health and increase the incidence of liver damage, SIRT1 presents a new pharmacological target for treating hepatic disease. This study was published in the April 2009 issue of the prestigious scientific journal *Cell Metabolism*.

The principal investigator of the study, [Xiaoling Li, Ph.D.](#), is the head of the [Mammalian Aging Group](#) at NIEHS, whose members all contributed as co-authors on the study. A native of China, Li received her Ph.D. in biological chemistry from the Johns Hopkins University School of Medicine and trained as a postdoctoral fellow at the Massachusetts Institute of Technology before joining NIEHS in 2007. She studies environmental, nutritional and hormonal factors that affect sirtuins — regulators of aging and longevity.



Biochemist Lutz Birnbaumer heads the Transmembrane Signaling Group in the NIEHS Laboratory of Neurobiology. (Photo courtesy of Steve McCaw)

In her recent [publication](#), Li utilizes knockout mice with hepatic deletion of SIRT1 to study liver function in search of regulators of lipid metabolism. SIRT1 is an enzyme that deacetylates histones — the structural components of chromosomes — and modulates their function. SIRT1 activity is dependent on the nutritional status of the cell and therefore can serve as a direct link between metabolism and chromosome structure. It translates what we eat into gene modification.

Li's team observed that under normal feeding conditions, hepatic knockout of SIRT1 causes no phenotypic changes in mice. However, SIRT1 knockout mice fed a high-fat diet have defective fatty acid metabolism, show signs of liver inflammation and have altered insulin signaling. SIRT1 knockout mice accumulate more fat in their livers and gain more weight in diet-induced obesity trials.

In previous studies, mice with whole body SIRT1 knockout suffered from physiological abnormalities and severe growth retardation that concealed the importance of SIRT1 in regulating liver function. This is one of the first studies using liver specific knockout mice to outline the molecular mechanism of SIRT1 function in liver and fat metabolism.

After extensive biochemical analysis, Li's team determined that SIRT1 interacts with and regulates a lipid sensor called the peroxisome proliferators-activated receptor alpha (PPAR α). PPAR α signaling is responsible for normal synthesis and elimination of lipids and fat. A coactivator of PPAR α , PGC-1 α , is also a SIRT1 substrate, and its activity is stimulated following deacetylation by SIRT1. The researchers examined 48 genes that are regulated by PPAR α , and found that 25 genes had decreased expression, indicating an impaired PPAR α signaling and fatty acid metabolism.

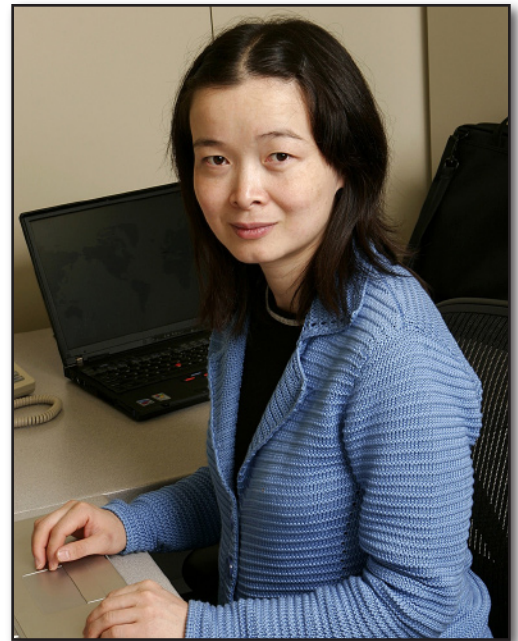
A healthy liver may contain up to 10 percent of its weight in fat. However, abnormal retention of fat and lipids within the liver can lead to inflammation and scarring of liver — a condition known as cirrhosis. If untreated, cirrhosis results in liver failure and death.

Risk factors for faulty fat metabolism and liver disease include diabetes, protein malnutrition, obesity, hypertension and excessive alcohol consumption. Fatty liver disease is preventable by maintaining a healthy weight, exercising and using alcohol only in moderation.

Citation: [Purushotham A](#), [Schug TT](#), [Xu Q](#), [Surapureddi S](#), [Guo X](#), [Li X](#). 2009. Hepatocyte-specific deletion of SIRT1 alters fatty acid metabolism and results in hepatic steatosis and inflammation. *Cell Metab* 9(4):327-338.

(Negin Martin, Ph.D., is a research fellow in the NIEHS Membrane Signaling Group. She was recently chosen as a 2009 Science Communication Fellow with *Environmental Health Sciences*.)

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Li heads a group in the NIEHS Laboratory of Signal Transduction that is striving to characterize molecular mechanisms that may hold the secrets of longer life and healthier aging. (Photo courtesy of Steve McCaw)



Visiting Postdoctoral Fellow Aparna Purushotham, Ph.D., was lead author on the paper. Li said of her colleague, "She has done a great job on this study and deserves recognition [for her important contributions]." (Photo courtesy of Steve McCaw)

Researcher Presents Strategy for Studying Environmental AhR Modulation

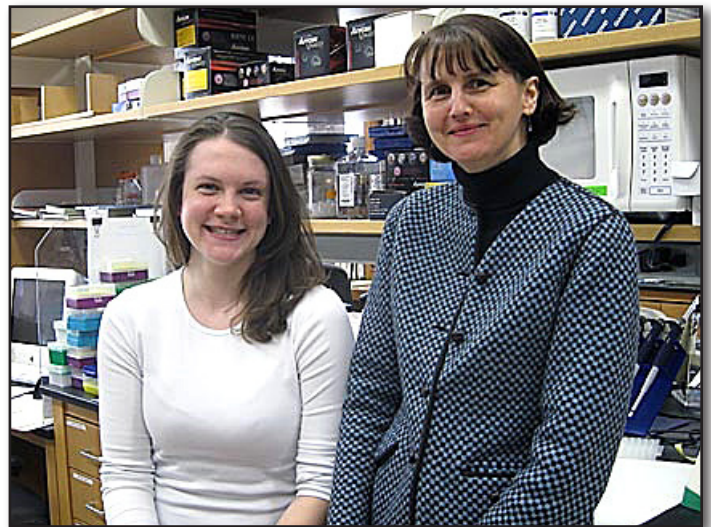
By Brian Chorley

In the wake of her 2008 study of dioxin's effects on the ligand-activated transcription factor aryl hydrocarbon receptor (AhR) and influenza A infection in mice, [NIEHS grantee](#) B. Paige Lawrence, Ph.D., has published a review of research on AhR modulation of anti-viral immunity that translates mechanistic research by her and others into a proposed research agenda based on a unified hypothesis — “that environmental signals delivered via the AhR influence anti-viral immune defenses.” The review is part of a special issue of the journal *Biochemical Pharmacology* devoted to “Biological Functions of the Ah Receptor: Beyond Induction of Cytochrome P450s.”

[Lawrence](#) is an associate professor of Environmental Medicine and Microbiology and Immunology at the University of Rochester School of Medicine and Dentistry. She and coauthor Jennifer L. Head argue in the [review](#) that more research could be useful in preparing for “the global health threat posed by viruses” and “stimulate new therapies to aid in the treatment of other diseases.” According to the review, better understanding of how pollutants deregulate anti-viral immunity could yield “new information regarding specific aspects of the disease process that are susceptible to modulation.” They propose that in addition to the canonical pathway of AhR-mediated transcriptional regulation, AhR modulation may work through interaction with signaling pathways, including non-genomic pathways, to influence immunity.

Much of the review focuses on the experimental mouse model of infection with human influenza A virus — the one Lawrence and colleagues used in their 2008 [study](#) of epigenetic alterations related to AhR activation. In those experiments, Lawrence's research team exposed pregnant and lactating mice to low doses of a common form of dioxin, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), thereby indirectly exposing fetuses and early postnatal pups during different periods of gestation and lactation. Depending on when the pups were exposed to TCDD, differential elements of the immune system were affected, purportedly through AhR modulation.

Specifically, after TCDD-exposed pups had matured, their ability to mount an immune response to influenza virus had diminished due to two separate mechanisms. It was observed that CD8+ T-cells decreased when pups were exposed to dioxin while nursing, and neutrophils increased if pups had been exposed during late gestation and nursing. These events were attributed to a diminished viral clearance and enhanced inflammation, respectively. Of note, the adult mother mice directly exposed to TCDD did not exhibit persistent defects in their immune response to viral infection, supporting the theory that these detrimental effects in the offspring were due to alteration during immune development.



Coauthors Jennifer Head, left, and Paige Lawrence are shown in their lab at the University of Rochester (UR). Head is a third-year graduate student at UR, supported by an NIEHS-funded Institutional Research Training Grant. (Photo courtesy of Paige Lawrence)

In their review, Head and Lawrence point to several additional areas of AhR modulation that have not received the attention they merit. They observe that “specific effects of AhR activation on the immune response to other viruses have not been specifically examined *in vivo*.” They also propose more research into the mechanisms that control excessive neutrophil recruitment during viral infection and into how AhR affects epithelial and endothelial cells, which are often overlooked as critical elements of innate host defenses.

Dioxin as a Model AhR Trigger

Dioxins directly affect biological systems via binding to cellular environmental sensors known as *Per-Arnt-Sim* proteins. One well-studied member of this family of proteins is the aryl hydrocarbon receptor (AhR), which readily binds many environmental contaminants, including dioxins, making AhR an important mediator of immune development and function.

Dioxins are a group of chemically related chemicals that are produced from the combustion of chlorine containing substances. Low levels of dioxin naturally result from volcanic and forest fire activity, but the advent of industrial processes in the mid-18th century has exponentially increased dioxin release into the atmosphere. Today, dioxin production has considerably lessened due to restrictions on industrial emissions. However, combustion of coal, municipal waste, treated wood, and other chlorine-containing substances still contribute substantially to environmental dioxin pollution.

Diet is the main source of dioxin exposure in humans. Dioxins are highly lipophilic in nature and bioaccumulate in the fats of animals over time, due to their slow rate of elimination. Red meats, dairy, and chicken products are common reservoirs. Once consumed, the ingested dioxins can remain in human fat storage for an estimated 8 years or even longer, resulting in long-term exposure. Because of their persistence in tissues and the environment, dioxins’ effects on physiology and health are of keen interest to researchers. Certain dioxins are known carcinogens, and a number of studies have found effects on reproduction, sexual development, and interrupted homeostasis of the epidermal, neurological and immune systems.

Because dioxin is quickly eliminated in about eight days from mice after exposure, study results are not directly translatable to humans; however, this physiologic aspect makes the mouse an excellent model to test for acute effects of dioxin exposure. Lawrence’s own results support the conclusion that permanent detrimental effects to the immune system can occur through dioxin-mediated AhR activation during development.

Since dioxin exposure can occur through consumption of a high fat diet, avoidance of these foods may offer one of the several ways that changing environmental exposures may modulate disease processes.

Citations:

Head JL, Lawrence BP. 2009. The aryl hydrocarbon receptor is a modulator of anti-viral immunity. *Biochem Pharmacol* 77(4):642-653.

Hogaboam JP, Moore AJ, Lawrence BP. 2008. The aryl hydrocarbon receptor affects distinct tissue compartments during ontogeny of the immune system. *Toxicol Sci* 102(1):160-170.

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Nobel Winner Andrew Fire to Give Distinguished Lecture

By Eddy Ball

On May 19, Nobel Laureate Andrew Fire will explore “Cellular Responses to Foreign Nucleic Acids” in the latest seminar of the 2008-2009 NIEHS Distinguished Lecture Series. NIEHS Immunology Group Principal Investigator [Farhad Imani, Ph.D.](#), will host the talk, scheduled to begin at 11:00 a.m. in Rodbell Auditorium.

[Fire](#) is a molecular biologist and professor of pathology and genetics at Stanford University. He and Craig Mello, Ph.D., of the University of Massachusetts Medical School shared the [2006 Nobel Prize in Physiology and Medicine](#) for their discovery of RNA interference (RNAi) — the way double-stranded RNA (dsRNA) can silence gene expression. Thanks to their groundbreaking work, researchers are now able to use RNAi techniques to quickly and randomly silence one gene at a time and identify even previously unknown genes involved in a specific pathway.

Fire’s current research focuses on the role of RNAi and other triggers and mechanisms that help an organism’s immune system identify and respond to foreign or unwanted nucleic acid. His lab primarily uses the nematode *C. elegans* as a model system to study the role of dsRNA, which is an essential component of most viruses, as a major mediator in gene silencing. Fire’s lab is particularly interested in the roles of gene silencing processes in viral pathogenesis and tumor progression in mammalian systems.

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This Month in EHP

By Eddy Ball

The May 2009 issue of *Environmental Health Perspectives* is now available on-line, with a feature story on environmental effects on the microbiota — the vast population of bacteria and other microbes that regulate health in the gut. The issue also includes a discussion of what is called “shotgun” proteomics and new studies of the autoimmune effects of the industrial solvent trichloroethylene (TCE) in mice and humans, non-food sources of bisphenol A (BPA), feminization of wild fish exposed to environmental estrogens, and the potential roles of folate and cysteine in facilitating arsenic methylation in children.

- **The Gut Reaction to Environmental Exposures** — Examining the complex relationship between flora in the human gastrointestinal tract and the gut’s ability to defend against environmentally linked disease



Distinguished Lecturer Andrew Fire (Photo courtesy of Linda A. Cicero of the Stanford News Service)



- **Boosting the Signal for Biomarker Discovery with “Shotgun” Proteomics** — Probing the potential of advances in omics technologies for streamlining biomarker discovery by narrowing the field of promising candidates for follow-up with targeted immunoassays
- **TCE and Autoimmune Disease** — Reviewing evidence that TCE is involved in the development of autoimmune disease in mice and humans and calling for additional work in this promising line of research
- **BPA Levels in Fasting NHANES Participants** — Analyzing data on fasting times in participants in the 2003-2004 National Health and Nutrition Examination Survey (NHANES) that suggest non-food sources of BPA and BPA accumulation in fat or other body tissues
- **Environmental Estrogens and Endocrine Disruption in Fish** — Estimating associations between feminization of wild fish and concentrations of estrogenic and anti-androgenic chemicals in the rivers where they live that support a multi-causal etiological link
- **Tailoring Nutritional Interventions for Children Exposed to Arsenic** — Teasing out the differences between arsenic-exposed adults and children in relation to their urinary arsenic metabolites and plasma levels of the nutrients folate, cobalamin, cysteine and homocysteine

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Extramural Update

NIH Pathways to Independence Awardees Recognized

The NIEHS Division of Extramural Research and Training (DERT) recently recognized three additional [NIH Pathway to Independence Award \(K99/R00\)](#) recipients for their successful transition to tenure track or equivalent status and officially welcomed them as members of the NIEHS grantee community.

After a project review of their research, training and career development accomplishments, the following recipients moved from an R99 mentored-postdoctoral phase of their training to R00 status as independent principal investigators:

- [Michelle Block, Ph.D.](#) — Assistant Professor of Anatomy and Neurobiology at the Virginia Commonwealth University School of Medicine, working under the grant [Reactive Microgliosis and Progressive Dopaminergic Neurotoxicity](#)
- [Dario Ramirez, Ph.D.](#) — Assistant Member in the Free Radical Biology and Aging Research Program at the Oklahoma Medical Research Foundation, working under the grant [Free Radicals and Redox Signaling Triggered by Lipopolysaccharide in Macrophages](#)



Block held postdoctoral fellowships at NIEHS and the Environmental Protection Agency. She was a member of the NIEHS Neuropharmacology Group. (Photo courtesy of Michelle Block)

- [Vishal Vaidya, Ph.D.](#) — Instructor in Medicine, in the Renal Division of Brigham and Women’s Hospital, working under the grant [Technology and Endothelial Biology of Kidney Injury Molecule-1](#)

The Pathway to Independence program is a way to increase and maintain a strong cohort of new and talented NIH-supported independent investigators by providing an opportunity for postdoctoral scientists to receive both mentored and independent research support from the same grant award. The award is for up to five years of support in two phases — from one to two years for the continuation and completion of mentored postdoctoral experience during the K99 phase and up to three years of research grant support in the independent R00 phase.

Applicants for the Pathways to Independence Award must have had fewer than five years of postdoctoral experience, still be in a mentored or postdoctoral position, and may not have had previous R01 or K-series grant support. Both U. S. citizens and non-U.S. citizens at domestic institutions, including intramural and extramural and for profit may apply.

Since the program was initiated in 2007, NIEHS has made approximately 25 K99 grant awards. So far, five of these K99 awardees have successfully transitioned to faculty positions and have been awarded the R00 grant funding. Several more have achieved faculty positions and R00 awards are pending.

For further information on the K99/R00 program contact: [Carol Shreffler, Ph.D.](#)

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Ramirez was a postdoctoral and research fellow in the NIEHS Free Radical Metabolism Group. (Photo courtesy of Dario Ramirez)



Vaidya was a postdoctoral fellow in the renal division of Brigham and Women’s Hospital, Harvard Medical School, supported by a grant from the National Kidney Foundation. (Photo courtesy of Vishal Vaidya)

Extramural Papers of the Month

By Jerry Phelps



- [Pesticide Exposure Raises Risk of Parkinson's Disease](#)
- [Solution Found to Increase Nanotube Luminescence](#)
- [Nasal Injury in Rats Exposed to Diacetyl May Be Predictive of Lung Injury in Humans](#)
- [Increased Immunoglobulin in Children with Autism](#)

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

Pesticide Exposure Raises Risk of Parkinson's Disease

NIEHS-funded epidemiologists at the University of California Los Angeles found that exposure to the combination of the fungicide maneb and the herbicide paraquat increased the risk of later development of Parkinson's disease. For people diagnosed with the degenerative disease prior to age 60, the risk was increased four- to six-fold.

The study reports that living within 500 meters of agricultural operations where the pesticides were sprayed increased residents' risk by 75 percent. The exposures occurred between 1975 and 1999, and the timing of the exposure proved to be a critical factor in the study. For people who were diagnosed at early ages, the exposure occurred when they were children, teens or young adults. The study participants included 368 long-term Central Valley residents with Parkinson's.

The research team developed a geographic information system approach for estimating exposure, based on California pesticide-use records. All addresses for the study participants were used to give an accurate estimate of their total exposure from 1974 through 1999, coinciding with the dates of the pesticide-use records.

According to the study's senior author, Beate Ritz, the new study confirms previous observations in animal studies that exposure to multiple chemicals may increase the effects of each chemical and that the timing of the exposure is an important risk factor.

Citation: [Costello S, Cockburn M, Bronstein J, Zhang X, Ritz B](#). 2009. Parkinson's disease and residential exposure to maneb and paraquat from agricultural applications in the central valley of California. *Am J Epidemiol* 169(8):919-926. Epub 2009 Mar 6.

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Solution Found to Increase Nanotube Luminescence

Chemists at the University of Connecticut have found a way to increase the luminescence efficiency of single-walled carbon nanotubes, which could lead to better use of nanotechnology in medical imaging and other applications. Increasing the luminescence efficiency of carbon nanotubes could lead to their use in detecting tumors, arterial blockages and other internal problems that are now diagnosed with potentially harmful x-rays, radioactive dyes or more invasive methods. Physicians could scan patients with a device that would capture a very sharp image from the light given off by the carbon nanotubes.

Previous work in this and other laboratories had been able to raise the light emitted from nanotubes by only 0.5 percent. The new discovery is best described as a chemical sleeve wrapped tightly around the nanotube, which reduces exterior defects. The chemical used is a derivative of vitamin B-12, also known as flavin. The flavin molecules “self-assemble” into a tube that adsorbs to the carbon nanotube.

The researchers claim that the act of self-assembly not only forms a new tubular structure, but that it actively cleans the surface of the underlying nanotube. The cleaned nanotubes achieve luminescence efficiency as high as 20 percent.

The researchers anticipate that a number of important applications may be possible as the result of their discoveries, including medical devices and biosensor applications.

Citation: Ju SY, Kopcha WP, Papadimitrakopoulos F. 2009. Brightly fluorescent single-walled carbon nanotubes via an oxygen-excluding surfactant organization. Science 323(5919):1319-1323.

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Nasal Injury in Rats Exposed to Diacetyl May Be Predictive of Lung Injury in Humans

Exposure to the butter flavor ingredients diacetyl and butyric acid has recently been found to cause a respiratory condition called bronchiolitis obliterans. The popular press has dubbed the condition “popcorn workers lung” because it is otherwise a rare condition, but strikes workers in the popcorn industry at a much higher rate than the general population. The condition causes scarring of the lungs that inhibits normal respiration.

NIEHS-supported scientists investigating the health effects of butyric acid and diacetyl have discovered that the severity of airway injuries in rats above the level of the lung are predictive of similar injuries in human lung tissue. The current results suggest that simultaneous exposure to butyric acid and diacetyl may increase the toxicity and potential lung injury caused by diacetyl.

Butyric acid is a potent inhibitor of an enzyme known as diacetyl reductase that metabolizes diacetyl. These findings highlight the need to consider the multiple components of butter flavoring vapors in comprehensive risk assessments and safety evaluations.

Citation: Morris JB, Hubbs AF. 2009. Inhalation dosimetry of diacetyl and butyric acid, two components of butter flavoring vapors. Toxicol Sci 108(1):173-183.

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Increased Immunoglobulin in Children with Autism

New data on autism from NIEHS-supported grantees at the University of California, Davis presents additional information that immune dysfunction is associated with autism disorders. Previous reports have shown abnormal immunoglobulin levels, including increases in blood levels of auto-reactive antibodies in people with autism.

Since IgG is the predominant antibody isotype found in the blood, the researchers hypothesized that an altered immune response could result in an abnormal IgG profile in children with autism. They measured plasma levels of four different isotypes of IgG in 241 children from the Childhood Autism Risks from Genetics and the Environment study — a large epidemiologic case-control investigation. The study included 114 children with autism disorder, 96 typically developing control children and 31 children with developmental delays.

They found significantly increased levels of the IgG4 subclass in children with autism disorder as compared to the control children and the children with developmental delays. The results suggest an underlying immunological abnormality in children with autism disorder. The researchers conclude that additional investigation is necessary to determine the relationship between immunological findings and behavioral impairments in autism.

Citation: [Enstrom A, Krakowiak P, Onore C, Pessah IN, Hertz-Picciotto I, Hansen RL, Van de Water JA, Ashwood P. 2009. Increased IgG4 levels in children with autism disorder. Brain Behav Immun 23\(3\):389-395.](#)

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

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Intramural Papers of the Month

By Robin Arnette

- [Telomere Length Is Associated with Obesity and Weight Gain](#)
- [Mouse Allergens Associated with Asthma Symptoms](#)
- [Female Mice Neonatally-Treated with Genistein Exhibit Reproductive Abnormalities](#)
- [Novel Role for Estrogen Receptor Beta in Granulosa Cells](#)

Telomere Length Is Associated with Obesity and Weight Gain

Investigators at NIEHS report that shorter telomeres — noncoding double-stranded repeats at the ends of chromosomes — are associated with higher body mass index (BMI) and weight gain in adulthood. Since short telomeres have been linked to an increased risk of developing age-related diseases, these findings support the hypothesis that obesity may accelerate the aging process. In addition, the findings highlight the importance of maintaining a healthy weight in adulthood.

The investigators studied 647 women from the approximately 50,000 women ages 35-74 who are participating in the Sister Study, a prospective study of environmental and genetic risk factors for breast cancer. The women's height, weight and waist circumferences were measured, and telomere length was estimated by extracting DNA from blood samples and subjecting the samples to real-time quantitative polymerase chain reaction (PCR).

There was an inverse relationship between telomere length and both current and past BMI. While telomere length was associated with weight gain and weight cycling, the results suggested that duration of obesity may be more important than weight gain, per se, since among women over 40, telomeres were shortest in women who were overweight or obese both in their 30s and when they enrolled in the study.

Citation: [Kim S](#), [Parks CG](#), [DeRoo LA](#), [Chen H](#), [Taylor JA](#), [Cawthon RM](#), [Sandler DP](#). 2009. Obesity and weight gain in adulthood and telomere length. *Cancer Epidemiol Biomarkers Prev* 18(3):816-820.

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Mouse Allergens Associated with Asthma Symptoms

Recent findings suggest that mouse allergen exposure in the home is an important risk factor for allergic asthma and contributes independently to asthma morbidity among allergic individuals. According to the research team, comprised of scientists from NIEHS and the Constella Group, LLC, levels of mouse urinary protein (MUP) greater than 1.6 µg/g in the home increased the odds of having asthma symptoms in the past year by two-fold. These results were generated as part of the National Survey of Lead and Allergens in Housing (NSLAH), the first study to evaluate the importance of residential mouse allergen exposures among the general U.S. population.

The NSLAH was a cross-sectional study that surveyed 2,456 individuals living in 831 housing units in 75 different locations throughout the U.S. Participants completed questionnaires that provided information on demographics, household characteristics and health status. Members of the research team vacuumed dust from various indoor sites and used a polyclonal immunoassay to determine the concentration of MUP.

Eighty-two percent of the homes surveyed had detectable levels of MUP, and 35 percent of the homes had MUP concentrations greater than 1.6 µg/g. Allergic individuals who were exposed to these elevated levels of MUP had an increased risk of experiencing asthma symptoms, while those who did not have allergies were unaffected.

Citation: [Salo PM](#), [Jaramillo R](#), [Cohn RD](#), [London SJ](#), [Zeldin DC](#). 2009. Exposure to mouse allergen in U.S. homes associated with asthma symptoms. *Environ Health Perspect* 117(3):387-391.

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Female Mice Neonatally-Treated with Genistein Exhibit Reproductive Abnormalities

The oviductal environment and uterus of female mice neonatally treated with genistein, a phytoestrogen found in soy products, develop abnormalities that contribute to reproductive failure. Investigations conducted by NIEHS researchers determined that although the eggs from these mice were normal, reduced embryo survival in the abnormal oviductal environment and the inability of the uterus to sustain pregnancy contributed to their complete infertility.

On neonatal Days 1–5, female mouse pups received subcutaneous injections of corn oil (control) or 50 mg/kg/day of genistein. At six to nine weeks of age, eggs were harvested following induced ovulation. Eggs from both groups were easily fertilized *in vitro* and one cell embryos could be cultured equally to the blastocyst stage. When these blastocysts were transferred to pseudopregnant recipients, the number of live pups produced was similar to controls. However, if embryos were left to develop in the oviduct, about half failed to develop to the blastocyst stage and most of the remaining embryos failed to implant; no pups were born.

Previous studies suggested that the uterus of genistein-treated mice is less responsive to estrogens. Because implantation is hormone-dependent, the authors propose that the limited response to hormonal cues could be responsible for reproductive failure.

Citation: Jefferson WN, Padilla-Banks E, Goulding EH, Lao SP, Newbold RR, Williams CJ. 2009. Neonatal exposure to genistein disrupts ability of female mouse reproductive tract to support preimplantation embryo development and implantation. *Biol Reprod* 80(3):425-431.

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Novel Role for Estrogen Receptor Beta in Granulosa Cells

According to NIEHS researchers, estrogen receptor beta (ER β) is required for the optimal accumulation of cAMP in follicle stimulating hormone (FSH)-stimulated mouse granulosa cells. The published findings are the first to indicate the role that ER β plays in the induction of the cAMP pathway in mouse granulosa cells and the negative effects on ovulation and fertility.

Previous *in vivo* and *in vitro* studies demonstrated that granulosa cells from ER β ^{-/-} preovulatory follicles exhibited a reduced response to FSH-induced differentiation as evidenced by an attenuated response to luteinizing hormone (LH). The research team furthered this research by using microarray analysis to identify genes that need ER β for induction by comparing granulosa cells from ER β ^{-/-} and ER β ^{+/+} mice following FSH exposure. In addition, the team used granulosa cell cultures to examine the purpose of ER β in the cAMP pathway.

Results indicated a 50 percent reduction in cAMP levels in ER β ^{-/-} compared to controls and a reduction in CREB phosphorylation in FSH-treated ER β ^{-/-} granulosa cells.

Citation: DeRoo BJ, Rodriguez KF, Couse JF, Hamilton KJ, Collins JB, Grissom SF, Korach KS. 2009. Estrogen receptor beta is required for optimal cAMP production in mouse granulosa cells. *Mol Endocrinol* Mar 26 [Epub ahead of print].

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Inside the Institute

Assembly of Laboratory Staff Elects Officers and Councilors

By Eddy Ball

On April 14, the NIEHS Assembly of Laboratory Staff (AoLS) announced the results of its online election of officers and councilors, paving the way for the first organization of its type at NIEHS to serve as an officially sanctioned advocate for the interests of laboratory technical staff — much as the Assembly of Scientists performs that role for the Institute's staff scientists and principal investigators. The initial group of officers and councilors includes five members of the AoLS steering committee, which hosted an [organizational meeting](#) on March 4.

Officers include President Gina Goulding, a biologist in the NIEHS [Gamete Biology Group](#), President-elect Paula Brown, also a biologist in the Gamete Biology Group, and Secretary Stella Sieber, a biological science laboratory technician in the [Microarray Core](#). They will serve two-year terms, with Brown rotating into the position of president on January 1 of the second year of her term, as Goulding assumes the post of past-president and ex-officio council member for an additional year.



The new officers gather for a group photo. In the front row, left to right, are Brown, Goulding, Ward, Foley and Sieber. In the back row are, left to right, Myers and DeGraff. (Photo courtesy of Steve McCaw)

Elected as councilors are Biological Science Laboratory Technician Laura Miller DeGraff of the [Molecular and Cellular Biology Group](#), [Special Techniques Group](#) Leader Julie Foley, Biologist Page Myers of the Comparative Medicine Branch and Biologist Toni Ward of the [Polypeptide Hormone Action Group](#). DeGraff and Myers were members of the AoLS Steering Committee.

Councilors are elected by the Assembly for terms of two years, with two to be elected each year. The first AoLS committee meeting will determine which two of the newly elected councilors will serve one-year terms to give the council its constitutionally mandated continuity.

The AoLS was created at the recommendation of the NIEHS Organizational Climate Committee “to develop training and career advancement opportunities, enhancing professional excellence and our contribution to the Institute goals. The Assembly will serve as a general forum for communication, as a means to formulate and express opinion, and as an instrument to render advice and to take action pursuant to the general objectives of the laboratory staff.” At its organization meeting, many attendees expressed an interest in working toward improving promotion and evaluation guidelines for laboratory staff, who are career employees working in general service grades 5 through 12.

The AoLS will meet in the spring and fall each year. Special meetings can be called by a vote of the council and in response to a written petition by at least ten members of the assembly.

(Note: The AoLS has a [website](#), which employees may access within the Institute's internal network or offsite via an NIH/NIEHS connection. Posted there are nominee statements by candidate for office.)

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Earth Week 2009 Kick Off

By Eddy Ball

NIEHS kicked off its annual celebration of Earth Week on April 21 with remarks by Director Linda Birnbaum, Ph.D., who addressed a group of staffers gathered on the patio outside the Institute's main building. Birnbaum's talk was the opening event of the three-day celebration sponsored and organized by the NIEHS Environmental Awareness Advisory Committee (EAAC), which was founded in 1991. The first Earth Day took place in 1970.

With the blue sky, the lush greenery of early spring and the waters of the campus lake as backdrop, Birnbaum urged listeners to make their personal commitment to increased environmental stewardship and promised that NIEHS would continue to be the "environmental institute at NIH" and work to improve global environmental health. She set a goal of environmental sustainability in every aspect of operations at NIEHS.

"Our research here at NIEHS reminds us continually that public health and environmental health can't be separated," Birnbaum began. "The overwhelming majority of scientists now believe that global climate change is a real threat, and there is an increasing awareness that changes in climate will impact our health."

As Birnbaum underscored the importance of environmental stewardship, she pointed to a "tradition of excellence" at NIEHS. She listed several impressive accomplishments, including the 2007 NIEHS Environmental Policy Statement, a comprehensive Environmental Management System, green building modifications, such as solar panels on the B-module, recycling two-thirds of the waste at the Institute, green purchasing and a water conservation program that saved NIEHS \$90,000 last year by reducing water consumption by 20 percent.

Birnbaum described some of the many ways individuals can make an impact at home and at work. She suggested that employees can use promotional tote bags as reusable grocery bags, get in the habit of turning off lights and computer monitors when they're not being used, buy local food, bring reusable containers to work and meetings, reduce printing, recycle electronics and choose products with less packaging.

Looking to the future, Birnbaum promised "to hold ourselves to a higher standard" in all aspects of sustainability at NIEHS. She said she plans to issue the first NIEHS Sustainability Report this summer that will summarize all of the Institute's accomplishments and challenges as well as identify areas of future opportunity, including bringing all buildings up to green certification standards.



Assistant Project Officer Essie Jones was on hand for the kick off — complete with re-usable water container and recyclable coffee cup. (Photo courtesy of Steve McCaw)



EAAC co-chair and Biologist Danica Andrews welcomed employees to the Earth Week kick off. EAAC is a volunteer group that advises the director on environmental issues and opportunities. (Photo courtesy of Steve McCaw)

At NIEHS, Earth Day has evolved into a sustainability awareness and educational fair showcasing the practical ways that people can reduce their impact on the environment. Features included lectures by horticulturist Jeff Taylor, gardener Jeff Tucker, and a representative of Progress Energy’s new green initiatives, free giveaways and samples, and a 5K EPA Fun Race.

EAAC members lured visitors with free cookies, organic, shade-grown coffee, and a book and video exchange to tabletop displays in the lobbies of Keystone and the main building. There, employees and contractors found tips for green cleaning, buying local, green home improvements, rain barrels, smart commuting and responsible disposal of hazardous waste.



“We know that Earth Day should be everyday for all of us,” Birnbaum told the audience as she encouraged everyone to take the NIEHS Earth Week Challenge. (Photo courtesy of Steve McCaw)



Visiting Fellow Xiaohua Gao, Ph.D., left, and Biologist Michelle Klippel look over their Earth Week Challenge forms as Birnbaum talked about how employees can do their part. (Photo courtesy of Steve McCaw)



EAAC co-chair and avid cyclist Dick Sloane prepares to get down as Andrews queues up James Brown’s “I Feel Good.” The patio challenge was one of the first times many employees has seen Sloane with a tie. (Photo courtesy of Steve McCaw)



Staff Scientist Gary Bird, Ph.D., and Biologist Becky Boyles get into the swing of Earth Week. (Photo courtesy of Steve McCaw)



IRB Administrator Craig Wladyka and Health Scientist Diane Spencer pose during the tabletop display at Keystone. Spencer is an EAAC member who baked cookies for the event. (Photo courtesy of Steve McCaw)



The tabletop displays included this information poster on rain barrels. Visitors could enter a drawing for the rain barrel beside the table. (Photo courtesy of Steve McCaw)

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NTP Staffer Writes of Inspiration, Faith and Encouragement

By Eddy Ball

National Toxicology Program (NTP) Administrative Specialist Carolyn Hall doesn't advertise her extracurricular talents, but the word is getting around on campus about her new book, *Intimate Journey: A Guide to Your Spiritual Path*.

Frequently writing in the second person, Hall punctuates her introspective motivational narrative and poetry with extended journaling sections that make her book an interactive and personalized experience for the reader. From the first page, when readers can sign their names as someone with "a purpose for living this life," they have many opportunities to write down their own thoughts about Hall's meditations on how she found greater meaning and happiness in her own life and to strive to improve their own experiences in life.

iUniverse, the publisher of *Intimate Journey*, has classified the book as "Religion/Spirituality," and at the center of Hall's story is her personal relationship with her creator. But Hall's faith is more than doctrinal or denominational. Instead, it focuses on the ability of each individual to develop a positive attitude and live a life of service to fellow human beings.

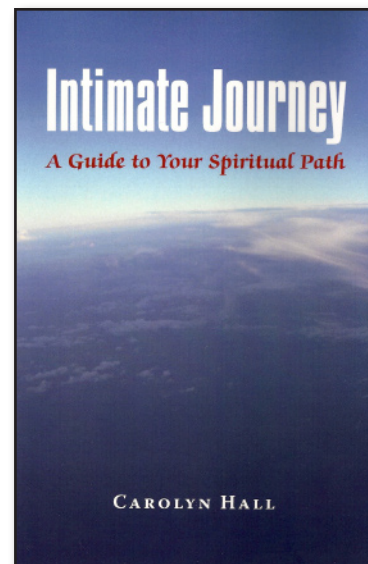


Hall joined NIEHS in 1991. She is part of the scientific support staff in the NTP Cellular and Molecular Pathology Branch headed by Robert Sills, D.V.M., Ph.D. (Photo courtesy of Steve McCaw)

Hall's faith in God is a faith in the rightness of the universe and the power of unconditional love. She envisions the journey toward serenity and self-confidence as a journey also to a heightened sense of responsibility toward others. "What really matters [ultimately]," she said, "is how you treat people."

Hall reminds readers of the seemingly little things — such as telling family members regularly how much they are loved — as well as the challenge of becoming a person who controls his or her emotions and everyday life, rather than being controlled by the negativity of others, regret over past failure or loss, and the uncertainties of life.

Hall is confident her story can be an inspiration for others, but she warns that there are no easy answers or shortcuts to happiness. She also won't rule out the possibility of a sequel as she continues on the next phase of her own intimate journey. "I think that faith is like anything else," Hall said of her experience. "You have to constantly work at it."



(*Intimate Journey* is available in print and electronic formats: ISBN 978-1-4401-1360-4, ISBN 978-1-4401-1362-8 and ISBN 978-1-4401-1361-1.)

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