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November 2008

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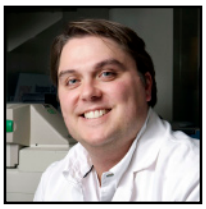

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Science Notebook

Distinguished Lecture on Biology of DNA

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GEMS Meeting Highlights Inflammation in Cancer

Members of the Genetics and Environmental Mutagenesis Society (GEMS) gathered in the Radisson Hotel in RTP for the group's 26th annual Fall Meeting on October 6. ...read more

Air Pollution Linked to Cognitive Deficits and Brain Abnormalities

A new NIEHS-funded study available online from the journal *Brain and Cognition* offers compelling evidence of the significant effects of ambient air pollution on structural alterations in brain and cognitive deficiencies in healthy children and dogs from two Mexican cities. ....read more

Vitamin D Insufficiency Common in Parkinson's Patients

A team of investigators at the Emory University School of Medicine, funded by an NIEHS grant and grants from other NIH institutes, recently reported that a significant portion of Parkinson's patients suffer from vitamin D insufficiency. ...read more

NIEHS Spotlight

Suk and Perera Honored for Advocacy

Veteran NIEHS leader Bill Suk, Ph.D., and NIEHS grantee Frederica Perera, Dr.PH., of Columbia University were honored for their advocacy of children's health in separate ceremonies held during October in Washington, D.C. and New York City by the Children's Environmental Health Network (CEHN). ...read more

NIH Holds Tribute for Johnson-Thompson

On October 9, NIH held its own tribute and reception for former NIEHS Director of Education and Biomedical Research Development Marian Johnson-Thompson, Ph.D., in the Cloisters Building on the Bethesda campus. ...read more

ICs Announce Epigenomics Grants

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Environmental Justice Advocate Speaks at EPA

As part of its ongoing Environmental Justice (EJ) Series, the Environmental Protection Agency (EPA) hosted Vernice Miller-Travis on September 30 at the EPA auditorium in RTP. ...read more

Working with the Media to Communicate Science

The NIEHS Office of Communications and Public Liaison (OCPL) recognizes the important role that the media can play in helping NIEHS communicate its research to the American public. ....read more

Science Notebook

Study Finds Elevated PBDEs in California

Investigators funded by an NIEHS Environmental Justice Program grant report high levels of polybrominated diphenyl ethers (PBDEs), ubiquitous compounds used as a fire retardant in furniture, in the house dust and serum of people living in California. Serum levels of the compound penta-BDE in residents of California were twice the national average. ...read more

Healing Process Found to Backfire in Lung Patients

A mechanism in the body that typically helps a person heal from an injury may actually be causing patients with idiopathic pulmonary fibrosis (IPF) to get worse, researchers at NIEHS and their collaborators have found. ...read more

Superfund Study Detects PCB11 in Ambient Air

A new year-long study conducted by researchers at the University of Iowa (UI) Superfund Basic Research Program (SBRP) reports finding unexpectedly high levels of polychlorinated biphenyls (PCBs), particularly PCB11 (3,3'-dichlorobiphenyl), pervasive in Chicago's urban air. ...read more

Inside the Institute

Hispanic Heritage Talk Focuses on U. S.-Mexico Binational Programs

On September 25 in Rodbell Auditorium, NIEHS Superfund Basic Research Program (SBRP) grantees Denise Moreno Ramírez and Monica Ramírez participated in the NIEHS Hispanic Heritage Month celebration with their joint presentation ...read more

Employee Services Holds Science Manager/ Leader Seminar

According to NIEHS Manager of Employee Services Dona McNeill, competent scientists stand to benefit from specialized training in how to be competent managers and leaders ...read more

Vocational Rehab Featured For Disability Awareness Month

October is National Disability Employment Awareness Month, and the NIEHS Disability Advocacy Committee (DAC) celebrated the contributions of "differently-abled" individuals by offering several events. ....read more

Hispanic Heritage Month Reception

Following the Hispanic Heritage Month Lecture on September 25, NIEHS staffers and guests flocked to the Rall Building Cafeteria for food, entertainment and a glimpse into the cultures of several Latin countries ....read more

Extramural Research

Extramural Update

As part of its role in the NIH Countermeasures Against Chemical Threats (CounterACT) program, NIEHS will provide oversight of one new Research Center of Excellence at the University of Alabama at Birmingham (UAB) and one project at Duke University created this summer to develop therapeutics for chlorine-induced pulmonary damage. These awards augment the existing NIEHS portfolio within the NIH CounterACT program to develop therapeutics for lung injury induced by chemical threats such as chlorine, sulfur mustard, sarin, phosgene and acrolein. ...read more

Extramural Papers of the Month

- Particulate Air Pollution Can Alter the Electrical Functioning in the Heart
- Acetaminophen May Increase the Risk of Developing Asthma
- Green Tea Polyphenol Combats Health Effects of High Fat Diet
- A Fruit Fly Model for Amyotrophic Lateral Sclerosis

Intramural Research

Intramural Papers of the Month

- Compact Fluorescent Light Bulbs Are Safe Substitutes for Standard Incandescent Bulbs
- Cadmium Produces Free Radicals in Rats
- The Case-Mother/Control-Mother Design Is Statistically Enhanced If We Account for Family Relationships
- Double-Strand Breaks Can Reconfigure Genome

Calendar of Upcoming Events

- **November 5 (Offsite Event)**, in the William T. Young Library Auditorium at the University of Kentucky, 8:30 – 12:00 — NIEHS Acting Deputy Director Bill Suk, Ph.D., and NIEHS grantee Phil Landrigan, M.D., present the inaugural keynote talks in the university's John P. Wyatt Lecture Series

- **November 6**, in Rodbell Auditorium, 8:30 – 5:00 — Science Day, Agenda TBA

- **November 7**, in Rodbell A, 10:30 – 12:30 — Laboratory of Reproductive and Developmental Toxicology Lecture Series with Frederike Jayes, D.V.M., Ph.D., addressing "Estrogen Receptor Function Within the Hypothalamic-Pituitary-Ovarian Axis"

- **November 8 (Offsite Event)**, at the Hamner Conference Center at 15 T.W. Alexander Drive in RTP. 4:00 — 2nd Biennial GlaxoSmithKline-American Foundation for Aging Research Symposium keynote talk on "Challenges and Opportunities in Aging Research" with Richard B. Hodes, M.D., follows a full day of student presentations and a 3:30 reception

- **November 13 - 14 (Offsite Event)**, at the Winfrey Hotel in Birmingham, Ala. — Breast Cancer and the Environment Research Centers 5th Annual Early Environmental Exposures Meeting

- **November 14 (Offsite Event)**, in Alumni Hall at the UNC-Chapel Hill Carolina Club, 8:00 – 6:00 — Carolina Center of Cancer Nanotechnology Excellence 2nd Annual Cancer Nanotechnology Symposium (Registration)

- **November 17 - 18 (Offsite Event)**, at the National Academy of Sciences Building in Washington, D.C. — "Value in Health Care: Accounting for cost, quality, safety, outcomes and innovation"

- **November 20 - 21**, in Rodbell Auditorium, 8:30 – 5:00 — NTP Board of Scientific Counselors Meeting

- **November 21 (Offsite Event)**, in G202 at the UNC-Chapel Hill Medical Biomolecular Research Building, 12:00 – 1:00 — NIEHS grantee Laura Niedernhofer, M.D., Ph.D., exploring "The Contribution of DNA Damage to Aging and Age-related Disease"

- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Workshop Explores Opportunities in the Green Economy

By Eddy Ball

From the manufacture of rain barrels to the retrofitting of older homes, the emerging green economy promises to have a fundamental impact on the way people will work and live in the future. That's the message attendees heard in one form or another throughout the NIEHS Worker Education and Training Program (WETP) Fall Awardee Meeting and Technical Workshop held October 15–17 at the Chapel Hill Sheraton Hotel.

Wilson praised the attendees for thinking "outside the box," and closed by telling the audience, "I applaud you for stepping up to the plate." (Photo courtesy of Steve McCaw)

Chaired by WETP Director Chip Hughes, the meeting was organized around the theme "Implications for Safety and Health Training in a Green Economy." The event featured two keynote talks, four plenary sessions and concurrent breakout sessions exploring the environmental, economic, social and philosophical dimensions of what many in the audience clearly envision as a revolution poised to happen. Background papers and other materials are available online at the WETP events page.

The meeting opened with a welcome from Hughes and an overview presented by NIEHS Acting Director Sam Wilson, M.D. Wilson, who described himself as a "big fan" of worker education and training, pointed to the prominent role of WETP in the NIEHS "rainbow" that spans its mission from basic research to the translation of findings onto the streets and into the workplaces of America.

Delivering the keynote talk on October 16 was Dave Foster, retired director of the United Steel Workers District 11 and currently executive director of the Blue-Green Alliance, a cooperative effort by environmentalists and labor to promote investment in the green economy. The Alliance, Foster explained, calls for spending $100 billion to create two million new jobs.

During his talk, Foster laid out the challenges of worker education in a green economy — to increase the number of safe, living-wage, career-track jobs that contribute directly to preserving or enhancing environmental quality. (Photo courtesy of Steve McCaw)

That investment could reduce unemployment to 4.4 percent, Foster continued, while also putting in place effective, energy efficient global warming solutions. "We have to construct a new economy," Foster urged, one that will redefine social values, promote environmental justice and strengthen the domestic economy.

Along with its obvious implications for education and training, vocation and lifestyle, several speakers in the plenary sessions observed, the green economy will also lead to a change in the mindset chemists, engineers and other scientists will bring to their work in the future.

John Warner, Ph.D., former chairman of the Department of Chemistry at the University of Massachusetts at Lowell and founder of the Warner Babcock Institute for Green Chemistry, was the first of several speakers who called for fundamental changes in science education and the invention/design process. Everyone, from the bench scientist to the worker on the job, needs to approach life and work with "new eyes and new ideas," he argued, and a clearer understanding of the implications in terms of environmental impact and social justice.

J. Phillip Thompson, MIT associate professor of urban politics and community development, and other speakers pointed to urban degradation, gentrification, environmental injustice and other failed energy policies as some of the problems the green economy can help address. (Photo courtesy of Steve McCaw)

Warner, who co-authored the twelve principles of green chemistry, was followed by Terrence Collins, Ph.D., director for the Institute for Green Science at Carnegie Mellon University, and Collins' former student, Evan Beach, Ph.D., a postdoctoral researcher at Yale University's Center for Green Chemistry and Green Engineering. Beach described examples of green engineering, such as new adhesive tape that mimics the biology of the gecko, and gave an overview of the twelve principles of green engineering that are taking his field well beyond traditional concerns with form, function and profitability at any environmental cost.

Warner gestured as he made a point about the current science education model. "Education in the sciences is broken," he said, "and we need to fix it." (Photo courtesy of Steve McCaw)

The other 14 plenary and breakout session speakers took the green economy back to shop floors, urban neighborhoods and classrooms where structural changes are already well underway. The keynote speaker on October 17, San Francisco State University Professor of Urban Studies Raquel Pinderhughes, explored the potential impact the green economy can have on addressing social and racial inequality, as outlined in her recent study.

Because green-collar jobs have relatively low barriers to entry and typically offer on-the-job training, Pinderhughes explained, they provide an excellent opportunity for creating dignified and meaningful work for the people who are the hardest to employ. "We're really building a social movement," she concluded, one that can lead to pervasive socioeconomic changes to reverse generations of disenfranchisement and injustice.

NIEHS National Clearinghouse Specialist Donald Elisburg, standing, took his conversation with Donele Wilkins of Detroiters Working for Environmental Justice offline, following her plenary session talk. (Photo courtesy Steve McCaw)

Pinderhughes discussed her Green Collar Job Training and Placement Model, which emphasizes the "soft" skills involved in getting and keeping jobs as well as the "hard" skills essential for the actual work performed. (Photo courtesy of Steve McCaw)

WETP Administrator and Industrial Hygienist Sharon Beard, left, shown talking with workshop attendee Alexander Prentzas of OAI, Inc., moderated the plenary session on "Environmental Justice and Good/Green Jobs for All." (Photo courtesy of Steve McCaw)

In his closing remarks, Hughes observed, "We've latched onto something that I think can carry us into the next decade," with the challenge of integrating the needs of the green economy into the WETP. (Photo courtesy of Steve McCaw)

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Postdocs Win SOT Awards

By Eddy Ball

Two NIEHS postdoctoral fellows will be adding to their CVs and their bank accounts as a result of their winning posters in the North Carolina Society of Toxicology (NCSOT) President's Award for Research Competition. The competition, a prelude to the group's annual Fall Meeting on October 23 in Rodbell Auditorium, resulted in the award of first place to Postdoctoral Fellow Erik Tokar, Ph.D., and second place to Postdoctoral Fellow Scott Auerbach, Ph.D.

As first place winner, Tokar received a cash award of $500 and the opportunity to give a 20-minute presentation of his research at the Fall Meeting. Tokar collaborated with his supervisor and mentor Research Pharmacologist Michael Waalkes, Ph.D., of the Environmental Toxicology Program and National Cancer Institute, on a study titled "Stem cell selection facilitates arsenic-induced malignant transformation via innate resistance, hyper-adaptability and over-production."

With his second-place win, Auerbach received a cash award of $250 and recognition by NCSOT. Auerbach collaborated with his NTP Toxicology Branch colleague, Chemist Richard Irwin, Ph.D., on the study titled "Prediction of hepatocarcinogenic potential in male rats using machine learning methods informed by genome-wide expression analysis."

The NCSOT meeting was organized around the theme of "Pharmaceuticals and Personal Care Products in the Environment."

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First place winner Erik Tokar (Photo courtesy of Steve McCaw)

Second place winner Scott Auerbach (Photo courtesy of Steve McCaw)

NIEHS Scientists Shine at Research Festival

By Eddy Ball

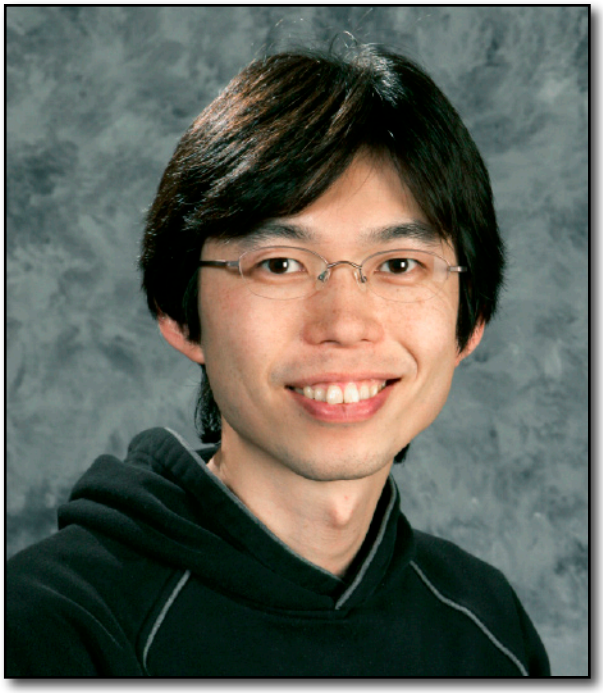
NIEHS and National Toxicology Program (NTP) scientists were among the thousands of people attending the 21st annual NIH Research Festival October 14-17 at the Masur Auditorium and Natcher Conference Center on the NIH campus in Bethesda, Md. The event included a plenary session on obesity, 18 concurrent symposia sessions, poster sessions with more than 500 entries, a Fellows Award for Research Excellence (FARE) program and award ceremony, a symposium and career fair for postdocs, and special exhibits spread over the three days.

Representing NIEHS on the program were three senior investigators presenting at a symposia on "Genetic Susceptibility — The Link between Environmental Exposure and Human Disease," chaired by NTP Acting Chief and Staff Scientist in the Host Susceptibility Branch Jef French, Ph.D. Seven NIEHS postdoctoral fellows (see text box) also made the trek to Bethesda, six of them to paricipate in the poster competition. An additional postdoctoral fellow did not attend the festival although his research was judged as part of the poster presentation.

Research Festival symposium chair Jef French, above, is shown at the Genetics and Environmental Mutagenesis Society Fall Meeting. French will become president-elect of the organization in January. (Photo courtesy of Steve McCaw)

In addition to serving as chair for the symposia, French made a presentation on analyzing DNA strand break repair and susceptibility to tumor suppressor gene loss associated with loss of heterozygosity in response to human carcinogen exposure. He was joined by NIEHS Senior Investigator and Chief of the Laboratory of Respiratory Biology Steve Kleeberger, Ph.D., and NTP Toxicology Branch Staff Scientist June Dunnick, Ph.D., who also spoke at the session.

In his presentation, Kleeberger described his work in identifying the transcription factor NRF2 as a critical determinant of susceptibility to hyperoxic lung injury. Dunnick's presentation explored how environmental factors may contribute to cardiac disease and how the NIEHS plans to use mouse models to identify highly penetrant allelic variants of genes that modify or influence cardiotoxicity in order to determine orthologous human genes. Two National Cancer Institute investigators, Kent Hunter, Ph.D. and Karlyne Reilly, Ph.D., also presented at the symposium.



Nakai's FARE award will help him attend additional professional development meetings to share his research and network with colleagues. (Photo courtesy of Steve McCaw)

One of the young scientists from NIEHS, Visiting Fellow Wataru Nakai, Ph.D., of the Chromosome Stability Group headed by Principal Investigator Mike Resnick, Ph.D.,

won a FARE Award for his research. His submission, “Transition of a Double-Strand Break to a Chromosome Break is Efficiently Prevented by RMX, Exonuclease I and MCD1,” was part of the Genetics/Genomics Poster Session on October 15.

NIEHS Postdoctoral Fellow Jennifer Adair served as a member of the FARE Committee for the Research Festival.

NIEHS Postdocs at the NIH Research Festival

The annual FARE competition, now in its 14th year, selects the top twenty-five percent of abstracts from fifty different study sections to receive a $1,000 travel award. In addition to Nakai, six other NIEHS fellows presented their work in the competition:

- Scott Auerbach, Ph.D., in the Cancer session
- Yin Li, Ph.D. in the Cell Biology session
- Yang Cao, Ph.D., in the Epidemiology session
- Xueqian (Shirley) Wang, Ph.D., in the Imaging session
- Jianxin Shen, Ph.D., in the Neurobiology and Behavior session
- Saurabh Chatterjee, Ph.D., in the Oxidative Stress session (in absentia)

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Health Research Loses Faithful Supporter

By Eddy Ball

On October 15, the health research community was saddened to learn of the death of retired U.S. Congressman Paul Rogers, 87, two days earlier at a hospital in Washington. Rogers, known as "Mr. Health" in legislative circles, was an enthusiastic and persistent advocate of legislation to improve the environment and healthcare, as well as promote the aggressive expansion of biomedical research at several ICs within the NIH, including NIEHS.

Former Representative Paul G. Rogers spoke at a Research!America Annual Meeting in March 2008 at the National Press Club in Washington. (Photo courtesy of Heather Jameson and Research!America)

Rogers was widely quoted as saying ,"Without research, there is no hope" — a statement now set in a marker on the NIH campus. In recognition of his advocacy for greater funding for research, in June 2001, Congress dedicated the plaza in front of Building 1 at NIH the Paul G. Rogers Plaza.

After they learned of his death, NIEHS Acting Director Sam Wilson, M.D., and NIH Director Elias Zerhouni, M.D., issued statements about Roger's contributions to medical research and expressed their condolences to his widow, Becky, and daughter, and the Rogers family.

"Paul played a key role in advancing the field of Environmental Health Sciences to include supporting the NIEHS request to establish an Institute of Medicine (IOM) Roundtable on EHS Research and Medicine in 1998," Wilson observed in his message to NIEHS employees. "It is with great respect and gratitude that we remember this special man and recognize his important legacy to environmental health research."

A Democrat who represented West Palm Beach, Fla. for 12 terms, Rogers was a member of Congress from 1955 to 1979 and chairman of the House Subcommittee on Health and the Environment for eight years. During that time, he sponsored or was instrumental in the passage of some of the most important pieces of health- and environment-related legislation introduced in the House of Representatives.

In his statement, Zerhouni pointed to several of Roger's key accomplishments, including his significant role in doubling the NIH budget over a five-year period. "Some of the prominent pieces of legislation which Paul sponsored and played a major role in enacting are the National Cancer Act of 1971 and 1977; the Heart, Blood Vessel, Lung and Blood Act; the Research on Aging Act; the Comprehensive Drug Abuse Prevention and Control Act of 1970; the Emergency Medical Services Act; the Clean Air Act; Safe Drinking Water Act; and the Radiation Health Safety Act," Zerhouni said.

In recent years, Rogers channeled much of his energy into health advocacy through the organization Research!America, where he served as a board member and chair emeritus. Research!America is the nation's largest not-for-profit public education and advocacy alliance that works with more than 500 member organizations, representing a vast array of medical, health and scientific fields. In 2006 Research!America established the Paul G. Rogers Society for Global Health Research with founding support from the Bill & Melinda Gates Foundation.

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Nobel Winner Is Superfund Grantee

By Eddy Ball

One of this year's Nobel Prize for Chemistry winners, Roger Tsien, Ph.D. has a history of grant awards from the NIEHS Superfund Basic Research Program (SBRP) to support second-generation development of his seminal discoveries. Working from the University of California at San Diego, Tsien has been an SBRP grantee since 2000.

Nobel Winner and current Superfund grantee Roger Tsien (Photo courtesy of the University of California at San Diego)

Tsien was honored along with colleagues Martin Chalfie, Ph.D., of Columbia University, also an NIH grantee, and a former NIH grantee, Osamu Shimomura, Ph.D., of the Marine Biological Laboratory in Woods Hole, Mass. The chemists discovered a fluorescent protein, GFP, in a colorful jellyfish and developed it into a key tool for observing previously invisible processes — such as the development of nerve cells in the brain or the way cancer cells spread.

In a statement issued October 8, NIH Director Elias Zerhouni, M.D., underscored the importance of Tsien's accomplishments in the conduct of basic research. "Roger Y. Tsien contributed to our general understanding of how GFP fluoresces," Zerhouni explained. "He also extended the color palette beyond green, allowing researchers to give various proteins and cells different colors. This enables scientists to follow several different biological processes at the same time."

Although Tsien's work has its roots in the 1955 discovery of the luminescence of hydromedusae and was well underway long before the establishment of NIEHS in 1966, SBRP has supported his research for the past eight years to extend applications of his discovery in the environmental health sciences. According to NIEHS SBRP Program Analyst Beth Anderson, Tsien received a grant in 2000 to study novel cell-based toxicity sensors identified by genome-wide screens and another in 2005 for work in molecular imaging.

With his first SBRP grant at UC San Diego, Tsien and his colleagues developed inexpensive and rapid screens for the presence of environmental hazards, for the hazards posed by mixtures of toxins, and for testing large numbers of field isolates. The 2005 grant funds an Imaging Core, where Tsien oversees the development and application of new fluorescence, biarsenical reporter and tetracysteine-based methods for the analysis of gene and protein expression and detection both in cultured cells and tissues.

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Suk and Perera Honored for Advocacy

By Eddy Ball

Veteran NIEHS leader Bill Suk, Ph.D., and NIEHS grantee Frederica Perera, Dr.PH., of Columbia University were honored for their advocacy of children's health in separate ceremonies held during October in Washington, D.C. and New York City by the Children's Environmental Health Network (CEHN).

Suk was presented his award by CEHN board member Joy Carlson at the Third Annual DC Children's Environmental Health Advocate Award Reception on October 20. Perera was presented her award by CEHN board member and NIEHS grantee Peggy Shepard at the First Annual NYC Children's Environmental Health Advocate Award Reception on October 7.

Suk, who has been a member of the senior leadership at NIEHS for more than 20 years, is director of the Superfund Basic Research Program and currently serves as NIEHS acting deputy director. According to CEHN Executive Director Nsedu Obot Witherspoon, Suk has been instrumental in collaborative efforts worldwide to improve the lives of children by working to improve the environment and understand better its impact on their health.

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

"Dr. Suk has been a great friend to the children's environmental health field and specifically the Children's Environmental Health Network since its start," Witherspoon explained. "He was instrumental in working with CEHN to set the first research agenda on children's environmental health in the early 90's and has served on our science committee for many years."

Perera, a professor of Environmental Health Sciences at Columbia's Mailman School of Public Health, is also the director of the NIEHS-funded Columbia Center for Children's Environmental Health (CCEH). She was also honored in May with the Measure of Children Award from the Healthy Schools Network.

Director of the Columbia Center for Children's Environmental Health Frederica Perera (Photo courtesy of Eric Evans and Columbia University)

"Dr. Perera pioneered the field of molecular epidemiology, beginning with studies of cancer and is now applying molecular techniques within studies of pregnant women and their children," Witherspoon said. "Her areas of specialization include prevention of environmental risks to children, molecular epidemiology, cancer prevention, environment-susceptibility interactions in cancer, developmental damage, asthma and risk assessment."

Honored along with Suk were Liz Blackburn, a leader in education, nursing and community service; Bettina Poirier, majority staff director and chief counsel of the Senate Environment and Public Works Committee; and Greg Famer, senior vice president of Government and Community Relations at Nortel. Also receiving an award in New York was Wendy Gordon, founder of the National Geographic Green Guide.

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CEHN Executive Director Nsedu Obot Witherspoon also serves as an NIEHS Public Interest Partner and National Advisory Environmental Health Sciences Council member. (Photo courtesy of Steve McCaw)

NIH Holds Tribute for Johnson-Thompson

By Eddy Ball

On October 9, NIH held its own tribute and reception for former NIEHS Director of Education and Biomedical Research Development Marian Johnson-Thompson, Ph.D., in the Cloisters Building on the Bethesda campus. Friends and colleagues from the Washington area and beyond gathered to add their praise and best wishes for a fruitful retirement to those expressed in a similar NIEHS ceremony held September 22.

Traveling to Bethesda from RTP were NIEHS Acting Director Sam Wilson, M.D., and Joan Packenham, Ph.D., director of the NIEHS Office of Research Compliance. Wilson made the opening remarks at the event and was followed by leaders in science education and minority involvement at NIH and elsewhere — as well by Johnson-Thompson's former students, mentees and husband.

Leading off the program was Vivian Pinn, M.D., director of the NIH Office of Research on Women's Health, who in 1967 was the only African American and only woman in her class to graduate from the University of Virginia School of Medicine. Pinn surveyed Johnson-Thompson's accomplishments from her childhood in Florida through her tenure at the University of the District of Columbia and at NIEHS.

Marian Johnson-Thompson (Photo courtesy of Steve McCaw)

Director of the National Center on Minority Health and Health Disparities John Ruffin, Ph.D., followed Pinn with observations on Johnson-Thompson's "ability to always see the bigger picture." Another colleague who spoke of her role in expanding educational opportunities for minorities was Lovell Jones, Ph.D., director of the Center for Research on Minority Health at the University of Texas M. D. Anderson Cancer Center and a former member of the NIEHS National Advisory Environmental Health Sciences Council.

Acknowledging Johnson-Thompson's dedication to students was longtime friend and colleague Freeman Hrabowski, Ph.D. Hrabowski is the president of the University of Maryland Baltimore County, home of the Meyerhoff Scholarship Program whose students honored Johnson-Thompson by naming her Mentor of the Year in 2001.

Speakers were also on the program offering their appreciation for Johnson-Thompson's work as a scientist and educator. Colleagues Agnes Day, Ph.D., chair of the Department of Microbiology at the Howard University College of Medicine, and former Chair of the University of the District of Columbia Department of Biology and Environmental Science Carolyn Cousin, Ph.D., talked about her contributions to the field of microbiology. Her former student, Morgan State University Provost Joan Robinson, Ph.D., and her current Meyerhoff mentee, Tamika John, offered their perspectives on Johnson-Thompson's transformative influence on their lives.

Johnson-Thompson's sisters in the Federal City Alumnae Chapter Delta Sigma Theta Sorority spoke of her dedication to community service, and her husband, Charles, talked of his pride in being a part of her life. He also added her service with the Susan G. Komen for the Cure at the N.C. Correctional Institution for Women on breast cancer awareness to her long list of accomplishments.

Johnson-Thompson closed out the tribute with a look back at her years as an educator, scientist and public servant and voiced her appreciation for the many people who have helped make her career so rich and rewarding.

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ICs Announce Epigenomics Grants

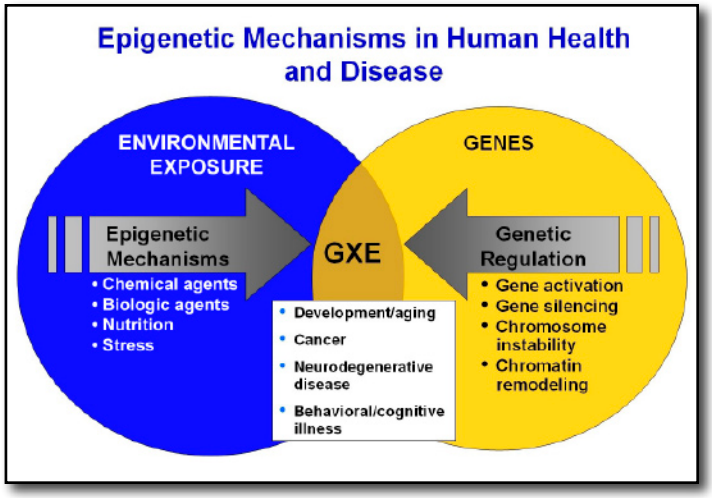
By Eddy Ball

NIEHS is one of six institutes and centers (ICs) that announced the award of $18 million in 2008 grants on September 29 as part of the $190 million, five-year trans-NIH Roadmap Epigenomics Program. The ambitious program will study epigenetic processes at a genome-wide scale to understand better how these processes control genes during different stages of development and affect gene expression. Because epigenetic alterations are potentially preventable and reversible, the research could have a major impact on the practice of medicine.

The twenty-two 2008 awards announced by NIH focus on four areas: epigenome mapping centers, epigenomics data analysis and coordination, technology development in epigenetics and the discovery of novel epigenetic marks in mammalian cells.

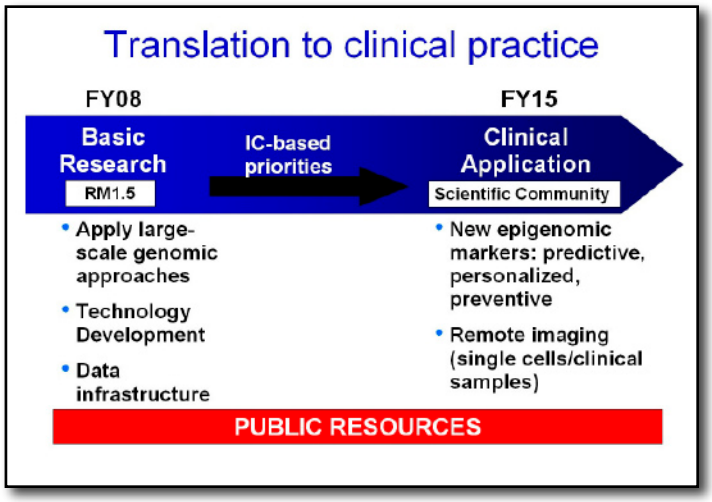
Wilson gave the NIEHS National Advisory Environmental Health Sciences Council an update on the planning stage of the Roadmap Epigenomics Program during its September 17–18, 2007 meeting. (Photo courtesy of Steve McCaw)

According to the NIH press release, the overall hypothesis of the NIH Roadmap Epigenomics Program is that the origins of health and susceptibility to disease are, in part, the result of epigenetic regulation of the genetic blueprint. Researchers believe that understanding how and when epigenetic processes control genes during different stages of development and throughout life will lead to more effective ways to prevent and treat disease. Epigenetic processes, such as modifications to DNA-associated proteins called histones, control genetic activity by changing the three-dimensional structure of chromosomes.



The initiative will focus on the potentially reversible and preventable changes in gene expression patterns triggered by environmental exposures. (Graphic courtesy of Sam Wilson)

The research will have a wide range of preventive and treatment applications, according to NIEHS Acting Director Sam Wilson, M.D. "The epigenetic regulation of gene expression is an emerging frontier in understanding human health and disease," he observed. "The information generated by this Roadmap program will be an invaluable resource for scientists studying normal biological processes, as well as a wide variety of diseases, including cancer, autoimmune diseases, developmental disorders, and neurological diseases such as autism."



The translational potential of the research is significant, with applications ranging from addiction and inflammation to birth defects, chronic diseases and cancers. (Graphic courtesy of Sam Wilson)

"Epigenomics-based research is now a central issue in biology. We will build upon our new knowledge of the human genome and move towards a deeper understanding of how DNA information is dynamically regulated through DNA histone modifications, as well as the emerging role of micro RNAs and other factors," explained NIH Director Elias A. Zerhouni, M.D. "The grants now funded through this program will provide reference data that the entire community can use to understand epigenetic regulation and how it affects health and disease."

In addition to NIEHS, participating ICs are the National Institute on Drug Abuse (NIDA), the National Institute on Deafness and Other Communication Disorders (NIDCD), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Center for Biotechnology Information (NCBI) of the National Library of Medicine. Their efforts are coordinated by the Office of Portfolio Analysis and Strategic Initiatives (OPASI) as part of the NIH Roadmap.

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Environmental Justice Advocate Speaks at EPA

By Eddy Ball

As part of its ongoing Environmental Justice (EJ) Series, the Environmental Protection Agency (EPA) hosted Vernice Miller-Travis on September 30 at the EPA auditorium in RTP. Miller-Travis, who is a leading figure in the movement, spoke to a group of EPA, NIEHS and community attendees on "The Unfinished Environmental Justice Agenda: Picking Up the Pieces."

Miller-Travis began with a review of the history of Environmental Justice and its relationship to civil rights before addressing the challenges that remain in the struggle to ensure that all communities are treated equally before the law. In the course of her narrative, she recounted the experiences that convinced her that "the real civil rights threat… was a whole other arena that no one had been paying attention to — the environmental threat that communities of color were facing."

The recipient of many awards for her work, Miller-Travis has spent the past 22 years in leadership positions in the EJ movement, including serving as the executive director of the Environmental Support Center (ESC) from 2005 to 2008. She first became involved in EJ in 1982 when she was a Columbia

"I feel like the hand of God grabbed me and said, 'This is the work you need to be doing, and this is the path you need to be on,'" Miller-Travis said of her 26 years of environmental rights advocacy. (Photo courtesy of Steve McCaw)

For EJ Activists, the Struggle Continues

People who attended the talk by Miller-Travis took away hard copies of *Toxic Wastes and Race at Twenty, 1987 - 2007: Grassroots Struggles to Dismantle Environmental Racism in the United States*. The report was prepared for the United Church of Christ Justice and Witness Ministries to celebrate the twentieth anniversary of the landmark study that grew out of Miller-Travis' work in Warren County, N.C.

The report uses 2000 census data, a current national database of commercial hazardous waste facilities and Geographic Information Systems to count persons living nearby to assess nationally the extent of racial and socioeconomic disparities in facility locations. It also examines racial disparities by region and state, as well as for metropolitan areas, where most hazardous waste facilities are located.

Several NIEHS EJ grantees were involved in the report, including principal author Beverly Wright, Ph.D., director of the Deep South Center for Environmental Justice at Dillard University. In addition to a detailed history and statistical analysis, the report includes contributions by Miller-Travis, NIEHS grantee Peggy Shepard and NIEHS Public Interest Partner and National Advisory Environmental Health Sciences Council member Nsedu Obot Witherspoon, executive director of the Children's Environmental Health Network.

These activists joined the more than 100 signers of an open letter to Congress on July 20, 2007 calling for leaders to address the continuing environmental and health disparities in low-income and people of color communities. "Environmental injustice in people of color communities," they wrote, "is as much or more prevalent today than 20 years ago."

University student living in Harlem and introduced herself to civil rights leader and Executive Director of the United Church of Christ Commission for Racial Justice (UCC-CRJ) Rev. Ben Chavis. Chavis, who is now known as Benjamin Chavis Muhammad, coined the term "environmental racism" and is considered by many to be the father of the EJ movement.

The first assignment Miller-Travis accepted with UCC-CRJ in 1986 was as a research assistant for the Special Project on Toxic Injustice in predominantly African-American Warren County, N.C. Miller-Travis worked with colleagues there, including UCC's Director of Research Charles Lee, overlaying EPA data on the location of hazardous waste sites throughout the United States with the racial and socio-economic profiles of residents in those zip codes to demonstrate the direct correlation between the two data sets.

Laura McKelvey welcomed attendees to the presentation and introduced Miller-Travis. McKelvey is a tribal representative in the EPA Office of Air Quality Planning and Standards. (Photo courtesy of Steve McCaw)

The landmark national study, *Toxic Waste and Race in the United States of America*, published in 1987, grew out of that research collaboration. "If I live to be a hundred," Miller-Travis said of the experience, "I don't think I will ever have the opportunity to work on something as significant as this report turned out to be.… We now had the data to prove that this [relationship] is not random."

Fourteen years after the 1994 Executive Order on EJ was signed by President Bill Clinton, the agenda is still "unfinished," Miller-Travis contended, because of several persistent challenges in ensuring equal opportunity before the law. Enforcement of environmental standards continues to be uneven, and people of color continue to be treated differently in such places as Dickson County, Tenn., when government officials are forced to take action against contaminated air and water, she maintained.

In response to a question from NIEHS Program Analyst Liam O'Fallon about the role of research in the EJ agenda, Miller-Travis acknowledged "the huge contribution that NIEHS and EPA have made in putting out the data." (Photo courtesy of Steve McCaw)

In addition, regulators are prohibited from considering the "big picture" when they rule on permits for hazardous waste and other environmentally impacting activities. Miller-Travis pointed to the siting of sewage treatment plants, like the one she has fought against in Harlem, and transit centers, the so-called "bus barns" that are major sources of diesel air pollution, in minority neighborhoods that already have waste sites.

Each permit is considered in isolation from pre-existing activities, she said. While the individual activity may not exceed air and water quality standards, the synergistic "mixture" of exposures from different activities may pose a significant threat to the health of residents. Harlem, for example, has the highest asthma rates in the world, and it is no coincidence, Miller-Travis argued, that Harlem is also the site of multiple environmentally impacting activities.

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Following her talk, Miller-Travis posed among wildflowers on the RTP campus with EPA EJ grantee Omega Wilson, center, and Lena Epps-Price, coordinator of the Environmental Justice Series at EPA. (Photo courtesy of Steve McCaw)

Working with the Media to Communicate Science

By Robin Mackar

The NIEHS Office of Communications and Public Liaison (OCPL) recognizes the important role that the media can play in helping NIEHS communicate its research to the American public. For this reason, much of late September and October was dedicated to media training and media outreach efforts.

On September 29 - 30, fifteen scientists from various divisions of the Institute, including NTP, DERT and DIR participated in one of three half-day personalized media training sessions. The sessions were held on the main campus of the NIEHS facility and were led by two communication coaches from The Communication Center, a Washington, D.C.-based company known for its expertise in training NIH scientists.

Thayer, above, was one of the scientists who participated in the interviews. "Certainly there were moments when I squirmed at my performance, especially during the video playback," she remarked, "but I now have a better sense of what I should do to increase the effectiveness and clarity of my communications with the press." (Photo courtesy of John Maruca)

"We really work to tailor the media training to meet the needs of our busy scientists," said Christine Flowers, OCPL Director. The training supported by OCPL and NTP included an overview on message development, tips on communicating complex information so it is clear, concise and quotable, delivery skills and providing scientists the confidence they need to maintain control of a media interview. Each participant was provided an on-camera opportunity to answer questions about their area of expertise.

Given that the majority of the NIEHS interview requests are phone interviews with print reporters, the training focused heavily on preparing scientists for print interviews. Each of the three sessions included an individual who participated in a pre-interview by phone with a reporter from The Communication Center. A newspaper article was developed based on each interview and brought to the training session. Participants read the stories and then a debriefing occurred, with the individual print reporter participating via telephone, giving the participants an opportunity to find out why specific quotes, headlines and details were selected for the story.

Flowers said she was pleased with comments by participants. NTP scientist Kristina Thayer, Ph.D., for example, described the media training as "very instructive and useful," and colleague Michelle Hooth, Ph.D., said, "I learned some good practical tips."

"This was the one training session where I actually came away with the feeling that I was given really good practical information," wrote one participant on the training evaluation form — giving Flowers and her staff added incentive to work toward providing additional training opportunities in the future to help scientists communicate their findings more effectively.

Annual Conference

In mid-October, Flowers and OCPL News Director Robin Mackar headed to Roanoke, Va. to communicate with journalists themselves. There they participated in the 18th Annual Conference of the Society of Environmental Journalists, which was attended by more than 800 reporters. The OCPL staffers met with many of the reporters, disseminated information, and supported the efforts of Gwenn Collman, Ph.D., and Jerry Heindel, Ph.D., of DERT as they participated in several events.

Collman served on a panel titled "Does Environment Trump Genetics? Teasing out the Factors Affecting Women's Health." Collman also participated in a "beat" dinner with about a dozen reporters where she highlighted the NIEHS Partnerships for Environmental Public Health (PEPH) program.

Heindel participated in a panel moderated by a reporter from the *Milwaukee Journal Sentinel* that focused on endocrine disruptors and toxicology. Heindel also talked to reporters during a lunch session on how to communicate information about epigenetics to the general public. *EHP* Editor Susan Booker also attended the conference.

"It was wonderful to see so many journalists from across the country, both free lance and those associated with newspapers and magazines, interested in the environment," Heindel said afterwards. "These people are really doing a great job of getting the word out about the importance of environmental exposures and diseases. They are helping us do our job."

(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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Science Notebook

Distinguished Lecture on Biology of DNA

By Robin Arnette

Many scientists have uncovered the mechanisms involved in DNA replication, repair and recombination. One of those researchers, Tom Ellenberger, D.V.M., Ph.D., visited NIEHS recently and gave a seminar that focused on his contribution to this body of knowledge. The presentation, titled "Structural Biology of DNA End Joining," took place at Rodbell Auditorium on October 14. Kasia Bebenek, Ph.D., a staff scientist in the Laboratory of Molecular Genetics, hosted the talk.

Ellenberger found some comic relief during his explanation of the ways ligases perform their crucial roles in DNA repair. (Photo courtesy of Steve McCaw)

Ellenberger is a Wittcoff Professor and head of the Department of Biochemistry and Molecular Biophysics at Washington University School of Medicine in St. Louis. His work provides a foundation for understanding how mutations affecting the proteins that are involved in these processes cause chromosomal instability and disease.

Ellenberger is particularly interested in why mammalian cells have three different families of DNA ligases — enzymes that join two DNA molecules together in an energy-dependent process — and what contributes to the biological specificities of those enzymes. Before Ellenberger delved into his research, he gave a brief overview of ligases and why they were important.

Bebenek introduced Ellenberger and monitored the questions from her colleagues in the Laboratory of Molecular Genetics and other labs. (Photo courtesy of Steve McCaw)

He said that most DNA damage is repaired by cutting out the damaged segment of DNA — whether it was a single nucleotide in the case of base excision repair (BER) or a stretch of nucleotides surrounding the damaged region in the case of nucleotide excision repair (NER). During the repair process, polymerase fills in the gap and. once the damaged segment is removed, the ligase completes the ligation reaction. "Since ligases are central in all manner of DNA repair activities, they are crucial to the maintenance and stable transmission of genetic information from generation to generation," he explained.

According to Ellenberger, there are three families of mammalian ligases.

- **Ligase I** has the most abundant activity in replicating cells and was involved in the repair of Okazaki fragments, short pieces of lagging strand DNA, that were generated during replication.

- **Ligase IV**, involved in a double-strand break repair pathway known as non-homologous end joining (NHEJ), has the ability to "paste" together two ends of broken DNA. It also plays a role in the immune system.

- **Ligase III** is a repair enzyme with some overlap activity with the other two mammalian ligases.

Postdoctoral fellow Raj Gosavi, Ph.D., followed the talk closely. Gosavi works in the Structure and Function Research Group, which is also known as the Collaborative Crystallography Group. (Photo courtesy of Steve McCaw)

"Ligases I and III are essential as they are required for mammalian development and the long-term viability of cells," Ellenberger said. "One reason why ligase III may be so important is it is the only identified ligase in mammalian mitochondria."

Ellenberger predicted that ligase I and ligase III were structurally similar, except for a unique zinc finger ligase III that had been previously described as a "DNA nick sensor." Biochemical and x-ray crystallographic studies of ligase III demonstrated that the enzyme had two separate DNA binding domains and was highly efficient at ligating together two DNAs, consistent with genetic studies showing that ligase III was involved in an alternative pathway of DNA double strand break repair.

Dmitry Gordenin, Ph.D., lead author of a new paper on the consequences of DNA double-strand breaks, was ready with a question for the speaker. Gordenin is a staff scientist in the Chromosome Stability Group. (Photo courtesy of Steve McCaw)

By constructing a structural database of DNA ligases bound to their substrates and crystal data from ligase III, Ellenberger's group inferred the types of motions that occurred in ligase III during the various steps of the ligation reaction. Ligase III had two separate nick-binding moieties, one at the amino-terminus and the other at the carboxyl-terminus. These two sites acted in sequence to repair the DNA. He said, "This turned into the jack-knife model, which says it's a series of flexible hinges that open and close in different ways during the course of recognizing the nick and catalyzing DNA end joining."

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GEMS Meeting Highlights Inflammation in Cancer

By Eddy Ball

Members of the Genetics and Environmental Mutagenesis Society (GEMS) gathered in the Radisson Hotel in RTP for the group's 26th annual Fall Meeting on October 6. True to tradition, the meeting featured talks by senior investigators on a topic of growing interest to biomedical researchers — the role of inflammation in tumor initiation and progression. There were also eight poster presentations and five submitted talks by talented students, trainees and junior investigators competing for awards (see text box).

Enjoying the high point of the event, Ross, left, and McGee, right, posed with Best Oral Presentation winner Jacquelyn Bower. GEMS devotes more than half of its annual fall meeting to showcasing the accomplishments of young scientists. (Photo courtesy of Steve McCaw)

The meeting opened with introductory remarks by GEMS President Rose Anne McGee, an NIEHS associate scientific review officer. The agenda was organized sequentially around the theme of "Inflammation in Cancer," moving from basic research into mechanisms of initiation and progression of cancer to a meta-analysis of studies of anti-inflammatory drug use in humans as a preventive strategy.

Moderating the meeting was GEMS President-Elect Jeffrey Ross, Ph.D., a molecular biologist and acting laboratory division director with the Environmental Protection Agency (EPA). Ross began his overview of the talks by observing that investigation into the link between inflammation and cancer has what he called "some history."

Samson's talk inspired several questions from people in the audience who were intrigued by the differing responses of target organs she observed in her experiments with transgenic and knock-out mice. (Photo courtesy of Steve McCaw)

Ross explained that speculation about the role of inflammation in cancer can be traced back as far as 1863 to the work of German pathologist Rudolph Virchow, M.D. However, Ross said, "there's really been a resurgence of interest in this field recently" with a steady growth of citations in the literature. He pointed to the more than 900 papers published in the first nine months of 2008 alone.

The first talk of the meeting featured NIEHS grantee Leona Samson, Ph.D., an American Cancer Society Research Professor and director of the Center for Environmental Health Sciences at the Massachusetts Institute of Technology. Samson discussed the ways "DNA damage induced by chronic inflammation contributes to carcinogenesis" by initiating the biological changes that ultimately lead to tumor development.

Using cell lines as well as transgenic and knock-out mice with altered DNA repair capabilities, Samson studies how exposures to alkylating agents, both exogenous and endogenous, such as the nitrosylation of amines and lipid peroxidation, and chronic conditions, such as obesity, can trigger an inflammatory cascade. Alkylating agents produce reactive oxygen and nitrogen species (RONS) that can, in turn, damage DNA, interfere with base excision repair and alter the expression of a host of genes implicated in cancer initiation and progression.

Following Samson, Elaine Lin, Ph.D., assistant professor in the Department of Medicine (Oncology) at the Albert Einstein College of Medicine of Yeshiva University, explored "The role of macrophages in tumor progression to malignancy." Lin's research has found that macrophages may manipulate the host immune system in such a way that it favors the survival and metastasis of the tumor.

Working with a mouse model of breast cancer, Lin has investigated several processes involved in what is known as the angiogenic switch — the mechanism that controls development of a vascular network in tumors — a crucial step for the transition of the tumor to malignancy. She has determined that blocking the essential factors that recruit macrophages to benign tumors can impair progression to malignancy.

Walkes explains the work behind his award-winning poster presentation to fellow attendees. (Photo courtesy of Steve McCaw)

Supporting Young Scientists

In her opening remarks, GEMS President Rose Anne McGee welcomed attendees and acknowledged the many sponsors of the meeting. McGee expressed her special gratitude to NIEHS for its "continued and generous support of GEMS," which "has helped make possible the more than $50,000 in travel grants GEMS has awarded over the past 25 years to encourage young scientists."

Winners typically use their grants for attending professional meetings they might otherwise have been unable to afford. The GEMS competition gives students and trainees from colleges in North Carolina, NIEHS and EPA an affordable opportunity to fine-tune their presentation skills, network with senior investigators and peers, and learn more about new trends in biomedical research.

Winners at the 2008 GEMS Fall Meeting reported on their ongoing research at Wake Forest University (WFU), North Carolina Agricultural and Technical State University (NC A&T), and the University of North Carolina (UNC):

Best Poster Presentation Awards ($250 each):

- Yu Cheng, lead author of "Genetic and epigenetic inactivation of TNFRSF10C gene in human prostate cancer." Cheng is a doctoral student in the WFU Molecular Genetics and Genomics program.

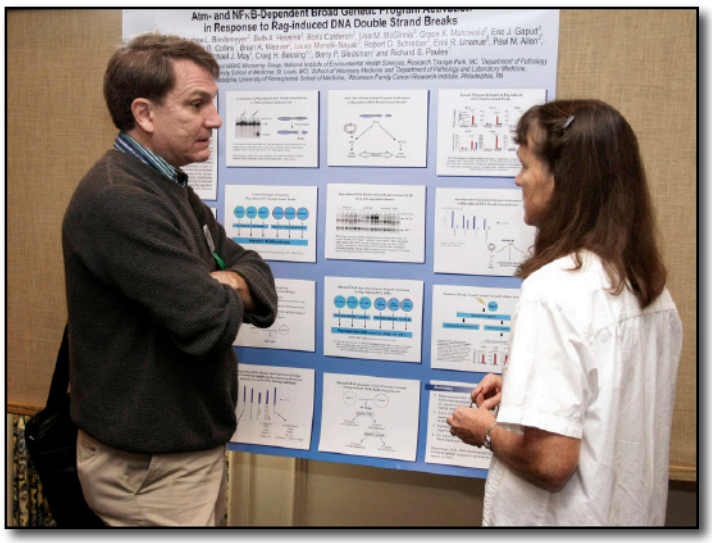
- Christopher Walkes, lead author of "Role of p38 in diepoxybutane-induced apoptosis in human lymphoblasts." Walkes is a master's student in the Department of Biology at NC A&T.

Best Oral Presentation Award ($1,500): Jacquelyn Bower, lead author of "ATM and topoisomerase IIα are required for the maintenance of chromosomal integrity through G2/M decatenation checkpoint signaling." Bower is a postdoctoral fellow in the Department of Pathology and Laboratory Medicine at the UNC Lineberger Comprehensive Cancer Center working with NIEHS grantee William Kaufmann, Ph.D.

The meeting's final invited speaker was Duke University epidemiologist and associate professor in the Department of Community and Family Medicine Patricia Moorman, Ph.D., whose talk was titled "Non-steroidal anti-inflammatory drugs (NSAIDs) as chemopreventives for cancer: Are they ready for prime time?" Moorman presented a meta-analysis of cohort and case control studies on the effects of NSAIDS in humans.

Despite promising results in animal studies, Moorman was guarded in her own conclusions from the review of human studies. She warned of the potentially serious side effects of NSAID use as well as the inherent weaknesses of population studies, which rely almost exclusively on self reporting for their data and are capable of establishing correlations but not direct causation. Moorman feels that considerably more study is needed to determine whether the regular use of NSAIDs can be effective in reducing the risk of developing cancer.

GEMS members mingled as they viewed posters. Shown here are Membership Coordinator Carolyn Harris, left, and NTP Biologist Diane Spencer, a member for 26 years and former GEMS president. (Photo courtesy of Steve McCaw)



NIEHS Health Science Administrator Dan Shaughnessy, Ph.D., left, talks with Biologist Cindy Innes about her research with the Environmental Stress and Cancer Group and Microarray Group at NIEHS. (Photo courtesy of Steve McCaw)

The seriousness of her topic, hepatocellular carcinoma, didn't stop NC A&T Biology Professor Minnie Holmes-McNary, Ph.D., from enjoying one of the lighter moments of her presentation. (Photo courtesy of Steve McCaw)

Moorman took questions following her talk, the final one of the day. Afterwards, Ross announced the winners of the poster and oral presentation awards. (Photo courtesy of Steve McCaw)

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Air Pollution Linked to Cognitive Deficits and Brain Abnormalities

By Shweta Trivedi

A new NIEHS-funded study available online from the journal *Brain and Cognition* offers compelling evidence of the significant effects of ambient air pollution on structural alterations in brain and cognitive deficiencies in healthy children and dogs from two Mexican cities. According to an editorial that will accompany the manuscript's publication later this year, the study provides additional support for the hypothesis that "the effects of air pollution go well beyond the expected pulmonary and cardiovascular implications… [and] have serious mental health and neurodevelopmental implications for children."

Calderón-Garcidueñas wrote that the study offers "encouragement that future, large-scale work in this area has great potential to give much-needed answers." (Photo courtesy of Lilian Calderón-Garcidueñas)

The trans-disciplinary team of investigators led by University of Montana pediatrician and neuroscientist Lilian Calderón-Garcidueñas, M.D., Ph.D., included specialists in psychiatry, psychology, radiology, toxicology, education and biostatistics. Among the contributing authors is former NIEHS/NTP Principal Investigator Robert Maronpot, D.V.M., who served as the veterinary pathologist on the study.

The study builds on previous work by Calderón-Garcidueñas and others showing that children exposed to high levels of air pollution experience chronic respiratory tract inflammation, changes in inflammatory mediators in blood and changes in brain tissue (see text box). She and her colleagues have also established in past studies that dogs can serve as a model for the health effects of air pollution in humans since they show similar patterns of neuroinflammation in response to inhaled particulate matter (PM).

Maronpot is a board-certified veterinary pathologist and toxicologist who has designed, conducted, and evaluated animal carcinogenesis studies for 40 years, including 26 years at NIEHS/NTP. (Photo courtesy of Steve McCaw)

The study was conducted with 55 children and 14 dogs in Mexico City, where residents are chronically exposed to high levels of ozone, PM and xenotoxic lipopolysaccharides associated with PM. The study used 18 children from the city of Polotitlán and 7 dogs from the city of Tlaxcala as controls.

Unlike Mexico City, the control cities have levels of air pollution that are within the current U.S. National Ambient Air Quality Standards. Children were matched in terms of age, health status and socio-economic status in an attempt to isolate air pollution as the variable responsible for outcomes. Dogs were age matched and raised in similar kennel conditions. Work in Mexico was coordinated through the Instituto Nacional de Pediatria in Mexico City, where Calderón-Garcidueñas holds an adjunct appointment.

The team of investigators assessed cognitive performance of the children with the Wechsler Intelligence Scale for Children-Revised (WISC-R) and structural changes in their brains with Magnetic Resonance Imaging (MRI). They also genotyped the children's blood samples for Apolipoprotein E (APOE) and Toll-like receptor 4 TLR4) polymorphisms.

With the canine studies, the investigators used the same protocol for scanning as they did for the children's studies. Following euthanasia, canine brain tissues were examined for cyclooxygenase-2 (COX-2), glial fibrillary acidic protein (GFAP) and Zonula occludens-1 (ZO-1) localization via histopathology. Subsequently, COX-2, IL-1β and CD14 mRNA were quantitated by real-time PCR.

Even after accounting for age differences among the subjects and controls, children from Mexico City received lower scores in terms of "performance age" than the children from Polotitlán on three important aspects of intelligence tested by the WISC-R — fluid cognition, memory and executive function. MRI tests showed that 56.5% of Mexico City children had evidence of hyperintense white matter prefrontal lesions compared to only 7.6% of the children from Polotitlán.

Because of the detrimental effects of air pollution on cognition and development manifest in the children and dogs from Mexico City, Engle emphasized, "Our findings have serious implications for public policy." (Photo courtesy of the Georgia Institute of Technology)

Gold Standard Evidence of Pre-clinical Neurodegeneration

In February of this year, Calderón-Garcidueñas and collaborators in Mexico City and the United States published a study in the journal *Toxicologic Pathology* that reported findings from 47 autopsies of clinically healthy, cognitively and neurologically intact children and adults who had died suddenly. Results indicated that lifelong exposure to high levels of pollutants was associated with neuroinflammation, altered immune response, ultrafine particulate deposition and disruption of the blood-brain barrier — along with an advanced rate of protein fibrillation and deposits of amyloid ß-42 and α-synuclein in the brains of children and young adults.

The cohort of 35 exposed subjects was comprised of residents of heavily polluted Mexico City. The 12 subjects in the control cohort were residents of two cities with lower levels of pollution, Tlaxcala and Vera Cruz. The subjects ranged in age from two to 45 years, with an average age of 25 ± 1.5 years. The researchers examined full histories and cause of death to exclude as much as possible pre-existing medical or lifestyle factors or causes of death that would confound results. Each of the 47 subjects was given a complete autopsy and tested for markers of inflammation and immune response.

The differences between the two groups led the researchers to speculate on the connection between pollution-induced neuroinflammation and the development of later-onset neurodegenerative disease. "We strongly propose that neuroinflammation as a result of exposure to air pollution could have a causative role in both Alzheimer's and Parkinson's diseases and that sustained brain inflammation confers a higher risk for the development of these two frequent neurodegenerative disorders."

The investigators found evidence of neuroinflammation and vascular lesions in canine brains from Mexico City. Canine MRI results were comparable to results for children, suggesting that the children were experiencing similar damage to their brains. The inflammatory markers COX-2 and IL-1β were also up-regulated in canine brain tissue pointing to the role of free-radical associated cell damage and modulation of cerebral function during neuroinflammation.

Senior author Randall Engle, Ph.D., professor and chair of the School of Psychology at the Georgia Institute of Technology, explained that "differences in cognition of the type measured in this study predict school performance, complex learning, ability to control attention and avoid distraction, reading and listening comprehension, reasoning, and the ability to block impulsive anti-social behavior."

Citation: Calderón-Garcidueñas L, Mora-Tiscareño A, Ontiveros E, Gómez-Garza G, Barragán-Mejía G, Broadway J, Chapman S, Valencia-Salazar G, Jewells V, Maronpot RR, Henríquez-Roldán C, Pérez-Guillé B, Torres-Jardón R, Herrit L, Brooks D, Osnaya-Brizuela N, Monroy ME, González-Maciel A, Reynoso-Robles R, Villarreal-Calderon R, Solt AC, Engle RW. 2008. Air pollution, cognitive deficits and brain abnormalities: A pilot study with children and dogs. Brain Cogn [Epub ahead of print], doi:10.1016/j.bandc.2008.04.008

(Shweta Trivedi, Ph.D., is a postdoctoral fellow in the Laboratory of Respiratory Biology Environmental Genetics Group)

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Vitamin D Insufficiency Common in Parkinson's Patients

By Brian Chorley

A team of investigators at the Emory University School of Medicine, funded by an NIEHS grant and grants from other NIH institutes, recently reported that a significant portion of Parkinson's patients suffer from vitamin D insufficiency. Their findings were published in the October issue of *Archives of Neurology*. Marian Evatt, M.D., assistant professor of Neurology at Emory and assistant director of the Movement Disorders Program at Wesley Woods Geriatric Hospital, was first author of the paper.

Neurologist and lead author Marian Evatt (Photo courtesy of Emory University)

Parkinson's disease is a neurodegenerative disorder in which substantia nigra, the locus of dopamine-producing nerve cells in the brain, dies or becomes impaired. Dopamine shortage causes difficulty with muscle coordination and control, the hallmark symptoms of Parkinson's disease. Approximately 1.5 million Americans are affected by this disease.

In this study, *insufficiency* was defined as 30 nanograms or less of the storage form of vitamin D, 25-hydroxyvitamin D, per milliliter of blood. *Deficiency* was defined as 20 nanograms per milliliter or less. The researchers reported that 55 percent of a Parkinson's cohort exhibited vitamin D insufficiency.

Insufficiency was noted in only 36 percent of healthy subjects, a significantly lower percentage. In addition, 23 per cent of the Parkinson's patients exhibited vitamin D deficiency, compared to 10 percent in the control group.

Vitamin D, a fat soluble pro-hormone, has been linked to maintaining physiologic function as well as preventing diseases, such as bone, cardiovascular, autoimmune and, notably, neurologic disorders. Synthesis occurs in the skin with UV-B radiation exposure, primarily from sunlight. Diet, such as fortified foods and certain fish, can also provide minor amounts of vitamin D. Deficiency can result from inadequate sun exposure, metabolism or absorption disorders, and other genetically influenced factors.

The researchers recognized that patients with chronic neurodegenerative disease commonly exhibited risk factors for vitamin D insufficiency, including advanced age, obesity and decreased sun exposure. The study limited potentially confounding effects of these factors by selecting individuals who resided in sunny southern locales, had paler complexion and were being treated in an outpatient clinic — making them more likely to have increased UV-B exposure.

Additionally, age was not a criteria inclusion, thereby minimizing age-related confounding effects. Intriguingly, Parkinson's patients were also more likely to exhibit vitamin D insufficiency than patients with another neurodegenerative disorder, Alzheimer's disease, 55 percent versus 41 percent. Although Evatt and colleagues suggested that a potential reason for this difference may be due to increased mobility issues more common in Parkinson's patients, they did not see a correlation between 25-hydroxyvitamin D insufficiency and symptom duration in either group. The investigators suggest that this phenomenon may therefore be unique to Parkinson's disease.

This study adds to the growing body of evidence in support of the notion that vitamin D deficiency may contribute to the pathogenesis of Parkinson's. Vitamin D regulates multiple cellular processes known to be abnormal in Parkinson's disease, including cellular differentiation, proliferation and apoptosis. Additionally, vitamin D receptor and activating enzyme are enriched in hippocampal and substantia nigra cells in the brain, problematic regions in Parkinson's patients. Evatt and her colleagues at Emory are currently researching the role of vitamin D in Parkinson's development and progression, as well as the therapeutic potential of vitamin D supplementation.

These findings could have immediate clinical implications. Potential risk of bone disorder, cancer and autoimmune diseases, such as diabetes mellitus, are associated with vitamin D deficiency. Evatt suggests that Parkinson's patients should be checked more regularly for low 25-hydroxyvitamin D levels as a strategy for minimizing further complications of an already debilitating neurodegenerative disease.

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.

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

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Study Finds Elevated PBDEs in California

By Eddy Ball

Investigators funded by an NIEHS Environmental Justice Program grant report high levels of polybrominated diphenyl ethers (PBDEs), ubiquitous compounds used as a fire retardant in furniture, in the house dust and serum of people living in California. Serum levels of the compound penta-BDE in residents of California were twice the national average. House dust levels in California ranged from 4 to 10 times levels found in homes in other parts of the United States — and 200 times levels reported in Germany.

Published online October 1 by *Environmental Science and Technology*, the study was a collaboration involving researchers at the Silent Spring Institute, the University of California Berkeley, Brown University and Communities for a Better Environment, a California-based environmental justice group. In addition to NIEHS financial support, which is overseen by NIEHS Program Analyst Liam O'Fallon, the study also received funding from the New York Community Trust.

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RESEARCHING THE ENVIRONMENT AND WOMEN'S HEALTH

Animal studies have demonstrated that PBDEs are associated with thyroid hormone disruption and adverse reproductive and neurodevelopmental effects. According to an Environmental Protection Agency review published earlier this year, the primary route of exposure is incidental ingestion and dermal contact with house dust, which raises special concerns about exposures in infants and toddlers.

Lead author Ami Zota (Photo courtesy of Ami Zota)

Although PBDEs have been banned by the European Union and 11 states in the U.S. — and U.S. manufacturers discontinued production of PBDEs in 2004 — the scientists maintain that a substantial exposure reservoir remains in the environment. Older furniture continues to be an important source of exposure, and imported furniture containing PBDEs is still sold in many states. California's levels may be higher, the authors of the study speculate, because of the state's stringent furniture flammability standards adopted more than 30 years ago and the potentially harmful substitutes for PBDEs now in use or proposed.

"Virtually all the penta-BDE produced globally was used to meet this [California] fire standard," explained lead author and Silent Spring Postdoctoral Research Fellow Ami Zota, ScD, "and now these chemicals have been detected in nearly every species across the globe."

The study, led by scientists from the Silent Spring Institute, compared the concentrations in dust collected in 49 California homes with concentrations in dust collected under the same protocol from 120 homes in Massachusetts. The researchers also compared concentrations in their studies to reports by other investigators. The study used data from the 2003-2004 National Health and Nutrition Examination Survey (NHANES) to compare serum levels of PBDEs in residents of California with those in participants living elsewhere in the U.S.

Although the study's authors acknowledged several limitations to the study, they argued that the ubiquity and persistence of the PDBE exposure reservoir should be a lesson for regulators. "These findings suggest the need for more anticipatory assessments of the environmental health impacts of consumer product decisions [about other untested flame retardants] prior to their implementation," they concluded.

The researchers also called on NHANES to reinstate its earlier practice of measuring thyroid hormone so that direct correlations between PBDE and thyroid can be made for humans participating in that large-scale annual survey.

Citation: Zota AR, Rudel RA, Morello-Frosch RA, Brody JG. 2008. Elevated house dust and serum concentrations of PBDEs in California: Unintended consequences of furniture flammability standards? Environ Sci Technol [Epub ahead of print] doi: 10.1021/es801792z

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Healing Process Found to Backfire in Lung Patients

By Robin Mackar

A mechanism in the body that typically helps a person heal from an injury may actually be causing patients with idiopathic pulmonary fibrosis (IPF) to get worse, researchers at NIEHS and their collaborators have found.

Lead author Stavros Garantziotis (Photo courtesy of Steve McCaw)

"We identified a new mechanism that explains why some patients with IPF get more short of breath than others, in spite of similar levels of lung scarring," said Stavros Garantziotis, M.D., an NIEHS staff clinician and lead author on the new paper highlighted on the cover of the November 1 issue of the *American Journal of Respiratory and Critical Care Medicine*.

Idiopathic pulmonary fibrosis is an incurable lung disease that affects approximately 50,000 people in the United States. In IPF, the lung tissue becomes scarred and patients have difficulty breathing, often resulting in death. The cause is unknown, though genes as well as environmental factors, such as smoking and exposure to metal dust particles, are thought to raise the risk.

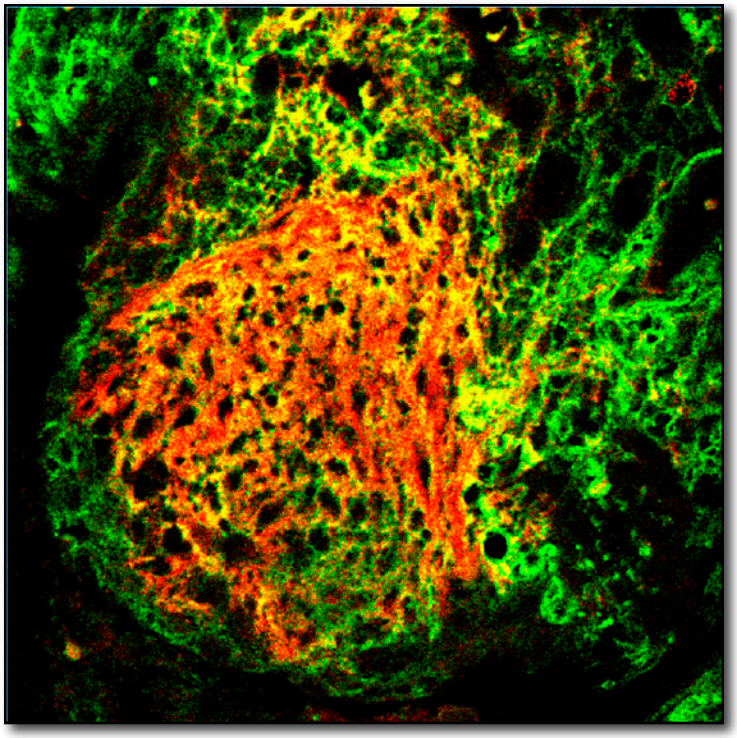
In healthy individuals, the body has a way of forming new blood vessels that can help heal an injury. For example, if you cut your finger, the body knows to deliver nutrients and cells to the injury site to promote wound healing. However, in patients with IPF, although there is a healing process that occurs, the researchers said the process backfires or is disrupted and may be doing the patients more harm than good. Garantziotis explained that this involves a blood protein called inter-alpha-trypsin inhibitor (IaI), which binds with a connective tissue molecule called hyaluronan to make new blood vessels.

In people without IPF, this produces a healing process in the lungs. But Garantziotis said something different happens in people with IPF.

"Instead of building healthy new tissue to heal the scarring in the lungs, patients with higher IaI levels develop vessels that are far away from where they should be, pushing the blood away from the lung and bypassing the area where the body gets its oxygen, thus causing more shortness of breath," Garantziotis explained. Patients with IPF may suffer from low oxygen levels and shortness of breath beyond the actual effects of lung scarring itself.

The researchers applied a true bench-to-bedside approach for this study. Starting with basic research findings from in vitro cell and experimental animal studies, they were then able to demonstrate, in patients with IPF, that higher IaI serum levels were associated with less ability to take up oxygen, thus worsening the patients' condition.

The researchers say there are at least two reasons why this study is important. First, it demonstrates for the first time the important role that a blood circulating protein plays in lung function. Secondly, it identifies a potential new therapeutic target for IPF.



The cover of the November 1 issue of the ***American Journal of Respiratory and Critical Care Medicine*** *features a photo of a fibroblastic focus (area of scarring) in a lung of a patient with pulmonary fibrosis stained for inter-alpha-trypsin inhibitor (red) and hyaluronan (green). Areas where the two molecules co-localize are stained yellow. (Photo courtesy of Stavros Garantziotis)*

In addition to the NIEHS, other collaborators on the paper include scientists affiliated with the Angiogenesis Core Facility, National Cancer Institute, Gaithersburg, Md.; Duke University Medical Center, Durham, N.C.; Vanderbilt University Medical Center, Nashville, Tenn.; Institute for Molecular Science of Medicine, Aichi Medical University, Aichi, Japan; National Jewish Medical and Research Center, Denver; and the National Heart, Lung, and Blood Institute, Bethesda, Md.

Citation: Garantziotis S, Zudaire E, Trempus CS, Hollingsworth JW, Jiang D, Lancaster LH, Richardson E, Zhuo L, Cuttitta F, Brown KK, Noble PW, Kimata K, Schwartz DA. 2008. Serum Inter-{alpha}-Trypsin Inhibitor and Matrix Hyaluronan Promote Angiogenesis in Fibrotic Lung Injury. Am J Respir Crit Care Med 178(9):939-947.

(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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Superfund Study Detects PCB11 in Ambient Air

By Melissa Fabiano

A new year-long study conducted by researchers at the University of Iowa (UI) Superfund Basic Research Program (SBRP) reports finding unexpectedly high levels of polychlorinated biphenyls (PCBs), particularly PCB11 (3,3'-dichlorobiphenyl), pervasive in Chicago's urban air. Keri Hornbuckle, Ph.D., professor of Civil and Environmental Engineering at UI and research engineer for IIHR-Hydroscience and Engineering, led the study with funding provided by NIEHS.

PCB production ceased in the 1970s due to the high toxicity of most PCB congeners and mixtures. PCBs are classified as persistent organic pollutants which bioaccumulate in animals.

"It has been assumed that PCBs would eventually be virtually eliminated," Hornbuckle explained, "[but] PCB11 is ubiquitous in air throughout the city of Chicago. We do not know if there are any health concerns associated with this [specific form of the] compound, but there are very few published studies of its toxic properties."

The study was posted online September 24 and will be published in an upcoming issue of *Environmental Science and Technology*. To the best of her knowledge, Hornbuckle explained, this "is the first published report on PCB11 in ambient air."

The air sampling was carried out in collaboration with Chicago's Mobile C.A.R.E. Foundation. This non-profit organization, which is dedicated to providing free asthma care and education to children in underserved areas of the city, allowed Hornbuckle's team to install high volume air sampling equipment on two health clinic vans. The equipment collected air samples at more than 37 sites in Chicago while C.A.R.E. staff provided health services to help diagnose and treat respiratory illnesses of elementary students and families.

Air samples were analyzed to determine the presence of any of the 209 PCB congeners or derivatives. Of the 184 samples collected, 91 percent contained PCB11. It is particularly interesting that, in some air samples, PCB11 comprised up to 15 percent of the total PCBs measured, raising concerns that there could be multiple current sources of the compound.

The PCB11 congener was found throughout Chicago's residential areas. Previous reports of PCB11 in wastewater effluent from pigment manufacturing suggest that the compound is either an historical or current component of consumer paint products. No confirmed source of PCB11 was identified.

Lead author Keri Hornbuckle, left in green sweater, discussed the equipment installation with van driver Roger Peck while UI graduate student Andres Martinez, foreground, enters data. (Photo courtesy of Keri Hornbuckle and Tim Schon online album)

Hornbuckle and Martinez checked the equipment before the van made one of its collection runs in Chicago neighborhoods. (Photo courtesy of Keri Hornbuckle and Tim Schon online album)

PCBs are manufactured chemicals. From the 1920-70s, the Monsanto Chemical Company manufactured and marketed PCB mixtures known as Aroclors. PCB11 is not a dominant component of Aroclor, but may be a byproduct of the degradation of paint, resins and pigments, such as diarylide yellow. In addition to PCB11 being widely distributed in Chicago's air, the congener has also been detected in the wastewater effluent and sediment samples collected downstream from industrial runoff.

PCB11 is one of the more volatile PCBs and, as a result, inhalation may be an important route for human exposure. For example, as Hornbuckle explained, if PCB11 is "present in interior paints, then indoor concentrations may be much higher" than reported in outdoor air. Hornbuckle concluded that further study is necessary because there is a possibility that "PCB11 is present not only in Chicago, but in air elsewhere and also in fish, soil, water, food and humans."

Citation: Hu D, Martinez A, Hornbuckle KC. 2008. Discovery of Non-Aroclor PCB (3,3′-Dichlorobiphenyl) in Chicago Air. Environ. Sci. Technol [Epub ahead of print] 10.1021/es801823r.

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

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Extramural Update

NIEHS Expands Role in CounterAct Program

As part of its role in the NIH Countermeasures Against Chemical Threats (CounterACT) program, NIEHS will provide oversight of one new Research Center of Excellence at the University of Alabama at Birmingham (UAB) and one project at Duke University created this summer to develop therapeutics for chlorine-induced pulmonary damage. These awards augment the existing NIEHS portfolio within the NIH CounterACT program to develop therapeutics for lung injury induced by chemical threats such as chlorine, sulfur mustard, sarin, phosgene and acrolein.

Sadis Matalon, Ph.D., a professor and the director of research in the Division of Critical Care and Perioperative Medicine at the UAB School of Medicine, will direct the Center. The Center represents a collaboration between UAB and Yale University in New Haven, Conn.

Duke University Professor Michael Gunn, M.D., is the principal investigator of the newly awarded research project, titled "Prevention of Inflammatory Lung Injury after Chlorine Exposure." Gunn is director of the Laboratory of Dendritic Cell Biology in the Duke Human Vaccine Institute.

As a result of solicitations for proposals for the CounterAct Research Network in 2006, NIH funded four Centers of Excellence, 24 individual research projects, six Small Business Innovation Research (SBIR) awards, two contracts and four interagency agreements with Department of Defense (DoD) laboratories. NIH was able to add two more Centers and seven new individual research projects in 2008.

NIEHS provides oversight of those CounterACT awards that focus primarily on pulmonary injury including two Centers of Excellence and six individual research projects. These projects are developing therapeutic agents against sarin, sulfur mustard, chlorine, phosgene, diphosgene, triphosgene, ammonia, acrolein, half mustard, 2-chloroacetophenone and sulfuric acid. While DoD has had an ongoing research program related to chemical threats, its interests are restricted to military populations. The NIH research agenda, for its part, includes the demographic diversity of the nation's civilian population. Sharing of information and resources among CounterACT investigators is facilitated by scientific interest groups that communicate frequently, as well as by annual symposiums of the entire Network.

With the attacks on the United States in 2001, the growing threat of terrorism has become a national security priority. In response to both the terrorist attacks and the anthrax scare that followed six weeks later, DHHS, through many NIH partners, developed a research agenda focused on meeting the needs of the civilian population in the event of a biological, radiological or chemical attack on our nation. Many of the same chemicals posing a threat as terrorist agents may also be released from transportation and storage facilities because of industrial accidents or natural disasters.

In addition to NIEHS, the CounterAct Research Network includes the National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Neurological Disorders and Stroke (NINDS), National Eye Institute (NEI), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and National Institute of General Medical Sciences (NIGMS). The overall goal of the CounterACT program is the development of new and improved medical countermeasures designed to prevent, diagnose and treat the conditions caused by potential and existing chemical threat agents.

CounterAct – A Collaborative Research Agenda

The funding opportunity announcements establishing the Network identified four groups of high priority chemical threats:

- Neurotoxic agents, such as organophosphorus nerve "gases"
- Vesicating agents, for example sulfur and mustard
- Pulmonary agents, such as chlorine gas
- Metabolic/cellular poisons, such as cyanide

Proposed research projects fell into five categories:

- Mechanistic research to identify targets for therapeutic/diagnostic development
- Development of *in vitro* and animal models for efficacy screening of therapeutic and diagnostic tools
- Efficacy screening of therapeutics/diagnostics using appropriate new and validated *in vitro* and animal models
- Advanced efficacy studies with appropriate animal models including non-human primates
- Clinical studies, including trials, when appropriate.

For more information regarding the CounterACT Research Network, see: www.ninds.nih.gov/counteract.

Contacts:
NIEHS: Elizabeth A. Maull, Ph.D., program administrator
NINDS: David A. Jett, Ph.D., lead program director for the NIH CounterAct program

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Extramural Papers of the Month

By Jerry Phelps

Particulate Air Pollution Can Alter the Electrical Functioning in the Heart

New research findings from NIEHS grantees suggest that exposure to the fine particulate air pollution and black carbon particles generated in areas of heavy traffic can adversely effect the heart's ability to conduct electrical signals in people with pre-existing coronary artery disease. The study, conducted with 48 Boston-area heart patients, found changes in the ST-segment of the patient's electrocardiograms, possibly indicating inadequate blood flow to the heart or inflamed heart muscle — even when breathing air is not considered hazardous.

All the patients had undergone in-hospital procedures to examine or open blocked coronary arteries. The ST-segment changes observed in the study were asymptomatic, but the findings expand the evidence that air pollution can affect heart health, either through inflaming the heart muscle or through reducing blood flow to the heart. The heart effects were highest within the first month after hospitalization and for heart attack patients or those with diabetes.

This study provides additional rationale for avoiding or reducing heavy traffic exposure for people with heart conditions because of the potential exposure to elevated levels of air pollution particles. The study authors suggest additional research is necessary to determine whether the pollution-related ST-segment changes are due to increased heart inflammation, reduced blood flow, oxidative stress or increased risk of arrhythmias.

Citation: Chuang KJ, Coull BA, Zanobetti A, Suh H, Schwartz J, Stone PH, Litonjua A, Speizer FE, Gold DR. 2008. Particulate air pollution as a risk factor for ST-segment depression in patients with coronary artery disease. Circulation 118(13):1314-1320.

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Acetaminophen May Increase the Risk of Developing Asthma

A new epidemiologic study, supported by NIEHS and conducted with 345 pregnant women, adds to the growing evidence suggesting a causal link between the use of the non-steroidal anti-inflammatory drug acetaminophen and the rise in the incidence of asthma in children.

Acetaminophen became the drug of choice for pain and fever relief after the FDA ordered manufacturers to place a warning label on bottles about the link between aspirin use and Reyes syndrome in 1986. Afterwards, pediatricians nationwide started noticing a rise in asthma incidence, and some suspected a link to acetaminophen. Unlike aspirin and ibuprofen, acetaminophen decreases the level of the antioxidant glutathione in the lungs and other tissues.

For the study, women responded to a questionnaire related to respiratory outcomes in their newborns during their first year of life. Use of acetaminophen in the second and third trimesters was significantly related to wheezing in the first year, a known symptom of asthma in young children.

The researchers will continue to follow these children until they reach five years of age to determine more precise estimates of asthma incidence. The researchers point out that this is only the second study of its type and that the link needs further research.

Citation: Persky V, Piorkowski J, Hernandez E, Chavez N, Wagner-Cassanova C, Vergara C, Pelzel D, Enriquez R, Gutierrez S, Busso A. 2008. Prenatal exposure to acetaminophen and respiratory symptoms in the first year of life. Ann Allergy Asthma Immunol 101(3):271-278.

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Green Tea Polyphenol Combats Health Effects of High Fat Diet

Green tea, consumed widely in East Asian countries, contains caffeine and polyphenolic compounds known as catechins. The most common catechin compound in green tea is epigallocatechin-3-gallate (EGCG). EGCG has been suggested as the catechin responsible for the potential health benefits experienced with long-term consumption of green tea, a link supported by findings from a new NIEHS-funded study.

In the study, mice were fed a diet containing 60% of energy as fat for 16 weeks, at which point some mice were given EGCG for another 16 weeks. Mice treated with EGCG had lower body weights, decreased insulin resistance and lower plasma cholesterol than the untreated mice. EGCG treatment also decreased liver weight and liver triglycerides. Subsequent histological examination of liver tissue revealed decreased lipid accumulation in the liver cells of the treated mice. In another experiment, obese mice given four weeks of EGCG treatment also showed decreased body fat and blood glucose as compared to the untreated controls.

These results indicate that physiological relevant doses of EGCG treatment can mitigate the development of obesity, symptoms of metabolic syndrome and liver fat accumulation. The researchers conclude that these effects could be mediated by decreased fat absorption, decreased inflammation or other mechanisms.

Citation: Bose M, Lambert JD, Ju J, Reuhl KR, Shapses SA, Yang CS. 2008. The major green tea polyphenol, (-)-epigallocatechin-3-gallate, inhibits obesity, metabolic syndrome, and fatty liver disease in high-fat-fed mice. J Nutr 138(9):1677-1683.

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A Fruit Fly Model for Amyotrophic Lateral Sclerosis

A multi-university research team funded by NIEHS has developed a new laboratory model for studying the motor neuron disease amyotrophic lateral sclerosis (ALS). The researchers created a transgenic fruit fly that is able to express human copper, zinc-superoxide dismutase (SOD1), an antioxidant enzyme that has been implicated in the hereditary form of ALS.

ALS is a progressive and fatal neurodegenerative disease of the motor nervous system. It is characterized by the loss of muscle function caused by dysfunction and death of motor neurons throughout the body. About one-fifth of hereditary ALS cases are linked to mutations in the gene encoding for SOD1. Uncovering how mutations in the enzyme lead to the dysfunction and death of motor neurons could illuminate how ALS develops and progresses in patients with both sporadic and hereditary forms of the disease.

In experiments using the new model, the researchers found that expression of the enzyme in the flies induced neurological damage along with accumulation of the enzyme in motor neurons accompanied by a stress response in the surrounding glial cells. This work suggests that SOD1 can cause cell-autonomous damage to motor neurons. It also highlights the usefulness of the fruit fly model for studying ALS.

Citation: Watson MR, Lagow RD, Xu K, Zhang B, Bonini NM. 2008. A drosophila model for amyotrophic lateral sclerosis reveals motor neuron damage by human SOD1. J Biol Chem 283(36):24972-24981.

(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

Compact Fluorescent Light Bulbs Are Safe Substitutes for Standard Incandescent Bulbs

NIEHS scientists have determined that energy-saving compact fluorescent light (CFL) bulbs should not aggravate skin rashes in people with skin disorders, as an earlier report had claimed. The NIH-funded research suggests that CFL bulbs are safe* and can be substituted for standard incandescent bulbs.

A February 3, 2008 article in *Parade* magazine titled "Bright Lights, Bad Headache?" stated that CFLs "can aggravate skin rashes in people with lupus, eczema, dermatitis or porphyria." The research team addressed the concern by calculating the potential photosensitization indices of protoporphyrin IX — a typical porphyrin that is present in the skin of porphyria patients — and riboflavin — a putative lens phototoxin — versus a 14 W CFL bulb, a 60 W soft white incandescent (SWIL) bulb and two 40 W cool white fluorescent (CWF) bulbs. High values would have indicated a greater possibility for photosensitization of the skin or eyes. The results indicated that a 14 W CFL bulb, which is comparable to a 60 W SWIL bulb, actually had a photosensitization index that was half of that for a 60 W SWIL bulb.

The team also compared the emission spectra of the three types of bulbs. The results indicated that while all three bulbs emitted low UVB, only the CFL and CWL bulbs emitted UVA. In addition, both CFL and CWL bulbs displayed similar emission spectra values. Taken together, the findings suggest that CFL bulbs will not increase the phototoxicity of porphyrins or riboflavin and are safe for people with skin irritations.

*This safety assessment relates only to the quality of light regarding its photosensitizing potential and does not consider the presence of mercury in fluorescent light bulbs, which may create a safety problem during lamp breakage.

Citation: Chignell CF, Sik RH, Bilski PJ. 2008. The photosensitizing potential of compact fluorescent vs. incandescent light bulbs. Photochem Photobiol 84(5):1291-1293.

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Cadmium Produces Free Radicals in Rats

The environmental and industrial pollutant cadmium (Cd) induces the *in vivo* generation of free radicals in murine liver cells, according to researchers from NIEHS. This work is the first to demonstrate that Cd-induced radical formation is dependent on the activation of Kupffer cells, liver macrophages and iron-catalyzed reactions.

Prior to this study, numerous journal articles had indicated that metals like Cd affected signaling pathways and produced radicals that caused DNA damage, altered gene expression, apoptosis and the oxidation of lipids and proteins, but no direct evidence had been reported. The research team used electron spin resonance (ESR) spectroscopy to examine which adducts were produced in rats following the administration of cadmium chloride (CdCl2) and the spin trapping agent α-(4-pyridyl-1-oxide)-*N*-*tert*-butylnitrone (POBN).

Depletion of hepatic glutathione by diethyl maleate significantly increased free radical production, whereas inactivation of Kupffer cells by gadolinium chloride and chelation of iron by desferal inhibited it. Treatment with the xanthine oxidase inhibitor allopurinol, the catalase inhibitor aminobenzotriazole or the cytochrome P-450 inhibitor 3-amino-1, 2, 4-triazol had no effect. This is the first study to show Cd generation of reactive oxygen- and carbon-centered radical species by involvement of both iron mediation through iron-catalyzed reactions and activation of Kupffer cells, the resident liver macrophages.

Citation: Liu J, Qian SY, Guo Q, Jiang J, Waalkes MP, Mason RP, Kadiiska MB. 2008. Cadmium generates reactive oxygen- and carbon-centered radical species in rats: Insights from in vivo spin-trapping studies. Free Radic Biol Med 45(4):475-481.

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The Case-Mother/Control-Mother Design Is Statistically Enhanced If We Account for Family Relationships

In research to identify the roles of genetic variants in young-onset conditions like birth defects and schizophrenia, there are two genomes to consider: that of the child and that of the mother. Epidemiologists can use a case-mother/control-mother design, where affected offspring and their mothers are genotyped, along with a control group of healthy offspring and their mothers. One then treats the mother-offspring pairs as the unit of analysis. Investigators from NIEHS and Radboud University in the Netherlands have shown that the statistical power of analyses based on this design can be improved by using models that impose some natural assumptions.

The simplest assumption is that transmissions from parent to child follow Mendelian laws; applying this insight brings substantial gains in power. One can additionally assume genetic symmetry between the mother and father, which provides still more power. A third assumption, involving "allelic exchangeability," confers additional gains.

Although an extra individual must be genotyped for every case under a case-mother/control-mother design — with equal numbers of case and control pairs — compared with a case-parent-triad design, for some risk scenarios the imposition of assumptions based on the family relationships can render the case-mother/control-mother design more powerful than a case-parent triads design.

Citation: Shi M, Umbach DM, Vermeulen SH, Weinberg CR. 2008. Making the most of case-mother/control-mother studies. Am J Epidemiol 168(5):541-547.

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Double-Strand Breaks Can Reconfigure Genome

Researchers from NIEHS, Duke University and Universidade Estadual de Campinas in Brazil report that DNA double-strand breaks (DSBs) that occur in repetitive elements of the genome of the budding yeast *Saccharomyces cerevisiae* often result in chromosome aberrations (CAs) that can reconfigure the genome. The authors believe that this reshaping of an organism's genome may drive evolutionary change.

The investigators used ionizing radiation to induce ~250 DSBs per diploid G2 cell and found that although the vast majority of breaks were repaired efficiently and accurately by homologous recombination (HR) between sister chromatids, multiple CAs among survivor colonies were frequent. CAs were initially identified using pulsed-field gel electrophoresis and then analyzed using comparative genome hybridization (CGH) to identify the breakpoints of rearranged chromosomes. Nearly all of the CAs resulted from HR between nonallelic repetitive elements, mainly Ty retrotransposons.

This study provides a possible mechanism for disease-associated CAs that may arise in humans and lends credence to the theory that HR between repetitive DNA is a source of genomic variation in humans.

Citation: Argueso JL, Westemoreland J, Mieczkowski PA, Gawel M, Petes TD, Resnick MA. 2008. Double-strand breaks associated with repetitive DNA can reshape the genome. Proc Natl Acad Sci USA 105(33):11845-11850.

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Inside the Institute

Hispanic Heritage Talk Focuses on U.S.-Mexico Binational Programs

By Melissa Fabiano

On September 25 in Rodbell Auditorium, NIEHS Superfund Basic Research Program (SBRP) grantees Denise Moreno Ramírez and Monica Ramírez participated in the NIEHS Hispanic Heritage Month celebration with their joint presentation, "Toward an Informed Mexican and Mexican-American Citizenry." The talk was sponsored by the NIEHS Diversity Council Hispanic Heritage Committee and hosted by NIEHS Health Disparities Postdoctoral Fellow Rose Marie Ramos, Ph.D.

Like their work in Arizona and Mexico, Monica Ramírez, left, and Denise Moreno Ramírez presented their talk as a collaborative effort. Several times in the talk, as shown above, they shared the lighter side of their work. (Photo courtesy of Steve McCaw)

The speakers are affiliated with The University of Arizona (UA) SBRP Community Outreach (CO) and Research Translation (RT) Cores, where Moreno Ramírez serves as CO Core and U.S.-Mexico Binational Center for Environmental Sciences and Toxicology coordinator and Ramírez is RT Core coordinator. The two programs highlighted in their presentation were CampCIENCIAS, a prototype science education program with a focus on high school students who live on and near the U.S.-Mexico border, and an ongoing series of training sessions for community health advocates, known in their communities as promotoras.

Since its inception, the mission of the UA SBRP and U.S.-Mexico Binational Center, Ramírez explained, has been "to reduce the burden of human illness and dysfunction from environmental exposures." Moreno Ramírez and Ramírez foster the growth and development of UA's unique international outreach program that targets Mexican and Mexican-American communities in the southwestern U.S., U.S.-Mexico border region and Mexico itself.

In addition to CampCIENCIAS and promotoras training, the program's outreach efforts have included collaboration with:

- Academic institutions, such as the Universidad Nacional Autónoma de México (UNAM)
- Government agencies, including the U.S. EPA Arizona/Sonora Border 2012 Waste and Enforcement Task Force
- Local industries for remediation of mine tailing, hazardous waste landfills and other environmentally impacting activities
- Community citizens through specialized workshops and the distribution of educational literature in English and Spanish on environmental health topics

These programs are just a few of the Cores' outstanding efforts to bridge the gap between academia and citizens. As Moreno Ramírez explained, the fundamental belief she and her colleagues bring to their work is that "citizens are well equipped to change social, political and environmental conditions since they are more knowledgeable about their own community and, therefore, ought to be considered 'local experts' in their own right."

To help put this theory of "citizens as experts" into practice, the CO/RT Cores strive to educate Mexican and Mexican-American residents through a "circle" of action. The circle is divided into four quarters — training, community needs, science translation and engagement — that the speakers said must be addressed in unison as the basis for a successful CO/RT program.

Case studies presented by the UA CO/RT Cores demonstrated that the circle concept can yield important benefits in terms of planning future training, developing local and non-governmental organizations in Mexico, creating and utilizing bilingual materials, and engaging appropriate governmental and grass roots organizations.

Moreno Ramírez and Ramírez expressed their hope that the CO/RT Cores will continue to successfully impact the U.S.-Mexico border environment and people. They want the Cores to encourage academics and government agencies to involve citizens and institutions to a greater extent when tackling local environmental issues. Together, Moreno Ramírez and Ramírez envision the CO/RT Cores playing an even more pivotal role in UA SBRP in the future.

Following the talk, the speakers joined members of the audience and others at NIEHS for refreshments and entertainment (see related story).

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

NIEHS Diversity Council Vice-Chair Brad Collins welcomed the audience to the talk. Collins is a chemist in the Laboratory of Pharmacology Chemistry Group. (Photo courtesy of Steve McCaw)

Hispanic Heritage Committee member Trisha Castranio was one of several NIEHS staffers who came to the talk. Castranio is a chemist in the Molecular Developmental Biology Group headed by Principal Investigator Yuji Mishina, Ph.D. (Photo courtesy of Steve McCaw)

Lecture host Rose Ramos moderated the question and answer session following the talk. (Photo courtesy of Steve McCaw)

Hispanic Heritage Committee Chair Veronica Godfrey, left, presented the speakers with a poster for their presentation as a memento of their visit to NIEHS. Godfrey is a biologist with the NIEHS Chemistry Group. (Photo courtesy of Steve McCaw)

Employee Services Holds Science Manager/Leader Seminar

By Eddy Ball

According to NIEHS Manager of Employee Services Dona McNeill, competent scientists stand to benefit from specialized training in how to be competent managers and leaders in addition to top performers at the bench. That was the rationale behind a custom-designed seminar held September 22 in Rodbell Auditorium and September 23 in the Rall Building E-450 conference room. A group of ten current and aspiring managers (see text box) attended the two-part seminar for management tips and hands-on activities to help them communicate more effectively.

Working with a focus group made up of NIEHS Division of Intramural Research (DIR) scientists, McNeill and colleague Cynthia Radford, central training manager, looked at various models and resources for ideas for the seminar. The group selected one of the models they reviewed and modified it to better meet the needs identified by the group.

As McNeill said to participants invited to the seminar, "Your science is very demanding and rewarding, but on top of that you are also expected to manage other scientists and administrative staff. That takes a whole skill set that is very different from your science skills."

McNeill, seated, and Radford of NIEHS Employee Services (Photo courtesy of Steve McCaw)

Focus Group and Attendees

The Science Manager/Leader Seminar focus group was made up of McNeill and Radford and six senior investigators:

- Principal Investigator Jean Harry, Ph.D., Neurotoxicology Group
- Acting Chief Paul Foster, Ph.D., Toxicology Branch
- Tenure-Track Investigator Honglei Chen, M.D., Ph.D., Aging and Neuroepidemiology Group
- Principal Investigator David Miller, Ph.D., Intracellular Regulation Group
- Staff Scientist John Roberts, Ph.D., Metastasis Group

Attending the first seminar, along with Foster, were nine current and aspiring scientist managers:

- Staff Scientist Nell Burch, Ph.D., Genotyping Core
- Biologist Natasha Clayton, Pathology Support Group
- Staff Clinician Stavros Garantziotis, M.D., Clinical Research Program
- Group Leader David Malarkey, D.V.M., Ph.D., NTP Pathology Group
- Chip Romeo, Ph.D., Laboratory of Neurobiology
- Deputy Scientific Director Bill Schrader, Ph.D.
- Chemist Cynthia Smith, Ph.D., of the Chemistry Group
- Acting Chief Ray Tice, Ph.D., NTP Biomolecular Screening Branch
- NTP Deputy Program Director for Science Nigel Walker, Ph.D.,

The group brought in Mary Charles Blakebrough of McBreakthrough Consulting to conduct the September 22 half-day session on "The Myers-Briggs Type Indicator (MBTI) – Review for Science Managers." Attendees took the personality type assessment and discussed the ways their types might best communicate with the other personality types they are sure to encounter in their groups and branches.

Sharon Milgram, Ph.D., director of the NIH Office of Intramural Training and Education, was recruited to chair the three-quarter day September 23 session on "Science Management/Leadership." Milgram's program covered the use of MBTI in the laboratory and office environment, motivating and developing others, team building as a leader and peer, managing conflict in the workplace, handling difficult conversations in the most constructive way and cooperative goal setting.

The seminar had its roots in a series of meetings earlier this year that McNeill held with lab and branch chiefs in DIR to ask for support for a specialized training module. She managed to get their support for the series and helpful suggestions for designing the content. The initial planning sessions also gave McNeill a pool of potential members for the focus group that crafted the seminar prototype.

With the first seminar completed and satisfied participants promoting it by word of mouth, McNeill and Radford are ready to take their lessons from the experience and move ahead by fine tuning the prototype. "The plan is to modify the program to make the fit even better and conduct the seminar several more times over the next year." McNeill said. "We also want to develop and deliver other seminar topics in the future to improve the management skills of leaders across the Institute."

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Vocational Rehab Featured For Disability Awareness Month

By Robin Arnette

October is National Disability Employment Awareness Month, and the NIEHS Disability Advocacy Committee (DAC) celebrated the contributions of "differently-abled" individuals by offering several events. On October 14, Jessie Pickett-Williams, M.S., CRC, LPC, unit manager for the Durham office of the North Carolina Division of Vocational Rehabilitation Services, presented a seminar titled "Images of Success" in Rodbell Auditorium. Pickett-Williams heads a staff whose sole purpose is to help individuals with disabilities access employment opportunities in North Carolina.

The North Carolina Division of Vocational Rehabilitation Services, known by its shortened name of "VR," has been in existence since 1920 and started offering services to its clients in 1921. VR is part of the North Carolina Department of Health and Human Services and has 32 unit offices, 17 independent living offices and 11 assistive technology offices throughout the state. Persons who have a documented disability — physical, mental, emotional, learning or substance abuse disorder — and who are able to participate in competitive work activities are eligible to apply to the program.

Pickett-Williams described the network of vocational rehabilitation services designed to help more workers enjoy gainful employment. (Photo courtesy of Steven McCaw)

Pickett-Williams said that VR provides a variety of core services:

- Treatment of impairments, including medical and surgical services, but not for acute conditions
- Counseling and guidance
- Training, such as college and university, community college, vocational and trade school programs
- Job-related services, including job search assistance, job placement and on-the-job support or coaching
- Rehabilitation technology

VR's support services include such things as transportation, equipment and licenses, interpreter services and the purchasing of required tools, to name a few. Pickett-Williams described what she and her staff do once they are contacted.

"We usually get referrals from doctors, social workers, mental health professionals or schools, but we can receive referrals from anyone," she said. "The cases are assigned to counselors who specialize in a particular area, whether it is [to assist] someone with a learning disability or someone who is hearing impaired. The counselors then obtain medical records and determine eligibility for services. Specialists, including vocational evaluators, assess the person's strengths and interests through testing and make recommendations. All of this information allows the counselor to manage the case from beginning to end."

When individuals from VR find and keep a job, they aren't the only ones who benefit. Employers who hire them can receive tax credits. Four are available:

- Work Opportunity Tax Credit
- Disabled Access Tax Credit
- Welfare to Work Tax Credit
- Architectural/Transportation Barrier Removal Deduction

Among the audience was Gerard Roman, an NIH Office of Equal Employment Opportunity specialist at NIEHS. (Photo courtesy of Steve McCaw)

Lecture host Jeannie "JJ" Bell-Nichols listened to an attendee during the quation-and-answer portion of the event. (Photo courtesy of Steve McCaw)

Pickett-Williams ended her talk with examples of VR participants who were happy and productive employees. DAC Vice-Chair Jeannie "JJ" Bell-Nichols hosted the seminar and said she was pleased to hear about the many success stories of disabled North Carolinians finding fulfillment in their work. DAC Chair Alicia Moore thanked Pickett-Williams for her dedication to working with individuals with disabilities. Both women, as well as the rest of the seminar audience, left Rodbell Auditorium knowing that VR is doing its part to strengthen and diversify North Carolina's workforce.

Hispanic Heritage Month Reception

By Eddy Ball

Following the Hispanic Heritage Month Lecture on September 25, NIEHS staffers and guests flocked to the Rall Building Cafeteria for food, entertainment and a glimpse into the cultures of several Latin countries at displays set up along the patio side of the cafeteria. The lecture itself was well attended (see related story), and the reception drew nearly three times that number from the offices and labs on campus — including such sympatico colleagues as NIEHS Acting Director Sam Wilson, M.D., and Acting Deputy Director Bill Suk, Ph.D., who showed their solidarity with the celebrants.

Biologist John Petranka was one of many visitors to the displays of photos, crafts and mementos from Latin American countries. (Photo courtesy of Steve McCaw)

Refreshments included food from local Hispanic eateries and authentic homemade desserts from NIEHS employees of Hispanic origin. Musical entertainment was provided by a lively group of costumed musicians known as the Mariachi Los Galleros de Mexico, who played their first number as they entered the cafeteria and made their way to the staging area.

The band was obviously well experienced in engaging their crowds and struck an emotional chord among Hispanic listeners as they played the nostalgic songs "En mi Viejo San Juan" ("In My Old San Juan") and "Y Volver" ("And to Return" or "Coming Back"). The audience sang along to the songs and swayed in unison as the musicians played the evocative ballads.

Biologist Elizabeth Padilla-Banks, left, posed with Hispanic Heritage Committee member Rose Ramos, Ph.D., in the display area prior to the arrival of the musicians. (Photo courtesy of Steve McCaw)

Written during World War II by Noel Estrada, "En mi Viejo San Juan" is one of the most famous ballads of Puerto Rico. The song captures the longing of Puerto Rican emigrants and soldiers for their distant homeland. For many Puerto Ricans, it remains today a kind of second national anthem, and it was adopted as the official city anthem of San Juan.

"Y Volver" reflects a similar longing for the past among people of Hispanic descent, but the song has a more specifically romantic theme of separation by a lover who promises to return to the arms of the beloved. Also known by the shorter title "Volver," it was featured in the Pedro Almodóvar film of that name and sung by the character Raimunda, played by Pénelope Cruz. The song has also been covered and adapted by such vocalists as Ry Cooder and Los Lobos.

Both songs are staples at weddings and other gatherings that celebrate cultural solidarity as well as the events themselves and are likely to bring listeners to tears under the right circumstances. At the Hispanic Heritage Month reception, the food, displays, nostalgic songs and other music by Mariachi Los Galleros de Mexico served to underscore the pride and love of their culture for the NIEHS staffers whose roots extend to the countries of South and Central America.

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Not surprisingly, the food and homemade desserts were extremely popular, and mid-way through the entertainment segment of the reception, most of these dishes were bare. (Photo courtesy of Steve McCaw)

As popular as the band's instrumentals were, it was the vocals that truly inspired audience involvement. (Photo courtesy of Steve McCaw)

Hispanic Heritage Committee Members

Rosemarie Ramos
Maria Sifre
Brad Collins
Lysandra Castro
Trisha Castranio
Eli Ney, Committee Co-Chair
Veronica Godfrey, Chair

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