



Environmental Factor

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December 2008

NIEHS Spotlight



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NIH Research Festival in October. ...[read more](#)



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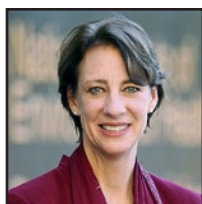
personal care products present in the[read more](#)



Lecture Series Recognizes Suk and Landrigan

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at the inaugural John P. Wyatt Lecture ...[read more](#)



Hrynkow Chosen as AAAS Committee Chair

Bethesda-based NIEHS Associate Director Sharon Hrynkow, Ph.D., has accepted a November 5 offer from the AAAS Board of Directors of

a one-year appointment as chair of the ...[read more](#)

Science Notebook



Sixth Annual Science Awards Day Honors Achievements

NIEHS Science Awards Day, held on the first Thursday of November each year, added a new category of award to the 2008 event to honor the year's

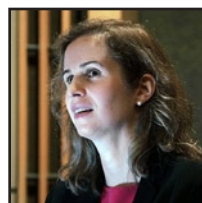
outstanding staff scientist. Now in its sixth year, the annual day-long event rewarded, ...[read more](#)



NIA Director Visits RTP to Address Students

National Institute on Aging (NIA) Director Richard Hodes, M.D., was the keynote speaker at the 2008 Symposium on the Biology of Aging

initiated by the American Foundation for Aging Research (AFAR) and the North Carolina GlaxoSmithKline Foundation. The symposium was held[read more](#)



Fibroids and the Black Women's Health Study

Lauren A. Wise, Sc.D., an Assistant Professor of Epidemiology at the Boston University School of Public Health, visited NIEHS recently to talk

about her work on uterine leiomyomata, also known as "fibroids." Wise presented "Risk Factors for Uterine Leiomyomata in the Black Women's[read more](#)



Global Warming and Insect Populations

The Scientific Research Society, Sigma Xi, headquartered in Research Triangle Park, N.C., hosted a presentation on November 17 by

North Carolina State University (NCSSU) ecologist Rob Dunn, Ph.D., as part of a monthly lunchtime lecture series. The talk, titled "Global Warming[read more](#)

NIEHS Spotlight



Tinkle Chairs Session at U.S.-China Symposium

NIEHS Office of the Director Senior Science Advisor Sally Tinkle, Ph.D., attended the First U.S.-China Symposium on Nanobiology and Nanomedicine in Beijing October 21 – 23. Interactions with Human Health and the Environment” ...[read more](#)



Taking Research from the Bench to the Community

This fall the Superfund Basic Research Program (SBRP) at the University of Arizona (UA) once again focused its Binational Center translation and outreach core activities on communities across the border in Mexico. On October 27 – 28,[read more](#)



Former Council Member Weinstein Mourned

On November 3, NIEHS lost a long-time friend and former member of its National Advisory Environmental Health Sciences Council with the death of I. Bernard (Bernie) Weinstein, M.D., Sci.D. (Hon.). ...[read more](#)

NIH Announces 2009 Roadmap Funding for New Investigators

On October 23, NIH issued a program announcement for the 2009 NIH Director's New Innovator Award program soliciting applications with an opening date of December 15, 2008. The program is tailored to early career investigators, with grants to cover up to \$1.5 million in direct costs over five years. NIH expects to fund 24 awards in September 2009.[read more](#)



Children's Health Symposium Tackles the Built Environment

With the help of contributions by platinum sponsor NIEHS and other supporters, the Children's Environmental Health Institute (CEHI) held its Fifth Biennial Scientific Symposium on October 30 – 31 in Austin, Texas. The focus of this[read more](#)

Science Notebook



NIEHS Investigator Advances Understanding of Heparin Biosynthesis

NIEHS Structure and Function Research Group Leader Lars Pedersen, Ph.D., and colleagues at the University of North Carolina (UNC) Chapel Hill have succeeded in creating a group of recombinant enzymes that synthesize novel varieties of heparan sulfate with unique biological functions ...[read more](#)



ADHD Medications Do Not Cause Genetic Damage in Children

In contrast to recent findings, two of the most common medications used to treat attention deficit hyperactivity disorder (ADHD) do not appear to cause genetic damage in children who take them as prescribed, according to a new study by researchers at the ...[read more](#)



Upcoming Distinguished Lecture by Gary L. Johnson

The 2008 – 2009 NIEHS Distinguished Lecture Series will feature a talk December 9 by Professor and Chair of the University of North Carolina Department of Pharmacology Gary L. Johnson, Ph.D. ...[read more](#)

Extramural Research

Extramural Update

Changes are in the works for the way grant applications are reviewed at the National Institutes of Health (NIH), and they are scheduled to be phased in beginning in January 2009. While the NIH peer-review system has received much praise over the years, it had not been scrutinized for potential improvements that could enhance a process that has been in place for more than a decade. It had also become clear that the burden of review could put enormous pressures on reviewers, and NIH decided ...[read more](#)

Inside the Institute



Disability Awareness Program Showcases Campus Talent

NIEHS concluded its observance of National Disability Employment Awareness Month (NDEAM) with an afternoon of events on October 28.

The highlights included a book reading in Rodbell Auditorium by EPA Environmental Engineer and novelist Marc Yves Menetrez, Ph.D., ...[read more](#)



Burning the (Weekend) Twilight Oil

Photographer Steve McCaw was on his way home from covering a meeting when he captured this image of NIEHS from across the campus lake on the

evening of Saturday November 8. ...[read more](#)



Chinese Delegation Visits NIEHS

On November 14, a contingent of Chinese government officials involved in a four-month executive education and English-language immersion

program at Duke University attended a half-day workshop at NIEHS as part of their series of weekly field experiences. The program was[read more](#)

Extramural Research

Extramural Papers of the Month

- [Parkinson's Disease Linked to Vitamin D Deficiency](#)
- [Nanoparticles Kill Blood Vessel Cells in the Human Brain](#)
- [Cytosine-DNA Methyltransferase Mediates Carcinogen-Induced Gene Promoter Methylation](#)
- [Gas Stove Emissions Worsen Asthma Symptoms](#)

Intramural Research

Intramural Papers of the Month

- [Crystal Structure of RACK1 in *Arabidopsis thaliana*](#)
- [SNPs in Human Ion Channel Genes Increase Susceptibility to Disease by Creating New Phosphorylation Sites in the Channel Proteins](#)
- [Cumene Exposure Leads to K-ras and p53 Mutations That Are Linked to Lung Tumors in Mice](#)
- [Inducible Nitric Oxide Synthase Is Involved With Streptozotocin-induced Diabetes](#)

Calendar of Upcoming Events

- **December 4**, in the Rall, Building Mall, 7:30–3:00 — Holiday Craft Fair
- **December 4 (Offsite Event)**, at The Weathervane at A Southern Season in Chapel Hill, 5:30–8:30 p.m. — North Carolina Special Libraries Association (NCSLA) Officer Installation Banquet with keynote talk by NIEHS Library Director and Chair of the SLA Centennial Commission Dav Robertson on “InfoPrognostications: 100 Years Past, 100 Years Future”
- **December 5**, in Rodbell Auditorium, 9:00–10:00 — Frontiers of Environmental Sciences Lecture Series
- **December 8**, in Rodbell Auditorium, 11:00–12:00 — Laboratory of Molecular Genetics Fellows Invited Guest Lecture with Jef Boeke, Ph.D., speaking on “Retrotransposons in humans and other mammals.”
- **December 9**, in Rodbell Auditorium, 11:00–12:00 — Distinguished Lecture Series featuring Gary Johnson, Ph.D., who discuss the topic of “Defining MAP3 Kinase Regulated Signaling Networks: From Metastasis to Tissue Stem Cells”
- **December 11**, in Rodbell Auditorium, 8:30–2:30 — Outstanding New Environmental Scientists (ONES) Seminar
- **December 11**, in Rall F-193, 1:00–2:00 — Laboratory of Structural Biology Seminar Series with Lee Pedersen, Ph.D., presenting a “Progress report on the atomic details of making thrombin”
- **December 16**, in Rodbell Auditorium A 11:00–12:00 —Biostatistics Branch Seminar with Ori Davidov, Sc.D., topic TBA
- **December 18**, in Rodbell Auditorium—Director’s Annual Honor Awards Ceremony and Reception
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

NIEHS Postdocs Honored with FARE Awards

By Eddy Ball

Ten NIEHS post-doctoral fellows (pictured) are among the winners of the 2009 Fellows Award for Research Excellence (FARE) presented at the NIH Research Festival in October. The winners will also be honored at the NIEHS Director's Annual Honors Award Ceremony December 18 in Rodbell Auditorium.

Winners of FARE awards will each receive a \$1000 stipend to attend a scientific meeting at which they will present their abstracts, either as a poster or a seminar. Fellows submit an abstract of their research, which is peer reviewed in a blind study section competition. More than 1,000 applicants competed for this year's awards.

The winners are also asked to present their work at a dedicated poster session on the day of the FARE awards presentation ceremony. In addition, the winners serve as judges for the following year's FARE competition.

The FARE program began in 1995 to provide recognition for the outstanding scientific research performed by intramural postdoctoral fellows. Winners are chosen by the [FARE Subcommittee](#) of the NIH Fellows Committee (FelCom).



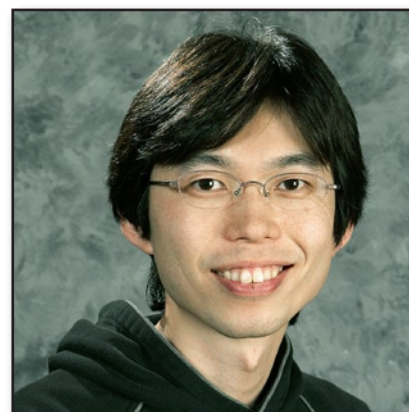
*Research Fellow Suraj Dhungana, Ph.D., Host Defense Group and Mass Spectrometry Group.
(Photo courtesy of Steve McCaw)*



*IRTA Fellow Xiaoming Hu, Ph.D., Neuropharmacology Group.
(Photo courtesy of Steve McCaw)*



*Visiting Fellow Yoshihiro Komatsu, Ph.D., Molecular Developmental Biology Group.
(Photo courtesy of Steve McCaw)*



*Visiting Fellow Wataru Nakai, Ph.D., Chromosome Stability Group.
(Photo courtesy of Steve McCaw)*



*Visiting Fellow Fanny Odet-Radvay, Ph.D., Gamete Biology Group.
(Photo courtesy of Steve McCaw)*



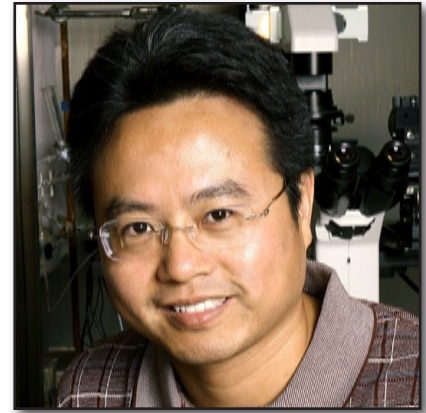
*IRTA Fellow Denise Ray, Ph.D., Metastasis Group.
(Photo courtesy of Steve McCaw)*



*IRTA Fellow Stephen Simons, Ph.D.,
Synaptic and Developmental
Plasticity Group.
(Photo courtesy of Steve McCaw)*



*Visiting Fellow Krisztian Stadler, Ph.D.,
Free Radical Metabolism Group.
(Photo courtesy of Steve McCaw)*



*IRTA Fellow Bin Tu, Ph.D.,
Ion Channel Physiology Group.
(Photo courtesy of Steve McCaw)*

Former NIEHS Postdoctoral Fellow Jennifer Adair, Ph.D., represented NIEHS on the 2009 subcommittee. Adair recently left the NIEHS for a position at the Fred Hutchinson Cancer Research Center in Seattle.

The annual FARE competition is open to intramural fellows, such as Intramural Research Training Award (IRTA), Cancer Research Training Award (CRTA), clinical/research and visiting fellows with no more than five years total postdoctoral experience in the NIH intramural research program. Visiting scientists and fellows must not have been tenured at their home institutions. Postdoctoral-level special volunteers and pre-IRTAs currently enrolled in a Ph.D. program and conducting their doctoral dissertation research at an NIH lab may also enter.

Along with support from FelCom, the FARE program is sponsored by the NIH scientific directors, the Office of Research on Women's Health, and the Office of Intramural Training and Education. The awards are funded by the scientific directors and the Office of Research on Women's Health.



*Visiting Fellow Adolfo Zurita, Ph.D.,
Transmembrane Signaling Group.
(Photo courtesy of Steve McCaw)*

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Dearry Explores Impact of Global Economy on Health

By Eddy Ball

On October 28, NIEHS Associate Director for Environmental Public Health Allen Dearry, Ph.D., offered public health specialists a compelling argument for instituting reforms related to the global economy as an effective intervention to impact climate change and health. Dearry's venue was the American Public Health Association (APHA) Annual Meeting in San Diego, where he presented research findings in a symposium titled "Trade and Transportation: Impact on Environmental Public Health."

In his talk, Dearry eschewed the popular icons of global warming — coal-fired power plants, fume-spewing school buses and vehicle-choked interstates — to turn the spotlight on the less publicized ways globalization is impacting public health worldwide.

Dearry's talk focused on global shipping and ports, overseas manufacturing and exports, and the growing number of the world's people involved in electronic waste (e-waste) recycling. Dearry's presentation was a call to the public and private sectors everywhere to abandon the "out of sight, out of mind" attitude that has allowed the global economy to flourish with minimal oversight or accountability — except to the financial bottom line of those who benefit most.

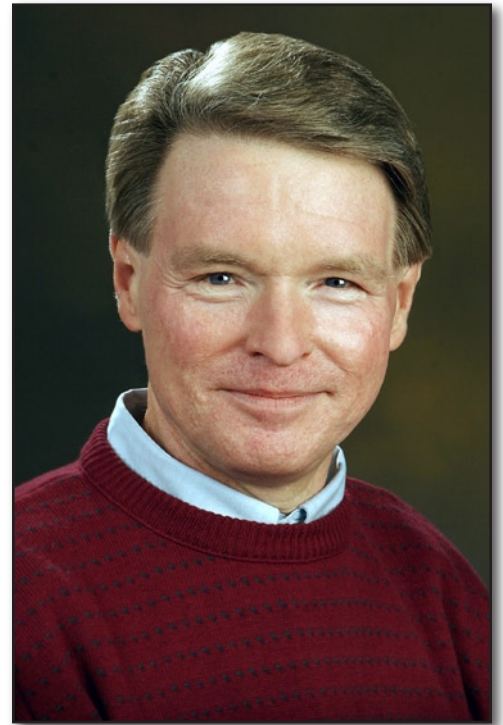
"Ships are an important source of carbon dioxide, the main driver of climate change and ocean acidification," Dearry explained. Their impact is felt in communities along coastlines adjacent to shipping lanes, along the world's busiest shipping lanes and in the oceanic ecosystem worldwide. Dearry also pointed to the health effects of goods movement. Particulate matter emissions alone from shipping account for approximately 60,000 cardiopulmonary and lung cancer deaths each year around the world.

Dearry focused on China, where 386,645 people died of work-related illnesses in 2005, as an example of the occupational health impact of feeding the American marketplace. Developing countries, such as China, rarely enforce the limits they have in place for workplace exposure to hazardous elements and compounds.

In China, "More than 200 million workers of China's labor force of 700 million were routinely exposed to toxic chemicals," Dearry observed. "China's carbon dioxide emissions doubled in five years, and it is likely the world's largest emitter." Most of this trend is driven by the manufacture of goods which are exported from China to developed countries.

Dearry turned finally to the dark side of America's love for the latest electronic gadget. "About 80 percent of US e-waste is exported to the developing world," he said. "E-waste is the most rapidly growing segment of the municipal waste stream in the world."

In a struggle to eke out a living, disadvantaged people in some developing countries often expose themselves to dangerous levels of the lead, barium, chromium, mercury, brominated flame retardants and polyvinyl chlorides present in discarded computers, televisions, cell phones and other e-waste exported from developing countries, Dearry maintained.



At the APHA meeting, the Environment Section presented its Distinguished Service Award to Dearry in recognition of his service to the section and organization, including the Environment Section chair and APHA governing council. (Photo courtesy of Steve McCaw)

The solutions that Dearry presented will involve concerted and aggressive efforts by business and governments at home and abroad. Some are so obvious that it's a wonder they weren't in place years ago, such as reducing the speed of ships at sea and "cold ironing" — requiring ships in port to plug into electricity rather than use their diesel engines. Others require hard-to-achieve universal agreement on international treaties, such as the Basel Convention of 1989 that has yet to be signed by several countries, to inform developing nations of all incoming shipments of hazardous waste, including e-waste.

Local and national governments can take action, as have New Jersey, Washington, California and Maryland, to promote green product design and control movement of e-waste. Governments of developing countries can put in place stricter workplace safety measures and limits on emissions. American retailers and manufacturers can oversee their offshore suppliers and facilities more effectively.

"Everyone has a stake in what is happening with our global economic system and its effects on climate change and public health," Dearry concluded, "and everyone bears some responsibility for the solutions."

Some Examples of the Effects of the Global Economy

Each of the three sections of Dearry's presentation offered some disturbing data about the sea transportation, offshore manufacturing and e-waste disposal that have proliferated in the growing global economy.

- According to International Maritime Organization estimates, ocean-going vessels released an amount of carbon dioxide in 2007 equivalent to the annual greenhouse emissions of 205 million cars — more cars than were registered in the US in 2006.
- The ports of Los Angeles/Long Beach emit more than 20 percent of Southern California's particulate pollution, which contributes to more than one million respiratory-related school absences, 62,000 cases of asthma symptoms and 2,400 premature heart-related deaths each year.
- China's exports to the US have grown to \$290 billion from \$51 billion just a decade ago, and more than 80 percent of the 6,000 factories in Walmart's worldwide database of suppliers are located in China.
- During the years 2002 to 2004, benzene levels in Chinese factories were more than 11 times the US EPA allowable level, contributing to China's dubious honor as the country which has more deaths per capita from work-related illnesses each year than any other country.
- Africa's largest port, Lagos, Nigeria, receives the equivalent of 400,000 computers or monitors each month, and nearly all of it is thrown into unlined and unmonitored landfills, which are close to groundwater and routinely set afire.
- In Guiya, China, 70 percent of families engage in e-waste recycling operations, most using primitive techniques, such as hammers and prying tools to separate the most valuable — and usually most hazardous — metals and compounds for re-sale.

Looking at Risks Posed by Drugs in the Environment

By Eddy Ball

In October and November, NIEHS helped support two scientific meetings investigating the potential threat to human health of pharmaceuticals and personal care products present in the environment.

On October 23, the Institute hosted the half-day [North Carolina Society of Toxicology \(NCSOT\)](#) Fall Meeting in Rodbell auditorium, which featured talks on the topic of “Pharmaceuticals and Personal Care Products in the Environment.” Two weeks later, with joint sponsorship by NIEHS, on November 10 – 11 the [Research Triangle Environmental Health Collaborative \(RTEHC\)](#) gathered 150 experts and stakeholders at the North Carolina Biotechnology Center in Research Triangle Park, N.C. for a two-day summit on “Pharmaceuticals in Our Water: What We Know, What We Don’t Know and What We Should Do.”

Concerns about the health effects of pharmaceuticals in drinking water accelerated with a series of reports in Spring 2008 that treated drinking water in Philadelphia, northern New Jersey, San Francisco and Washington tested positive for traces of prescription drugs. Despite some evidence of adverse effects in fish, amphibians and insects, the threat to human health of such drugs as antibiotics, mood stabilizers and sex hormones diluted in drinking water remains unclear.

Both meetings featured keynote talks by Hal Zenick, Ph.D., director of EPA’s National Health and Environmental Effects Research Laboratory (NHEERL), who discussed the [scientific background](#) of the issue of pharmaceuticals in the environment (PiE). At the larger RTEHC meeting, Zenick was joined by colleagues from the U.S. Geological Survey, EPA, the Food and Drug Administration and England’s Brunel University who offered their perspectives on the scientific and regulatory issues involved.

NIEHS grantee Richard Di Giulio, Ph.D., of Duke University and scientists from North Carolina state agencies, the University of North Carolina, GlaxoSmithKline and other organizations spoke during the RTEHC summit. Investigators from Baylor University, EPA and Sygenta Crop Science gave presentations for attendees of the NCSOT meeting.

Speakers at both meetings called for more data and careful interpretation to assess the dangers posed by PiE. There was a general agreement that physicians, pharmacists and patients need to be educated about responsible prescribing of drugs and disposal of pharmaceuticals. In addition, governments have an obligation to assign specific responsibilities to agencies regulating and monitoring PiE.



Zenick, shown addressing the NCSOT meeting, underscored regulators’ need for more data about the health effects of pharmaceuticals and personal care products diluted in drinking water. (Photo courtesy of Steve McCaw)



Olden is busy at his new job setting up the nation’s first urban school of public health at the City University of New York. However, he has remained active in the Research Triangle environmental public health community. (Photo courtesy of Harvard University)

The NCSOT holds annual spring and fall meetings, which have convened in NIEHS and EPA facilities on their RTP campuses in recent years. Many of the chapter's members will also attend the 48th Annual Meeting and ToxExpo of the [Society of Toxicology](#) to be held in Baltimore, Md. March 15–19, 2009.

The RTEHC summit is the organization's kickoff event. As the group's chairman, NIEHS Director Emeritus Ken Olden, Ph.D., described the organization, RTEHC is committed to "provid[ing] a neutral forum to host candid discussions and to provide advice on the most significant issues facing environmental health and related public policy." RTEHC executive committee members envision the organization as hosting annual environmental health summits; serving as a clearinghouse and promoter of seminars, workshops and conferences occurring at various public and private organizations; and assisting organizations by facilitating meetings and by enhancing collaborative ventures.

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Lecture Series Recognizes Suk and Landrigan

By Eddy Ball

NIEHS Acting Deputy Director Bill Suk, Ph.D., and NIEHS grantee Phil Landrigan, M.D., were honored November 5 as the keynote presenters at the inaugural John P. Wyatt Lecture in Environmental Health and Disease. Their talks took place in the William T. Young Library Auditorium on the campus of the University of Kentucky (UK) in Lexington.

The event launched a series of annual lectures sponsored by the Dr. John P. Wyatt Endowment at UK, as well as by the UK Office of the Vice President for Research, the UK College of Agriculture and the NIEHS-funded UK Superfund Basic Research Program.

[Suk](#) spoke on the topic "Environmental Exposure and Disease Links in Global Health: Addressing Health Needs and Disease Outcomes," one of several environmental health issues he addresses as acting deputy director. Prior to his acting appointment, Suk was the director of the NIEHS Superfund Basic Research Program.

Suk has published extensively on issues linking exposures with disease and on research and prevention strategies to reduce risks of environmentally induced diseases and disorders. Among his numerous honors, he was selected as a fellow of the [Collegium Ramazzini](#) and has been a National Science Foundation fellow.

Landrigan, who directs the Mount Sinai School of Medicine Children's Environmental Health Center, spoke about "Children's Health and the Environment: The Problem and the Solution." He is a pediatrician, epidemiologist and internationally recognized leader in public health and preventive medicine.

[Landrigan](#) is a member of the Institute of Medicine of the National Academy of Sciences. Prior to joining Mount



*Acting Deputy Director Bill Suk.
(Photo courtesy of Steve McCaw)*

Sinai, he was a medical epidemiologist at the Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health.

Suk and Landrigan were joined at the Wyatt Lecture by UK doctoral student Zuzana Majkova, UK postdoctoral scholar Jignesh Pandya, Ph.D., and Michigan State University doctoral student Haitian Lu. The students each gave 15-minute presentations on their current research.

John P. Wyatt, M.D., was director of the University of Kentucky Tobacco and Health Research Institute from 1974 until January 1980. He was a pulmonary diseases researcher who published over 100 articles covering viruses and diverse lung injuries.

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*NIEHS grantee Phil Landrigan.
(Photo courtesy of Phil Landrigan
and the Mount Sinai School of Medicine)*

Hrynkow Chosen as AAAS Committee Chair

By Eddy Ball

Bethesda-based [NIEHS Associate Director Sharon Hrynkow, Ph.D.](#), has accepted a November 5 offer from the AAAS Board of Directors of a one-year appointment as chair of the organization's Committee on Science, Engineering and Public Policy (COSEPP). Hrynkow has served on the committee as a member and federal liaison for four years.

Hrynkow will assume her new position on February 17, 2009. She describes her new role as one that will give her an opportunity to make certain that environmental health sciences issues have a place in the policy decision-making process.

"I am honored to be asked to lead COSEPP, particularly at a time when the discourse on science and technology policy is increasingly at the fore in federal, state and international agendas," Hrynkow said. I look forward to working with COSEPP and AAAS colleagues as we explore a range of critical issues, including the linked agendas of climate change and health, ethical issues surrounding deployment of new technologies, and building the pipeline of next generation scientists, among so many other priority areas."

Communicating the offer to Hrynkow, [AAAS Science and Policy Programs](#) Associate Director Stephen D. Nelson used the superlatives "significant and highly valued" to describe Hrynkow's contributions to COSEPP. "It was the Board's feeling that you are exceptionally qualified to provide effective leadership for COSEPP," he continued, "and we hope you will be willing and able to serve."



*Incoming chair of the AAAS Committee on
Science, Engineering and Public Policy Sharon
Hrynkow. (Photo courtesy of Steve McCaw)*

Created by AAAS in 1973, COSEPP grew out of a Science and Public Policy Studies Group formed by science, engineering and public policy scholars in the late 1960s. The committee serves as the principal advisory body for AAAS activities in science and technology policy, primarily, but not exclusively, at the federal level. The committee also oversees several specific policy-related programs within AAAS.

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Tinkle Chairs Session at U.S.-China Symposium

By Eddy Ball

NIEHS Office of the Director Senior Science Advisor Sally Tinkle, Ph.D., attended the First U.S.-China Symposium on Nanobiology and Nanomedicine in Beijing October 21 – 23. At the precedent-setting event, she co-chaired a session on “The Molecular Basis for Engineered Nanomaterial Interactions with Human Health and the Environment” with Chinese Academy of Science (CAS) Professor Zhifang Chai, Ph.D..

The [symposium](#) was sponsored on behalf of NIH by NIEHS and the National Cancer Institute (NCI). Chinese sponsors were CAS and the National Natural Science Foundation of China.

The NIH contingent was led by NIH Deputy Director for Intramural Research Michael Gottesman, M.D. Tinkle and [NIEHS Acting Director Sam Wilson, M.D.](#), served as members of the U.S. National Steering Committee.

According to Tinkle, the symposium established important ties between U.S. and Chinese nanomaterial/nanomedical investigators, set the stage for partnerships to coordinate and leverage research programs, and was an opportunity to discuss the new NIH/NIEHS NanoHealth Enterprise Initiative with an international audience of materials scientists. “By the close of the meeting,” she said, “we identified several action steps to support these goals — including a web portal for contact information, the cataloguing of resources and potential collaborative projects.”

NIEHS provided four members of the U.S. Select Speaker Faculty participating in the symposium. They included Professor Andre Nel, M.D., Ph.D., University of California Los Angeles; Vicki Colvin, Ph.D., Rice University; Paul Howard, Ph.D., Food and Drug Administration National Center for Toxicological Research; and Brian Thrall, Ph.D., Pacific Northwest National Laboratory.

As a follow up to the symposium, Tinkle said that Gottesman will contact Director of the Fogarty International Center Roger Glass, M.D., about exploring opportunities for student and post-doctoral exchange programs during his visit to China this month.

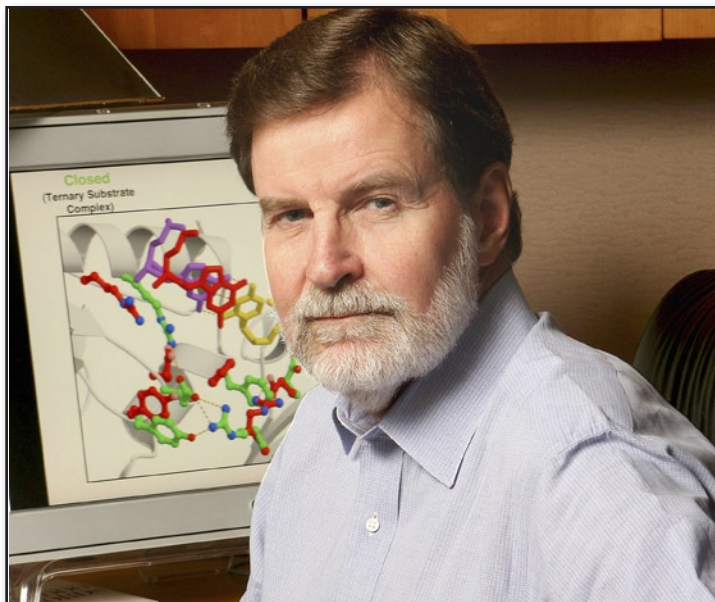
According to Tinkle, the symposium was a natural next step in her efforts on the behalf of NIEHS as a member of the NIH Nano Task Force Health Implications Working Group of the Nanoscale Science, Engineering and



Tinkle was a prime mover in the development of the NIEHS NanoHealth Initiative and the natural choice to represent NIEHS at the symposium. (Photo courtesy of Steve McCaw)

Technology Subcommittee since 2004, as NIEHS representative to the NIH Nano Task Force and as chair of the Nanomaterials Health Implications Working Group. “Through its NanoHealth Enterprise Initiative, NIEHS increases its scientific leadership position in the fields of nanotoxicology and human health,” Tinkle explained.

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Wilson was one of the three signers of the NIH proclamation accepting an invitation to co-sponsor the symposium. The others were former NIH Director Elias Zerhouni, M.D., and NCI Director John Niederhuber, M.D. (Photo courtesy of Steve McCaw)

Taking Research from the Bench to the Community

By Denise Moreno Ramírez and Eddy Ball

This fall the Superfund Basic Research Program (SBRP) at the University of Arizona (UA) once again focused its Binational Center translation and outreach core activities on communities across the border in Mexico. On October 27 – 28, the program held its sixth Specialized Workshop in Ciudad Obregón in the state of Sonora. It was attended by 236 Mexican students, faculty and senior investigators, health advocates and governmental personnel.

The workshop, titled “Health Impacts, Management and Treatment of the Most Prevalent Contaminants in Southern Sonora,” was conducted on the campus of the Instituto Tecnológico de Sonora (ITSON). The workshop’s goal was to provide the attendees with the most pertinent scientific information emerging from years of research funded by NIEHS, EPA and other sources and conducted by the [UA SBRP](#) and collaborators in Mexico.



Speakers who gathered at a panel session during the workshop included, left to right, UA Professor Wendel Ela, Ph.D.; ITSON Professor María Mercedes Meza Montenegro, Ph.D.; Instituto Nacional de Salud Pública researcher Lizbeth Teresita López Carrillo, Ph.D.; UA Professor Walter Klimecki, Ph.D.; and UNISON Professor Diana Maria Meza Figueroa, Ph.D. (Photo courtesy of UA SBRP)

The training included fifteen sessions taught by UA and ITSON scientists and their colleagues from the Mexican government and two additional Mexican research institutions — the Universidad Autónoma de Coahuila (UAC) and Centro de Investigación Científica y de Educación Superior de Ensenada (CICESE).

The focus of the workshop was regional environmental and health impacts in southern Sonora. The program was divided into three sessions:

- ***Arsenic Toxicology and Treatment of Water***

— Focusing on the toxicology of arsenic and its carcinogenicity, its presence in water and dust, and remediation in potable water sources

- ***Solid Waste and Municipal Landfills*** — Exploring the environmental engineering perspective on landfills and a pilot project at the Ensenada municipal landfill

- ***Pesticides*** — Surveying the impact of pesticides in the Yaqui Valley and the human health effects of exposures to individual pesticides and mixes

The workshop also included a special promotora training session that targeted health workers involved in outreach activities with Yaqui indigenous communities emphasizing the fundamentals of toxicology and research ethics when working with human subjects.

The conference concluded with remarks by ITSON president, Gonzalo Rodríguez Villanueva, Ph.D., stressing the importance of collaborative binational investigations. He pointed to the accomplishments of the collaboration of Mexican researchers with the UA [U.S.-Mexico Binational Center for Environmental Sciences and Toxicology](#), which helped to train three of the Mexican scientists speaking at the conference. The three U.S. researchers presenting at the workshop are SBRP-funded investigators who serve as mentors of Binational Center trainees and fellows.

(Denise Moreno Ramírez serves as coordinator of the UA SBRP Community Outreach Core and U.S.-Mexico Binational Center.)

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Participants lined up to sign in for the workshop in the new Centro de Estudios Estratégicos y de Negocios building at ITSON. (Photo courtesy of UA SBRP)



UAC researcher and former Binational Center trainee Pablo Ruiz, Ph.D., spoke to community health workers on the specifics of filling out surveys and obtaining samples for testing. (Photo courtesy of UA SBRP)



The workshop organizers had reason to smile over a job well done. Shown left to right are Binational Center Co-Director James A. Field, Ph.D., with Program Coordinators Rocio Estrella and Denise Moreno Ramirez. (Photo courtesy of UA SBRP)

Former Council Member Weinstein Mourned

By Eddy Ball

On November 3, NIEHS lost a long-time friend and former member of its National Advisory Environmental Health Sciences Council with the death of I. Bernard (Bernie) Weinstein, M.D., Sci.D. (Hon.). Weinstein's nearly five-decade career in cancer research came to close when he died in New York City at age 78 after experiencing kidney failure.

At the time of his death, [Weinstein](#) was the Frode Jensen professor of medicine, professor of Genetics and Development, and professor of Public Health at the Columbia University Medical Center. He was also director emeritus of the Herbert Irving Comprehensive Cancer Center.



Bernard Weinstein (Photo courtesy of Franklin P. Salisbury Jr. and the National Foundation for Cancer Research)

Weinstein was engaged in an aggressive research agenda elucidating the fundamental molecular mechanisms involved in multistage carcinogenesis as a quest to develop more effective prevention and treatment strategies. He received many honors in recognition of his scientific and medical contributions, including selection as a fellow of the American Academy of Arts and Sciences.

When he learned of his friend's death, NIEHS Acting Director Sam Wilson, M.D., praised Weinstein's contributions to the Institute. "He was an advisor to the director and deputy director on many topics in the environmental health sciences," Wilson wrote, "and he was instrumental in helping the Institute launch the Environmental Genome Project in the late 1990s."

In a [tribute](#) by the National Foundation for Cancer Research (NFCR), where he was a fellow, Weinstein was described as a pioneer in the fields of molecular carcinogenesis, preventive oncology and molecular epidemiology. Similarly, the American Association for Cancer Research (AACR), which posted an [obituary](#) of the AACR member of 45 years, praised Weinstein's "seminal contributions to basic cancer research, cancer prevention and translational research during his long and productive career."

Weinstein is survived by his wife, Joan, three children and two grandchildren. He was buried in Forest Hills Cemetery in Madison, Wis., where he attended college and medical school at the University of Wisconsin and which he considered home.

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NIH Announces 2009 Roadmap Funding for New Investigators

By Eddy Ball

On October 23, NIH issued a program announcement for the [2009 NIH Director's New Innovator Award](#) program soliciting applications with an opening date of December 15, 2008. The program is tailored to early career investigators, with grants to cover up to \$1.5 million in direct costs over five years. NIH expects to fund 24 awards in September 2009.

To be eligible for the awards, applicants must have received a doctoral degree or completed medical internship and residence within the previous ten years and be committed to dedicating at least 25 percent of their research effort to their projects. Because the program is geared toward new investigators, applicants must not have been a principal investigator on a prior NIH Research Project (R01) or similar grant. The eligibility criteria were clarified on November 4 to include current or past recipients of an R00 Pathway to Independence award if they meet all the other eligibility criteria.

The New Innovator Award program is designed to support exceptionally creative new investigators who propose highly innovative projects that have the potential for unusually high impact on an important biomedical or behavioral research problem. The evaluation procedure for applications under the New Innovator Award program is distinct from the traditional NIH peer review “study section” process.

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Children's Health Symposium Tackles the Built Environment

By Rosemarie Ramos

With the help of contributions by platinum sponsor NIEHS and other supporters, the Children's Environmental Health Institute (CEHI) held its Fifth Biennial Scientific Symposium on October 30 – 31 in Austin, Texas. The focus of this year's meeting was “Blueprint for Children's Health and the Built Environment.” What emerged from the [CEHI](#) symposium was a consensus that sustainable building and urban planning decisions must include an essential consideration of the long-term impact on human health and development.

As in previous years, the 2008 symposium brought together stakeholders from various disciplines to identify persistent and emerging children's environmental health issues. Speakers emphasized that this responsibility needs to be shared by stakeholders from the scientific, public health and non-scientific communities.

The forum featured a number of high-profile environmental public health experts that included Phil Landrigan, M.D., director of the NIEHS-funded Children's Environmental Health Center at Mt. Sinai School of Medicine; Anila Jacob, M.D., of the Environmental Working Group (EWG); Don Mattison, M.D., senior scientific advisor at the



NIEHS attendees Ramos, right, and Environmental Health Perspectives Writer/Editor Martha Dimes, Ph.D., posed outside the conference facility — a barn moved from New York State and retrofitted with environmentally friendly features. (Photo courtesy of Rosemarie Ramos)

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; and Howard Frumpkin, M.D., Dr.P.H., director of the CDC National Center for Environmental Health.

Presentations included an overview of the current centers funded by the NIH for the National Children’s Study by Mattison, Landrigan, and Donald Dudley, M.D., co-investigator of the National Children’s Study at the University of Texas Health Science Center in at San Antonio. Frumpkin’s presentation offered an historical perspective regarding the human health impact on such conditions as childhood obesity and respiratory disease of urban planning decisions over the last few decades that have failed to promote physical activity and healthy air quality.

Speaking from the perspective of urban planning and building design, John Poretto, former executive vice president for administration and finance at the University of Texas Health Science Center in Houston, and Steve McDowell, architect-owner of BNIM architects of Kansas City, Mo., presented their collaboration on building projects on UT campuses. These projects are now required to undergo a mandatory environmental health impact assessment prior to implementation.

Jacob and renowned neurotoxicologist Steven Gilbert, Ph.D., discussed the critical need to expand the definition and sources of environmental exposures, as well as the importance of assessing the long-term health impact from low-dose chronic exposures to lead and mercury. Jacob presented the latest project of the EWG titled “10 Americans” — highlighting the fact that no environmental exposure is as critical as those occurring in the intrauterine environment.

Fittingly, the venue for this year’s event was the historic Barr Mansion, one of the former cotton plantation houses that populated the Blackland Prairie in the 1800’s. Today, the property includes a ballroom facility that serves as a venue for meetings, receptions and weddings. The Barr Mansion boasts of being a certified organic venue serving only organic-certified meats and vegetables, much of it purchased from local growers.

(Rosemarie Ramos, Ph.D., is the health disparities postdoctoral fellow in the Metastasis Group.)

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NIEHS grantee Phil Landrigan, left, and colleague Donald Dudley were featured presenters at the symposium. (Photo courtesy of Rosemarie Ramos)



CEHI Executive Director Janie Fields, right, took time out from the proceedings for a photo with CEHI Board Member and NASA Astronaut David Wolfe, M.D. In the 1990s, Fields was instrumental in getting a commitment of financial support by NIEHS from then Deputy Director Sam Wilson, M.D. (Photo courtesy of Rosemarie Ramos)



In 1980, private investors purchased the Barr Mansion and restored the property, which is now listed in the National Register of Historical Places. (Photo courtesy of Rosemarie Ramos)

Science Notebook

Sixth Annual Science Awards Day Honors Achievements

By Eddy Ball

NIEHS Science Awards Day, held on the first Thursday of November each year, added a new category of award to the 2008 event to honor the year's outstanding staff scientist. Now in its sixth year, the annual day-long event rewarded the achievements of postdoctoral fellows in juried competition, recognized the cumulative achievements of early-career and senior investigators, and celebrated the spirit of scientific inquiry across the spectrum of Division of Intramural Research (DIR) laboratories and branches.

2008 awards included plaques for all the winners and \$1,000 travel grants for the outstanding postdoctoral investigators:

- **Scientist of the Year Award** – Michael Resnick, Ph.D., Chromosome Stability Group principal investigator, speaking on “Endgame: DNA Breaks and Genome Stability”
- **Early Career Award** – Michael Fessler, M.D., Host Defense Group Response principal investigator, speaking on “Back to the Past: New Paradigms for Host Defense in Host Cholesterol and Membrane Homeostasis”
- **Outstanding Staff Scientist Award** – Freya Kamel, Ph.D., Chronic Disease Epidemiology Group staff scientist, speaking on “Environmental Neurotoxicants and ALS [amyotrophic lateral sclerosis]: Incidence and Progression”
- **Mentor of the Year** – Ronald Mason, Ph.D., Free Radical Metabolism Group principal investigator
- **Best Poster Presentation in Environmental Biology** – Stephanie Nick McElhinny, Ph.D., DNA Replication Fidelity Group, for Ribonucleotide misincorporation by eukaryotic replicative polymerases



Resnick, second from the right, was a winner in two ways — as Scientist of the Year and as mentor and co-author for former postdoctoral fellow Francesca Storici, Ph.D., second from the left, lead author on the Paper of the Year. Abramowitz, left, and Blackshear, right, joined the winners. (Photo courtesy of Steve McCaw)



Gilchrist, above, was one of six speakers vying for Best Oral Presentation. (Photo courtesy of Steve McCaw)



Fessler explained that his award-winning research “challenges the canonical view of apolipoprotein A-1” by demonstrating that it induces proinflammatory signals in macrophages. (Photo courtesy of Steve McCaw)

- **Best Poster Presentation in Environmental Diseases and Medicine** – Päivi Salo, Ph.D., Environmental Cardiopulmonary Diseases Group, for Exposure to dog (Can f 1) and cat (Fel d 1) allergens in U.S. homes and current asthma

- **Best Poster Presentation in Environmental Toxicology** – Marcelo Bonini, Ph.D., Free Radical Metabolism Group, for MnSOD (SOD2) peroxidase activity, a novel mitochondrial redox sensor, linking oxidative stress and energetic metabolism

- **Best Oral Presentation** – Daniel Gilchrist, Ph.D., Transcriptional Responses to the Environment Group, for Pol II stalling can enhance gene expression by blocking promoter-proximal nucleosome assembly

- **Paper of the Year** – Laboratory of Molecular Genetics: Former Postdoctoral Fellow Francesca Storici, Ph.D., Staff Scientist Katarzyna Bebenek, Ph.D., Principal Investigator Thomas Kunkel, Ph.D., Staff Scientist Dmitry Gordenin, Ph.D., and Principal Investigator Michael Resnick, Ph.D. 2007. RNA-templated DNA repair. *Nature* 447: 338-341.

This year's event, like its predecessors, was sponsored by the NIEHS Office of the Scientific Director and moderated by Special Assistant to the Scientific Director Joel Abramowitz, Ph.D. Judges included members of the NIEHS Board of Scientific Counselors and investigators from the NIEHS Extramural and Intramural scientific communities.

The full-day event featured a morning session of oral presentations by fellows, students and technicians, midday poster sessions showcasing 68 abstracts by postdoctoral fellows and an afternoon session of talks by award-winning career investigators. Afterwards, Abramowitz and Acting Scientific Director Perry Blackshear, M.D., D.Phil., presented awards to winners in the several categories. The Mentor of the Year, chosen by the NIEHS Trainees Assembly (NTA), was also recognized.

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Kamel smiled as she answered questions about her ongoing quest to understand the disease that killed baseball great Lou Gehrig. (Photo courtesy of Steve McCaw)



Mentor of the Year Mason, center, poses with Abramowitz, left, and Visiting Fellow and NTA Steering Committee member Rajendrakumar Gosavi, Ph.D. (Photo courtesy of Steve McCaw)



Posters by NIEHS trainees snaked through the hallways of the Rall Building — giving trainees and investigators an opportunity to network with their colleagues from other labs and branches. (Photo courtesy of Steve McCaw)

NIA Director Visits RTP to Address Students

By Eddy Ball

National Institute on Aging (NIA) Director Richard Hodes, M.D., was the keynote speaker at the 2008 Symposium on the Biology of Aging initiated by the American Foundation for Aging Research (AFAR) and the North Carolina GlaxoSmithKline Foundation. The symposium was held November 8 at the North Carolina Biotechnology Center in Research Triangle Park.

Hodes' talk on "Challenges and Opportunities in Aging Research" concluded a full-day agenda of platform and poster presentations by AFAR awardees from universities throughout the US.

The symposium enjoys generous support from the North Carolina GlaxoSmithKline Foundation, as well as from NIEHS, the North Carolina Biotechnology Center and Whole Foods of Raleigh. Contributions from these and other supporters and individuals contributing through the Combined Federal Campaign have allowed AFAR to distribute hundreds of thousands of dollars in fellowships over the last thirty years to the next generation of researchers studying aging and age-related health problems.

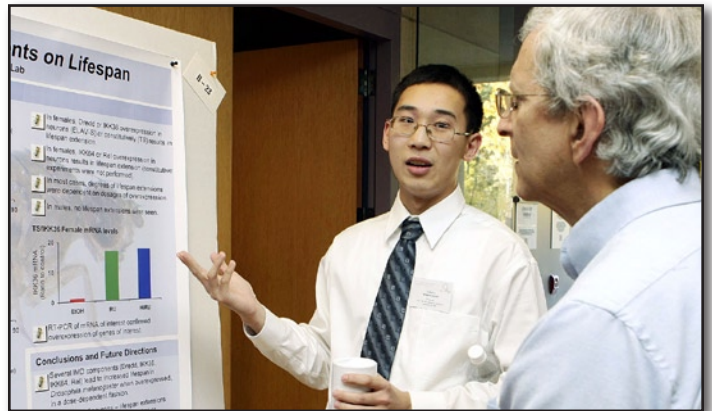
Beginning with an overview of the demography of aging as a framework for the challenges facing scientists and practitioners, Hodes pointed to "a very steep increase of people over 65, particularly those 85 or older." For what is certainly the first time in history, he continued, "somewhere around the middle of the next decade, there are going to be more older adults than there are young [under five years old] kids."

Commenting on "the nearly unbelievable demographic trends" and the "concern on the part of many" about the impact of increased longevity on quality of life (QOL), Hodes nevertheless found some reason for optimism in data on long-term care. Studies comparing the estimated increase in disability among older people, based on trends in 1982, have shown a surprising decline in the rate of disability, which is down from a projected 10 million to 7.5 million people currently.

Hodes observed that "the challenge that this creates, of course, is to understand just what are some of the factors



Toward the end of his talk, Hodes mentioned two NIA grants geared toward encouraging young investigators to enter the field of aging research — the Promoting Careers in Aging and Health Disparities Research awards and the Paul B. Beeson Career Development Awards in Aging. (Photo courtesy of Steve McCaw)



Hodes, in profile right, spoke with student Daniel Lu of the Helfand Lab at Brown University about his research on the lifespan of fruit flies. (Photo courtesy of Steve McCaw)



The symposium's poster session spread through the Glaxo Galleria of the North Carolina Biotechnology Center. (Photo courtesy of Steve McCaw)

that caused this [decline]” and to maintain this trend in the face of rising rates of obesity and diabetes. He turned to examples of significant recent epidemiological and biochemical investigations in the field. These include a large-scale study that demonstrated the efficacy of lifestyle changes, as compared to preventive medications, in preventing diabetes — even among the oldest groups enrolled — and studies of the relationships of caloric restriction, social interaction, the compound resveratrol, which is found in wines and berries, and familial determinants to QOL and longevity.

When Hodes, who maintains an active research program in the areas of cellular and molecular immunology and the biology of telomerase, turned to preliminary studies and speculation about ways to manipulate the “mitotic clock” that regulates the body’s progress to cellular senescence, the students were ready with questions. These ranged from queries about the development of epigenetic mapping for understanding how cancer genes are controlled to efforts to manipulate the expression of telomerase — the enzyme that determines the replicative capacity of cells — to prolong healthy cell viability and control cancer cell proliferation.

Hodes concluded his talk with a sobering reflection on current trends in NIH funding that have resulted in a marked decline in real dollars since the end of steady funding increases in 2003. Asserting that “you are the group that we’re all most interested in supporting,” he reinforced the commitment of NIH to supporting young investigators to the greatest extent possible with diminishing resources. He also expressed his hope that a growing older population will press for increased support of research that affects them so directly.

Founded in 1979, [AFAR](#) is recognized by the IRS as a national charity and describes itself as “the only organization supporting education and research in aging through fellowships to graduate and undergraduate students.” It has been awarded the Independent Charities Seal of Excellence for its exceptional standards of public accountability, program effectiveness and cost effectiveness.

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AFAR Founder and President Paul Agris, Ph.D., center, is an advisor and mentor to the students, who typically spend several years as AFAR fellows. He is a professor of Molecular and Structural Biochemistry at North Carolina State University. (Photo courtesy of Steve McCaw)



AFAR Program Assistant and Development Officer Mary Beth Hollman, right, talked with student Catherine Choi during the second poster session. Choi is investigating the pathogenesis of Parkinson’s disease as part of her studies at the Institute for Cell Engineering at Johns Hopkins University School of Medicine. (Photo courtesy of Steve McCaw)



The students spent most of their time engaged in their science, but they also had an opportunity to enjoy the autumn beauty of the grounds surrounding the North Carolina Biotechnology Center. (Photo courtesy of Steve McCaw)

Fibroids and the Black Women’s Health Study

By Robin Arnette

Lauren A. Wise, Sc.D., an Assistant Professor of Epidemiology at the Boston University School of Public Health, visited NIEHS recently to talk about her work on uterine leiomyomata, also known as “fibroids.” Wise presented “Risk Factors for Uterine Leiomyomata in the Black Women’s Health Study” during the Epidemiology Branch seminar held on November 3. The talk took place in Rodbell Auditorium and was hosted by Mitch Eddy, Ph.D., a senior investigator in the Laboratory of Reproductive and Developmental Toxicology.

Wise said that fibroids were benign tumors that arose from smooth muscle cells of the uterus in women. She explained that many fibroids were asymptomatic and didn’t cause major morbidity, but they could be a huge problem for some women. Symptoms included menorrhagia or heavy menstrual bleeding, pelvic pressure, pain, infertility, reproductive dysfunction and complications in labor and delivery.

Wise also revealed the toll that fibroids exact on the nation’s healthcare system. “Fibroids are the fifth leading cause of hospitalization for nonpregnancy-related conditions in reproductive-aged women and the leading cause of hysterectomy,” she said. “This means they account for high healthcare costs — over \$2.1 billion each year in the U.S.”

Wise’s interest in studying these tumors began during her days as a doctoral student at Harvard when she analyzed data from the Black Women’s Health Study (BWHS) for her dissertation. Conducted by investigators from Boston University and Howard University, the study examined why black women tend to be disproportionately affected by certain illnesses, including breast cancer, diabetes, and fibroids.

“Black women have two to three times the incidence of fibroids compared to white women,” Wise said. “This has been documented not only in the Nurses’ Health Study II, an ongoing U.S. prospective cohort



Guest lecturer Lauren Wise reported on an epidemiological study that has significant health disparities implications. (Photo courtesy of Steve McCaw)



Lecture host Mitch Eddy listened as Wise responded to questions about the study’s findings in relation to smoking status. (Photo courtesy of Steve McCaw)



The meeting drew several members of the NIEHS Epidemiology Branch, such as Principal Investigator Donna Baird, Ph.D., center, who has also conducted research on uterine leiomyomata in black and white women. (Photo courtesy of Steve McCaw)

study, but also by a study by [Donna D. Baird, Ph.D.](#) Black women have an earlier age of diagnosis and hysterectomy, and they have larger and more numerous tumors at the time of diagnosis.”

The BWHS started in 1995 and is a prospective cohort study of 59,000 black women aged 21–69 at baseline. The team enrolled participants through mailed questionnaires sent to subscribers of Essence Magazine and members of black professional health organizations. The questionnaires posed a series of questions dealing with demographics, lifestyle, anthropometric factors, reproductive and medical history, and diet. The team relied on self-reported diagnoses of fibroids confirmed by ultrasound, a noninvasive screening procedure with high sensitivity and specificity relative to histologic evidence. The data were updated every two years, and the cohort retention rate was approximately 80 percent.

Wise and her colleagues found an inverse association between age of menarche (i.e., first menstrual period) and fibroids. Women who started their periods at age 15 or older had a 30 percent decreased risk of developing fibroids compared with women who started menstruating at age 11 or younger. The team also found a 30 percent reduced risk of developing fibroids in women who have had children relative to women who had not given birth. Both findings may be explained by hormonal mechanisms, as fibroids are thought to be hormone-dependent tumors. “Women who have a later age at menarche or who have babies tend to have fewer menstrual cycles and, therefore, a reduced cumulative exposure to endogenous estrogens, which appear to promote fibroid growth,” she said.

The BWHS also examined whether alcohol and smoking were possible risk factors for fibroids. Although Wise and colleagues published data showing a weak positive association between alcohol consumption and fibroids, and a weak inverse association between smoking and fibroids, repeated analysis after 6 additional years of follow-up yielded a stronger association with pack years of smoking staving off fibroids. Wise added, “Of course we wouldn’t recommend that women start smoking to prevent fibroids, but it is an interesting finding from an etiologic point of view.”

Wise’s future research goals include examining environmental and early life exposures, diet, and genetics in relation to uterine fibroids.

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Global Warming and Insect Populations

By Eddy Ball

The Scientific Research Society, Sigma Xi, headquartered in Research Triangle Park, N.C., hosted a presentation on November 17 by North Carolina State University (NCSU) ecologist Rob Dunn, Ph.D., as part of a monthly lunchtime lecture series. The talk, titled “Global Warming and the Neglected Majority,” explored the impact of climate change on invertebrates — and ultimately humans — by focusing on ants, one of the best studied insect species.

Dunn is part of the NCSU Conservation Ecology Research Group, which uses integrated approaches to study diversity, rarity, extinction and conservation. Within the group, research interests include microcosms, large-scale experiments on corridors, studies of rarity and diversity at continental scales, and diverse modeling approaches. Dunn is the author of a new book, *Every Living Thing: Man’s Obsessive Quest to Catalog Life, from Nanobacteria to New Monkeys*.

“What I want to talk about today,” Dunn began, “is what we can project about the ecological aspects of the future.” What he also did was to turn the attention of his audience away from global warming icons, such as the polar bear and its Arctic habitat, to the temperate areas of the world where humans and their often unseen invertebrate neighbors coexist.

According to Dunn, these areas include the back yards of residents of central North Carolina where an average of 30 species of ants can be found. The back yard is also where people may encounter the three major invasive species of ants that “are doing better and better each year” in North Carolina, he added — the fire ant, the Argentine ant and the aggressive Asian needle ant (*Pachycondyla chinensis*), whose painful sting can trigger anaphylactic reactions in as many as one out of every 100 people it stings.

Dunn described the contributions of insects, some of them members of endangered species that could be threatened by global warming, as sources of pharmaceuticals, dispersers of seeds and pollen, and mediators of many, if not most, ecological processes. He added, however, that insects also make up the majority



Although the Asian needle ant, above, was probably not actually in the auditorium, it was mentioned several times during the talk and, according to Dunn, could likely be found somewhere on the grounds of Sigma Xi building. (Photo courtesy of Benoit Guenard)



“I think the big story of climate change has much more to do with small things,” Dunn explained, which in turn can impact human health and lifestyle. (Photo courtesy of Steve McCaw)



The audience included NIEHS employees, such as Postdoctoral Fellow Patrick Brandt, Ph.D., center; who works in the Molecular and Genetic Epidemiology Group. (Photo courtesy of Steve McCaw)

of pests, are capable of destroying crops and buildings, and can serve as disease vectors.

From what Dunn and other investigators have learned about the central importance of temperature to insect populations, global warming is likely to help at least some species of ants and other insects invade parts of the world where they are now less prevalent, such as higher elevations and, for fire ants, the interior of forests. Climate change is also likely to accelerate the dominance of invasive species — many of which, like the Asian needle ant, perform fewer ecologically beneficial activities and can pose a threat to human health and quality of life.

“It doesn’t take much,” Dunn asserted, “to go from a community [of insects] dominated by the processes we [humans] like to a community with a whole bunch of invasive species doing some pretty nasty things.”

Dunn concluded his talk by re-emphasizing how little scientists understand about the world of insects and the specifics of what a warmer world will be like for humans and the “neglected [insect] majority.” He noted that many of the tens of millions of insect species estimated to exist are still undiscovered. Even today, he observed, “You could still go out in Central Park and find a new species.”

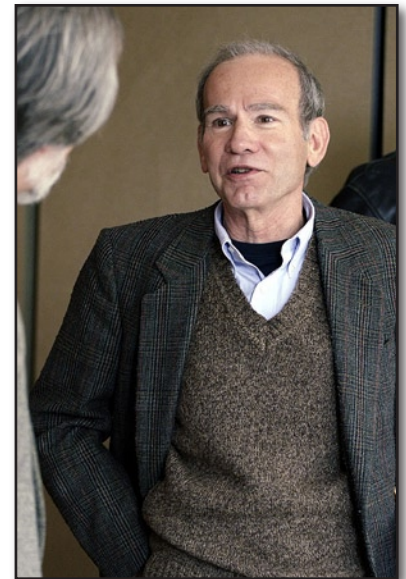
Because so much remains to be discovered about insects, human attempts to control them can easily backfire — just the way that the use of DDT ironically ended up accelerating the northwards spread of fire ants by ten or twenty years.

(Individuals interested in attending the Sigma Xi lunchtime lecture series should contact series organizer [Catherine Clabby](#), associate editor of American Scientist.)

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Lecture host Anna Lena Phillips, assistant book reviewer at American Scientist, talked with visitors following the lecture. (Photo courtesy of Steve McCaw)



Monte Basgall, senior science writer at Duke University, shared his thoughts about Dunn’s presentation following the talk. (Photo courtesy of Steve McCaw)



Burroughs Wellcome Fund communications officer Russ Campbell, right, and American Scientist senior writer and columnist Brian Hayes clearly appreciated Dunn’s humor and irony. (Photo courtesy of Steve McCaw)

NIEHS Investigator Advances Understanding of Heparin Biosynthesis

By Brian Chorley

NIEHS Structure and Function Research Group Leader [Lars Pedersen, Ph.D.](#), and colleagues at the University of North Carolina (UNC) Chapel Hill have succeeded in creating a group of recombinant enzymes that synthesize novel varieties of heparan sulfate with unique biological functions — offering potential for advancing future research and for developing new therapeutic applications. The [findings](#) of their research, which was funded in part by NIEHS, appeared online November 20 ahead of print on the *Proceedings of the National Academy of Sciences (PNAS)* web site.

Heparin is a naturally occurring molecule produced in many living organisms. The mechanisms governing heparin biosynthesis are highly conserved among species, lending credence to the idea that heparin and heparin-like molecules are critical for life.

In the medical world, heparin is primarily utilized as an anticoagulant. One of the oldest drugs still commonly used today, heparin is widely available, cheap to manufacture, and easy to store and administer.

In a natural context, heparin and heparin-like molecules participate in development, inflammatory response and normal physiology. In addition to heparin's use as an anticoagulant, many scientists believe that there is great therapeutic potential for heparin-like molecules. Current research has suggested its use for symptomatic treatment of asthma, cancer and inflammatory bowel syndrome, as well as other conditions.

Heparin, a highly sulfated form of heparan sulfate, is a linear polysaccharide. Its differential sulfation patterns determine both form and function. Much of today's commercially available heparin is a heterogeneous mixture of heparin moieties. The focus of current heparin research is to discover the specific therapeutic qualities, as well as deleterious side effects, of the various forms of the compound.

Synthesis is dependent on a number of specialized enzymes, including a group of sulfotransferases. In their report, Pedersen and colleagues dissected the enzymatic process of the heparan sulfate 2-O-sulfotransferase (2OST). 2OST is known to sulfate two specific moieties of the heparan sulfate chain. One variant is more common in nature than the other, and the biological role of the rare sulfated form is not well understood.

In the study, the researchers report finally solving the crystal structure of the catalytic portion of 2OST using a recently developed technique of structurally guided mutagenesis. "The structure of this enzyme was something we have been going after for a long time," Pedersen said.



Along with its own research, Pedersen's group develops three-dimensional structural characterization using molecular biology, biochemistry and X-ray crystallographic techniques for other NIEHS researchers. (Photo courtesy of Steve McCaw)

By comparing and contrasting known structures of other sulfotransferases, the researchers identified regions important for enzymatic activity, complex formation and substrate specificity. This information aided the team in developing a host of 2OST mutant enzymes. The mutants possess a range of activity levels and substrate specificities. One mutant form, to the delight of Pedersen and the research team, demonstrated almost complete propensity to manufacture the rare sulfated unit on the heparan sulfate polysaccharide chain.

Pedersen explained that there are likely potential benefits in producing homogenous preparations of heparin, such as those manufactured by recombinant biosynthetic enzymes. For example, a known side effect of general heparin treatment is a condition called thrombocytopenia, or a dangerously low platelet count.

Research with homogenous preparations of heparin may be able to identify variants which have reduced side effects yet retain anticoagulant properties. Additionally, some variants that do not function as an anticoagulant may prove to be most effective for other therapeutic uses. “You don’t necessarily want to give [heparin that functions as an] anticoagulant as cancer therapy,” Pedersen summarized.

In addition to Pedersen, members of the UNC Eshelman School of Pharmacy’s Division of Medicinal Chemistry and Natural Products participated in the research. The UNC team included principal investigator, Jian Liu, Ph.D, as well as co-authors Heather Bethea and Ding Xu. The research was funded by the American Heart Association, National Institutes of Health and the Division of Intramural Research at NIEHS.

Citation: [Bethea HN](#), [Xu D](#), [Liu J](#), [Pedersen LC](#). 2008. Redirecting the substrate specificity of heparan sulfate 2-O-sulfotransferase by structurally guided mutagenesis. *Proc Natl Acad Sci U S A*. Nov 20. [Epub ahead of print]

(Brian Chorley, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

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ADHD Medications Do Not Cause Genetic Damage in Children

By Robin Mackar

In contrast to recent findings, two of the most common medications used to treat attention deficit hyperactivity disorder (ADHD) do not appear to cause genetic damage in children who take them as prescribed, according to a new study by researchers at the National Institutes of Health (NIH) and Duke University Medical Center.

The [study](#) published online this month in the *Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP)* provides new evidence that therapeutic doses of stimulant medications, such as methylphenidate and amphetamine, do not cause cytogenetic (chromosomal) damage in humans. The researchers looked at three measures of cytogenetic damage in white blood cells of each child participating in the study and found no evidence of any changes after three months of continuous treatment.

“This is good news for parents,” said Kristine Witt, a genetic toxicologist at the NIEHS/National Toxicology Program (NTP) and co-author on the study, which was funded through the Best Pharmaceuticals for Children Act by NIEHS and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). “Our results indicate that methylphenidate- and amphetamine-based products do not induce cytogenetic damage in children.”

The researchers involved emphasize that the findings should not be interpreted as final proof of the long-term safety of stimulant drugs for the treatment of ADHD. “More research and close monitoring of children taking these medications for extended periods of time is needed to fully evaluate the physical and behavioral effects of prolonged treatment with stimulants,” noted Scott Kollins, Ph.D., co-author of the paper and director of the Duke ADHD Program, where the study was conducted.

ADHD is a disorder characterized by attention problems, impulsivity, and hyperactivity. About 3 to 5 percent of children in the United States have been diagnosed with the disorder, although several studies suggest 7 to 12 percent of children may be affected.

The current study included 63 children, ranging from 6–12 years of age, who met full criteria for ADHD but who had not previously been treated with stimulant medications. Children in the study were divided into two groups and treated by a board-certified child psychiatrist with either methylphenidate (commercially available as Ritalin LA and Concerta) or with mixed amphetamine salts (Adderall and Adderall XR). Blood samples were taken before the medication was started to establish baseline values for the cytogenetic measures that were analyzed in the study, and a second sample was collected after three months of continuous treatment. Forty-seven children completed the full three-month treatment schedule.



Along with Witt, above, NIEHS co-authors were NTP Director of the Center for the Evaluation of Risks to Human Reproduction Mike Shelby, Ph.D., and NIEHS Biostatistics Branch Staff Scientist Grace Kissling, Ph.D. (Photo courtesy of Steve McCaw)

The researchers found no significant differences between the two groups of children with regard to age, gender, race, body weight, height, or ADHD subtype. The groups also showed very similar ADHD symptom levels at initial screening and children in both groups responded equally well to the medication.

The study was designed to determine the reproducibility of findings from a previously published paper that reported methylphenidate-induced chromosomal changes in children with ADHD. The current study was not able to replicate the findings from the previous study. The new JAACAP paper extends the literature by using a larger sample size than previous studies, investigating more than one commonly prescribed medication and providing well-characterized results that can be generalized to other ADHD populations.

Citation: Witt KL, Shelby MD, Itchon-Ramos N, Faircloth M, Kissling GE, Chrisman AK, Ravi H, Murli H, Mattison DR, Kollins SH. 2008. Methylphenidate and amphetamine do not induce cytogenetic damage in lymphocytes of children with ADHD. J. Am. Acad. Child Adolesc. Psychiatry 47(12):DOI 1375Y1383.

(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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Upcoming Distinguished Lecture by Gary L. Johnson

By Eddy Ball

The 2008 – 2009 NIEHS Distinguished Lecture Series will feature a talk December 9 by Professor and Chair of the University of North Carolina Department of Pharmacology Gary L. Johnson, Ph.D. Johnson will discuss the topic of “Defining MAP3 Kinase Regulated Signaling Networks: From Metastasis to Tissue Stem Cells” at 11:00 in Rodbell Auditorium.

Johnson’s laboratory defines the “signal relay” systems initiated by various cellular stimuli including cytokines, growth factors, antigens and drugs used to treat human disease. The unifying hypothesis directing the lab’s work is that the differential expression and spatial organization of signal relay proteins control the responsiveness of different cell types to specific stimuli.

According to Johnson, aberrant spatial and temporal control of signal relay systems is a major contributing factor to human diseases including cancer, cardiovascular disease and autoimmunity. The primary signal relay systems studied in the lab involve the mitogen activated protein kinase (MAPK) pathways and how they regulate gene expression, cell growth, development and apoptosis.



*Distinguished Lecturer Gary Johnson
(Photo courtesy of Gary Johnson)*

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Extramural Update

Peer Review at NIH and NIEHS – A Thank You for NIEHS Reviewers

Changes are in the works for the way grant applications are reviewed at the National Institutes of Health (NIH), and they are scheduled to be phased in beginning in January 2009. While the NIH peer-review system has received much praise over the years, it had not been scrutinized for potential improvements that could enhance a process that has been in place for more than a decade. It had also become clear that the burden of review could put enormous pressures on reviewers, and NIH decided it was time to evaluate the process (see <http://enhancing-peer-review.nih.gov/>).



Staff of the NIEHS Scientific Review Branch, shown above, are left to right seated, Linda Bass, Ph.D., and Nesbitt. Standing, left to right, are Janice Allen, Ph.D., Rose Anne McGee, Sally Eckert-Tilotta, Ph.D., and Leroy Worth, Ph.D. (Photo courtesy of the Division of Extramural Research and Training)

As a result, a variety of changes to peer review at NIH will be piloted in coming months. These changes have come about from recommendations designed to reduce the burden on reviewers in the future. Two of the early pilots include shortening the length of applications and decreasing the number of amended applications allowed. The latter has been announced in the NIH Guide for Grants and Contracts: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-016.html>. There is enthusiasm among reviewers and administrators for shortening the summary statement by focusing the critique on the merit of the science presented and for improving the rating system to make it more useful to both the applicant and NIH staff.

Most importantly, NIH staff members recognize that the cornerstone of review quality is recruiting and retaining excellent reviewers. NIH has planned several pilot studies in an attempt to determine the most effective changes for reaching this goal.

NIEHS, the Division of Extramural Research and Training (DERT), and Scientific Review Branch staff want to extend sincere thanks to the hundreds of people who have taken the time and made extraordinary efforts to serve as reviewers in the many peer-review meetings for the Institute. Reviewers' written critiques and oral comments have led to scoring and budgetary recommendations that are critical in achieving the goal of funding the most meritorious science. Indeed, without their sacrifices to this end, staff could not do the day-to-day business of supporting the environmental sciences and the investigators who do the work.

For more information, contact:
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Extramural Papers of the Month

By Jerry Phelps

Parkinson's Disease Linked to Vitamin D Deficiency

Fifty–five percent of Parkinson's disease (PD) patients are insufficient in vitamin D, according to new research findings from an NIEHS-supported study at the Emory University School of Medicine. The number of Parkinson's patients with vitamin D deficiency was higher than either healthy elderly people in the control group or Alzheimer's disease patients. This finding adds to the evidence that low vitamin D levels are associated with Parkinson's disease.

Most Americans get sufficient amounts of vitamin D through exposure to sunlight or by dietary supplements. However, the body's ability to produce vitamin D in response to sun exposure decreases with age making elderly people more at risk for vitamin D deficiency.

Currently it is unclear whether there is a cause and effect relationship between vitamin D and Parkinson's. The connection could be partly related to the decreased mobility of Parkinson's patients, which may result in less sun exposure, or there could be a direct link between vitamin D insufficiency and the onset or progression of the disease.

Previous studies have shown that the region of the brain, the substantia nigra, which produces dopamine and is most affected by Parkinson's disease, has high levels of vitamin D receptors — suggesting that vitamin D may be important for the normal function of these cells. Emory doctors are conducting additional research to investigate whether vitamin D insufficiency is a cause or a result of having Parkinson's.

Citation: Evatt ML, DeLong MR, Khazai N, Rosen A, Triche S, Tangpricha V. 2008. Prevalence of vitamin D insufficiency in patients with Parkinson disease and Alzheimer disease. Arch Neurol 65(10):1348-1352.

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Nanoparticles Kill Blood Vessel Cells in the Human Brain

A study funded in part by the Superfund Basic Research Program at NIEHS shows that nanoparticles of aluminum oxide can adversely affect and even kill specialized endothelial cells that line blood vessels in the human brain.

The researchers designed this study to determine the effects of nanoscale particles of aluminum oxide on the human blood-brain barrier. In cell culture systems, endothelial cells that line the interior of blood vessels in the brain were treated with nano-alumina, normal sized alumina particles, carbon nanoparticles or normal sized carbon particles. After exposure, the researchers assessed cell structure, cell death, mitochondrial effects and tight junction proteins. Laboratory rats were given intravenous doses of nano-alumina.

In 2005, aluminum oxide nanoparticles accounted for 20 percent of the world production of nanoparticles. The particles are used in a variety of applications in the ceramics, electrical, engineering, and biomedical fields. Increases in the production and expansion of the uses of these particles will inevitably lead to greater human exposure.

According to the researchers, the nanoscale alumina and carbon particles were much more toxic than their respective compounds of normal particle size. Nano-alumina significantly increase cellular oxidative stress and disrupted the expression of tight junction proteins. The whole animal experiments confirmed the protein alteration with a loss of critical proteins in the cerebral blood vessels.

Citation: [Chen L, Yokel RA, Hennig B, Toborek M](#). 2008. Manufactured aluminum oxide nanoparticles decrease expression of tight junction proteins in brain vasculature. *J Neuroimmune Pharmacol* 3(4):286-295.

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Cytosine-DNA Methyltransferase Mediates Carcinogen-Induced Gene Promoter Methylation

NIEHS-supported researchers studying the basic cellular and molecular events that occur after exposure to carcinogens report differences in DNA repair capacity in bronchial epithelial cell lines after low-dose treatment with methylnitrosourea and benzo(a)pyrene-diolepoxide. They also found that levels of cytosine-DNA methyltransferase 1 (DNMT1) increased significantly during the carcinogen exposure and were linked to promoter-hypermethylation of several genes in each transformed cell line. These findings may have implications for preventing lung cancer in smokers.

When the researchers employed strategies to reduce the production of the DNMT1 protein, cell transformation and gene silencing were reversed. Reduced DNMT1 production prior to carcinogen exposure prevented transformation and gene methylation.

These studies and findings describe a mechanistic link between increased DNMT1, methylation of tumor suppressor genes and reduced DNA repair capacity that together appear to cause cancer-like changes in lung epithelial cells. The study also provides evidence for the use of demethylation strategies to prevent lung cancer in smokers.

Citation: [Damiani LA, Yingling CM, Leng S, Romo PE, Nakamura J, Belinsky SA](#). 2008. Carcinogen-induced gene promoter hypermethylation is mediated by DNMT1 and causal for transformation of immortalized bronchial epithelial cells. *Cancer Res* 68(21):9005-9014.

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Gas Stove Emissions Worsen Asthma Symptoms

Johns Hopkins scientists supported by NIEHS report that high levels of nitrogen dioxide gas from cooking and heating stoves in indoor environments aggravate asthma symptoms in inner-city children — especially preschool-aged children. Nitrogen dioxide gas is most prevalent in industrial settings, but it is also found at high levels in many poor, inner-city homes that have unvented gas stoves.

The research team compared the nitrogen dioxide levels in the homes of 150 inner-city Baltimore children aged 2-6 to the frequency and intensity of coughing, wheezing, shortness of breath and chest tightness. Each 20-point increase in nitrogen dioxide levels led to 10 percent more days of coughing and 15 percent more days of limited speech due to wheezing. Eighty-three percent of the homes had gas cooking stoves and 72 percent were heated with natural gas. Forty-two percent of the households had annual incomes less than \$25,000.

Asthma is the most common pediatric chronic disease affecting 6.2 million children in the United States alone. 28

It is widely known that severe asthma is most prevalent in the inner-city environment. The authors conclude that physicians caring for children with asthma should ask about their home's heating and cooking appliances and recommend using alternatives if possible — or at least encourage the parents to have the stoves properly vented.

Citation: Hansel NN, Breyse PN, McCormack MC, Matsui EC, Curtin-Brosnan J, Williams DL, Moore JL, Cuhran JL, Diette GB. 2008. A longitudinal study of indoor nitrogen dioxide levels and respiratory symptoms in inner-city children with asthma. *Environ Health Perspect* 116(10):1428-1432.

(Jerry Phelps is a program analyst in the Program Analysis Branch of 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

Crystal Structure of RACK1 in *Arabidopsis thaliana*

Researchers at NIEHS and Howard University have crystallized an isoform of the activated C-kinase 1 (RACK1) protein from the plant *Arabidopsis thaliana*. The crystal structure of RACK1, a scaffolding protein implicated in signaling pathways, revealed that the protein contained highly conserved surface residues that could be involved in vital protein-protein interactions. These data provide a future framework for studying RACK1's role in cellular stress, protein translation and developmental processes in both plants and animals.

Work from other labs determined that RACK1 was a member of the WD40 repeat family of β -propeller proteins, and early biochemical efforts used the β subunit of mammalian G proteins (G_{β}) as a model. However, the model lacked precise structural detail with regard to diverse loop regions and surface side chain conformations that make RACK1 and G_{β} functionally distinct. As mammal and plant forms of RACK1 have failed to crystallize on their own, the NIEHS team fused the c-terminal of a mutant maltose binding protein (MBP) — specifically designed to improve the chances of crystallization — to the n-terminus of the *A. thaliana* isoform RACK1A and solved the structure at 2.4 Å.

RACK1A is a canonical seven-bladed β -propeller with each propeller blade consisting of a four-stranded antiparallel β -sheet. The blades are arranged around an axis that creates a water accessible channel in the middle of the propeller. Earlier mutational studies have implicated blades 5 and 6 as important docking stations for a host of signaling proteins.

Citation: Ullah H, Scappini EL, Moon AF, Williams LV, Armstrong DL, Pedersen LC. 2008. Structure of a signal transduction regulator, RACK1, from *Arabidopsis thaliana*. *Protein Sci* 17(10):1771-1780.

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SNPs in Human Ion Channel Genes Increase Susceptibility to Disease by Creating New Phosphorylation Sites in the Channel Proteins

NIEHS scientists have determined that a common single nucleotide polymorphism (SNP) in a cardiac potassium channel gene, hERG1, creates a phosphorylation site within the human Kv11.1 channel protein that inhibits channel activity. Kv11.1 channels are necessary for rhythmic excitability of cardiac muscle and endocrine cells, and they are regulated by hormonal signaling through the phosphatidylinositol 3-kinase (PI3K), which normally increases channel activity by stimulating a protein phosphatase, PP5, which dephosphorylates the channel protein.

However, in human channels with the K897T polymorphism, in which a single nucleotide change alters the translation of codon 897 from a lysine to a threonine, hormonal signaling through PI3K has the opposite effect on phosphorylation of the channel and on its activity. With a threonine (Thr) instead of a lysine at residue 897, hormonal signaling through PI3K leads to channel phosphorylation on Thr 897 by the Akt protein kinase, and to inhibition of channel activity. Human cardiac myocytes with less Kv11.1 channel activity have longer action potentials, as indicated by longer QT intervals in the electrocardiogram, and an increased risk of developing an arrhythmia, which can be fatal.

The finding suggests that human genetic differences can alter susceptibility to disease by changing phosphorylation sites in proteins and altering their regulation, a phenomenon the authors have named “phosphorylopathy.” The paper also reports the results of a bioinformatics search for other SNPs in human ion channel genes that are known to be associated with disease. The authors identify 15 other SNPs in nine genes that are predicted to create or destroy putative phosphorylation sites. They are currently investigating these genes in collaboration with clinical investigators at NIEHS.

Citation: [Gentile S, Martin N, Scappini E, Williams J, Erxleben C, Armstrong DL](#). 2008. The human ERG1 channel polymorphism, K897T, creates a phosphorylation site that inhibits channel activity. *Proc Natl Acad Sci USA* 105(38):14704-14708.

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Cumene Exposure Leads to *K-ras* and *p53* Mutations That Are Linked to Lung Tumors in Mice

B6C3F1 mice treated with the solvent cumene had significantly greater incidences of alveolar/bronchiolar adenomas and carcinomas than control mice according to a team of researchers from NIEHS. The team evaluated the cause of these lung neoplasms and determined that the mutations occurred in the *K-ras* oncogene and *p53* tumor suppressor gene, the same genes that are often mutated in human lung cancer.

Cumene, also known as isopropylbenzene, is a component of crude oil and is mainly used to produce acetone and phenol. Humans are probably exposed to the chemical by breathing air-borne cumene molecules during petroleum refining or the combustion of petroleum products. Using PCR-amplified DNA isolated from paraffin-embedded neoplasms, the researchers detected *K-ras* mutations in 87 percent of cumene-induced lung neoplasms. The most common mutations were exon 1 codon 12 G to T transversions and exon 2 codon 61 A to G transitions.

p53 protein expression was detected by immunohistochemistry in 56 percent of cumene-induced lung neoplasms, and mutations were detected in 52 percent of lung neoplasms. In addition, cumene-induced lung carcinomas exhibited loss of heterozygosity (LOH) on chromosome four and six, while no LOH occurred in spontaneous carcinomas or normal lung tissue.

The *K-ras* and *p53* pattern of mutations suggested that DNA damage and genomic instability contribute to the development of lung cancer in mice that may be of relevance to humans.

Citation: [Hong HH, Ton TV, Kim Y, Wakamatsu N, Clayton NP, Chan PC, Sills RC, Lahousse SA. 2008. Genetic alteration in *K-ras* and *p53* cancer genes in lung neoplasms from B6C3F1 mice exposed to cumene. Toxicol Pathol 36\(5\):720-726.](#)

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Inducible Nitric Oxide Synthase Is Involved With Streptozotocin-induced Diabetes

Recent studies from researchers at NIEHS and the Universidad de la Republica in Uruguay indicate that inducible nitric oxide synthase (iNOS) is a significant source of the free radical intermediates that are formed in streptozotocin (STZ)-induced diabetic rats. The finding sheds new light on the mechanisms involved in diabetes.

Diabetes mellitus leads to a myriad of medical complications in humans, with cardiovascular disease and atherosclerosis being significant causes of death. Earlier published reports, using STZ-induced diabetic rats as a model, suggested that oxidative stress and free radicals are contributing to diabetes and its complications through various mechanisms. To determine the source of the free radicals, the research team employed electron paramagnetic resonance (EPR) spectroscopy, in vivo spin-trapping, isotope labeling experiments and immunological techniques.

The results indicated that iNOS was the main source of radical generation, and isotope labeling determined that the lipid-derived radicals detected by EPR spectra were induced by hydroxyl radicals. L-arginine pretreatment and 1400W, a specific iNOS inhibitor, reduced EPR signals to baseline levels, which indicated that peroxynitrite was the source of the hydroxyl radicals. Immunohistochemistry of the liver and kidney of the diabetic rats determined the correlation and co-localization between iNOS, nitrotyrosine and 4-hydroxynonenal as a lipid peroxidation end product in the tissues.

Citation: [Stadler K, Bonini MG, Dallas S, Jiang J, Radi R, Mason RP, Kadiiska MB. 2008. Involvement of inducible nitric oxide synthase in hydroxyl radical-mediated lipid peroxidation in streptozotocin-induced diabetes. Free Radic Biol Med 45\(6\):866-874.](#)

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Inside the Institute

Disability Awareness Program Showcases Campus Talent

By Eddy Ball

NIEHS concluded its observance of National Disability Employment Awareness Month (NDEAM) with an afternoon of events on October 28. The highlights included a book reading in Rodbell Auditorium by EPA Environmental Engineer and novelist Marc Yves Menetrez, Ph.D., and a reception in the NIEHS cafeteria following the reading. Both events were sponsored by the Diversity Council's Disability Advocacy Committee (DAC) and drew fans of homegrown talent from both sides of the lake.

As people entered Rodbell Auditorium, they were greeted with piano music by DAC member Jennie Foushee and a slide show produced by DAC Chair Alicia Moore highlighting famous people with disabilities. Following a welcome by DAC member Molly Vallant and an introduction by his long-time EPA associate and friend, NIEHS Deputy Associate Director for Management Chris Long, Menetrez spoke to the audience about his novel, *The Scent of Wildflowers*, and read excerpts from the story.

Like the protagonist of the story, Trey Barbette, Menetrez was injured in an accident that left him wheelchair bound and facing life on much different terms. In the saga that unfolds in Menetrez's story, Trey encounters and overcomes the deep despair of his loss as he works with his family and physical therapist, Raney Currin. The two help each other with their individual disabilities — in Raney's case a psychological trauma from her past — and fall in love.

Menetrez described writing his first novel as a “catharsis” and conceded that, like most first novels, “this one has autobiographical elements.” Asked about his experience as a prolific author of scientific articles writing a novel, Menetrez said that he felt liberated and “inebriated by the emotion” of creating a fictional



Long opened the program with a short biography of Menetrez and joked about the Canadian-born author's distinctive accent, which he acquired growing up in Brooklyn. (Photo courtesy of Steve McCaw)



Menetrez spoke and read from his seat at the front of the auditorium, creating a atmosphere of intimacy with his audience as he shared his — and his protagonist's — struggles with and triumph over extreme physical challenges. (Photo courtesy of Steve McCaw)



Zeldin, who was still reading the novel at the time of Menetrez's visit to NIEHS, also expressed his respect for the author's scientific publications. “I've cited his work in my own research,” Zeldin explained. (Photo courtesy of Steve McCaw)

world — a marked contrast to his feelings when he writes about his research on radioactivity and biological contaminants.

The program concluded with remarks by NIEHS Acting Clinical Director Darryl Zeldin, M.D. Zeldin described Menetrez as an embodiment of the theme of NDEAM —“America’s People... America’s Talent... America’s Strength” — and offered to help the author share his experiences as a recuperating patient with medical students at UNC and Duke, where Zeldin holds adjunct appointments.

Moore returned to the NDEAM theme as she gave Menetrez a special thanks for sharing his book. She also referred to theme as she served as mistress of ceremony during the reception program that followed. Moore introduced the musical entertainment, gave an inspirational reading of her own about living with a disability and welcomed EPA chemist Elin Ulrich, Ph.D., who talked enthusiastically about the rewards of her volunteer work as a walker for guide dogs in training, such as her companion, Lucky, a seven-month-old Golden Labrador Retriever.

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Burning the (Weekend) Twilight Oil

By Eddy Ball

Photographer Steve McCaw was on his way home from covering a meeting when he captured this image of NIEHS from across the campus lake on the evening of Saturday November 8. McCaw didn’t stop in to see just who was still at the benches and computers at a time when most people were making dinner plans or getting ready for a night on the town. Still, judging from the number of lights on, it’s probably safe to say that more than a handful of overachievers were still on the job.

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Alexander Drive Band trumpeter Mike Humble, left, and alto saxophonist Lisa Chadwick of NIEHS waited for their cue with tenor saxophonist Stan Malette, right — their instruments at the musicians’ equivalent of parade rest. (Photo courtesy of Steve McCaw)



Shown above, left to right, vocalists Jennie Foushee of NIEHS, Elin Ulrich of EPA, Nancy Powell and Alyson Scoltock of NIEHS, and Joyce Terry of EPA covered “What the World Needs Now” and other favorites. (Photo courtesy of Steve McCaw)



The evening light gives the Institute’s main building an other-worldly aspect as electric light from the building and the evening’s purple sky reflect in the still waters of the lake. (Photo courtesy of Steve McCaw)

Chinese Delegation Visits NIEHS

By Eddy Ball

On November 14, a contingent of Chinese government officials involved in a four-month executive education and English-language immersion program at Duke University attended a half-day workshop at NIEHS as part of their series of weekly field experiences. The program was organized by Public Affairs Specialist John Peterson and program chair and Deputy Scientific Director Bill Schrader, Ph.D.

NIEHS Acting Scientific Director Perry Blackshear, M.D., D.Phil., National Toxicology Program (NTP) Associate Director John Bucher, Ph.D., and Division of Extramural Research and Training (DERT) Acting Director Dennis Lang, Ph.D., presented overviews of the scientific activities and organizational structure of their respective areas during the first session of the workshop.

The Chinese delegates are involved in a broad range of government functions — science and technology, accounting and financial management, foreign affairs, and policy and legal affairs. Most of their questions during the first session focused on the structure of NIH and NIEHS, the Institute's role policy making, its funding mechanisms and its interactions with other government agencies and interest groups.

The second session of the workshop featured Chinese-born scientists working at NIEHS, who presented talks in their native Mandarin Chinese:

- *Environmental Health Perspectives (EHP)* International Program Manager and Editor Hui Hu, who discussed the journal's quarterly Chinese language edition, its student edition and science education resources, and its partnership with the Shanghai Municipal Center for Disease Control and Prevention
- Epidemiology Branch Tenure-track Investigator Honglei Chen, M.D., Ph.D., who reviewed his research into the genetic and environmental causes of Parkinson's disease, as well as his upcoming Shanghai Parkinson's Study, which will investigate environmental, genetic and biomarker risk factors in Chinese women



Xiaoling Li, right, shares a joke with Meng (Max) Shuchu following her presentation, which marked the end of the program. Shuchu, who works in the General Office of the Central Committee of the Chinese Communist Party, was head monitor of the delegation. (Photo courtesy of Steve McCaw)



Event organizer Peterson, center, talked with epidemiologist Chen prior to the meeting. Deputy General Director Wang (Sam) Chenghuan, Hainan Provincial Office of the State Administration of Industry and Commerce, waited in the background. (Photo courtesy of Steve McCaw)



As the meeting's chair and facilitator, Schrader made the visitors comfortable, introduced the speakers and kept the event on schedule. (Photo courtesy of Steve McCaw)

- Biostatistics Branch Principal Investigator Leping Li, Ph.D., who uses computer-based analytical models and methods to detect and discover functional elements in the promoter regions of genes involved in transcription
- Laboratory of Signal Transduction Principal Investigator Xiaoling Li, Ph.D., who studies the interaction of genes and environment in the progress of aging by focusing on the genetic pathways that play regulatory roles in this process

Following the talks and a tour of the investigators' lab facilities, the delegation rejoined Program Assistants Jessica Sapaugh and Derek DeLong for the trip back to the [Duke Center for International Development](#), where they will pursue their intensive studies through mid-December.



Lang's account of DERT partnerships with universities and institutes appealed to the audience of party officials and civil servants. (Photo courtesy of Steve McCaw)



Bucher discussed the organizational structure of NTP and its role in providing regulatory agencies with solid scientific evidence for their regulatory decisions. (Photo courtesy of Steve McCaw)



When Hu, the first of the scientists on the schedule, began her presentation in Mandarin, the audience began to feel more confident about participating with questions and comments. (Photo courtesy of Steve McCaw)



By the time Chen took to the podium, the audience was relaxed and ready to appreciate his humor — as well as the seriousness of his research into neurodegenerative diseases. (Photo courtesy of Steve McCaw)



Leping Li gestured to make a point about his bioinformatics-based estimations of transcriptional responses. (Photo courtesy of Steve McCaw)



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