



Environmental Factor

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January 2009

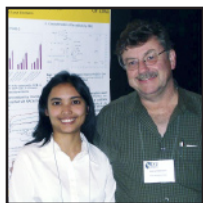
NIEHS Spotlight



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2008 ONES Awardees Speak at NIEHS

The 2008 winners of the Outstanding New Environmental Scientists (ONES) awards gathered in Rodbell Auditorium December 11

for their first group visit to NIEHS and presentations to Institute scientists. ...[read more](#)

Science Notebook



LMG Fellows Host Talk on Endogenous Mutagenesis

On December 8 in Rodbell Auditorium, the NIEHS Trainee Action Committee (TAC) of the Laboratory of Molecular Genetics (LMG) welcomed the most

recent researcher in its trainee-invited speaker series. ...[read more](#)



Folic Acid Supplements May Have Adverse Epigenetic Effects

A team of U.S. and Norwegian researchers, funded in part by NIEHS, report evidence of a possible

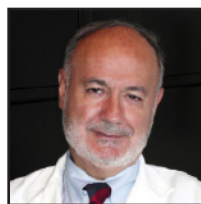
downside to the practice of maternal folic acid supplementation in the first trimester of pregnancy to reduce the risk of neural tube defects and other congenital malformations. ...[read more](#)



Yeast Model Used to Explore Genomic Hypermutation

A recent discovery by researchers at NIEHS sheds new light on the mechanisms of the unintentional changes in DNA that may lead to

cancer and genetic disease.[read more](#)



Upcoming Distinguished Lecture by Salvatore DiMauro

The 2008 – 2009 NIEHS Distinguished Lecture Series will welcome its next speaker, Salvatore DiMauro, M.D., at 11:00 a.m. January

13 in Rodbell Auditorium, when he explores the topic of “Mitochondrial Medicine.”[read more](#)

NIEHS Spotlight



Global Health Meeting Highlights International Partnerships

As part of the ongoing cooperative agreement between NIEHS and the World Health Organization (WHO),

the NIEHS Division of Extramural Research and Training (DERT) hosted a mini-symposium on global environmental health December 4 in Rodbell Auditorium ...[read more](#)



Study Examines Women's Household Exposure Experiences

A new report, funded in part by an NIEHS Environmental Justice grant, indicates that women are increasingly concerned

with the chemicals in their household environment — and that learning about their own “exposure experiences” can help to shape understanding of the common sources of chemical exposures[read more](#)



NIEHS Represented at EcoHealth Conference

The Yucatan Peninsula city of Merida served as the venue for the International EcoHealth Forum 2008 December 1-5 . Hosted by Mexico's

National Institute of Public Health and sponsored in part by NIEHS, the conference provided a forum for exchange of the latest information on ecological issues, including land use patterns, biodiversity loss, and conservation programs and their relationships to human health. ...[read more](#)



WE ACT Conference To Address Climate Justice

West Harlem Environmental Action, Inc. (WE ACT) for Environmental Justice, an NIEHS

grantee, is currently accepting registrations for its 20th Anniversary National Climate Justice Conference January 29 – 30 to be held at Fordham University School of Law in New York City.[read more](#)

Extramural Research

Extramural Update

The NIEHS Superfund Basic Research Program (SBRP) has announced that Laura Senier of Brown University is the recipient of the eleventh annual Karen Wetterhahn Memorial Award. The award was presented to Senier on December 9 at the SBRP Annual Meeting in Pacific Grove, California.

...[read more](#)

Extramural Papers of the Month

- [Microglial Cell Enzyme Involved in Neuronal Cell Death](#)
- [Discovery of Gene Variant for Cleft Lip](#)
- [Antioxidant Administration Reduces Lung Injury from Chlorine Exposure](#)
- [Consumption of Foods with High Soy Content is Associated with Lower Sperm Concentrations in Men](#)

Intramural Research

Intramural Papers of the Month

- [Damaged Single-Strand DNA Formed at Double-Strand Breaks and Uncapped Telomeres](#)
- [RhoX13 Is a Novel RhoX Gene in Rats and Mice](#)
- [The DSS1 Protein Requires the R3IM Motif for Proteasome Interaction](#)
- [The Nrf2 Pathway Protects Against RSV Disease in Rodents](#)

NIEHS Spotlight



Humane Society and Procter and Gamble Recognize NTP for Advancing Alternatives to Animal Testing

On December 18, the Humane Society of the United States (HSUS) and Procter and Gamble presented Ray Tice, Ph.D., of the National Toxicology Program (NTP) an award for the outstanding scientific contributions that he and others are making to advance viable alternatives to animal testing.[read more](#)

Inside the Institute



Director's Annual Honor Awards Ceremony

NIEHS honored employees at the 2008 Director's Annual Honor Awards Ceremony in Rodbell Auditorium on December 18. ...[read more](#)



Native American Heritage Features Lumbee Entrepreneur

The NIEHS Diversity Council welcomed vintner Darlene Gabbard as guest speaker at the NIEHS Native American Heritage Month celebration November 21 in Rodbell Auditorium. ...[read more](#)

Calendar of Upcoming Events

- **January 5**, in Rodbell Auditorium, 10:00–11:00 — Laboratory of Molecular Genetics Fellows Invited Guest Lecture with Susan Rosenberg, Ph.D., speaking on “Mutation as a Stress Response and the Regulation of Evolvability”
- **January 6**, in Rodbell A, 11:00–12:00 — David Banks, Ph.D., presenting a Biostatistics Branch seminar on “Statistical Issues in Metabolomics”
- **January 9**, in Rodbell Auditorium, 9:00–10:00 — Frontiers of Environmental Sciences Lecture Series featuring a seminar on “How Should we Respond to Uncertain Environmental Risks of Nanomaterials?” by Mark R. Wiesner, Ph.D.
- **January 13**, in Rodbell Auditorium, 11:00–12:00 — Distinguished Lecture Series presentation by Salvatore DiMauro, M.D., on “Mitochondrial Medicine”
- **January 16**, in Rodbell Auditorium, 11:00–12:00 — Laboratory of Reproductive and Developmental Toxicology Seminar Series featuring Lora Hedrick Ellenson, M.D., speaking on “The Molecular Genetics Of Endometrial Carcinoma: Of Mice And Women”
- **January 22**, in Rall D-350, 11:00–12:00 — Robert T. Truckner, M.D., speaking on “Human Environmental Exposure Research: Ethical And Safety Issues”
- **January 22**, in Rall F-193, 1:00–2:00 — Laboratory of Structural Biology Seminar Series presentation on “Ataxia-telangiectasia mutated (ATM)-mediated Cell Cycle Checkpoint in Response to Inhibition of Poly (ADP-ribose) Polymerase (PARP) Activity during Base Excision Repair” with Michael Carrozza, Ph.D.
- **January 29–30 (Offsite Event)**, at the Fordham University School of Law, New York City — Advancing Climate Justice: Transforming the Economy, Public Health and Our Environment
- **January 30**, in Rodbell Auditorium, 9:00–10:00 — Frontiers of Environmental Sciences Lecture Series, speaker and topic TBA
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Wilson and Yakel Honored as AAAS 2008 Fellows

By Eddy Ball

In December, the American Association for the Advancement of Science (AAAS) announced that two NIEHS scientists are among the 486 AAAS 2008 Fellows, an honor bestowed upon AAAS members by their peers. According to AAAS, NIEHS Acting Director Sam Wilson, M.D., and Principal Investigator Jerry Yakel, Ph.D., were awarded this honor in recognition of their “distinguished efforts to advance science or its applications.”

The AAAS 2008 Fellows will be presented with an official certificate and a gold and blue rosette pin, representing science and engineering, respectively, on February 14 at the AAAS Fellows Forum during the [2009 AAAS Annual Meeting](#) in Chicago. This year’s AAAS Fellows were announced in the AAAS News and Notes section of the journal *Science* on December 19.

Wilson was selected by the AAAS Section on Biological Sciences for his “seminal contribution to the understanding of structure-function relationships of the mammalian repair DNA polymerase, elucidation of its protective role against alkylating agents and for leadership in academia.” In addition to serving as [acting director](#), Wilson is the principal investigator in the Laboratory of Structural Biology and head of the [DNA Repair and Nucleic Acid Enzymology Group](#) in the Laboratory of Structural Biology.

Yakel was selected by the AAAS Section on Medical Sciences for his “distinguished contributions to neuroscience, particularly the role of nicotine receptors in brain function, and for his efforts in mentoring the next generation of biomedical scientists.” A member of the Laboratory of Neurobiology, Yakel is head of the [Ion Channel Physiology Group](#).

The tradition of AAAS Fellows began in 1874. Currently, members can be considered for the rank of Fellow if nominated by one of the steering groups of the Association’s 24 sections, by any three Fellows who are current AAAS members — so long as two of the three sponsors are not affiliated with the nominee’s institution — or by the AAAS chief executive officer.

Each steering group then reviews the nominations of individuals within its respective section and a final list is forwarded to the AAAS Council, which votes on the aggregate list.



Along with his considerable leadership responsibilities, AAAS Fellow Wilson, above, has maintained an aggressive research agenda. (Photo courtesy of Steve McCaw)



AAAS Fellow Jerry Yakel (Photo courtesy of Steve McCaw)

The Council is the policymaking body of the Association, chaired by the AAAS president and consisting of the members of the board of directors, the retiring section chairs, delegates from each electorate and each regional division, and two delegates from the National Association of Academies of Science.

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Superfund Comes of Age

By *Melissa Fabiano-Scheuer*

The NIEHS Superfund Basic Research and Training Program (SBRP) marked 21 years of research and training success at the Asilomar Conference Grounds in Pacific Grove, Calif. December 7–9. This year’s meeting, “Innovative Science and Technology for Mitigating Human, Ecological and Environmental Risks,” was hosted by the University of California, Davis (UC Davis) and sponsored by the NIEHS.



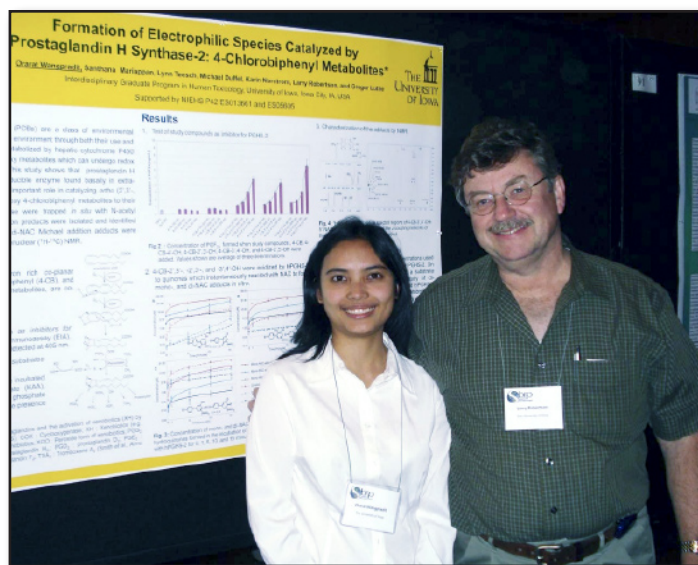
The meeting convened Sunday evening with the first of two poster sessions. Poster participants included postdocs, researchers and students, with the latter group participating in the annual student poster competition. All posters presented corresponded to Monday’s agenda highlighting SBRP analytical/bioanalytical research and improvements and advancements related to environmental contaminants that comprise the listed Superfund chemicals.

Each of the morning sessions opened with a keynote presentation. On Monday, Arlene Blum, Ph.D., a biophysical chemist and visiting scholar with the Department of Chemistry, University of California, Berkeley (UC Berkeley), discussed “The Fire Retardant Dilemma: Balancing Fire Safety, Human Health and Environmental Protection.” She emphasized the importance of looking at science from past and present perspectives. Blum argued that once individuals take that holistic perspective, they will then have the ability to make more informed decisions about the future.

Blum’s presentation underscored the conference’s central theme — without the knowledge of past scientific research and policy, the reinstatement of dangerous chemicals can endanger the global future. Blum brought this point home as she emphatically stated, “Toxic chemicals could be as threatening to our world as climate change.”

Tuesday morning’s keynote speaker, sociologist Martin Kenney, Ph.D., professor of Human and Community Development, UC Davis, explored the topic, “Is the Mandatory Invention Ownership University TLO [Technology Licensing Organization] the Best Method of University Technology Transfer?”

In his talk, Kenney argued that the United States should reconsider its current position with regard to the ownership of intellectual property derived from publicly-funded research. He highlighted the



Orarat Wangpradit and Larry W. Robertson, Ph.D., M.P.H., principal investigator from the University of Iowa, pose in front of Wangpradit’s research poster. (Photo courtesy of Bernhard Hennig, Ph.D., Director, UK Superfund Basic Research Program)

challenges of the Baye-Dole Act of 1980, advocating that a university-based inventor should own and develop his or her own intellectual property on an individual basis.

Kenney's keynote presentation was a session topic that was evidently on the minds of many conference participants — indeed, a complete session was dedicated to intellectual property and implications for the university, scientists and business. These talks stemmed from the second Green Technology Entrepreneurship Academy (GTEA), which took place this July ([see related story](#)). The session was followed by an interactive panel discussion led by

NIEHS SBRP Program Analyst Beth Anderson, which included panelists, entrepreneurs and scientists Raina Maier, Ph.D., Robert Hurt, Ph.D., Rolf Halden, Ph.D., and student 2008 GTEA attendee Collette Quinn.

The second evening poster session Monday evening gave attendees a taste of the next day's agenda. The focus remained on Superfund chemicals, with an emphasis on their effects on human and environmental health, risk exposure assessments and new applications related to real-world scenarios.

On Tuesday morning, NIEHS Acting Deputy Director William Suk, Ph.D., announced the selection of Laura Senier, a doctoral candidate in the Department of Sociology at Brown University, as the eleventh recipient of the Karen E. Wetterhahn Memorial Award ([see Extramural Update in this issue](#)).

Senier highlighted her contributions to Brown University's SBRP Community Outreach Core in her presentation, "Public Schools and Contaminated Land in Rhode Island: Using SBRP Research Translation and Community Outreach to Foster Research and Advocacy." This research focuses on the ways translation and outreach activities can engage community groups while supporting policy in public health and environmental justice.

Following Senier's presentation, Claudia Thompson, Ph.D., acting director of the NIEHS SBRP, presented the Student Poster Awards for outstanding presentations to Stephen Richardson of the University of North Carolina at Chapel Hill (UNC-CH), for Sunday's session, and Courtney Kozul of Dartmouth College, for Monday's session.

The meeting wrapped up with closing remarks by Michael Denison, Ph.D., of UC Davis. Denison noted that the meeting had advanced its mission, improving measurement tools for monitoring human and ecological exposure and biological/toxicological effects of Superfund chemicals, and that such advances will facilitate a future of more accurate risk assessment of Superfund chemicals in the present global environment.

(Melissa Fabiano-Scheuer is a communications specialist for MDB, Inc., a contractor for the NIEHS SBRP and the Worker Education and Training Program. She is a regular contributor to the *Environmental Factor*.)



Meeting attendees had the opportunity to enjoy beautiful sunsets such as this one in Pacific Grove, Calif. The beach was within walking distance of the Asilomar Conference Grounds. (Photo courtesy of Bernhard Hennig, Ph.D., Director, UK Superfund Basic Research Program)

SBRP Successes

The SBRP has had many successes during the past 21 years. Several of these accomplishments are listed below.

Kent Udell, Ph.D., University of California-Berkeley SBRP, developed the Steam Enhanced Extraction (SEE) technique for remediation of volatile hydrocarbons from soil. This SBRP-funded research generated a new national and international industry, and provided a technical basis for U.S. Environmental Protection Agency (EPA) policy on source removal for soil and groundwater cleanup.

Michael Denison, Ph.D., University of California-Davis SBRP, developed and validated a rapid and inexpensive recombinant cell bioassay system for the detection and relative quantification of dioxin-like chemicals. The XDS-CALUX[®] bioassay costs are 40 percent to 70 percent lower than the traditional High Resolution Gas Chromatography/Mass Spectrometry (HR GC/MS) method.

Michael Hooper, Ph.D., University of Washington SBRP, showed that wildlife biomonitoring provides a practical and sensitive means for determining whether the contaminants at hazardous waste sites find their way into the food chain at biologically significant levels. His work supported EPA remediation efforts in Colorado, South Carolina, Kentucky and Washington.

Lucio Costa, Ph.D. and Clement Furlong, Ph.D. University of Washington SBRP, discovered the importance of genetic variability in the human paraoxonase (PON1) gene in determining sensitivity to specific organophosphate exposures. This information provided regulators with data that was important in the EPA's negotiating removal of chlorpyrifos and diazinon from retail sales and home use.

Robert Hurt, Ph.D., Brown University SBRP, engineered prototype sorbent-containing packaging and disposal bags to capture mercury from broken compact fluorescent lamps and/or for use in recycling efforts. Brown University has applied for federal patents covering the mercury-absorption packaging and the absorbent material and plans to begin discussions with companies on manufacturing the new technology.

Josh Hamilton, Ph.D., Dartmouth College SBRP, was the first to report that arsenic is a potent endocrine disrupter and that endocrine disruption is one of the principal means by which arsenic is able to influence a wide array of disease risks, including various cancers, diabetes, cardiovascular disease and developmental problems.

Martyn Smith, Ph.D., University of California-Berkeley SBRP, used detection of genetic translocations in children with acute myeloid leukemia to provide unambiguous evidence of prenatal origin of the disease and suggest that exposures of the fetus before birth could be critical in producing childhood leukemia.

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NTP Unveils New Non-Cancer Study Criteria

By Eddy Ball

The National Toxicology Program (NTP) is trying to bring the same rigorous standards it uses for classifying the outcomes of its cancer studies to many of its non-cancer studies, according to presentations made by speakers at the NTP Board of Scientific Counselors (BSC) meeting November 20 in Rodbell Auditorium. The Board voted to accept three working group reports addressing the establishment of new criteria for future NTP immunotoxicology, reproductive and developmental studies.

The three sets of criteria were presented by BSC Criteria Working Group (CWG) chairs Nancy Kerkvliet, Ph.D., who chaired the immunotoxicology group, and Edward Carney, Ph.D., who chaired the reproductive and developmental groups. The criteria are similar to those used with the agency's gold-standard cancer studies, which are based on five levels of evidence ranging from clear evidence to no evidence and inadequate study.

Toxicology Branch Acting Chief and reproduction and development discipline leader [Paul Foster, Ph.D.](#), opened the discussion by explaining why NTP decided to establish the strength of evidence criteria. "We've had a goal now for the best part of 18 months to employ the same rigorous standards used historically to review our carcinogenicity bioassays with the NTP non-cancer studies," he said. He also noted that the NTP did not undertake this effort in isolation and emphasized the critical role the working groups played in helping establish the criteria for the various studies. The working groups, made up of representatives from government, industry and academia, met in late summer 2008.

"We have a desire to have uniform [non-cancer] criteria for chemicals across studies and for studies across chemicals, much as we have for the cancer bioassays," Foster continued, "so that the Board, the NTP staff and the public can have some kind of consistency in the ways these findings are reported."

Foster and Toxicology Branch immunology discipline leader [Dori Germolec, Ph.D.](#), expressed their confidence that the new criteria will give NTP non-cancer studies the same rigor, consistency and authority that NTP cancer reports have enjoyed for decades. The criteria, they maintained, will increase the utility of the non-cancer studies for regulatory agencies by clarifying the official government opinion of the hazards posed by chemicals.



Foster, center, set the stage for the Board's input when he conceded, "We understood that it wasn't going to be as straightforward as taking them [cancer study criteria] and dropping them into this [non-cancer] template and making them work." He is shown with NTP Deputy Program Director for Science Nigel Walker, Ph.D. (Photo courtesy of Steve McCaw)



Germolec, above, noted, "The NTP uses functional and quantitative measures of the immune response, so that we can evaluate the biological plausibility of the changes that we observe in our studies." (Photo courtesy of Steve McCaw)

Following presentations by the chairs of the three CWGs, Board members engaged in a lively discussion before giving NTP the go-ahead to progress to the next phase of finalizing the criteria. NTP scientists agreed to address Board concerns about terminology that might lead to misinterpretation by those not as familiar with toxicology.

In the course of the Board's discussion, Foster, Germolec and NTP Associate Director John Bucher, Ph.D., emphasized that the non-cancer studies will be clearly presented as hazard studies with multiple interrelated end points and not as risk assessments, which require exposure data not always available for non-cancer studies. The levels of evidence, they assured the Board, will be noted as applying under the conditions of the individual study in regard to specific sexes of specific species for the particular studies.

All CWGs proposed four levels of evidence: clear evidence, some evidence, equivocal evidence and no evidence. The reproductive and developmental toxicity CWG also included the category "inadequate study" for studies with qualitative or quantitative limitations that could not be interpreted for toxicity — a category that will also be incorporated into the final immunotoxicology criteria.

Timeline for Non-Cancer Criteria

According to Foster and Germolec, revisions to the levels of evidence statements for the three sets of criteria incorporating the Board's recommendations should be completed by the end of January 2009.

The proposed criteria are slated for formal presentation to attendees at the [Society for Toxicology \(SOT\) 48th Annual Meeting and ToxExpo](#) March 15 – 19 in Baltimore by Foster and Germolec.

Germolec expects to begin applying the immunotoxicology criteria to studies for peer review by the end of 2009. Foster said that the first reproductive and developmental studies featuring the new criteria could appear as early as 2010.



Kerkvliet, above, said her immunotoxicology CWG was gratified at the level of agreement that members reached independently when applying the proposed criteria to several earlier studies. (Photo courtesy of Steve McCaw)



*Carney, left, pondered the comments of Board members about his presentations of findings of the reproductive and developmental CWGs. To his left sat *ad hoc* member and North Carolina State University zoologist John Vandenberg, Ph.D. (Photo courtesy of Steve McCaw)*



Board member David Wegman, M.D., center, said that NTP was going “in the right direction” and acknowledged that the innovative criteria were “a work in progress.” Wegman is a professor and former dean of the School of Health and the Environment at the University of Massachusetts Lowell. Member and University of Michigan geneticist Diane Robins, Ph.D., right, listened intently. (Photo courtesy of Steve McCaw)



American Cancer Society statistician Kenneth Portier, Ph.D., chaired the deliberations over the immunotoxicology criteria because of BSC Acting Chair Kirkvliet’s role as chair of that CWG. (Photo courtesy of Steve McCaw)

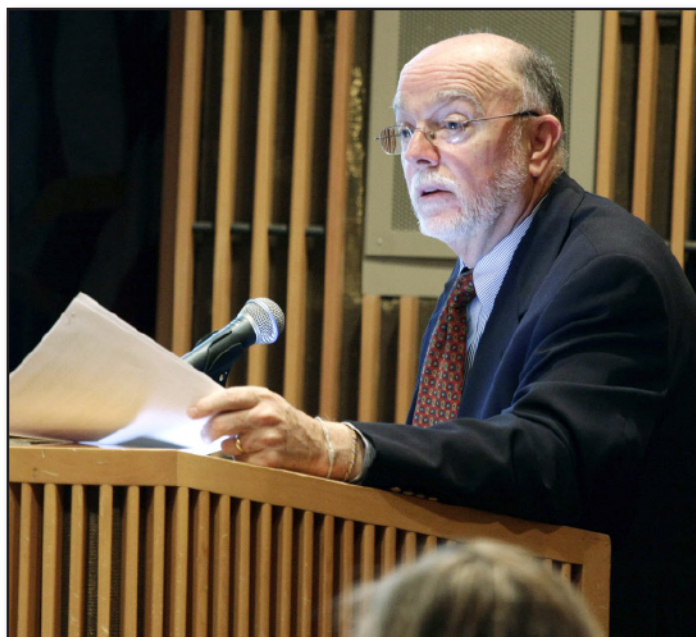
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2008 ONES Awardees Speak at NIEHS

By Eddy Ball

The 2008 winners of the Outstanding New Environmental Scientists (ONES) awards gathered in Rodbell Auditorium December 11 for their first group visit to NIEHS and presentations to Institute scientists. The young investigators were welcomed by NIEHS Acting Deputy Director Bill Suk, Ph.D., who described the event as “a proud day for DERT [Division of Extramural Research and Training].” Suk also called attention to incoming NIEHS Director Linda Birnbaum, Ph.D., who was in the audience.

The ONES winners are a diverse group, with specialized research interests in epidemiology, toxicology, biology and chemistry, who share a common goal of establishing themselves as independent principal investigators. Their research ranges across what Suk described as the NIEHS “rainbow” from fundamental research in molecular toxicology to the application of their findings for the prevention and treatment of disease.



Suk described NIEHS as “an enabling institute..., one of the most public-health oriented of all the institutes at NIH.” (Photo courtesy of Steve McCaw)

In her opening remarks, ONES Program Director and meeting chair Carol Shreffler, Ph.D., explained that the ONES grants are R01 awards specially designed to help junior investigators at the start of their careers “put in the foundation for a successful research career.” The grants fund five years of research at \$250,000 per year and support equipment purchases and career enhancement activities with an additional \$150,000 during each of the first two years.

“This award is intended to be highly selective for the most talented scientists,” Shreffler continued. “We only allow one application per school within an institution.” There are also several other requirements that limit the pool of applicants, such as time since earning a Ph.D., tenure-track status, substantial institutional support, a commitment to spending 80 percent of their time on research, and a rigorous peer review process.

“We indeed have made this a very competitive process,” she concluded, “and we look forward to having these awardees make some very seminal contributions to the future of our Institute.”

The new ONES winners include six outstanding junior investigators:

- University of Michigan epidemiologist Marie Sylvia O’Neill, Ph.D., who is studying the exposures of pregnant women to air pollution in Mexico City and the link to preterm births through *in vitro* and *in vivo* studies of inflammatory response to air pollutants
- Duke University pulmonary and critical care physician John Hollingsworth, M.D., whose goal is to better understand the role of innate immunity in environmental airway disease and how exposure to ambient ozone can modify subsequent innate adaptive responses in the lung
- Hamner Institutes for Health Sciences physician-scientist Jingbo Pi, M.D., Ph.D., who seeks to elucidate the paradoxical roles of transcription factor Nrf2-mediated response to antioxidants in type 2 diabetes caused by arsenic exposure as the foundation for developing more effective preventive measures and therapies
- Duke University chemist Heather Stapleton, Ph.D., who will continue her investigation into the extent to which children are exposed to polybrominated diphenyl ethers (PBDEs) — flame-retardant chemicals that are present in indoor air and dust — and their link to thyroid dysfunction



“One of things that we found was that a lot of people who were successful in getting their first grant had trouble getting the renewal of the grant because, during this first phase of their career, they didn’t have access either to additional equipment or career enhancement opportunities,” Shreffler told the audience. (Photo courtesy of Steve McCaw)



Stapleton plans to enroll 100 children in her study to assess their exposures to PBDEs and their thyroid hormone levels. She plans to combine her field work with lab work to assess the metabolism of PBDEs in human liver and brain cells. (Photo courtesy of Steve McCaw)

- University of Rhode Island pharmacologist/toxicologist Angela Slitt, Ph.D., who plans to use her grant to explore how the expression of drug transporters affect chemical disposition and toxicity, and the ways nutrition and intake of dietary antioxidants affect the process
- Vanderbilt University neurobiologist Aaron Bowman, Ph.D., who seeks to characterize the gene-environment interaction between Huntington's Disease and manganese exposure, which may account for significant differences in the points at which the genetic condition manifests in different individuals

The morning presentations were part of a day-long agenda for the awardees that included lunch with DERT staff, and afternoon meetings with intramural scientists and postdoctoral fellows. The ONES awardees will make additional presentations at NIEHS over the course of their grants.



Slitt's research is concerned with two aspects of nutrition — the relationship of caloric restriction to longevity, and how body mass impacts the ability of the liver to transport heavy metals and endocrine disruptors. (Photo courtesy of Steve McCaw)



Pi tackled questions from the audience about the paradox inherent in his findings about arsenic — that exposure triggers the induction of antioxidant enzymes to protect cells from reactive oxygen species and at the same time appears to impede glucose-mediated oxidative stress that promotes insulin secretion. (Photo courtesy of Steve McCaw)



Hollingsworth, right, took advantage of the morning break to confer with DERT Science Administrator Srikanth Nadadur, Ph.D. (Photo courtesy of Steve McCaw)

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Global Health Meeting Highlights International Partnerships

By Eddy Ball

As part of the ongoing cooperative agreement between NIEHS and the World Health Organization (WHO), the NIEHS Division of Extramural Research and Training (DERT) hosted a mini-symposium on global environmental health December 4 in Rodbell Auditorium. The program, which featured talks by researchers in the Americas, Asia, Europe and Africa, was chaired by NIEHS Center for Risk and Integrated Sciences Acting Branch Chief Claudia Thompson, Ph.D., and organized with the help of a WHO employee in residence at NIEHS, Kathy Prout of the WHO Interregional Research Unit.

The talks presented research findings from around the world as one speaker after another addressed the importance of communications, training and multidisciplinary collaboration for impacting global health issues. Speakers offered specific examples of productive international collaborations and a bi-directional exchange of data and solutions.

The opening talk was presented by Fernando Díaz-Barriga, Ph.D., of Mexico's Autonomous University of San Luis Potosí on the topic "Environmental Health Issues and Vulnerable Populations in Latin America: Do We Need a New Agenda?" Díaz-Barriga described his group's work among the people in *favelas*, the poor areas adjacent to urban centers in South and Central America, and urged his audience to be receptive to findings of scientists in developing countries — to be prepared to "go south for solutions, not just for samples."

The next talk, by Chulabhorn Research Institute Principal Investigator Mathuros Ruchirawat, Ph.D., emphasized the productive "Collaborative Initiatives on Arsenic and Health in Southeast Asia" with NIEHS grantees from Columbia University, the Massachusetts Institute of Technology (MIT) and the University of Arizona. Expanding her work beyond the borders of her native Thailand, Ruchirawat has established relationships with scientists and government officials in Vietnam and Korea.

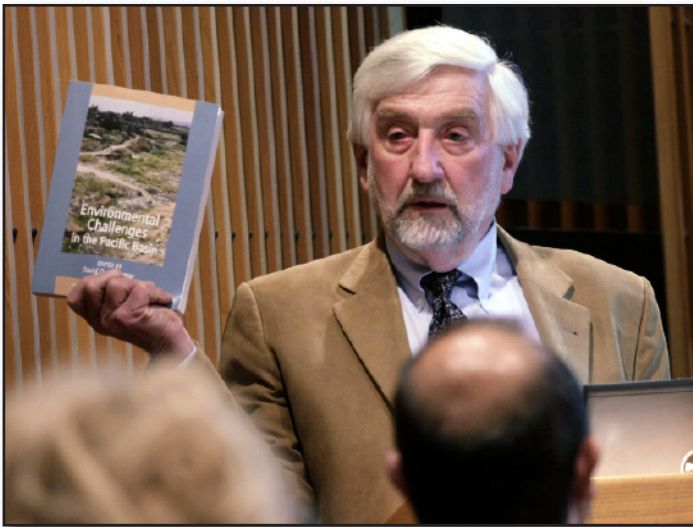
Later in the program, University of Albany Director of the Institute for Health and the Environment David Carpenter, M.D., addressed the topic of "Fostering International Collaborative Research through Scientific Meetings." He began by noting that although international scientific meetings and training may be easy targets for cutbacks in times of budgetary restraints, both are critical to establishing productive collaborations.



Díaz-Barriga, above, gestured to make a point as he answered the rhetorical question posed in his title. "It is time for intervention," he said, as he surveyed the litany of environmental exposures faced by the vulnerable populations of Mesoamerica. (Photo courtesy of Steve McCaw)



Ruchirawat, above, described her work with collaborators investigating the health of residents of Vietnam's Red River delta, where as many as ten million people are exposed to high levels of arsenic. (Photo courtesy of Steve McCaw)



Carpenter pointed to a very tangible outcome of international scientific meetings, *Environmental Challenges in the Pacific Basin*, a collection of papers presented at the 2007 meeting of the Pacific Basin Consortium for Environment and Health. Carpenter is editor of the anthology. (Photo courtesy of Steve McCaw)



Despite the high percentage of deaths in Africa caused by environmental factors — 23 percent and rising — Pronczuk pointed to the Libreville Declaration and new “south-to-south” collaborations between such countries as Argentina and Zambia as hopeful signs in an otherwise bleak panorama of environmental health. (Photo courtesy of Steve McCaw)

These activities are all about bringing parallel research interests and strangers together, Carpenter observed, noting his own record of more than 100 joint publications with researchers from nine other countries. Pointing to Ruchirawat’s training at MIT under NIEHS grantee Leona Samson, Ph.D., and Ruchirawat’s subsequent collaborations with Samson and NIEHS grantees Joe Graziano, Ph.D., of Columbia University and Vas Aposhian, Ph.D., of the University of Arizona, he argued that exchange programs and networking can establish valuable life-long research partnerships for the scientists who participate in them.

The meeting’s final speaker, WHO Department of Public Health and Environment Medical Officer Jenny Pronczuk, M.D., concluded her talk with a telling example of what international collaborations have accomplished in Africa. Faced with seemingly insurmountable threats to environmental health, including frequent “environmental health emergencies,” all 53 African nations in August signed the “Libreville Declaration on Health and Environment in Africa.”

In the declaration, the countries’ ministers reaffirmed their commitment to implement all conventions and declarations that bear on health and environment on their continent. The bulk of those conventions and declarations were established through international collaborative research and issued at scientific meetings of the kind fostered by WHO, NIEHS and other funding sources.

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NIEHS staff posed with presenters following the meeting. (Photo courtesy of Steve McCaw)

Study Examines Women’s Household Exposure Experiences

By Dixie-Ann Sawin

A new report, funded in part by an NIEHS Environmental Justice [grant](#), indicates that women are increasingly concerned with the chemicals in their household environment — and that learning about their own “exposure experiences” can help to shape understanding of the common sources of chemical exposures. The [study](#), led by sociologist Rebecca Gasior Altman, Ph.D., used a novel approach that communicated data produced by biomonitoring body fluids and testing household air and dust.

After reviewing their personal chemical exposure data, most women were surprised and puzzled at the number of contaminants detected. They initially had difficulty relating the chemical results for their homes, located in rural and suburban communities, with their images of environmental problems, which they associated with toxic contamination originating outside the home from military or industrial activities, accidents or dumping.

Through thirty in-depth interviews, the researchers conducted a qualitative assessment of 25 women’s responses to personal exposure information, as part of a collaborative effort to uncover links between environmental exposures and breast cancer. The subjects had all participated in and responded to the earlier multi-component [Household Exposure Study \(HES\)](#), which characterized common chemical exposures in everyday indoor environments and was among the first such studies to report both community- and individual-level exposure data to enrollees.

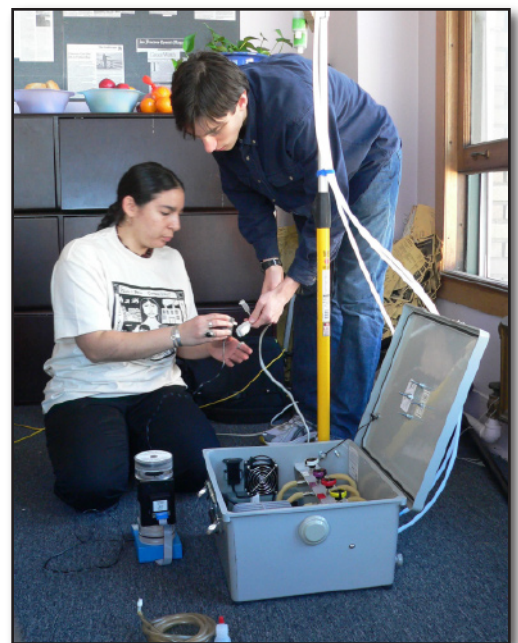
Carried out by co-authors Ruthann Rudel and Julia Brody Ph.D., of the Silent Spring Institute, the HES sampled 120 homes for 89 environmental chemicals in Cape Cod, Mass. The chemicals selected for the study were ones previously linked to endocrine disruption and included alkylphenols, parabens, phthalates, polychlorinated biphenyls (PCBs), flame retardants, pesticides and phenols.

The interview protocol for this follow-up study involved 55 semi-structured questions about participants’ interpretation and impressions of the results and their associated responses to the information. The protocol allowed researchers to ask follow up questions when necessary to probe further the women’s responses.

“Our interviews indicate that study participants wanted their results and appreciated the opportunity to receive them,” Altman and colleagues observed. They concluded, “Our findings raise the importance of reporting even uncertain science and underscore the value of a community-based reporting strategy.”



Working on her Ph.D., which she completed in 2008, Altman served as a graduate student research assistant on a grant held by Silent Spring Institute with collaborators Phil Brown, Ph.D., of Brown University and Rachel Morello-Frosch, Ph.D., of the University of California Berkeley. (Photo courtesy of Rebecca Gasior Altman)



Silent Spring technicians are shown conducting the kind of biomonitoring that produced data from Cape Cod homes. (Photo courtesy of Silent Spring)

Although some scientists and government officials worry such information will provoke fears, Altman explained, the interdisciplinary team discovered instead that people who learned about chemicals in their homes and bodies were eager for more, not less, information about how typical household products can expose them to chemicals that may affect health.

According to the authors, the study represents one of the first detailed accounts of its kind and offers insights into the ways future exposure studies should report results to participants. It is also a response to a call by the National Research Council in its 2006 report, *Human Biomonitoring for Environmental Chemicals*, for more research on how participants react to results from surveillance and personal exposure studies in the context of their unique social and historical settings.

This effort by researchers at Brown University, the University of California Berkeley and the Silent Spring Institute appeared in the December issue of the American Sociological Association's *Journal of Health and Social Behavior*.

To extend this work and investigate the experience of study participants from different historical, environmental and social contexts, the research team is repeating both the household sampling and qualitative interviews in a California community of predominantly low-income Latino and African American residents.

Citation: Altman RG, Morello-Frosch R, Brody JG, Rudel R, Brown P, Averick M. 2008. Pollution Comes Home and Gets Personal: Women's Experience of Household Chemical Exposure. Journal of Health and Social Behavior 49(4): 417-435.

(Dixie-Ann Sawin, Ph.D., is a post-doctoral research fellow in the Laboratory of Neurobiology Neurotoxicology Group.)

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NIEHS Represented at EcoHealth Conference

By Eddy Ball

The Yucatan Peninsula city of Merida served as the venue for the International EcoHealth Forum 2008 December 1-5. Hosted by Mexico's National Institute of Public Health and sponsored in part by NIEHS, the conference provided a forum for exchange of the latest information on ecological issues, including land use patterns, biodiversity loss, and conservation programs and their relationships to human health.

NIEHS played a prominent role at the [meeting](#) through a panel discussion on Energy and Health. Chaired by NIEHS Associate Director [Sharon Hrynkow, Ph.D.](#), the Institute's lead on climate change, the panel session focused on links between energy strategies and use and public health. Joining the NIEHS in supporting the panel was the United Nations Foundation.



Along with concerns about the disparities in wealth and resources between developed and developing nations, Hrynkow, above, has also been an advocate of pursuing gender equality worldwide as part of the global health agenda. (Photo courtesy of Steve McCaw)

In her opening comments, Hrynkow remarked on the glaring inequities evident in energy use and availability worldwide. “2.4 billion people in the poorer parts of the world do not have access to clean energy,” she explained, “while those in wealthier nations use a disproportionate share of the world’s energy resources.”

Pointing to the growing middle class in emerging economies of China, India and other nations and the attendant demands for goods, services and energy, Hrynkow cautioned that the world’s energy path is unsustainable. As energy policies evolve, she continued, “It will be critical to understand health impacts, both positive and negative, of the energy choices societies are about to make.”

The distinguished panel of speakers included [Jonathan Patz, M.D.](#), professor at the Nelson Institute for Environmental Studies at the University of Wisconsin - Madison, who addressed the health and economic co-benefits of energy choices such as walking and biking. He was joined by NIEHS Laboratory of Molecular Toxicology Postdoctoral Fellow Julia Gohlke, Ph.D., who described a holistic framework for assessing a range of energy choices and used a case study of coal-fire power plants to identify gap areas in our knowledge base.

A third panelist, London School of Hygiene and Tropical Medicine Reader in Environmental Epidemiology [Paul Wilkinson, M.D.](#), shared results of a modeling study in London that demonstrated that local programs to decrease greenhouse gas emissions would not be sufficient to improve health due to regional weather patterns that deposit particulate matter and other factors broadly. He called for concerted mitigation efforts at the local, regional and global level.

In addition to the panel session hosted by Hrynkow, the nearly weeklong conference also featured pre-forum events on November 30 and December 1, when attendees were welcomed formally by the governor of Yucatan and the Mexican ministers of Health and Ecology. The next three days offered participants full-day symposia, oral and multimedia presentations, and poster sessions structured around the themes of each day’s plenary session. On the final day of the forum, participants who stayed over at the conference were able to enjoy ecological site visits to Celestúm, Yaxcabá or San Felipe.

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Patz, shown at his April [lecture](#) at NIEHS, shared the 2007 Nobel Peace Prize awarded to the Intergovernmental Panel on Climate Change and Al Gore. (Photo courtesy of Steve McCaw)



Gohlke, above, has been active in climate change conferences as a part of her postdoctoral experience, including a January presentation with colleagues Melissa Chan, Ph.D., and NIEHS Associate Director of the Office of Risk Assessment Research Chris Portier, Ph.D. (Photo courtesy of Steve McCaw)

WE ACT Conference To Address Climate Justice

By Eddy Ball

West Harlem Environmental Action, Inc. (WE ACT) for Environmental Justice, an [NIEHS grantee](#), is currently accepting registrations for its 20th Anniversary National Climate Justice Conference January 29 – 30 to be held at Fordham University School of Law in New York City. The conference theme is “Advancing Climate Justice: Transforming the Economy, Public Health and Our Environment.” NIEHS is providing sponsorship for what organizers describe as a “[ground-breaking conference](#)” through the [Columbia University NIEHS Center for Environmental Health in Northern Manhattan](#).



According to WE ACT, “Environmental justice advocates, community leaders and stakeholders from New York City and other parts of the nation [will] come together to raise our voices and lead our community and country down the path toward achieving a just, responsible and sane climate-changed future by advocating for policies and programs that protect the most vulnerable communities of our country and demanding action to create a just transition to a clean, renewable energy economy and future.”

Major sponsors include the Centers for Disease Control and Prevention, the Ford Foundation, the Women’s Holistic Empowerment and Development Organization, The Mary Ann Liebert journal *Environmental Justice*, the New York University Law School Environmental Law Society and the Earth Institute at Columbia University.

The planning committee includes NIEHS Office of Environmental Public Health Associate Director Allen Dearry, Ph.D., and two grantees from the Columbia University NIEHS Center for Environmental Health in Northern Manhattan, [Joseph Grazziano, Ph.D.](#), and [Regina Santella, Ph.D.](#) Dearry and NIEHS Environmental Justice grantee [Beverley Wright, Ph.D.](#), will be among the guest speakers at the conference.

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Humane Society and Procter and Gamble Recognize NTP for Advancing Alternatives to Animal Testing

By Robin Mackar

On December 18, the Humane Society of the United States (HSUS) and Procter and Gamble presented Ray Tice, Ph.D., of the National Toxicology Program (NTP) an award for the outstanding scientific contributions that he and others are making to advance viable alternatives to animal testing.

The North American Alternative Awards were presented at HSUS' Washington office by the executive vice president of the HSUS, Andrew Rowan, Ph.D., and Len Sauers, Ph.D., vice president of product safety, regulatory and technical relations for Procter and Gamble. The awards recognize the efforts of the recipients to work toward the elimination of animal testing for consumer product safety while ensuring safe products for consumers and the environment.

Raymond Tice, Ph.D., chief of the NTP Biomolecular Screening Branch and deputy director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods, was joined by colleagues Christopher Austin, M.D., of the National Human Genome Research Institute (NIGRI) and Robert Kavlock, Ph.D., of the Environmental Protection Agency (EPA) to receive the award. The award includes a \$25,000 grant to support the ongoing alternative methodologies efforts.



Humane Society and Procter and Gamble award winner Ray Tice (Photo courtesy of Steve McCaw)

The three agencies signed a [Memorandum of Understanding \(MOU\)](#) in February 2008 to use the NIH Chemical Genomics Center's (NCGC) high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals. The award will be used to develop toxicity signatures that help determine how toxic a chemical might be and what type of toxicity it might cause.

“I am pleased that we are receiving recognition by our stakeholders for our efforts,” said Tice. “The NTP and our sister agencies are working hard to implement the vision set out by the National Research Council’s 2007 Report, [Toxicity Testing in the 21st Century: A Vision and a Strategy](#).”

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Science Notebook

LMG Fellows Host Talk on Endogenous Mutagenesis

By Stephanie Nick McElhinny

On December 8 in Rodbell Auditorium, the NIEHS Trainee Action Committee (TAC) of the Laboratory of Molecular Genetics (LMG) welcomed the most recent researcher in its trainee-invited speaker series. The guest lecturer, Jef Boeke, Ph.D., of the Johns Hopkins University School of Medicine, presented his group's latest research results and diagnostic advances in a seminar titled "Retrotransposons in Humans and Other Mammals." Yong Yang, Ph.D., a visiting fellow in the LMG Chromosome Stability Group, was the seminar host.

A professor of Molecular Biology and Genetics and the founder and director of the High Throughput Biology (HiT) Center at Johns Hopkins, [Boeke](#) investigates the mechanism and regulation of retrotransposons — mobile genetic elements that insert copies of themselves at new locations in the genome. "Transposable elements are the endogenous mutagen of every organism," Boeke stressed, "and are very important for the ongoing evolution and molding of genome structure and content."

In his talk, Boeke focused on the most abundant transposon in the human genome, the LINE-1 element (L1). L1 insertions have the potential to alter gene expression and cause human disease via several different mechanisms, such as insertion into the coding or functional sequences of a gene, which is predicted to disrupt gene function. Boeke explained, however, that the outcomes of insertion can be much more subtle, and he noted that "many of the alleles believed to be normal, because they have normal exon sequences, might actually contain mutations that are not appreciated."

According to Boeke, most L1 insertions occur in introns or between genes, and his group has recently shown that L1 insertion into the intron of a gene can attenuate transcription of that gene, leading to a decrease in protein levels. He emphasized that such intronic insertions are likely to have a significant impact on gene function and human disease but, because of their genomic location, are often overlooked.



Boeke opened his lecture with kind words for his colleagues at NIEHS. "One of my formative experiences as a graduate student was attending a Gordon Conference on Mutagenesis where I heard talks by Jan Drake and Tom Kunkel. That meeting was such an exciting experience, and I knew then that I had found my niche in science." (Photo courtesy of Steve McCaw)



The near-capacity audience failed to keep DNA Replication Fidelity Group Postdoctoral Fellows Andreas Larrea, Ph.D., and Scott Lujan, Ph.D., from finding a place to sit during the presentation. (Photo courtesy of Steve McCaw)

To investigate whether L1 insertions in non-coding sequences contribute to human disease, Boeke's group has developed a transposon insertion-site profiling chip (TIP-chip) to map the location of L1 insertions throughout the human genome. The goal of these efforts is to identify new candidate disease genes by mapping novel L1 insertions in clinical samples.

The preliminary results from this work with the TIP-chip are promising. Novel L1 insertions were detected in samples from patients affected by X-linked familial disorders, but Boeke noted that identical L1 insertions were also detected in samples from healthy individuals. Thus, while these L1 insertions may be contributing to the disease phenotype, they alone are not sufficient to cause disease.

Boeke believes the TIP-chip will prove particularly important for identifying genes linked to diseases with complex traits, such as cancer susceptibility and schizophrenia. These diseases are likely to be enriched for mutations that cause only a partial loss in gene function, which is the anticipated consequence of most L1 insertions.

Boeke is also investigating L1 retrotransposition using a synthetic biology approach. Boeke's group has created a synthetic L1 element, ORFeus, which is 200-fold more active in transposition than the original element. When inserted into a mouse model, an inducible version of ORFeus transposed randomly and generated a high frequency of both heritable and non-heritable mutations, producing the first evidence of regulated retrotransposition from a single integrated donor copy of L1 in cells. Boeke hopes to use the inducible ORFeus mouse as a tool to identify novel modifier genes of human disease, with current efforts focused on liver cancer.

(Stephanie Nick McElhinny, Ph.D., is a postdoctoral fellow in the LMG DNA Replication Fidelity Group.)

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Folic Acid Supplements May Have Adverse Epigenetic Effects

By Eddy Ball

A team of U.S. and Norwegian researchers, funded in part by NIEHS, report evidence of a possible downside to the practice of maternal folic acid supplementation in the first trimester of pregnancy to reduce the risk of neural tube defects and other congenital malformations. Their study, published online December 3 by the journal *Archives of Disease in Childhood*, found a six to nine percent increase in relative risk for wheeze and lower respiratory tract infections in exposed infants and toddlers — along with a 24 percent increase in risk for hospitalization for lower respiratory tract infections.

Citing the results of animal studies, the investigators speculated that the increased risk may be the result of epigenetic alteration of methylation levels impacting the development of the immune system of the fetus during the first trimester of pregnancy. “These findings are in agreement with the hypothesis that early childhood



Boeke and lecture host Yong Yang, right, fielded questions from fellows and senior investigators following the lecture. (Photo courtesy of Steve McCaw)

respiratory health may be affected by the possible epigenetic influences of methyl donors in maternal diet during pregnancy,” the researchers concluded.

While the findings are preliminary and the protective effects of folic acid supplementation on neural tube defects are still thought to outweigh the possible adverse effects on early childhood airway inflammation, the study advances understanding of the complex effects of maternal diet on fetal development. The results also point to the need for further investigations into the evidence for recommending specific levels of maternal supplementation during early pregnancy.

The [study](#) was led by NIEHS Special Volunteer Siri Håberg, Ph.D., who is also affiliated with the Division of Epidemiology at the Norwegian Institute of Public Health. The team included NIEHS Genetics Epidemiology Group Principal Investigator Stephanie London, M.D., as second author, and three colleagues from the Norwegian Institute of Public Health and the University of Oslo.

The team used data on the first 32,077 children up to the age of 18 months born of mothers enrolled in the Norwegian Mother and Child Cohort Study (MoBa), a large population-based study with information on supplementation from several time points in pregnancy. Because food in Norway, unlike food in the U.S., is not fortified with folic acid, assessment of supplementation by MoBa subjects was much simpler to determine.

The researchers acknowledged that several other factors related to supplement use may potentially influence the risk of disease in the MoBa children and strengthen or weaken the associations found in the study. These included such variables as the socio-economic status and health of the mother, as well as genetic polymorphisms in folate metabolism among mothers and children.

Citation: [Håberg SE, London SJ, Stigum H, Nafstad P, Nystad W. 2008. Folic acid supplements in pregnancy and early childhood respiratory health. Arch Dis Child. doi:10.1136/adc.2008.142448 \[Epub ahead of print\].](#)

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Lead author Siri Håberg (Photo courtesy of Siri Håberg)



Second author Stephanie London, who was Håberg's mentor at NIEHS (Photo courtesy of Steve McCaw)

Yeast Model Used to Explore Genomic Hypermutation

By Brian Chorley

A recent discovery by researchers at NIEHS sheds new light on the mechanisms of the unintentional changes in DNA that may lead to cancer and genetic disease. The Chromosome Stability Group, led by Michael Resnick, Ph.D., in the Laboratory of Molecular Genetics, found common sources of DNA mutation that persist with high tolerance and may predispose individuals to genetic disease. The group's [study](#), featuring Visiting Fellow Yong Yang, Ph.D., as first author and Staff Scientist Dmitry Gordenin, Ph.D., as principal investigator, appeared in the open-access journal *PLoS Genetics*.

Unintended genomic mutations can arise from multiple sources, including errors in DNA replication and repair and environmental DNA damage — usually with no obvious consequences. Some mutations, however, may be deleterious or beneficial to an organism by increasing or decreasing adaptation to the environment and may be passed to offspring. Mutation, therefore, performs an important role in evolution.

Some mutations are important to normal biological function. For example, the immune system utilizes a highly regulated process strictly confined to immunoglobulin locus known as somatic hypermutability, which generates variable recognition sites in a subpopulation of B-cells that recognize foreign antigen with different affinities. B-cells with receptors for best affinity to a particular antigen are then selected for an individual's immune response. Importantly, the rest of the genome is free from a mutation burden.

Other sites of unregulated localized hypermutability are known to exist. Regions of the genome that have undergone double-strand break repair exhibit higher frequencies of mutation. Additionally, dysfunctional chromosomal ends, known as “uncapped” telomeres, indicated hypermutability in yeast. Common intermediates in these events are long stretches of single-stranded DNA (ssDNA). Since prevention of DNA mutation depends on repair mechanisms that act primarily on double-stranded DNA, it has been theorized that ssDNA is a likely target of hypermutation.

To address this theory, the research team developed two sophisticated yeast models that allowed selection of subpopulations that had undergone double-strand break repair or transient uncapping of a telomere. These subpopulations were exposed to UV light or a chemical mutagen, methyl methanesulfonate, which induced DNA damage and subsequent mutation. Types and frequency of mutations were then assessed by reporter genes incorporated into the model yeast strains.



Visiting Fellow Yong Yang was first author on the study. (Photo courtesy of Steve McCaw)



Gordenin, above, also worked with Chromosome Stability Group co-authors Biologist Joan Sterling and former Postdoctoral Fellow Francesca Storici, Ph.D., who is now with the Georgia Institute of Technology. (Photo courtesy of Steve McCaw)

The study found that multiple types of mutation occurred in ssDNA with frequencies reaching one per 400 to 800 bases of DNA. This high mutation frequency is comparable to somatic hypermutability in immunoglobulin genes. In addition, the researchers found that mechanisms which direct hypermutability in immunoglobulin genes also direct hypermutability in ssDNA. They then used yeast strains deficient in specific components of DNA repair to verify that the error-prone polymerase ζ activity was essential.

Importantly, yeast survival was high in populations that exhibited hypermutability. The incidence of genome-wide mutation was low compared to regions near the double-strand break after mutagen exposure. Cellular mechanisms in place that prevent accumulation of wide-spread genomic mutation did not recognize the localized mutation in these colonies.

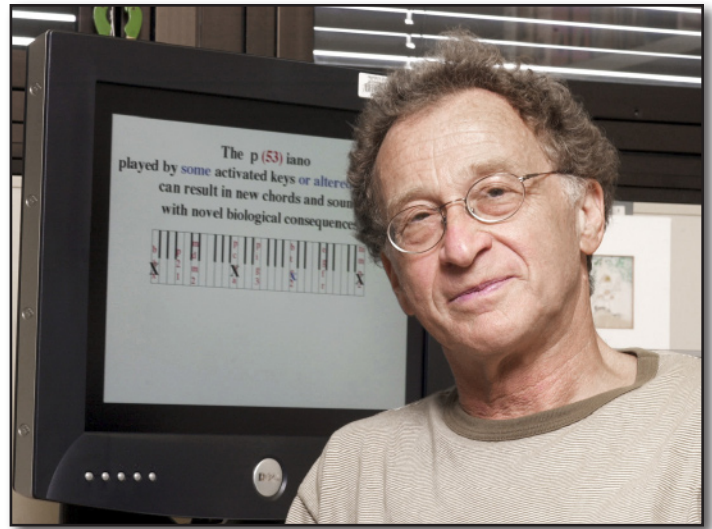
Circumstances where ssDNA occur in yeast also exist in mammalian cells. This is true both for double-strand breaks and during periods of DNA replication and gene transcription. Yang speculated that hypermutability of ssDNA is a mechanism for genomic mutation in humans and suggested this process has consequences for predisposition to genetic disease — notably cancer. Model studies such as these may therefore lead to association of human disease with hypermutation susceptibility. “Human health is our final goal,” stated Yang.

The researchers hope to develop their tool for use in a semi-high-throughput manner. Yang explained that this would allow more rapid identification of chemical mutagens amenable to hypermutation. Gordenin added that in addition to meticulously built model systems, the development of highly efficient technologies for whole-genome sequences opens new opportunities for investigators. This development will allow researchers to trace multiple mutation tracks left by transient localized hypermutability all over genomes and to evaluate environmental damage to genes and detect alterations that may lead to disease susceptibility.

Citation: [Yang Y, Sterling J, Storici F, Resnick MA, Gordenin DA. 2008. Hypermutability of damaged single-strand DNA formed at double-strand breaks and uncapped telomeres in yeast *Saccharomyces cerevisiae*. PLoS Genet 4\(11\):e1000264. Epub 2008 Nov 21.](#)

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

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Chromosome Stability Group Head Mike Resnick is NIEHS Scientist of the Year. (Photo courtesy of Steve McCaw)

Upcoming Distinguished Lecture by Salvatore DiMauro

By Eddy Ball

The 2008 – 2009 NIEHS Distinguished Lecture Series will welcome its next speaker, Salvatore DiMauro, M.D., at 11:00 a.m. January 13 in Rodbell Auditorium, when he explores the topic of “Mitochondrial Medicine.” The lecture hosts will be NIEHS Mitochondrial DNA Replication Group Principal Investigator Bill Copeland, Ph.D., and National Toxicology Program Toxicologist Kristine Witt, M.Sc., of the Toxicology Branch.

DiMauro is the Lucy G. Moses Professor of Neurology at the Columbia University College Medical Center and a trustee of the United Mitochondrial Disease Foundation (UMDF). His research focuses on genetic errors of energy metabolism, and he defines disease entities using both biochemical and molecular approaches.

In his talk, DiMauro will review the wealth of knowledge that has accumulated over the past fifty years about the etiology of mitochondrial diseases, which are caused primarily by mutations in mitochondrial DNA, but also by mutations in nuclear DNA. He plans to discuss the current understanding of the pathogenic mechanism of the disease, which he describes as “very limited,” and the few therapeutic options now available to treat symptoms or slow disease progression. He will also explore experimental approaches aimed at correcting the biochemical or molecular error itself.

While individual mitochondrial diseases are generally considered to be rare, collectively they constitute a significant burden on health, causing premature aging and severe neuromuscular pathologies. As the UMDF website emphasizes, “Every thirty minutes, a child is born who will develop a mitochondrial disease by age 10.” Most childhood patients with mitochondrial disease will die by age 20, according to host Bill Copeland.

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*Distinguished Lecturer Salvatore DiMauro
(Photo courtesy of Salvatore DiMauro)*

Extramural Update

Laura Senier Receives the 2008 Karen Wetterhahn Memorial Award

The NIEHS Superfund Basic Research Program (SBRP) has announced that Laura Senier of Brown University is the recipient of the eleventh annual [Karen Wetterhahn Memorial Award](#). The award was presented to Senier on December 9 at the SBRP Annual Meeting in Pacific Grove, California ([see related story](#)).

The SBRP presents this annual award to an outstanding scholar to pay tribute to the life and scientific accomplishments of Karen E. Wetterhahn, Ph.D., former director of the Superfund Basic Research Program at Dartmouth College. Wetterhahn died in 1997 as a result of accidental exposure to dimethylmercury.

An acknowledged international expert on the effects of heavy metals on biologic systems, Wetterhahn was a leader in conducting research on how metals initiate cancer and other metal-induced human diseases at the molecular level. She fostered links among biology, chemistry, environmental studies, engineering and medical science, insisting that “the life sciences are interdisciplinary.”



2008 *Wetterhahn Memorial Award* winner
Laura Senier (Photo courtesy of Brown University)

Senier is a doctoral candidate in the Department of Sociology at Brown University. Following her graduation *cum laude* from Colby College, she earned an M.A. from Brown University and an M.P.H. from Boston University. Senier is currently working on her dissertation under the guidance of Professor of Sociology and Environmental Studies and Director of the Brown University SBRP Community Outreach Core [Phil Brown, Ph.D.](#) Her research examines how genomics is influencing public health research and practice in the United States, especially in the area of breast cancer research.

Since joining the Brown University Community Outreach Core in 2005, Senier has coordinated research and communication activities with many community partners, including the [Environmental Neighborhood Awareness Committee of Tiverton](#) and the Woonasquatucket River Watershed Council. Her deep sensitivity to these communities allows her to find creative ways to use university resources to assist under-funded and under-staffed groups to facilitate their interaction with state agencies.

Senier’s accomplishments include serving as first-author on a May 2008 article in *Environmental Science & Technology* about the Tiverton experience, preparation of a first-authored article for *Organization and Environment* and publication of her M.A. thesis in a special issue of *Sociological Inquiry* edited by the renowned sociologist Lee Clark. In the spring of 2007, Senier’s strengths and abilities were further recognized with the receipt of a [Robert and Patricia Switzer Foundation Fellowship Award](#). Brown describes his colleague as “a multi-talented person,” who has been “central” to Brown University’s SBRP Community Outreach Core’s successes.

The staff of the NIEHS SBRP congratulates Ms. Laura Senier on her research accomplishments and wishes her continued success in her scientific career.

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Extramural Papers of the Month

By Jerry Phelps

Microglial Cell Enzyme Involved in Neuronal Cell Death

An international research team funded by NIEHS reported the discovery of the involvement of microglial cell I κ B kinase in excitotoxin-induced neurodegeneration. This discovery identifies a target for preventing mass cell death due to traumatic brain injury, stroke or neurodegenerative diseases.

The team employed a special strain of knock-out mice that have no gene for the I κ B kinase enzyme in specific cells of myeloid lineage including microglia — cells that act as the first and main form of active immune defense in the central nervous system. The gene deletion reduced the I κ B kinase activity in cultured microglia by up to 40 percent compared to microglia from normal mice.

Kainic acid-induced hippocampal neuronal cell death was reduced by 30 percent in the knock-out microglia. The reduction in neuronal cell death was followed by decreases in kainic acid-induced glial cell activation and expression of proinflammatory genes such as tumor necrosis factor and interleukin. Additional studies utilizing brain tissue slices in culture showed decreased susceptibility to kainic acid-induced excitotoxicity in knock-out mice brain tissue.

The discovery identifies I κ B kinase as a possible target for therapeutic interventions to ameliorate or prevent additional cell death following serious brain injuries or as a result of neurodegenerative disease.

Citation: [Cho IH, Hong J, Suh EC, Kim JH, Lee H, Lee JE, Lee S, Kim CH, Kim DW, Jo EK, Lee KE, Karin M, Lee SJ. 2008. Role of microglial IKKbeta in kainic acid-induced hippocampal neuronal cell death. Brain 131\(Pt 11\):3019-3033.](#)

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Discovery of Gene Variant for Cleft Lip

About one-fifth of isolated cleft lip may be due to a single nucleotide difference in the DNA sequence of a gene involved in facial development, according to new research findings from an international research team funded in part by NIEHS. Isolated cleft lip is one of the most common birth defects. The research team said this discovery could lead to DNA tests to help couples better understand their risk of having a child with a cleft lip.

This research finding has its origin in research conducted six years ago when the team discovered that a gene called IRF6 is involved with a rare condition called Van der Woude syndrome. About 15 percent of people with the syndrome have malformations that are clinically indistinguishable from isolated cleft lip, which suggested that the gene might be involved in both conditions. Through studying the gene's sequence, they discovered a single sequence variant in a section of DNA that is almost identical across twelve different animals.

The team determined that the substitution of a single adenine molecule in place of a guanine in the IRF6 gene alters the binding site for a protein called AP-2alpha. The protein is known to be involved in craniofacial

development and, when altered, causes a syndrome that involves clefts. These findings may not only lead to improvements in predicting clefts but, possibly, also to better interventions to prevent them.

Citation: [Rahimov F, Marazita ML, Visel A, Cooper ME, Hitchler MJ, Rubini M, Domann FE, Govil M, Christensen K, Bille C, Melbye M, Jugessur A, Lie RT, Wilcox AJ, Fitzpatrick DR, Green ED, Mossey PA, Little J, Steegers-Theunissen RP, Pennacchio LA, Schutte BC, Murray JC. 2008. Disruption of an AP-2alpha binding site in an IRF6 enhancer is associated with cleft lip. Nat Genet 40\(11\):1341-1347.](#)

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Antioxidant Administration Reduces Lung Injury from Chlorine Exposure

Dosages of vitamin C and other low molecular weight antioxidants may help prevent chlorine-induced lung injury that occurs after railroad tanker spills or that could occur as a result of terrorist attacks, according to NIEHS-supported researchers. The levels of chlorine exposure used in the research study mimic those seen during accidental exposures.

The research team exposed laboratory rats to chlorine gas at either 184 or 400 parts per million for 30 minutes in controlled environmental chambers. These levels are similar to those measured near chlorine tanker spills. Just one hour after exposure, the rats showed evidence of decreased arterial blood oxygen, increased blood carbon dioxide and acidosis, and increased markers of inflammation in respiratory fluid samples. In a subsequent experiment, administration of a mixture of antioxidants, which included ascorbic acid (vitamin C), deferoxamine and N-acetyl-L-cysteine, prior to exposure to 184 parts per million chlorine dramatically reduced the respiratory effects seen in the previous experiment.

These experiments suggest that antioxidant administration may be useful for preventing the serious lung injury and death that can occur as a result of chlorine gas exposure. Additional studies will be necessary to confirm these findings, but these results suggest that hazardous materials responders and rescue crews may benefit from prophylactic antioxidant administration prior to responding to a chlorine spill.

Citation: [Leustik M, Doran S, Bracher A, Williams S, Squadrito GL, Schoeb TR, Postlethwait E, Matalon S. 2008. Mitigation of chlorine-induced lung injury by low-molecular-weight antioxidants. Am J Physiol Lung Cell Mol Physiol 295\(5\):L733-L743.](#)

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Consumption of Foods with High Soy Content is Associated with Lower Sperm Concentrations in Men

New research reports that men who eat a high amount of soy-based food products have lower total sperm counts. Soy is rich in estrogenic compounds known as isoflavones including genistein, daidzein and glycitein.

The medical literature is replete with reports of steep drops in sperm count over the last 60 years in the U.S. and Europe. Possible explanations implicate increased exposure to endocrine disruptors and natural and synthetic estrogens.

In the current study, the 99 research subjects, who were the male partners of couples being evaluated at a fertility center, were asked to complete a questionnaire on the foods they eat regularly, which included 15 common soy-based foods such as tofu, soy milk, tempeh, tofu burgers, miso soup and drinks containing soy protein. Men who were in the highest category of soy intake ate one half of a serving each day of a soy-based food. Their sperm counts were on average 41 million sperm per milliliter of semen lower than men who ate no soy foods. Normal sperm counts range from 80 to 120 million per milliliter.

This study suggests that soy foods could have a deleterious effect on sperm production and might need to be avoided by men who have low sperm counts if they are trying to conceive children.

Citation: Chavarro JE, Toth TL, Sadio SM, Hauser R. 2008. Soy food and isoflavone intake in relation to semen quality parameters among men from an infertility clinic. *Hum Reprod* 23(11):2584-2590.

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Intramural Papers of the Month

By Robin Arnette

Damaged Single-Strand DNA Formed at Double-Strand Breaks and Uncapped Telomeres

In an article published in *PLoS Genetics*, NIEHS scientists reported that many kilobases of single-strand DNA created in the vicinity of double-strand breaks or at uncapped telomeres of the chromosomes of the budding yeast *Saccharomyces cerevisiae*, can be restored to viable double-strand form even if it contains multiple damages. In the process of such restoration the damages were turned into mutations by error-prone translesion DNA polymerase zeta.

The researchers wanted to investigate the molecular mechanisms that could provide simultaneous mutations long sought as a source of high fitness alleles in evolution and cancer. Team members constructed yeast strains using PCR-based gene disruption and genome modification by oligonucleotides. They then assessed the strains for mutagenesis associated with double-strand break repair and uncapped telomere arrest.

This work establishes a simple molecular mechanism for simultaneous generation of multiple mutations spanning over several kilobases without severe mutation load in the rest of the genome and puts forward questions about the share of damaged single-strand DNA in various kinds of environmental, occupational and drug-related mutagenesis. It also suggests a tool for genome-wide detection of transient long single-strand DNA regions formed during DNA replication double-strand break repair and telomere metabolism.

Citation: Yang Y, Sterling J, Storici F, Resnick MA, Gordenin DA. 2008. Hypermutability of damaged single-strand DNA formed at double-strand breaks and uncapped telomeres in yeast *Saccharomyces cerevisiae*. *PLoS Genetics* 4(11):e1000264.

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***Rhox13* Is a Novel *Rhox* Gene in Rats and Mice**

Found on the X chromosome of rodents, the reproductive homeobox (*Rhox*) gene cluster contains over 30 genes encoding transcription factors involved in development of various reproductive organs. However, recent studies performed by researchers at NIEHS have discovered a novel *Rhox* gene that is also located on chromosome X, but does not appear to be expressed in Sertoli cells or extraembryonic tissues like other *Rhox* genes. Called *Rhox13*, the gene may regulate a subset of genes in the prenatal ovary as well as the prenatal and postnatal testis.

The investigators knew that the previously characterized reproductive *Rhox* genes overlapped each other in terms of expression, so they set out to fully characterize this gene. The team used several techniques including northern blotting, RT-PCR, western blotting, immunohistochemistry and expression of recombinant RHOX13.

Rhox13 is similar to other *Rhox* genes in that it has a homeobox domain and lacks a paired domain, but its expression pattern is uniquely germ cell-specific. *Rhox13* transcripts are first found in the testis and ovary at 13.5 days post coitum (dpc). *Rhox13* transcription in the testes continues through adulthood, while in the ovary, transcription stops by three days post partum (dpp). The RHOX13 protein is expressed in a subset of germ cells, namely those spermatogonia and oogonia that have differentiated to enter meiosis. Future studies will be aimed at revealing the role of *Rhox13* in differentiation of germ cells in the testis and ovary.

Citation: Geyer CB, Eddy EM. 2008. Identification and characterization of *Rhox13*, a novel X-linked mouse homeobox gene. *Gene* 423(2):194-200.

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The DSS1 Protein Requires the R3IM Motif for Proteasome Interaction

A recent study determined that human Deleted in Split hand/Split foot 1 (HsDSS1) formed a complex with the proteasome via a specific subunit, which then bound with the ubiquitin-proteasome system (UPS), thus regulating ubiquitin-mediated protein degradation. Specifically, the amino-terminus of HsDSS1 contained an RPN3/S3-interacting motif (R3IM) that interacted with RPN3/S3, and this interaction had the capacity to not only control UPS, but also alter the steady state levels of important ubiquitinated substrates such as the tumor suppressor protein, p53. The work was performed collaboratively by a group of scientists from NIEHS and Alpha-Gamma Technologies Inc.

The investigators used several research methods to uncover DSS1's role in eukaryotic organisms, but one experiment, using siRNA to knockdown endogenous levels of HsDSS1, resulted in an increase in p53. This study was the first to demonstrate this action. The team uncovered several other findings from the data.

- An Asp/Glu-rich region of the R3IM in HsDSS1 regulated the proteasome interaction and degradation of ubiquitin-conjugated substrates.
- The interaction between HsDSS1 and RPN3/S3 was highly conserved, from nematodes to humans.
- The HsDSS1/RPN3/S3 proteasome complex was required for p53 targeting.
- The PCI/PINT domain, located within the RPN3/S3, was needed for binding to HsDSS1 and the proteasome.

The research has implications in many disease states such as cancer, aging, inflammation-related and neurodegenerative disorders.

Citation: Wei SJ, Williams JG, Dang H, Darden TA, Betz BL, Humble MM, Change FM, Trempus CS, Johnson K, Cannon RE, Tennant RW. 2008. Identification of a specific motif of the DSS1 protein required for proteasome interaction and p53 protein degradation. *J Mol Biol* 383(3):693-712.

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The Nrf2 Pathway Protects Against RSV Disease in Rodents

Researchers from NIEHS, Johns Hopkins University School of Medicine, the INFANT Foundation in Argentina and the Tohoku University Graduate School of Medicine in Japan determined that the Nrf2-antioxidant response element (ARE) pathway played a key role in protecting murine airways against respiratory syncytial virus (RSV) disease and oxidative stress. The finding is the first to demonstrate the importance of Nrf2-mediated antioxidant mechanisms in host viral infection and provides a possible means for therapeutic intervention.

RSV, the leading cause of severe lower airway disease in infants, young children and immune compromised adults, is characterized by bronchiolitis and respiratory failure in highly susceptible individuals. Because of these health implications, the investigators wanted to understand the pathogenesis of the infection. The team had two major objectives: (1) To determine the functional role of Nrf2 in RSV disease, and (2) whether the induction of Nrf2 and antioxidant enzymes would lessen the oxidant airway injury by RSV.

To address the first goal, the team infected Nrf2-deficient mice (Nrf2^{-/-}) and wild-type mice (Nrf2^{+/+}) with RSV or vehicle. Nrf2^{-/-} mice exhibited augmented bronchopulmonary inflammation and injury and suppressed antioxidant induction compared to Nrf2^{+/+} mice. For the second aim, Nrf2^{-/-} and Nrf2^{+/+} mice were orally treated with sulphoraphane, a naturally occurring antioxidant and Nrf2-ARE inducer, prior to infecting with RSV. Sulphoraphane pre-treatment dramatically limited lung RSV replication and virus-induced inflammation in Nrf2^{+/+} but not in Nrf2^{-/-} mice. This research suggests that targeting oxidative stress may limit RSV infectivity and improve human respiratory health.

Citation: Cho HY, Imani F, Miller-Degraff L, Walters D, Melendi GA, Yamamoto M, Polack FP, Kleeberger SR. 2008. Antiviral activity of Nrf2 in a murine model of respiratory syncytial virus (RSV) disease. *Am J Respir Crit Care Med* [Epub ahead of print].

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Inside the Institute

Director's Annual Honor Awards Ceremony

By Robin Arnette

NIEHS honored employees at the 2008 Director's Annual Honor Awards Ceremony in Rodbell Auditorium on December 18. Presenters included Acting Director Samuel Wilson, M.D., Acting Deputy Director William Suk, Ph.D., Executive Officer Marc Hollander, Division of Extramural Research and Training (DERT) Interim Director Gwen Collman, Ph.D, and Deputy Scientific Director Steven Akiyama, Ph.D. Christine Bruske Flowers, Director of the Office of Communications and Public Liaison, was Mistress of Ceremonies.

Program Analyst and NIEHS Awards Coordinator Diane Crawford organized the event and contacted the winners of the NIH Merit Award, Service Award and Fellows Award for Research Excellence (FARE) Award prior to the ceremony, but the winners of the Unsung Hero and Peer Awards were announced during the celebration.

NIH Merit Award Winners

Individuals

Office of the Director (OD) — Hugh Tilson, Ph.D.

Division of Intramural Research (DIR) — Patricia Deese and Ronald Melnick, Ph.D.

Office of Management (OM) — Marc Hollander

Groups

DIR — Joseph Roycroft, Ph.D., and Molly Vallant

OM — Gregory Holland, Paul Johnson, Christopher Hunt Jr., John McLamb, Scott Merkle, Richard Sloane, William Steinmetz, and William Fitzgerald Jr.



Molly Vallant accepts her DIR NIH Merit Award from Acting Director Samuel Wilson "for significant and sustained contributions to the high quality of studies conducted for the National Toxicology Program." (Photo courtesy of Steve McCaw)



Jerrold Heindel and Kimberly Gray pose with Wilson after receiving their Peer Awards. Peer Awardees also receive a \$600 cash prize. (Photo courtesy of Steve McCaw)

DEPT — Sally Eckert-Tilotta, Ph.D., J. P. (Pat) Mastin, Ph.D., Cindy Lawler, Ph.D., Christina Drew, Ph.D., J. T. (Chip) Hughes, Caroline Dilworth, Liam O’Fallon, Carolyn Mason, Jerry Phelps, Gwen Collman, Ph.D., Sharon Beard, Kimberly Gray, Ph.D., Michael Humble, Ph.D., Beth Anderson, Theresa Nesbitt, Ph.D., and Frederick Tyson, Ph.D.

Cross-divisional Collaboration — Denise Lasko, Robin Mackar, Allen Dearry, Ph.D., Mary Wolfe, Ph.D., Diane Spencer, John Bucher, Ph.D., Kristina Thayer, Ph.D., Michael Shelby, Ph.D., and Paul Foster, Ph.D.

Cross-divisional Collaboration — Kenneth Olden, Ph.D., and Trevor Archer, Ph.D.

Cross-divisional Collaboration — Leroy Worth Jr., Ph.D., Srikanth Nadadur, Ph.D., Michael Loewe, David Balshaw, Ph.D., J. P. (Pat) Mastin, Ph.D., Laurie Johnson, Christina Drew, Ph.D., Astrid Haugen, Bennett Van Houten, Ph.D., Jerrold Heindel, Ph.D., Frederick Tyson, Ph.D., and Kimberly McAllister, Ph.D.

Cross-divisional Collaboration — Raymond Tice, Ph.D., Cynthia Smith, Ph.D., Mary Wolfe, Ph.D., Nigel Walker, Ph.D., Robert Sills, Ph.D., John French, Ph.D., and Paul Foster, Ph.D.

Unsung Hero Awards

Sharon Soward, Susan Booker, Grace Kissling, Ph.D. Dori Germolec, Ph.D., and Joel Abramowitz, Ph.D.

Peer Awards

Kimberly Gray, Ph.D., and Jerrold Heindel, Ph.D.

FARE Awards

Suraj Dhungana, Ph.D., Yoshihiro Komatsu, Ph.D., Wataru Nakai, Ph.D., Fanny Odet, Ph.D., Denise Ray, Ph.D., Stephen Simons, Ph.D., Krisztian Stadler, Ph.D., Bin Tu, Ph.D., and Adolfo Zurita, Ph.D.



Several members of OM receive an NIH Merit Award “for exemplary teamwork in developing an Environmental Management System in accordance with Executive Order 13423.” From left to right: Scott Merkle, William Fitzgerald Jr., Christopher Hunt Jr., Paul Johnson, William Steinmetz, Gregory Holland, John McLamb and Wilson. (Photo courtesy of Steve McCaw)

Service Awards

30 years — Antoinette Bridges, Donald Cozart, Deitra Lunney, James Patterson, Denise Warren-Hinton, Richard Irwin, Ph.D., Michael Resnick, Ph.D., Annette Rice, Ph.D., Richard Rowley, Dale Sandler, Ph.D., Emily Starnes, and Molly Vallant

40 years — Joyce Goldstein, Ph.D., and Hannah Harris



NIEHS employees who participated in a cross-divisional collaboration receive an NIH Merit Award “for exemplary service in facilitating and organizing the evaluation of the bisphenol A report.” From left to right: Paul Foster, John Bucher, Mary Wolfe, Kristina Thayer, Robin Mackar, Diane Spencer, Denise Lasko, Michael Shelby and Allen Dearry. Steven Akiyama, Wilson and William Suk pose with the group. (Photo courtesy of Steve McCaw)

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Native American Heritage Features Lumbee Entrepreneur

By Eddy Ball

The NIEHS Diversity Council welcomed vintner Darlene Gabbard as guest speaker at the NIEHS Native American Heritage Month celebration November 21 in Rodbell Auditorium. Gabbard was introduced by NIEHS Chemist and Diversity Council Chair Brad Collins, host of the lecture and one of the organizers of the event — which also featured a reception in the NIEHS cafeteria immediately after the talk and an off-site wine tasting later in the evening.

Gabbard is a member of North Carolina’s Lumbee people, a writer and musician, and a successful farmer and businesswoman. She entertained the NIEHS audience with a unique story about how her



Gabbard explained that getting into the winery business was pure serendipity. She was searching for a way to use a bumper crop of fruit when she came across a book on winemaking at her local library. (Photo courtesy of Steve McCaw)

Native American cultural heritage was shaped by the forces of modern capitalism to inspire her to create the first American Indian-owned winery in the United States, which she operates on a working farm near Lexington, N.C. In the course of her talk, she also shared stories of her Lumbee childhood and recounted the history of the tribe and its continuing struggle to gain federal recognition.

Gabbard and her family have been producing fruit wines for the [Native Vines Winery](#) label for the past nine years and sell gemstone soaps, crafts and wine jellies, as well their books and music. They live on a 36-acre farm that has been in the family since the original Wachovia Land Grants of the 1750s. Her Native American heritage is reflected in her farming practices, which she describes as “biodynamic farming,” and she has made them a central part of her successful business.

Her acute sense of what her customers prefer has helped make her line of fruit and grape wines popular with ecotourists and a number of customers who buy her wines from a growing network of restaurants and retailers in North Carolina. Native Vines produces about 2,000 cases per year, and Gabbard hopes ultimately to double production to meet growing demand.

Producing a bounty of crops without commercial fertilizers or pesticides, the Gabbards rely on their farm animals to provide manure for fertilizer and to help keep weeds under control. Geese and barn swallows living on the farm do their part by eating insects that threaten her crops. They follow the old ways of agriculture in that they plant by the signs of the Zodiac and phases of the moon and perform most of the farm and winery labor by hand.

“We’re not trying to control nature,” she explained. “We’re letting nature control us.” In return, nature has been generous to Gabbard — allowing her to flourish as an entrepreneur, pursue her many interests and maintain harmony between her native past and the modern marketplace.

(In addition to Collins, the members of the planning committee for the event were Eli Ney, Angela King-Herbert, D.V.M., and Jerry Phelps)

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Collins, above, introduced the speaker and after the talk thanked her as fellow council member Eli Ney presented her with a poster for the event. (Photo courtesy of Steve McCaw)



The centerpiece of Native Vines wines remained uncorked — until they were taken off-site for an after-hours tasting. (Photo courtesy of Steve McCaw)



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