

# Environmental Factor

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September 2008

## NIEHS Spotlight



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### Summers of Discovery Recognizes Interns' Accomplishments

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[...read more](#)



### Wilson Meets at USC to Brief Stakeholders

NIEHS Acting Director Samuel Wilson, M.D., traveled to California to meet on May 27 with veteran University of Southern California (USC) grantee John Peters, M.D., Sc.D. and two U. S. Congresswomen, Lucille Roybal-Allard and Hilda Solis. [....read more](#)



### Superfund Grantee Honored by American Chemical Society

Louisiana State University (LSU) chemist and Superfund Basic Research Program (SBRP) grantee Barry Dellinger, Ph.D., was one of three scientists who received the prestigious Astellas USA Foundation Award [...read more](#)

## Science Notebook



### Modifying Risk Factors in Neurodegenerative Diseases

Parkinson's disease (PD), multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS) are debilitating neurodegenerative illnesses, but many researchers are making strides in understanding these conditions and developing treatment and prevention strategies. [...read more](#)



### Alcohol Binges Early in Pregnancy Increase Risk of Infant Oral Clefts

A new study by NIEHS epidemiologists shows that pregnant women who binge drink early in their pregnancy increase the likelihood that their babies will be born with oral clefts. The study appeared online July 30 in the *American Journal of Epidemiology*. [...read more](#)



### Gene Expression in Respiratory Disease

Noted research pulmonologist Ron Crystal, M.D., presented a lecture to NIEHS scientists on August 5 in Rodbell Auditorium titled "Why Are Some Individuals More Sensitive to the Environment than Others? [....read more](#)



### UNC Research Day Highlights Human Neurological Disorders

A contingent of NIEHS scientists joined colleagues from Duke University and the University of North Carolina (UNC) on August 15 for Research Day 2008, hosted at the Chapel Hill Campus by the UNC Department of Cell and Molecular Physiology. [...read more](#)

## NIEHS Spotlight



### The Meyerhoff Model

Twenty years later, the University of Maryland, Baltimore County's efforts to increase the number of minorities pursuing graduate STEM degrees have become something to study and replicate. [...read more](#)



### Van Houten Moves to Posts at University of Pittsburgh

In August, Ben Van Houten, Ph.D., left his positions as branch chief and senior investigator at NIEHS to accept dual appointments at the University of Pittsburgh (UP) School of Medicine and the UP Cancer Center in Pennsylvania [...read more](#)



### Olden Leaves NIH to Start New School of Public Health

After a successful career as NIEHS Director Emeritus and Principal Investigator, Ken Olden, Ph.D., has left the Institute to set a precedent in public health education with the creation of the new School of Public Health on the Hunter College campus of the City University of New York (CUNY). [...read more](#)



### Beard Recognized by Boston Training Program

Graduation day on June 12 at the Suffolk University Law School was a time to celebrate for the students receiving diplomas and certificates from JFYNetWorks, Boston's largest workforce and career development training center for youth and adults. [...read more](#)



### Superfund Research Publication Reaches 5000

The Superfund Basic Research Program (SBRP) publication, *Research Brief*, grew out of a 1997 conversation involving Sam Wilson, M.D., now NIEHS acting director, Beth Anderson, SBRP program analyst, and NIEHS Acting Deputy Director William Suk, Ph.D. [...read more](#)

## Science Notebook



### Grantee Presents Prize-Winning Environmental Justice Research

Edward Emmett, M.D., spoke to an audience of NIEHS and Environmental Protection Agency (EPA) scientists gathered in Rodbell Auditorium on July 24. Hosted by NIEHS Program Analyst Liam O'Fallon, Emmett's talk on "Perfluorooctanoate (PFOA) from Teflon Manufacture: Studies of Community Exposure, Potential Risks and Effects of Intervention" was part of the NIEHS Frontiers of Environmental Sciences Lecture Series. [...read more](#)



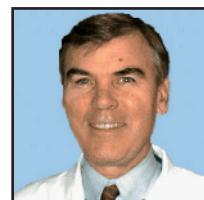
### Expert Panel Conducts Scientific Review of Styrene

On July 21-22, 2008, an expert panel met at the Radisson Hotel Research Triangle Park, N.C. to evaluate styrene, which was nominated for possible listing in the 12<sup>th</sup> *Report on Carcinogens (RoC)*. A majority of the panel members voted to recommend listing the compound as reasonably anticipated to be a human carcinogen. [...read more](#)



### Evolutionary Implications for Double-Strand DNA Breaks

A collaborative study, recently published in the *Proceedings of the National Academy of Science* by researchers from the NIEHS, Duke University and Brazil's Universidade Estadual de Campinas determined how DNA double-strand breaks (DSBs) in chromosomes can lead to chromosomal aberrations (CAs) and reshape the genome. [...read more](#)



### Upcoming Distinguished Lecturer Richard Boucher

The 2008 – 2009 NIEHS Distinguished Lecture Series will welcome its first speaker, Richard Boucher, M.D., at 11:00 a. m. September 8 in Rodbell Auditorium. Boucher will speak on "Cystic Fibrosis: A Failure of Lung Defense Against the Environment." [... read more](#)

## Inside the Institute



### A Fond Farewell to Ben Van Houten

When his friends and colleagues decided to mark the departure of Ben Van Houten to his new position at the University of Pittsburgh, they decided to go all out. The more than 200 people who gathered in the NIEHS Cafeteria on July 30 found a wide range of refreshments lining the central buffet bar, decorations and a carefully planned program of reflection and tribute ...[read more](#)



### Science Camp Revamped for Third Successful Year

The Durham Alumnae Chapter of Delta Sigma Theta marked several firsts when its members welcomed students to the third annual Science and Everyday Experiences (SEE) Summer Camp on June 28 at the chapter house in Durham. ...[read more](#)



### Health and Wellness Seminar Targets Nutrition

On August 19, NIEHS staffers gathered in Rodbell Auditorium to learn more about the integrative health/natural medicine approach to wellness in a talk on "The Science of Nutrition: How a Healthy Diet Creates a Healthy Future." ...[read more](#)

## Extramural Research

### Extramural Update

New Grant Opportunities on Functional Characterization of Genetic Variants and Interactions

NIEHS and the National Institute on Drug Abuse (NIDA) have announced a pair of funding opportunities on behalf of the NIH Genes, Environment and Health Initiative. The closing date for applications under RFA-DA-09-003 and RFA-DA-09-004 is October 17, 2008.

[...read more](#)

### Extramural Papers of the Month

- Mercury Vapor Captured from Compact Fluorescent Bulbs
- Breathing Polluted Air Raises Blood Pressure
- Link Between Thunderstorms and Asthma Attacks in the Atlanta Metro Area
- Over-the-Counter Pain Medicines May Reduce Risk of Diabetes

## Intramural Research

### Intramural Papers of the Month

- Exposure to Lead May Prolong ALS Survival
- The Involvement of RAP80 Following DNA Damage
- Liver X Receptor Regulates Pulmonary Innate Immunity
- Differential Regulation of an ERK Protein Scaffold to Control Gene Transcription

## Calendar of Upcoming Events

- **September 3**, in Rodbell Auditorium, 8:30 - 5:00 — NIEHS-EPA Air Pollution Cardiovascular Research Grantees Meeting
- **September 4 – 5 (Offsite Event)**, at the Sheraton-Chapel Hill — Genetic Susceptibility to Air Pollution Conference
- **September 8**, in Rodbell Auditorium, 11:00 - 12:00 — Distinguished Lecture Seminar Series featuring Richard Boucher, M.D., speaking on “Cystic Fibrosis: A Failure of Lung Defense Against the Environment”
- **September 9**, in Rodbell Auditorium, 8:00 - 5:30 — NAEHS Council Meeting
- **September 9**, in D-250, 1:00 - 3:00 — Seminar on Aging and Arthritis - Quality of Life and Issues Related to Disability with Leigh Callahan, Ph.D.
- **September 11 – 12**, in Rodbell Auditorium, 8:30 - 5:00 — High Throughput Screening Approaches for Toxicology
- **September 15**, in Rodbell Auditorium, 10:00 - 11:00 — LMG Fellows Seminar with Christophe Herman, Ph.D., speaking on “Beyond Mutation: Transcription and Protein Folding Errors Generate Heritable Epigenetic Change”
- **September 21 – 24 (Offsite Event)**, Cluj-Napoca, Romania — Central and Eastern European Conference on Health and the Environment: The Environment - A Platform for Health
- **September 22**, in Rall Cafeteria, 2:30 - 4:00 — Marian Johnson-Thompson, Ph.D., retirement reception
- **September 25**, in Rall Building Executive Conference Room, 11:00 - 12:30 — Hispanic Heritage Month Seminar with Denise Moreno
- View More Events: [NIEHS Public Calendar](#)

# NIEHS Spotlight

## Trainees Look Ahead to a New Year

By Eddy Ball

The NIEHS Trainees Assembly (NTA) held its first General Assembly of the 2008-2009 year on July 25 in Rodbell Auditorium. The event gave trainees an opportunity to hear NIEHS Acting Director Sam Wilson, M.D., and NIEHS Office of Fellows Career Development (OFCD) Acting Director Diane Klotz, Ph.D., discuss NIH and NIEHS resources for trainees, learn more about what the NTA can offer trainees from Steering Committee members and offer suggestions for training and activities for the year.

The meeting opened with a welcome from Steering Committee Chair **Stephanie Nick McElhinny, Ph.D.**, who introduced Wilson, the keynote speaker at the event. An NIH fellow himself early in his career, Wilson reinforced the NIEHS senior administration's commitment to quality training for the non-tenured and non-tenure track fellows. "I can't think of a group here at the Institute that we in the senior leadership are more dedicated to and more excited about than your group," Wilson said.

As Wilson talked about the importance of research at NIEHS and the critical need to network and "leverage the strengths of the Institute," he reflected on the aspects of scientific investigation that he cherishes most. He encouraged his audience to make time for "what's really fun for you" in science.

"For me, it is reading about research progress... and making time to have a really peaceful, solitary experience of thinking about what I've read and wondering what the answers could be," Wilson said. "Make sure you carve out enough time to have fun and develop those lines of thinking."

Following Wilson's talk, Steering Committee members **Rose Ramos, Ph.D.**, co-chair, and **Jennifer Adair, Ph.D.**, joined Nick McElhinny in a series of short presentations on the mission of the NTA and its collaborative advocacy and training activities. Ramos covered several of the networking,



*"I'm hoping that when you leave here and think about the presentation, you'll remember what I said about the commitment of the senior leadership to your training and your careers and your life here at the Institute," Wilson told the trainees.*

*(Photo courtesy of Steve McCaw)*



*"The NTA has influence on all levels of the administration, both here and at NIH," Nick McElhinny explained. "You need to let us know what you want to happen as far as training and workshops, so we can communicate with the appropriate people."*

*(Photo courtesy of Steve McCaw)*

career development and support initiatives sponsored by NTA to further its mission — as well as the ways NTA represents trainee interests at the NIEHS, NIH and national levels in such areas as training and education, working conditions, career development, taxes and stipends.

Adair discussed the volunteer opportunities available for trainees who want to get involved and said that “volunteering opens up excellent networking opportunities.” The Steering Committee strives to include a representative from each of the Institute’s labs, Nick McElhinny added, and the 12th Annual Biomedical Career Fair, sponsored jointly by NIEHS and the US Environmental Protection Agency and scheduled for May 1, 2009, will need volunteers in a variety of roles.

According to Nick McElhinny, the NTA prides itself on its good working relationship with OFCD, which is part of the Office of the Scientific Director in the Division of Intramural Research and a direct link to NIH trainee education and support resources. “The NTA and OFCD work together toward a common goal of providing resources for training and career development, but they approach this goal from different vantage points,” she explained.

Echoing the theme of working together for a common goal, Klotz described her role as OFCD acting director. “The purpose of my office existing,” she said, “is to give you opportunities to get the information you need to go further in your career.” She pointed to the curriculum vitae workshop and the K99/R01 grant-writing workshop as examples.

## Career Development Opportunities for NIEHS Trainees

by Rosemarie Ramos and Stephanie Nick McElhinny

Over the past year, career development programs for trainees at NIEHS have continued to grow with continued support from the NIEHS Office of the Director and Office of the Scientific Director. These programs offer trainees opportunities to develop skills that will help them stand out in a highly competitive job market:

- A new collaboration between the NTA and the *Environmental Factor* which provides a way for trainees to hone their non-technical writing skills — For those who have been in the job market or will be in the near future, this has become a highly sought-after skill (even for biomedical scientists). The opportunity is similar to that offered by a program developed a year ago for NIH fellows on the Bethesda campus which has been very well received.
- Career Counseling specifically for postdocs available on a regular basis under the leadership of Sharon Milgram, Ph.D., director of the NIH Office of Intramural Training and Education (OITE) — Trainees can meet individually with a professionally trained career counselor who understands the challenges facing today’s postdocs as they make their next career move. The service includes advice on preparing a CV or resume, converting a CV to a resume and developing effective interviewing skills.
- Individual Development Plan (IDP) counseling with Diane Klotz to help trainees outline career goals and determine what steps they can take to meet those goals — Klotz’s unique background and experience as an NIEHS postdoc, scientist and the former president of the National Postdoctoral Association has given her insight into the special needs of fellows here at NIEHS.
- An in-depth course on teaching at the college level — This course will cover course design, teaching philosophy and much more, virtually everything bench scientists need to know to begin a career in the classroom.
- The NTA is currently planning its second Fellows Orientation program to be held this fall.

(Rosemarie Ramos, Ph.D., is the health disparities postdoctoral fellow in the Metastasis Group. Stephanie Nick McElhinny, Ph.D., is a postdoctoral fellow in the DNA Replication Fidelity Group.)

Klotz announced that in addition to existing workshops OFCD will offer sessions on alternative career options such as Teaching at the College Level, Academic Track Series and Industry Track Series in the coming year. OFCD also plans to offer Leadership Training and Laboratory Management Training, two workshops that she said are pertinent to both tenure-track investigator and alternative career development.



Ramos also serves as NIEHS representative to the [National Postdoctoral Association](#), an advocacy group that lobbies Congress and employers on behalf of trainees. "Membership is free," she added. (Photo courtesy of Steve McCaw)



As Klotz explained, new workshops have been developed to complement fellows' experiences at NIEHS with training that they normally would not receive in the lab. (Photo courtesy of Steve McCaw)



Klotz and Adair, above, urged trainees to complete the surveys available at the meeting and online. "The survey is really the best way for you to give us information on what you want out of your training experience," she explained. (Photo courtesy of Steve McCaw)



Steering Committee member Abee Boyles, Ph.D., above, represents the Epidemiology Branch. Most of the committee's lab representatives attended the meeting. (Photo courtesy of Steve McCaw)



The event attracted new postdocs, such as Rebecca Long, Ph.D., who can benefit from working with Klotz on an Individual Development Plan at the outset of her fellowship. Long works with Stavros Garantziotis, M.D., head of the Matrix Biology Group. (Photo courtesy of Steve McCaw)



Veteran postdocs, such as Jeffrey Stumpf, Ph.D., also learned about new training that can be useful as the time for a job search approaches. Stumpf works with Bill Copeland, Ph.D., in the Mitochondrial DNA Replication Group. (Photo courtesy of Steve McCaw)

# Summers of Discovery Recognizes Interns' Accomplishments

By Eddy Ball

The NIEHS Summers of Discovery class of 2008 and its mentors enjoyed their annual day in the sun on June 30 when the program held its annual poster competition in the mall area of the Rall Building on the main campus in RTP. Two days later, on August 1 in Rodbell Auditorium, program coordinator Charle League awarded three of the young scientists awards for their work — Anand Kornepati, Nishant Shah and Cynthia Willson, Ph.D.

Winners were selected by a group of volunteer postdoctoral fellows who served as judges. The judges ranked posters in three categories based on each of the three intern educational levels — high school, college undergraduate and graduate/professional school. Although the 2008 interns came from educational institutions throughout the United States, the poster winners all turned out to be students at William G. Enloe High School and North Carolina State University (NCSU) in nearby Raleigh, N.C.

The poster competition and the awards ceremony were well attended by interns and their mentors, and this summer marked a high point in intern participation in the poster competition. According to League, 32 of the 36 interns in the 2008 Summers of Discovery program took advantage of the opportunity to showcase their research achievements, as well as one intern who participated in the August 7 NIH summer poster session in Bethesda.

NIEHS Acting Director Sam Wilson, M.D., opened the awards ceremony by congratulating League and the interns and offering a few comments about the importance of the summer experience for young scientists. "The NIH is recognized as the leading medical research organization worldwide," he said. "I think it's really exciting and really wonderful for you to have a chance to spend time doing medical research and interacting with veteran scientists who have been doing some of the leading work here."



*Enloe High School student Anand Kornepati, left, received his award from League. (Photo courtesy of John Maruca)*

## The Winners

- High School — Anand Kornepati, a rising junior at Enloe, for his work in the Laboratory of Respiratory Biology Matrix Biology Group: "The Role of Inter- $\alpha$ -trypsin Inhibitor in Endotoxin-induced Endothelial Injury," with NIEHS Biologist Vandy Parron, Brown University Oncologist Yow-Pin Lim, M.D., and NIEHS Principal Investigator Stavros Garantziotis, M.D.
- Undergraduate: Nishant Shah, a rising senior at NCSU, for his work in the Laboratory of Molecular Genetics Chromosome Stability Group: "Measurement of DNA Strand Breaks and Repair in Human Lymphoid Cells Using the Epstein-Barr Virus Episome," with Postdoctoral Fellow Christopher Halweg, Ph.D., and Principal Investigator Michael Resnick, Ph.D.
- Graduate/Professional: Cynthia Willson, Ph.D., a rising second-year Veterinary Medicine student at NCSU, for her work in the National Toxicology Program's Cellular and Molecular Pathology Branch: "Protein Expression Changes During Bladder Tumor Development Induced by o-Nitroanisole in F344 Rats," with Branch Chief Robert Sills, D.V.M., Ph.D., Biologist Tiwanda Masinde, Biologist Natasha Clayton and NTP Pathologist Mark Cesta, D.V.M.

Following Wilson, Acting Deputy Director Bill Suk, Ph.D., urged the interns to remember that “you really are the future of this institute and of NIH and of the environmental health sciences.... This is an outstanding opportunity that you have to develop as a scientist and to help define what your career goals will be.” Suk encouraged the young people to be proactive in seeking out what they need to make their opportunities as productive as possible.

As League prefaced her announcement of the winners, she offered “kudos to everyone who participated for the outstanding quality of the submissions.” She also encouraged interns to put the competition into the perspective of individual career development. “It [the judging] is not the point of the summer experience,” she said, “but rather it’s the value of the practice itself.... It’s also a good experience for the postdocs involved in judging the posters.”

League also took occasion to thank the many people who worked behind the scenes to make the 2008 Summers of Discovery program a success. “It takes a community to run a program like this,” she concluded, as she encouraged everyone to enjoy the ice cream reception that followed.



Resnick, left, joined NCSU student Shah, League and Halweg, right, for the presentation. (Photo courtesy of John Maruca)



Cesta, left, was one of the colleagues who worked with NCSU veterinary student Willson on her award-winning poster presentation. (Photo courtesy of John Maruca)

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The ice cream reception has become a tradition in the Summers of Discovery program. Shown here, left to right, are Kornepati, Richa Tawari, Ray Dong and Waynekid Kam selecting toppings for their treats. (Photo courtesy of John Maruca)

# Wilson Meets at USC to Brief Stakeholders

By Jon Nalick and Eddy Ball

NIEHS Acting Director Samuel Wilson, M.D., traveled to California to meet on May 27 with veteran University of Southern California (USC) grantee John Peters, M.D., Sc.D. and two U. S. Congresswomen, Lucille Roybal-Allard and Hilda Solis. Wilson participated in an information session to brief the representatives about current NIEHS-funded research and new initiatives in the areas of air pollution and children's health.

Peters is the Hastings Professor of Preventive Medicine and director of the Division of Environmental Health at the USC Keck School of Medicine and an NIEHS grantee for more than a decade. Rep. Roybal-Allard and Rep. Solis represent districts that include parts of greater Los Angeles.

The visit was part of an on-going effort by Wilson, NIEHS Acting Deputy Director William Suk, Ph.D., and others in the NIEHS Office of the Director to support grantees and inform stakeholders of the Institute's commitment to basic research in the environmental health sciences, the well-being of the nation's children, environmental justice, community involvement and community-based participatory research. Their travels have taken the emissaries throughout the United States and overseas during the past year, as they have visited grantee institutions, professional meetings, town halls and information sessions.

Peters is the principal investigator of the Children's Health Study, which has followed 11,000 children, for periods as long as 13 years, in Southern California communities to learn the effects of air pollution on the health of their lungs. He is also the principal investigator of an NIEHS-funded project to continue to follow these children into adulthood.

For the past ten years, Peters has directed the Southern California Environmental Health Sciences Center, an NIEHS-supported center which is based at the USC and includes faculty members from both USC and the neighboring University of California at Los Angeles, where NIEHS also supports research programs. The Center focuses on the full range of environmental health problems that humans face and endeavors to understand more completely how host factors and environmental exposures interact to produce human disease.



*Wilson gestured as he emphasized a point about the new initiatives NIEHS is now pursuing — including research on more sophisticated monitors to measure individual exposures to air pollution. (Photo courtesy of Jon Nalick and USC News)*



*Roybal-Allard, left, and Congressional Field Representative Michelle Esperanza sat beside Peters, right, as he described efforts to translate the center's research into measures to help prevent respiratory disease in children. (Photo courtesy of Jon Nalick and USC News)*

Now in her eighth term, Rep. Roybal-Allard is the first Mexican-American woman to serve in Congress and currently sits on the House Appropriations and Standards of Official Conduct committees. She has served as the Chair of the California Democratic Congressional Delegation and the Congressional Hispanic Caucus. She has also been active on the Congressional Children's Caucus, Democratic Homeland Security task force and the livable communities task force.

Rep. Solis, who was elected to her seat in 2000 with 79 percent of the vote, is an advocate for the promotion of environmental justice and for addressing health disparities. Among her other proposals, she has supported legislation to reduce the number of teen pregnancies within the Latina and African-American community.

(Jon Nalick is editor of the USC Health Sciences Campus newsletter *HSC weekly*, which ran a [story](#) about the meeting in its June 6 issue.)

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*Solis, sitting to Wilson's left, emphasized the needs of children living in congested urban areas and near major expressways.*  
*(Photo courtesy of Jon Nalick and USC News)*

## Superfund Grantee Honored by American Chemical Society

*By Eddy Ball*

Louisiana State University (LSU) chemist and Superfund Basic Research Program (SBRP) grantee Barry Dellinger, Ph.D., was one of three scientists who received the prestigious Astellas USA Foundation Award August 17 in Philadelphia at the Presidential Symposium of the 236th National Meeting of the American Chemical Society (ACS). Dellinger was honored for his significant contributions to scientific research that improved public health through his studies in the chemical and related sciences.

As part of the award, which carries with it a check for \$30,000, Dellinger was invited to present a lecture in translational chemistry at the national symposium. In his talk, he described his group's investigations into the mechanisms of formation of combustion-generated nanoparticles known as environmentally persistent free radicals (PFRs).

"We believe it is possible that some health effects attributed to molecular pollutants may actually be due to the PFRs," Dellinger said when he received the award, "and the concentration of PFRs may ultimately be shown to correlate with health effects of fine particles in epidemiologic studies."



*Astellas Award Winner Barry Dellinger*  
*(Photo courtesy of Barry Dellinger and Louisiana State University)*

PFRs are a by-product of any flame-producing chemical reaction, including coal and fuel power plants and burning wood. Because they are persistent, lasting for much longer than previously assumed, the microscopic PFRs are a threat to human heart and lung health and, under the right conditions, could cause health risks similar to smoking a pack of cigarettes a day. Dellinger's findings help explain why non-smokers, who make up nearly 15 percent of lung cancer cases, are also susceptible to the disease.

According to Dellinger, an estimated 50,000 Americans die annually from illness linked to PFRs. PFRs reside on fine particulate matter with a mass mean aerosol diameter of less than 2.5 microns, which allows them to evade the lung's filtering efforts, enter the blood stream and generate reactive oxygen species that can result in DNA strand breakage. Over time, this damage to DNA can result in the development of various cancers and cardiovascular disease.

Dellinger's findings grew out of a three-year SBRP grant, "Development of a Demonstrable Model of Dioxin Formation," administered by Center for Risk and Integrated Sciences Program Administrator Heather Henry, Ph.D. Dellinger conducted research on the emissions from hazardous waste incinerators, especially the highly toxic dioxins, polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/F), in order to better understand how the by-products of combustion, rather than toxic chemical itself, pose a risk to health.

During the week-long meeting, Dellinger also chaired an all-day session on the Health and Environmental Impacts of Combustion-Generated Nanoparticles that included several researchers supported by research centers funded as part of the Superfund Basic Research Program

Along with Dellinger, ACS also honored his colleague Isiah M. Warner, Ph.D., LSU Boyd Professor and Philip W. West Chair in Analytical and Environmental Chemistry, at the meeting. Warner was presented with the ACS Division of Analytical Chemistry Award in Spectrochemical Analysis recognizing research that has advanced the field of spectrochemical analysis and optical spectrometry.

The Astellas Award is the latest of several honors Dellinger has received for his work. He is the Patrick F. Taylor Chair of Environmental Chemistry at LSU and has been recognized with the Charles A. and Anne Morrow Lindbergh Foundation Certificate of Merit, the Wohleben-Hochwalt Research Award and the Environmental Protection Agency STAR (Science to Achieve Results) Award.

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# The Meyerhoff Model

By David Pluviose

(Editor's note: This story, originally published online in *Diverse: Issues In Higher Education* 22:47, highlights the successes of a scholarship program which has received ongoing support from the Division of Minority Opportunities in Research [MORE] at NIH/NIEHS.)



(Image courtesy of *Diverse: Issues In Higher Education*)

*Twenty years later, the University of Maryland, Baltimore County's efforts to increase the number of minorities pursuing graduate STEM degrees have become something to study and replicate.*

In a sea of bad news concerning the lack of Black male representation on college campuses, an oasis of minority male scholarship exists at the University of Maryland, Baltimore County, through the Meyerhoff Scholarship Program.

Launched in 1988 via the generous philanthropy of real estate entrepreneur Robert Meyerhoff and his wife, Jane, the Meyerhoff program was initially focused on increasing the number of Black males pursuing higher education in the fields of science, technology, engineering and math (STEM) but now has been expanded to include women and other underrepresented students.

In April, the Meyerhoff program held a two-day 20th Anniversary Research Symposium and Celebration, bringing back many of the 200 alumni who have completed doctorates, medical degrees and other STEM graduate degrees.

Meyerhoff alum Dr. Kafui Dzirasa, who is on the verge of adding a medical degree to the Ph.D. in neurobiology he's already earned while enrolled in a dual-degree program at Duke University, attended the Meyerhoff 20th anniversary celebration and called it "absolutely amazing, just to see the summation of 20 years. Everyone in the room seemed to be a doctor of some sort. I've never seen anything like it."

Dr. Crystal Watkins, a Meyerhoff alum who went on to earn a M.D./Ph.D. from Johns Hopkins University and recently wrapped up a stint as chief resident in psychiatry at JHU, says she felt "overwhelming emotion" while standing in a room with many of her Meyerhoff colleagues who are already trailblazing scientists and physicians.

"For the alumni it's just amazing because you have so many talented people that are this critical mass. And you're really saying, 'Wow, look at what kind of force we could be in changing the face of science,'" says Watkins, who has accepted an assistant professorship at Hopkins. "When I say the face of science, [I mean] not just the color of the people that are practicing it, but even just the way we teach education and the way we reach out to young people in the inner-city that are interested in being scientists."



*Dr. Crystal Watkins, a Meyerhoff alum who went on to earn a M.D./Ph.D. from Johns Hopkins University, says she and her fellow scholars can be an influential force in changing the face of science. (Photo courtesy of *Diverse: Issues In Higher Education*)*

## The Journey Begins

The Meyerhoff program is the brainchild of Dr. Freeman A. Hrabowski, UMBC president and a civil rights activist who graduated from Hampton University at age 19 with the highest honors in mathematics. As one of a small cadre of Black men in the United States holding advanced degrees in mathematics and statistics, Hrabowski has a particular passion for guiding young minorities towards STEM doctorates through the Meyerhoff program.

“Our challenge is both socioeconomic and racial. African-American and Hispanic children rarely see examples of successful scientists and engineers looking like themselves, and so people tend to aspire to be like those they admire. And unfortunately, the popular culture doesn’t often sing the praises of Black scientists,” Hrabowski says.

Noting that 20 Black Meyerhoff alums are completing Ph.D.s or medical degrees this year alone, Hrabowski says a key component of the program’s success is buy-in from UMBC research faculty, the majority of whom are White.

“Any institution will have supportive minority staff members, and they are very important, of course,” Hrabowski says. However, “it takes researchers to produce researchers, and unfortunately, very few of the scientific researchers in our country are African-American or Hispanic. And so we need Whites to become involved in this work, because the paucity of minority scientists is not simply a minority issue; it is an American issue,” he adds.

Meyerhoff alum and University of Maryland Medical Center emergency medicine resident Dr. Adrienne M. McFadden says UMBC staff treat Meyerhoff students like family. For example, when Meyerhoff scholars “get together a few times a semester, they call it a family meeting, so it is all in all considered a family from the beginning to the end,” she says.

When meeting other minority graduate students while completing her medical and law degrees at Duke University, McFadden says many of them complained about the lack of a support system at the colleges they attended, which is in stark contrast to the cocoon of support the Meyerhoff program has built for its minority scholars.

## Bridge to Success

Dzirasa says the six-week summer bridge program that all Meyerhoff scholars enroll in after high school is crucial to building a foundation of success for the scholars, many of whom never studied in groups during high school. However, many Meyerhoff scholars find that the group-study concept ingrained within the program and emphasized during the summer bridge is key to successfully tackling the rigorous math and science courses at UMBC.

“For me, I never studied in groups in high school, I never saw the benefit of it,” says Dzirasa, who was a chemical engineering major at UMBC. “But then again, I did moderately well, but never achieved up to the level of my potential. From the summer bridge experience, I learned how to start working in groups, and that was something that took my classmates and I all the way through undergrad.”



*Dr. Freeman A. Hrabowski, President, University of Maryland Baltimore County (Photo courtesy of [Diverse: Issues In Higher Education](#))*

As an example of the effectiveness of the group-study concept, Dzirasa says of the six Meyerhoff scholars that were chemical engineering majors at UMBC, “We had the top six scores in all of our classes because we worked very efficiently together.

“Of those, there are three M.D./Ph.D.s, one Ph.D., one M.D., and one person with a master’s in systems engineering from Columbia,” Dzirasa adds. “The notion that all of us succeeded together is the idea that drove all of us forward.”

McFadden says the Meyerhoff program is “a well-oiled machine,” in that Meyerhoff faculty and staff know that many of the high-achieving students coming into the program “tended to do things on our own and excelled on our own.” And they know that group-study “is a new concept for many of us, but they encourage us to enter into study groups and find a support system of students who are going to be in our classes so we have them to lean on and help us in our weaknesses in certain subjects.”

## **Replicating Success**

Annually, Hrabowski says, the Meyerhoff program gets around 2,000 nominations from high school principals, guidance counselors and teachers; and 1,000 applications for 80 Meyerhoff seats at UMBC. Nevertheless, Hrabowski says the concepts of group study and forging relationships with faculty mentors emphasized through Meyerhoff have been replicated among the general population of students at UMBC, and other colleges have taken their cues from Meyerhoff’s success. Louisiana State and Cornell universities are just two of the institutions that have modeled programs after Meyerhoff.

Dzirasa recalls a meeting of Meyerhoff students in which they discussed how the success of Meyerhoff could be replicated at other institutions. He says that what “people don’t realize is that Dr. Hrabowski is constantly in the process of replicating himself in the people that are coming through the program.

“Even if it’s something that may not show in five or six years, going back to the reunion, I’m now seeing my classmates and the people who tutored me who are professors at Michigan, professors at Yale, professors at Harvard, and you see this subtle thing happening, where indeed, he has replicated himself,” Dzirasa adds.

Ultimately, McFadden says, Hrabowski’s insistence that he get nothing but the best from his Meyerhoff scholars has paid great dividends.

“An underlying theme of great expectations is why Dr. Hrabowski was successful,” McFadden says. “If you have great expectations for yourself, then you will rise to the level of great accomplishment. What he always reinforces in all of his Meyerhoffs and in all of the students at UMBC is to expect the best from themselves.”

(Reprinted with permission from *Diverse: Issues In Higher Education*)

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# Van Houten Moves to Posts at University of Pittsburgh

By Eddy Ball

In August, Ben Van Houten, Ph.D., left his positions as branch chief and senior investigator at NIEHS to accept dual appointments at the University of Pittsburgh (UP) School of Medicine and the UP Cancer Center in Pennsylvania — returning to the state where he grew up on a small farm and first discovered his fascination with what he called “the beautiful and intricate spider web of biology.”

At UP, Van Houten will be the Richard M. Cyert Professor of Molecular Oncology in the Department of Pharmacology and Chemical Biology and at the same time serve as the head of the Molecular and Cell Biology Program in the Hillman Cancer Center. The center is the flagship treatment and research facility of the UPMC Cancer Centers network with the region’s most advanced imaging technologies for detecting cancer and monitoring treatment. Hillman is also home to a component of the NIH-funded General Clinical Research Center, which also provides support for the conduct of clinical trials.

After holding professorships at the University of Vermont and University of Texas Medical Branch, Van Houten began his career at NIEHS in 1999 with a precedent-setting dual appointment in the Division of Extramural Research (DERT) and Division of Intramural Research. In his work with DERT, Van Houten headed the Program Analysis Branch, which evaluates the Institute’s extramural grant portfolio in order to set priorities, formulate strategic plans and assure the maximum benefits of research funding.

Among many evaluation tasks, Van Houten and his group were charged with tracking the productivity and science emanating from the portfolio of awards of the extramural grantees. Working with colleagues at NIEHS, Van Houten helped to create a web-based tool for bibliometric analyses of publications and grant productivity. What emerged three years later was the Scientific Publications Information Retrieval System (SPIRES), a model now used across the NIH.

The SPIRES query screen enables searching by publication parameters or by project parameters, and the search can yield a detailed publication summary, including an impact factor that is used as a metric for evaluating the significance of the science. SPIRES is being run and maintained by NIH Information Technology Specialist Paul Jordan.

As principal investigator of the DNA Repair and Mitochondrial Damage Group in the Laboratory of Molecular Genetics, Van Houten was responsible for training fellows and performing cutting-edge research. He quickly became known as a nurturing mentor with loyal trainees. Two of them, Visiting Fellows Ye Ping, Ph.D., and Hong Wang, Ph.D., plan to work with him in Pittsburgh.

During his tenure at NIEHS, Van Houten was recognized as a leading authority in DNA repair and mitochondrial disease. His research interests also included omics methodologies and systems biology approaches.



*As “hard as it is for me leave NIEHS,” Van Houten, above, said he envisions the move to Pittsburgh as the logical next step in his efforts to build a program to understand the intricate web of cancer biology. (Photo courtesy of Steve McCaw)*

Among his many recent research accomplishments at NIEHS are two examples of transformative research that demonstrate the breadth of his scientific mastery, as well as his use of new approaches for investigating his research interests. In a study of innovative treatments for patients with the mitochondrial disease Friedreich's ataxia, a degenerative neurological condition, Van Houten's team used microarray analysis of gene expression to evaluate the effectiveness of antioxidant therapy. His group more recently employed nanotechnology to mark proteins with quantum dots for the first time to monitor DNA repair molecule by molecule in real time.

Van Houten has authored over 121 scientific articles, as well as 17 book chapters and reviews. He currently serves on the editorial boards of the *Journal of Biological Chemistry*, *Mutation Research*, *DNA Repair* and *Mitochondrion*. He was the chair of the 2005 Gordon Research Conference on Genetic Toxicology and co-chair of the 2007 Gordon Research Conference on Oxidative Stress and Disease.

Since joining the NIEHS, Van Houten has been recognized with five NIH Merit Awards and an NIH Director's Award. In May, he received the "Medal of the Slovak Academy of Sciences (SAS) for Support of Science," the most recent of many honors and awards.

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## Olden Leaves NIH to Start New School of Public Health

By Eddy Ball

After a successful career as NIEHS Director Emeritus and Principal Investigator, Ken Olden, Ph.D., has left the Institute to set a precedent in public health education with the creation of the new School of Public Health on the Hunter College campus of the City University of New York (CUNY). It will be the first such program designed with an urban focus, and it offers Olden the natural next step in his career in the environmental health sciences.

Hunter College is a senior unit of CUNY, and its location gives Olden an opportunity to pursue several of his public health research interests in a ready-made laboratory literally just outside his door. The city is home to several vigorous environmental justice programs and the kinds of public health issues, such as health disparity, that are especially relevant in urban settings.

In 2006, CUNY Chancellor Matthew Goldstein announced plans to open a School of Public Health at Hunter College by 2010, making it the first public school of public health in New York City. The proposed School of Public Health will offer graduate degree programs and possibly selected undergraduate degree programs with an urban focus in the five core areas of public health — biostatistics, epidemiology, social and behavioral sciences, health care administration and policy, and environmental and occupational health.

Public health, community-based participatory research, children's health and environmental justice were strongly emphasized during



Shown at Harvard University during his 2007 sabbatical, Olden remained active in public health venues even after he returned to the bench in 2005. (Photo courtesy of Harvard University)

Olden's tenure as NIEHS director from 1991 to 2005. In 1994, NIEHS published a strategic plan, *Vision for the Future*, that set the stage for integrating the Institute's basic research, toxicology, public health and environmental justice initiatives and positioning NIEHS to play an increasingly important role as "public policy makers struggle to balance human health needs with the economic benefits of commercial processes that might endanger that health."

He assumed the position at a time when the Institute had experienced a downturn in the constant dollars of its budget, and within two years he had gained NIH support for increasing the NIEHS share of resources. By working to increase the Institute's visibility and serving as an advocate for increased funding, Olden helped to increase the NIEHS budget more than four-fold over his tenure.

After his retirement as director, Olden continued to pursue his interests in public health while also serving as a principal investigator in the Laboratory of Molecular Carcinogenesis Metastasis Group. After receiving his Ph.D. from Temple University in 1970 and completing postdoctoral work at Harvard Medical School, Olden had joined the National Cancer Institute (NCI) in 1974 where he rose to become a tenured principal investigator in 1977.

In 1980, Olden joined the Howard University Cancer Center as scientific director in 1980 and took over direction of the Howard University Cancer Center in 1985. During the next six years, he revitalized the center and regained the core funding from the NCI that had been lost earlier.

When Olden came to NIEHS, he said his goal for NIEHS was to raise the institute's image among key officials of the executive and legislative branches to make the NIEHS more familiar at budget time and a "prime time player in environmental health" nationally and worldwide. His success in accomplishing those goals bodes well for the visionaries at Hunter who chose him to take on this historic public health education challenge during a time of spending constraints.

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## Beard Recognized by Boston Training Program

*By Eddy Ball*

Graduation day on June 12 at the Suffolk University Law School was a time to celebrate for the students receiving diplomas and certificates from JFYNetWorks, Boston's largest workforce and career development training center for youth and adults. The event was also a time for the non-profit organization to thank people who work behind the scenes to support the center's work, including NIEHS Worker Education and Training Program (WETP) Administrator and Industrial Hygienist Sharon Beard.

At the ceremony, Beard received the JFYNetWorks award for Distinguished Service to Workforce Development. She was honored for her work coordinating, evaluating and improving the



*Beard, second from right, is shown at the graduation with JFY staffers Paul Morse, Gary Kaplan and Craig Slatin.  
(Photo courtesy of Paula Paris and JFYNetWorks)*

nationwide program, especially in the Minority Worker Training Program area, as well as administering several Superfund/WETP grants to such organizations as the Center for Construction Research and Training, which helps provide support for the Environmental Technology job training curriculum at JFY.

Beard was one of three public sector officials recognized at the agency's 31st annual graduation ceremony. JFY deputy director Paula Paris and director Gary Kaplan also presented awards to Massachusetts State Senator Anthony Galluccio, commencement speaker and recipient of the Distinguished Service to Education Award, and Massachusetts Secretary of Labor and Workforce Development Suzanne Bump. JFY graduated 14 students from the GED program, 17 from the ESOL program and 29 from the Environmental Technology Program, most of them already employed or set to begin work after graduation.

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## Superfund Research Publication Reaches 5000

By Melissa Fabiano



The Superfund Basic Research Program (SBRP) publication, *Research Brief*, grew out of a 1997 conversation involving Sam Wilson, M.D., now NIEHS acting director, Beth Anderson, SBRP program analyst, and NIEHS Acting Deputy Director William Suk, Ph.D., about ways to communicate scientific breakthroughs and new events related to SBRP-funded research. This summer, 164 issues later, the publication marked an important milestone as its e-mail distribution list grew to include more than 5,000 unique e-mail addresses.

The *Research Brief* highlights accomplishments of diverse research projects funded by the SBRP. Maureen Avakian, an SBRP contractor, maintains consistent contact with SBRP grantees and proactively works with the NIEHS library staff to stay informed about soon-to-be published papers. Due to this steady communication between the program and its grantees, news regarding environmental health breakthroughs and SBRP-related events are reported in a timely manner.

Every month, the *Research Brief* performs the important service of providing relevant information in an easy-to-read format. As a result, the publication continues to be very well received, as its distribution keeps growing. Since 2000, the *Research Brief* list-serv has grown by 4,100 addresses, and the number of subscribers surpassed the 5000 mark on July 16.

The mission of each *Research Brief* is three-fold — to translate science into a language and format appropriate for diverse audiences, to highlight research related to human and environmental health and to provide complete contact information so that readers can reach SBRP grantees if they have specific questions. The publication is targeted primarily to EPA and Agency for Toxic Substances and Disease Registry risk assessors and hazardous waste site managers, but is also sent to representatives of state and local environmental agencies, public health agencies, industry, engineering firms, academics and not-for-profit organizations.

Past *Research Briefs* reported on the development of nanomaterials to prevent exposures to mercury in compact fluorescent light bulbs, community outreach efforts resulting in changes in state legislation regarding lead exposures, and the development of a recently approved Environmental Protection Agency method for analysis of dioxin-like halogenated aromatic hydrocarbons in environmental matrices.

Subscriptions are free through a link at the SBRP *Research Brief* [home page](#).

(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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# Science Notebook

## Modifying Risk Factors in Neurodegenerative Diseases

By Robin Arnette

Parkinson's disease (PD), multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS) are debilitating neurodegenerative illnesses, but many researchers are making strides in understanding these conditions and developing treatment and prevention strategies. One of these investigators, Alberto Ascherio, M.D., Dr.P.H., a professor of Epidemiology and Nutrition at Harvard School of Public Health, presented a distinguished lecture at NIEHS titled "Environmental Risk Factors and Biomarkers of Neurodegenerative Diseases." Honglei Chen, M.D., Ph.D., a tenure track investigator in the Epidemiology Branch, hosted the seminar in Rodbell Auditorium on August 12.

**Ascherio** began his talk by identifying three major roles that the field of epidemiology contributes to public health: preventing disease, targeting individuals at high risk for disease and determining neuroprotective factors that could be used for people who have the disease. In the case of PD, Ascherio and others have investigated several factors associated with the disease, including smoking and the use of tobacco products, caffeine consumption, pesticide exposure and family history. His work with smoking and caffeine, however, has yielded surprising results.

"We used data from several longitudinal studies and continued them by sending follow-up questionnaires to participants," he said. "People who were current smokers or who had recently stopped smoking had a 70 percent lower chance of developing PD than those who had never smoked." He added, "Although smoking is a major cause of morbidity and mortality, that shouldn't blind us to the possibility that there is something among the hundreds of chemicals in cigarette smoke that is important in preventing PD."

Coffee, tea and soda also have hundreds of components, but a cohort that Ascherio led determined it was caffeine that protected against PD. Middle-aged men documented their caffeine consumption, and their health was monitored for the next 15 years. Decaffeinated coffee and non-coffee drinkers exhibited a higher risk of PD than those who regularly consumed caffeinated beverages.

Despite the findings with cigarette smoke and caffeine, Ascherio said that studies with the antioxidant urate were the most exciting. "[The elevated amount of] serum urate not only predicted a lower risk of PD, but also a slower progression of the disease," he said. To pursue the finding further, Ascherio and Michael Schwarzschild, M.D., Ph.D., from the MassGeneral Institute for Neurodegenerative Disease, are collaborating on a project to examine the safety and efficacy of elevating urate levels in patients with early PD. The work is being funded by the Michael J. Fox Foundation for Parkinson's Research.



*Ascherio, above, emphasized the potential of his findings about elevated urate levels. "This is the first molecular marker directly linked to both the risk of development and progression of PD."* (Photo courtesy of Steve McCaw)

In regard to MS, Ascherio said that Americans who lived in northern states had a higher risk of MS than those who lived in the South or Midwest; however, if a person from the North moved to the South, his or her risk decreased. One hypothesis suggested that the difference in MS risk was due to a reduction in vitamin D; people in higher latitudes receive less sunlight and are prone to vitamin D deficiency.

To test the idea, Ascherio measured 25-hydroxyvitamin D (25OHD) levels — a good marker for vitamin D — in blood samples from the Department of Defense Serum Repository and found an inverse relationship between 25OHD blood levels and risk of developing MS. Ascherio said, “If this is true, it suggests that MS is largely a preventable disease. If we could increase vitamin D levels within the U.S. population, we could reduce the risk of MS by one-half.”

Ascherio ended the presentation with ALS research and highlighted a well-known study that found a relationship between veterans of the first Gulf War and ALS. He said that his group also found an increased incidence of ALS in military personnel who served during WWII, Korea and Vietnam. He said assembling over one million people for his next ALS cohort will be crucial. He noted, “Large longitudinal studies incorporating both genetic paths and biomarkers and environmental exposures are our best hope in finding or modifying risk factors in neurodegenerative diseases.”



*Not surprisingly, the lecture attracted several of Chen's colleagues in the NIEHS Epidemiology Branch, including biostatistician David Umbach, Ph.D., above. (Photo courtesy of Steve McCaw)*



*Visiting Predoctoral Fellow Fang Fang turned to watch speakers during the question and answer session. Fang works with Staff Scientist Freya Kamel, Ph.D., in the Epidemiology Branch. (Photo courtesy of Steve McCaw)*



*Ascherio's epidemiological studies also appealed to toxicologists, such as Rajendra Chhabra, Ph.D., center, group leader of the NIEHS General Toxicology Group. (Photo courtesy of Steve McCaw)*

# Alcohol Binges Early in Pregnancy Increase Risk of Infant Oral Clefts

By Robin Mackar

A new study by NIEHS epidemiologists shows that pregnant women who binge drink early in their pregnancy increase the likelihood that their babies will be born with oral clefts. The study appeared online July 30 in the *American Journal of Epidemiology*.

The researchers found that women who consumed an average of five or more drinks per sitting were more than twice as likely than non-drinkers to have an infant with either of the two major infant oral clefts — cleft lip with or without cleft palate or cleft palate alone. Women who drank at this level on three or more occasions during the first trimester were three times as likely to have infants born with oral clefts.

“These findings reinforce the fact that women should not drink alcohol during pregnancy,” said Lissa A. DeRoo, Ph.D., a staff scientist in the NIEHS Chronic Disease Epidemiology Group and author on the study. “Prenatal exposure to alcohol, especially excessive amounts at one time, can adversely affect the fetus and may increase the risk of infant clefts.” The causes of clefts are largely unknown, but both genetic predisposition and environmental factors are believed to play a role in their development.

The population-based study was conducted in Norway, which has one of the highest rates of oral clefts in Europe. The investigators contacted all families of newborn infants born with clefts between 1996 and 2002. The study included 573 mothers who had babies born with cleft lip with or without cleft palate and cleft palate only, as well as 763 mothers randomly selected from all live births in Norway. The average age of the mostly married mothers was 29 years.

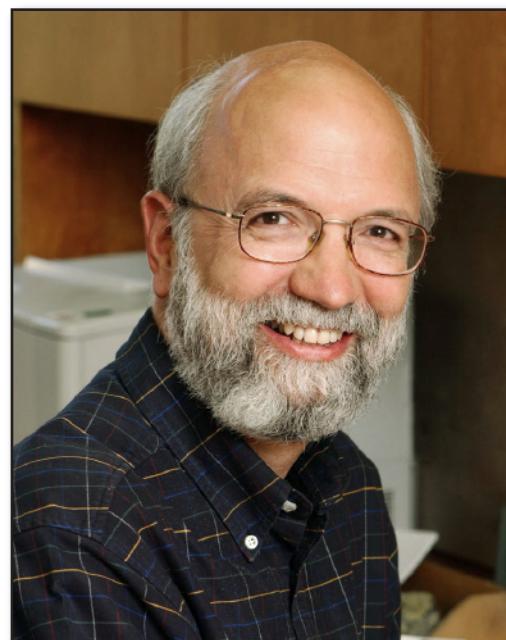
Mothers completed a self-administered mailed questionnaire focused heavily on the mother’s lifestyle and environmental exposures during her first three months of pregnancy when a baby’s facial development takes place.

The researchers found increased risks of orofacial clefts among infants whose mothers reported binge-level drinking of an average of five or more drinks per occasion during the first trimester compared to non-drinkers. Risk was further increased among women who drank at this level most frequently.

Both animal and human data suggest that it is the dose of alcohol consumed at one time during pregnancy rather than the frequency or total amount over time that matters most. “The greater the blood alcohol concentration, the longer the fetus is exposed. A single binge during a critical period of an infant’s development can be harmful,” DeRoo emphasized.



Staff Scientist and study author Lissa DeRoo  
(Photo courtesy of Steve McCaw)



In recognition of his “major contributions in making epidemiology one of the central disciplines in modern medicine,” Wilcox, above, was awarded an honorary doctoral degree on August 29 by the University of Bergen. (Photo courtesy of Steve McCaw)

"Fortunately, heavy maternal drinking is uncommon in many populations, but the fact that it is happening at all tells us we need to do a better job of letting mothers know about the effects that alcohol can have on their baby's development," explained Allen J. Wilcox, M.D., Ph.D., principal investigator in the NIEHS Environmental Toxins and Human Reproduction Group and co-author on the paper. In Norway, a separate study found that 25 percent of Norwegian women reported at least one binge-drinking episode during early pregnancy.

Alcohol is a recognized teratogen, an environmental agent that can cause malformations of an embryo or fetus. One of the most severe outcomes of heavy maternal drinking is fetal alcohol syndrome, a lifelong condition that causes physical and mental disabilities, including craniofacial malformations. There has been little research to determine if alcohol consumption is related to oral cleft risk.

The research was supported by the Intramural Research Program of the NIH, NIEHS. Researchers at the University of Bergen, the University of Oslo and the Medical Birth Registry of Norway also contributed to this study.

*Citation:* DeRoo LA, Wilcox AJ, Drevon CA, Lie RT. 2008. First-trimester maternal alcohol consumption and the risk of infant oral clefts in Norway: a population-based case-control study. Am J Epidemiol Epub ahead of print July 30, 2008, doi: 10.1093/aje/kwn186.

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

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## Gene Expression in Respiratory Disease

By Shweta Trivedi

Noted research pulmonologist Ron Crystal, M.D., presented a lecture to NIEHS scientists on August 5 in Rodbell Auditorium titled "Why Are Some Individuals More Sensitive to the Environment than Others? Genetic Variation and Modulation of Gene Expression in the Human Airway Epithelium." NIEHS Division of Extramural Research and Training Acting Deputy Director Pat Mastin, Ph.D., hosted the talk and encouraged the audience to consider future collaborations in translational research on the environmental dimensions of respiratory diseases.

Crystal is currently professor of Medicine and chair of the Department of Genetic Medicine at Weill Cornell Medical College and chief of the Division of Pulmonary and Critical Care Medicine at The New York Presbyterian Hospital. He served as the chief of the Pulmonary Branch, National Heart, Lung and Blood Institute from 1975 to 1993.



*Following the lecture, Crystal, right, spoke with NIEHS Acting Director Sam Wilson about ways his research approach can also offer insight into other environmental exposures' effects on respiratory diseases. (Photo courtesy of John Maruca)*

According to Crystal, his group utilizes microarray technologies for genome-wide characterization of gene expression, single nucleotide polymorphism and copy number variation profiles on clinical samples to identify candidate genes associated with complex diseases such as chronic obstructive pulmonary disease (COPD). “The first [hypothesis driving our research] is that transcriptional analysis of the small airway epithelium will lead to identification of the genes relevant to the risk from the environment,” he told the audience, “and the second is that variations in the response of the small airway transcriptome in response to the environment reflect genetic differences.”

Crystal compared his use of the Small Airway Epithelium (SAE), which he called “the canary of the lung,” for assessing the lung disease phenotype at biologic levels to the use of songbirds to warn miners of dangerous gases. Crystal uses fiberoptic bronchoscopy to brush airway epithelium to produce robust samples for RNA extractions.

The study populations include smokers who are “healthy” in terms of their lung functioning and imaging, healthy non-smokers, LENS (lung emphysema with normal spirometry) smokers and COPD smokers. One of Crystal’s significant findings was that, despite variability among individuals, more genes were found to be up- or down-regulated in SAE of healthy smokers, well before any functional changes were manifest, than in healthy non-smokers — with some genes differing as much as 60-fold.

Xenobiotic- and oxidant-related genes such as *nrf2* and glutathione pathway genes were expressed differentially in SAE of healthy smokers compared to healthy non-smokers. Surprisingly, immune response genes were found to be mostly down-regulated. Composite indices of gene expression in SAE were utilized to assess variability, including *nrf2* index, inflammation index, proliferation-related genes index and overall index of gene expression. Healthy non-smokers had the least variable gene expression. Healthy smokers were divided into low and high responders, and COPD smokers, the gold standard of disease phenotype, were high responders.

SNP analyses on five candidate genes — CHUR1, SNHG5, GPR135, CHP2 and ADRBK2 — revealed that there was a pairing control in SNP that could be correlated to gene expression in SAE. Copy number variations, where segments in the genome are missing or duplicated, also influenced the level of gene expression. The example Crystal highlighted from SAE was that of Glutathione-S-Transferases (GSTs). He suggested that it would be interesting to study the biologic influence of GST gene deletion in SAE of healthy smokers versus healthy non-smokers.

When Crystal compared DNA from SAE of healthy smokers to the DNA of their autologous blood, he observed that the genomes of SAE in healthy smokers had more cancer-related copy number variations — multiple deletions and amplifications — than the genomes of healthy non-smokers, indicating that there are acquired as well as SNP variations involved.

Turning to the future directions of his research, Crystal pointed to further exploration of signaling pathways from SAE and, for larger studies, trachea epithelium transcriptome to refine understanding of susceptibility. He also hopes to assess the effectiveness of interventions by characterizing their influence on gene expression.

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

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# UNC Research Day Highlights Human Neurological Disorders

By Eddy Ball

A contingent of NIEHS scientists joined colleagues from Duke University and the University of North Carolina (UNC) on August 15 for Research Day 2008, hosted at the Chapel Hill Campus by the UNC Department of Cell and Molecular Physiology. The day-long event featured keynote talks on autism and Alzheimer's disease by NIH grantees Joseph Piven, M.D., and Sangram Sisodia, Ph.D., as well as poster sessions for students and postdoctoral trainees in the [department](#).

The morning lecture, "Imaging the Developing Brain in Autism," was by [Piven](#), who is the Sarah Graham Kenan Professor of Psychiatry, Pediatrics and Psychology and director of the Neurodevelopmental Disorders Research Center at UNC. In his introduction, UNC Professor Manzoor Bhat, Ph.D., faculty organizer for the event, described Piven as "a world-renowned authority on autism... [whose] work has been cited thousands of times."

Along with his cutting edge research in imaging the brains of autistic children that was the core of his [April lecture](#) at NIEHS, Piven described efforts to identify children with autism as early as possible and better understand what he described as the spectrum of "autisms" that clinicians encounter. As Piven explained, "I'm really interested in going beyond these kind of crude behavioral phenotypes that we have in autism" to develop quantitative measures to add specificity to the list of criteria in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV).

"I often think that you could read DSM-IV on autism," Piven began, "and then sit on a bus next to somebody with autism and you probably wouldn't know it." However, by using a principal components approach, researchers can identify patterns of perception and social orienting that relate to different autism spectrum disorder phenotypes.

By combining brain imaging results with principal component analysis and genetic studies of people with autism, Piven contended, researchers can come closer to sorting through what he called "the laundry list" of candidate genes involved in autism to "disaggregate the syndrome." This approach could help scientists tease apart the substantial heterogeneity in this condition, link genetic abnormalities to specific brain-behavior phenotypes and develop more rationally derived approaches to early intervention.



Department Chair James Anderson, M.D., Ph.D., welcomed visitors from Duke and NIEHS to the 12th annual Research Day, which is held at the beginning of the academic year "to share our science and celebrate the diversity of our research programs" in physiology. (Photo courtesy of Steve McCaw)



In his introduction of Piven, Bhat, above, joked that Piven learned only the day before that he and Sisodia had been in different departments at Johns Hopkins University at the same time. (Photo courtesy of Steve McCaw)

Sisodia's afternoon talk focused on findings from his group's integrated genetic, neurobiological, molecular and cellular research with an exploration of "Function and Dysfunction of Presenilins in Alzheimer's Disease (AD)." Bhat introduced [Sisodia](#) with a photo on the screen behind him of the 51-year-old woman who was the first patient described with the disease by German neuropathologist Alois Alzheimer, M.D., in 1907.

Sisodia is the Thomas Reynolds Sr. Family Professor of Neurosciences in the University of Chicago's Department of Neurobiology, director of the Center for Molecular Neurobiology there and a leading expert on the biochemistry and genetics of AD.

The Sisodia group's investigations are focused on understanding the normal biology of proteins involved in the development of Alzheimer's disease, including amyloid precursor protein (APP), presenilin 1 (PS1) and presenilin 2 (PS2). The researchers seek to elucidate the molecular and cellular mechanisms by which mutated versions of these proteins promote the amyloid plaque and neurofibrillary tangles that are characteristic of what he predicts will be "an epidemic of staggering proportions" by 2050, when it is estimated that 25 percent of the population will be over 65 years old.

Sisodia's approach in studying these proteins has been to develop cell biological strategies together with specific transgenic mouse models to better understand development of Alzheimer's disease. According to him, these models could be useful for addressing issues relevant to the selective vulnerability of specific CNS systems and the pathophysiological sequelae, providing opportunities to test agents that block these processes.

His group recently reported that enriched environments and exercise modulate the metabolism and deposition of toxic amyloid peptides in the brains of transgenic animals, adding support to the theory that activity, exercise and mental stimulation may be protective, delaying onset of AD by stimulating adult hippocampal neurogenesis.

## Expanding the Autism Data Base

Toward the end of his talk, Piven lamented a common shortcoming of autism research. "One of the things that bedevils this research," he said, "is the sample size."

That situation could begin to change in 2009 with enrollment of subjects in a new large-scale epidemiological study of gene-environment interactions being supported by NIEHS grants managed by Health Science Administrator Cindy Lawler, Ph.D. Piven said that he will be pairing up with the [Early Autism Risk Longitudinal Investigation \(EARLI\) Network](#), a ten-year study of mothers of autistic children and their newborn siblings headed by Principal Investigator Craig J. Newschaffer, Ph.D., of Drexel University.

The network plans to implement a core epidemiologic data collection protocol focusing on prospective documentation of exogenous exposures, continuous autistic spectrum disorder (ASD) behavioral domains during pregnancy and early life, collection and banking of biological samples and follow-up of 1,200 newborn siblings through 36 months of age.

"The focus of their [EARLI] study is environmental," Piven said. "We're going to join up with them and add a genetics component with genome-wide data and look at the relationship with environmental factors."

With this increase in the data researchers need to truly understand the various linkages among genes, behavior and biology, investigators may be able to identify genetic, biological and family pedigree predictors of autism much earlier than the six-month point where Piven has found brain enlargement in autistic children.



*"What has become apparent in the past fifteen years is that autism is a genetic disorder,"* Piven maintained, "[but] none of the studies performed so far have achieved what is called 'genome-wide significance.'"

(Photo courtesy of Steve McCaw)



NIEHS Staff Scientist Gary Bird, Ph.D., who is a member of the Calcium Regulation Group, was among the scientists from NIEHS at Piven's talk. (Photo courtesy of Steve McCaw)



*"PSI is at the middle of the story,"* Sisodia explained. Mutations of PSI interfere with protein transport and trigger alterations in amyloid metabolism that result in plaque deposition.

(Photo courtesy of Steve McCaw)



NIEHS Summers of Discovery intern Catherine Ferguson, center, a student at Eastern Virginia Medical School, listened intently to Sisodia's talk. Sitting directly behind her were NIEHS Health Science Administrators Kimberly McAllister, Ph.D., left, and Annette Kirshner, Ph.D., right. (Photo courtesy of Steve McCaw)

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# Grantee Presents Prize-Winning Environmental Justice Research

By Eddy Ball

Edward Emmett, M.D., spoke to an audience of NIEHS and Environmental Protection Agency (EPA) scientists gathered in Rodbell Auditorium on July 24. Hosted by NIEHS Program Analyst Liam O'Fallon, Emmett's talk on "Perfluorooctanoate (PFOA) from Teflon Manufacture: Studies of Community Exposure, Potential Risks and Effects of Intervention" was part of the NIEHS Frontiers of Environmental Sciences Lecture Series.

Emmett is a professor in the University of Pennsylvania (UP) School of Medicine, deputy director of the Center of Excellence in Environmental Toxicology and director of the Community Outreach and Education Core. Emmett reported on the studies he and colleagues conducted on the effects of PFOA, a persistent and ubiquitous compound also known as C8, in water provided by the Little Hocking Water Authority (LHWA) in southeastern Ohio — and their innovative protocol for disseminating results to affected residents and impacting public health practice and policy in the area.

Emmett began his talk with photos of the Ohio River, the Dupont Teflon-producing plant in West Virginia that is the source of PFOA and, just across the river from the plant, the intake for drinking water distributed by LHWA to homes in Ohio as far as 20 miles away. "Community concern really started in 2001," he explained, "when PFOA was found in production wells of the Little Hocking Water Association at concentrations between 0.8 and 7.8 parts per billion."

As Emmett explained, with NIEHS funding to correct an "information discrepancy..., [the researchers] set about creating an environmental justice partnership [made up of] an environmental scientist, a local health care provider and the community association... to make sure the right questions were being asked and to empower those affected by providing the information necessary for informed action."



*Emmett recalled that industrial, legal and media representatives were inconvenienced by having to travel to the community to learn the results of the study. "I think that [community first communication] was extremely important to the community."* (Photo courtesy of Steve McCaw)



*O'Fallon, above, manages an NIEHS grant portfolio made up of projects, like Emmett's, designed to empower victims of environmental injustice. (Photo courtesy of Steve McCaw)*

In a random stratified sampling of groups with differing patterns of air exposure to PFOA, the investigators determined that the source was indeed water and that levels in humans varied depending on the source of the water. They also found that the median PFOA in LHWA customers averaged 386 ppb compared to a level of 5 ppb in the general population and approached levels found in production workers, with levels highest in the very young and the very old.

Even though the team found no association between serum PFOA and biomarkers or an increase in liver or thyroid disease, the team prepared a set of recommendations for consumers, industry and regulators. They disseminated the results of the study and their recommendations through a protocol that marked a paradigm shift in communication of research findings by notifying individuals in the study and the community first through personal letters, consultation, public meetings, a web site and a newsletter. Only after the people affected understood the results were the scientific community and the media informed in such a way that the partnership controlled the message.

This empowerment model proved to be very successful. It convinced Dupont on the afternoon that results were released to offer free bottled water to affected households and led eventually to construction of a new treatment plant. According to results of a follow-up study of the affected population, 78.6 percent accepted Dupont's offer of bottle water, 95 percent made some change in water supply, and there was a 26 percent reduction in PFOA levels.

Several published studies emerged from the investigators' work, along with a first prize at the EPA Science Fair in 2000, and the publications won the American College of Occupational and Environmental Medicine Authorship Award for the year. In May of this year, Emmett and Decatur Community Association Community Coordinator Ellen Mumma accepted the Community-Campus Partnerships for Health Award for 2008.

The research also inspired a chapter in Callie Lyons' provocatively titled 2007 book, *Stain-Resistant, Nonstick, Waterproof, and Lethal: The Hidden Dangers of C8*. So far at least two states, New Jersey and Minnesota, have used the team's research as the basis of safe water standards.



*The possible effects of PFOA on reproduction drew basic scientists, such as Principal Investigator Ken Korach, Ph.D., above, to the lecture. (Photo courtesy of Steve McCaw)*



*National Toxicology Program researcher Ron Melnick, Ph.D., commented on evidence of PFOA's effects on the early growth development of children of mothers with elevated levels. (Photo courtesy of Steve McCaw)*

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# Expert Panel Conducts Scientific Review of Styrene

On July 21-22, 2008, an expert panel met at the Radisson Hotel Research Triangle Park, N.C. to evaluate styrene, which was nominated for possible listing in the *12<sup>th</sup> Report on Carcinogens (RoC)*. A majority of the panel members voted to recommend listing the compound as reasonably anticipated to be a human carcinogen.

Styrene is a monomer used worldwide in the production of polymers that are incorporated into products such as rubber, plastic, insulation, fiberglass, pipes, automobile parts, food containers and carpet backing.

After receiving oral public comments from a number of groups, the expert panel carried out an in-depth review of the draft background document on styrene identifying edits to the text and additional references for inclusion. Following completion of the peer review, the expert panel discussed the scientific evidence regarding the carcinogenicity of styrene and recommended (8 yes / 2 no) that styrene be listed in the *12<sup>th</sup> RoC* as reasonably anticipated to be a human carcinogen based upon sufficient evidence from studies in experimental animals and limited evidence from studies in humans.

Next, the NTP will solicit public comment on the expert panel's listing recommendation and scientific justification through the Federal Register and finalize the background document, taking into consideration the panel's recommended edits and public comments.

Information about this meeting and the review of styrene is available by contacting the [RoC Office](#).

(Reprinted from the August 2008 *NTP Update*)



Bucher began the meeting with a description of the [revised multi-step review protocol](#) adopted for the *12<sup>th</sup> RoC* in 2007. "In this new arrangement," he explained, "the public meetings occur very early in the process." (Photo courtesy of Steve McCaw)



Panel Chair David Phillips, Ph.D., DSc., with *RoC* Group Director Ruth Lunn, Dr.P.H., following the public comment portion of the meeting. Phillips is a professor of Environmental Carcinogenesis at the University of London Institute of Cancer Research. (Photo courtesy of Steve McCaw)



Panel member Scot Eustis, D.V.M., Ph.D., left, looked on as colleague Lauren Zeise, Ph.D., referred to one of the studies cited in the *Draft Document for Styrene*. Eustis is a veterinary pathologist now in private practice, and Zeise is a risk assessment specialist with the California Environmental Protection Agency. (Photo courtesy of Steve McCaw)

Lorenz Rhomberg, Ph.D., was one of eight industry representatives speaking during the public comment session. He is a principal of Gradient Corporation who spoke on behalf of the National Marine Manufacturers Association. (Photo courtesy of Steve McCaw)

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# Evolutionary Implications for Double-Strand DNA Breaks

By Dixie-Ann Sawin

A collaborative study, recently published in the *Proceedings of the National Academy of Science* by researchers from the NIEHS, Duke University and Brazil's Universidade Estadual de Campinas determined how DNA double-strand breaks (DSBs) in chromosomes can lead to chromosomal aberrations (CAs) and reshape the genome. In a collaboration between the NIEHS Chromosome Stability Group of Michael Resnick, Ph.D., and the Duke Genetics and Molecular Biology laboratory of Tom Petes, Ph.D., highly sophisticated molecular tools were used to analyze CAs that arose from random DSBs induced by ionizing radiation.

Although the link between ionizing radiation or X-rays and CAs has been known for quite some time, the underlying mechanisms remain unknown. This study highlights the importance of DSBs in creating genetic variation and evolutionary change in organisms. Although DSBs can be efficiently repaired in nearly all organisms, the investigators wanted to know the extent to which they could change the genome even under conditions of maximal repair through homologous recombination (HR).

HR is the process of physical exchange between homologous chromosomes or sister chromatids following replication of a chromosome. This process occurs naturally during chromosomal crossovers in eukaryotic organisms undergoing meiosis and results in a shuffling of genetic material. HR is also involved in repair of DSBs, where organisms repair a damaged region using the material from a partner chromosome as a template. HR can also be utilized as a tool for targeting genetic changes into an organism. HR in eukaryotes has the additional role of protecting organisms from cancer.

This [study](#) differs from earlier ones because previous studies used techniques that selected for unique types of genetic events at specific chromosomal positions rather than sampling the entire genome. In this study, budding yeast were employed because of their genetic and molecular accessibility and the fact that yeast are often considered as model organisms for understanding events in human cells.

Diploid cells that were arrested in the G2 phase of the cell cycle were exposed to 80 krad (800 Gray) of radiation. This corresponds to 250 DSBs produced per cell. Diploid rather than haploid cells were used because it was anticipated that they could tolerate many types of CAs. Although the majority of DSBs were effectively repaired through HR between sister chromatids or homologous chromosomes, Jim Westmoreland, Ph.D., in the Resnick lab showed that approximately 2% produced CAs. Juan Lucas Argueso, Ph.D., the first author of the paper, showed that most of the generated CAs resulted from HR between small transposable element sequences called Ty retrotransposons that are located across the genome. The CAs were characterized by microarray-based comparative genomic hybridization (CGH array) to identify contiguous genomic segments.

Using a “molecular autopsy” approach that involved CGH of chromosomes newly generated by DSBs, the investigators were able to identify a variety of chromosomal changes. The DSB-induced changes primarily involved recombinational interactions between the Ty elements. These findings show that these scattered



Principal Investigator Mike Resnick (Photo courtesy of Steve McCaw)

sequences could effectively compete with sister chromatids and homologous chromosomes in the HR repair of DSBs. Included among the CAs were deletions, interstitial duplications and nonreciprocal translocations. In addition, mitotic recombination between homologous chromosomes, resulting in loss of heterozygosity (LOH), was also observed. CAs and LOH are common in cancer cells.

This study showed that DSBs can lead to increased genomic plasticity through recombination of repetitive DNA elements. These types of rearrangements can be either advantageous or deleterious to the organism. In fact, as the study suggests, “a compromise between opportunities for variation and excessive genome instability...” may contribute to increased genomic variation in humans.

*Citation:* Argueso JL, Westmoreland J, Moiczkowski 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.

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

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## **Upcoming Distinguished Lecturer Richard Boucher**

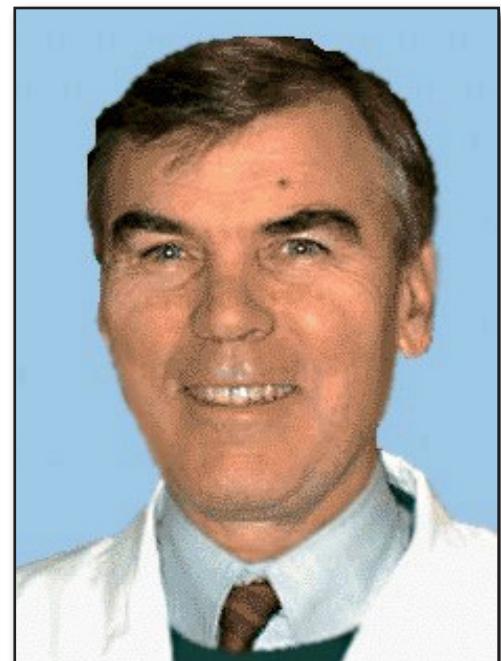
*By Eddy Ball*

The 2008 – 2009 NIEHS Distinguished Lecture Series will welcome its first speaker, Richard Boucher, M.D., at 11:00 a. m. September 8 in Rodbell Auditorium. Boucher will speak on “Cystic Fibrosis: A Failure of Lung Defense Against the Environment.”

Boucher is the Kenan Professor of Medicine and director of the Cystic Fibrosis/Pulmonary Research and Treatment Center at the University of North Carolina at Chapel Hill. His lab’s major interest lies in basic and translational research into the functions of airway epithelia in health and disease. The group investigates the physiology of airway surface liquid at the microscopic and the integrated (alveolar/airway) macroscopic levels, the sites and regulation of Na<sup>+</sup> transport in the conducting airways, the role of extracellular nucleotides in airway homeostasis and gene therapeutic approaches to cystic fibrosis lung diseases.

The talk will be hosted by Principal Investigator Jim Putney, Ph.D., of the Calcium Regulation Group.

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*Distinguished Lecturer Richard Boucher  
(Photo courtesy of UNC)*

# Extramural Update

## New Grant Opportunities on Functional Characterization of Genetic Variants and Interactions

NIEHS and the National Institute on Drug Abuse (NIDA) have announced a pair of funding opportunities on behalf of the NIH Genes, Environment and Health Initiative. The closing date for applications under [RFA-DA-09-003](#) and [RFA-DA-09-004](#) is October 17, 2008.



These grants are intended to encourage functional characterization of genetic variants believed to be associated with a particular disease or disorder outcome through gene discovery approaches, such as genome-wide association studies, candidate gene approaches and sequencing studies. Measuring the discrete contribution of a particular variant or environmental factor for the condition and being able to assess them in combination with other alleles/environmental factors is an integral component of the NIH Genes, Environment and Health Initiative (GEI).

Understanding the function of the gene variants identified through genome-wide association studies (GWAS) and other gene discovery approaches and elucidating the mechanisms of how they contribute to disease is an obvious next step towards realizing how best to relate the genomic data obtained from GWAS approaches to improving public health. One of the biggest challenges in functional genetics is establishing that a particular SNP or gene variant in a disease-associated region is indeed the variant contributing to or causing the disease. Innovative approaches utilizing computational and systems biology and the integration of “-omics” methodologies, such as genomics, comparative genomics, proteomics, transcriptomics, metabolomics, epigenomics and informatics, with such high-throughput technologies as RNAi, tissue arrays and others into comprehensive pathway-driven approaches are encouraged for applications to this initiative in order to understand functionally and mechanistically the role of environment, development and genetics in complex human diseases.

Areas of interest include relatively low throughput approaches, for example transgenic mouse approaches, to test some of the most promising variants for changes in function and high-throughput tests, such as yeast, *C. elegans*, cell culture systems or computational approaches, to look at different aspects of variant function. Model organisms and/or human studies are also encouraged, as is utilizing state-of-the-art technologies to explore cellular, physiological and/or behavioral function of the whole organism. This funding opportunity will use the R21 and R03 mechanisms with the R03 applications focused on projects that are pilot studies in nature and may not have preliminary data.

The GEI is a four-year, NIH-wide program to support efforts to identify major genetic susceptibility factors for diseases of substantial public health impact and to develop technologies for reliable and reproducible measurement of environmental exposures that interact with genetic susceptibility to influence health and disease. The program is being coordinated and implemented by an NIH-wide GEI Coordinating Committee, administratively led by NIEHS and the National Human Genome Research Institute (NHGRI).

For more information on the GEI program see: <http://www.gei.nih.gov/index.asp>

### Contacts

NIEHS: Kimberly McAllister, Ph.D. | [mcallis2@niehs.nih.gov](mailto:mcallis2@niehs.nih.gov)

NIDA: Joni Rutter, Ph.D. | [jr295m@nih.gov](mailto:jr295m@nih.gov)

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# Extramural Papers of the Month

By Jerry Phelps

## Mercury Vapor Captured from Compact Fluorescent Bulbs

Brown University researchers supported by the NIEHS Superfund Basic Research Program have developed a nanomaterial that absorbs the toxic mercury vapor in compact fluorescent light bulbs. Compact fluorescent bulbs are the increasingly popular swirl-shaped bulbs that use 75 percent less energy than incandescent bulbs and have been touted as one method to save energy and fight climate change. However, there is a major environmental concern; they emit mercury vapor when broken or damaged.

The research team developed a nanomaterial that readily absorbs the gas. It can be used in packaging of new bulbs and disposal of burned-out or broken bulbs. The researchers have applied for patents and expect to enter into licensing negotiations with companies that could manufacture the packaging.

The material is a variant of nanoselenium and was developed by Robert Hurt and Brown engineering student Natalie Johnson. It absorbs virtually all the mercury vapor given off by broken bulbs. Hurt thinks the packaging can be developed at a low cost since only one to five milligrams of nanoselenium is needed to absorb the mercury from a single bulb. The team has also developed plastic bags that could be used to dispose of burned-out or broken bulbs.

*Citation:* Johnson NC, Manchester S, Sarin L, Gao U, Kulaots I, Hurt RH. 2008. Mercury Vapor Release from Broken Compact Fluorescent Lamps and In Situ Capture by New Nanomaterial Sorbents. Env Sci, & Tech 42(15):5772-5778.

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## Breathing Polluted Air Raises Blood Pressure

A new study by cardiovascular researchers at the Ohio State University Medical Center is the first to report a direct link between air pollution and high blood pressure.

The research team exposed rats to levels of airborne pollutants that humans breathe on a regular basis. The levels were much lower than those seen in developing areas of China and India and some regions of the US. They found that short term exposure to these pollutants, over a 10-week period, elevated blood pressure in rats that were predisposed to the condition. These results are consistent with human observational studies that demonstrate similar blood pressure increases within hours to days following exposure.

Rats were exposed to concentrations of particulate matter air pollution comparable to levels seen in US cities with heavy commuter traffic. When rats were given angiotensin II, a naturally occurring hormone involved in blood pressure regulation, and exposed to particulate pollution, their blood pressure rose sharply as compared to rats that breathed filtered air.

A continuation of this work is being conducted in Beijing in association with the Summer Olympics. The researchers will measure vascular function in people before and after stringent air quality improvements are made for the games.

*Citation:* Sun Q, Yue P, Ying Z, Cardounel AJ, Brook RD, Devlin R, Hwang JS, Zweier JL, Chen LC, Rajagopalan S. 2008. Air Pollution Exposure Potentiates Hypertension Through Reactive Oxygen Species-Mediated Activation of Rho/ROCK. *Arterioscler Thromb Vasc Biol* [Epub ahead of print].

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## Link Between Thunderstorms and Asthma Attacks in the Atlanta Metro Area

In a study co-funded by NIEHS and the EPA, researchers report discovering a link between asthma attacks and thunderstorm activity in the Atlanta metro area, home to more than five million people.

While a relationship between thunderstorms and increased hospital visits for asthma attacks has been known and studied worldwide, this study is the first to combine epidemiology and climatology in a research effort in the American South.

The research team used a database of more than 10 million emergency room visits over an 11-year period and found a 3 percent higher incidence of visits related to asthma on days following thunderstorms. A likely hypothesis offered by the research team for the increase in asthma is that pollen grains may rupture upon contact with rainwater, releasing respirable-sized allergens, and that gusty winds associated with the storm help to spread these particles. Exposure to certain pollen allergens is a known risk factor for asthma attacks.

The research team will continue its work to better understand the mechanistic basis of thunderstorm-induced asthma in an effort to improve intervention strategies and planning for emergency room services. They point out that this is particularly important considering that severe thunderstorms are estimated to double in the Atlanta area in this century.

*Citation:* Grundstein A, Sarnat SE, Klein M, Shepherd M, Naeher L, Mote T, Tolbert P. 2008. Thunderstorm associated asthma in Atlanta, Georgia. *Thorax* 63(7):659-660.

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## Over-the-Counter Pain Medicines May Reduce Risk of Diabetes

Researchers supported by NIEHS have added to a growing body of literature showing that standard dosages of several over-the-counter analgesics may prevent or delay the onset of Type 2 diabetes. The researchers used laboratory mice fed a high fat diet that triggered impaired glucose tolerance, a hallmark of Type 2 diabetes. They compared biologically relevant dosages of acetaminophen, naproxen, ibuprofen and aspirin for their respective effects on protecting against the development of a pre-diabetic condition in these mice.

Glucose tolerance was improved in the mice receiving acetaminophen and aspirin and to a lesser extent ibuprofen. Naproxen had no effect on glucose tolerance. The over-the-counter drugs partially prevented an increase in body fat, with acetaminophen and ibuprofen performing better than naproxen and aspirin. In liver mitochondria, the drugs inhibited succinate-dependent hydrogen peroxide production and lipid peroxidation. The researchers conclude from these findings that the over-the-counter analgesics diminished pro-oxidant processes that exacerbate inflammation and a pre-diabetic state.

With the rise in obesity in the US come increasing rates of Type 2 or noninsulin dependent diabetes. The common, readily available and relatively inexpensive drugs tested in this study may represent valuable therapies to delay or prevent the onset of Type 2 diabetes.

*Citation:* Kendig EL, Schneider SN, Clegg DJ, Genter MB, Shertzer HG. 2008. Over-the-counter analgesics normalize blood glucose and body composition in mice fed a high fat diet. Biochem Pharmacol 76(2):216-224.

(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*

### Exposure to Lead May Prolong ALS Survival

Previous studies of lead suggested that the highly toxic metal was associated with increased risk of developing amyotrophic lateral sclerosis (ALS), but a team of scientists from NIEHS, Social and Scientific Systems, Inc., Westat and the University of Michigan reported that lead exposure was also associated with longer survival in ALS cases.

The authors said that given the small sample size and the unexpected results, the finding should be interpreted with caution. However, if the result is confirmed by other studies, it may contribute to understanding the mechanisms of disease progression and to developing therapies that prolong the lives of ALS sufferers.

The team measured levels of lead in blood and bone (in the tibia and patella) from 110 cases who participated in a case-control study conducted in New England in 1993–1996.

The researchers found the strongest association with survival in patients who had high levels of lead in the tibia, although those with high blood and patella lead levels also had prolonged survival. Conversely, shorter survival was associated with older age at diagnosis, being female, decreased lung function, shorter interval between symptom onset and diagnosis, and bulbar onset of disease (difficulty in speech or swallowing).

*Citation:* Kamel F, Umbach DM, Stallone L, Richards M, Hu H, Sandler DP. 2008. Association of lead exposure with survival in amyotrophic lateral sclerosis. Environ Health Perspect 116(7):943-947.

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## The Involvement of RAP80 Following DNA Damage

NIEHS researchers showed that a mutant of the tumor suppressor breast cancer-1 (BRCA1), which is associated with an increased risk of breast cancer, was unable to both interact with RAP80 and translocate to ionizing radiation-induced foci (IRIF). Previous work had demonstrated that RAP80, a nuclear protein containing two ubiquitin-interacting motif (UIMs), was associated with BRCA1 and mediated the translocation of BRCA1 to IRIF following ionizing radiation (IR) and ultraviolet light (UV) treatment. Their experiments demonstrated that RAP80 is involved in several types of DNA damage responses.

Earlier research from the group had determined that ataxia-telangiectasia mutated (ATM) kinase phosphorylated a specific serine residue (Ser205) in RAP80 *in vitro*. To study this mechanism and its molecular implications in more detail, the team generated rabbit polyclonal antibody against phosphorylated Ser205 and used it to track RAP80 in MCF-7 cells treated with IR. The data indicated that phosphorylation occurred less than five minutes after radiation treatment and was independent of BRCA1. The team concluded ATM was responsible for the phosphorylation since RAP80 wasn't phosphorylated when the same experiment was performed in A-T cells, a cell line that lacks ATM.

UV also induced phosphorylation of RAP80 at Ser205 and its translocation to DNA damage foci in response IR. This translocation event was dependent on the UIMs of RAP80 and RAD3-related kinase (ATR), an ATM-like kinase.

*Citation:* Yan J, Yang XP, Kim YS, Jetten AM. 2008. RAP80 responds to DNA damage induced by both ionizing radiation and UV irradiation and is phosphorylated at Ser205. *Cancer Res* 68(11):4269-4276.

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## Liver X Receptor Regulates Pulmonary Innate Immunity

The lung and the neutrophil are novel *in vivo* targets for pharmacologic Liver X Receptor (LXR) activation according to researchers at NIEHS and the National Jewish Medical and Research Center. The studies identify LXR stimulation as a potential tool for modulation of innate immunity in the lung.

The lungs, like the rest of the body, are exposed to potentially damaging agents, such as inflammatory environmental stimuli and bacterial infections. To fend off these attacks, the host organism's immunological response, in particular the recruitment of polymorphonuclear neutrophils (PMNs) — white blood cells that kill microorganisms by engulfing them — must be precisely regulated. Since work from other labs found that the  $\alpha$  and  $\beta$  forms of LXR, a nuclear receptor, were involved in proinflammatory gene expression, the team theorized that LXR regulated PMN recruitment to the lung when it was infected or inflamed.

To test this hypothesis, the researchers confirmed that LXR was expressed in the lung, and then treated mice with a synthetic LXR agonist prior to exposing their lungs to lipopolysaccharide (LPS), KC chemokine or the gram-negative bacterium *Klebsiella pneumoniae*. The team found that the LXR agonist attenuated PMN recruitment to the lungs and impaired pulmonary host defense.

*Citation:* Smoak K, Madenspacher J, Jeyaseelan S, Williams B, Dixon D, Poch KR, Nick JA, Worthen GS, Fessler MB. 2008. Effects of liver X receptor agonist treatment on pulmonary inflammation and host defense. *J Immunol* 180(5):3305-3312.

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# Differential Regulation of an ERK Protein Scaffold to Control Gene Transcription

Extracellular signal-regulated kinases 1 and 2 (ERKs 1 and 2) differentially regulate transcriptional pathways by forming stable complexes with other proteins. Such a complex containing ERK1 was found to be present in neuronal nuclei and to respond differently to synaptic or depolarizing stimulation, whereas monomeric ERK1 responds equally well to both types of stimulation. The NIEHS researchers who report the finding believe that this protein scaffolding mechanism allows neuronal stimulation to regulate gene transcription differentially depending on whether the stimulation is normal or pathological.

Data indicated that because of its size, the large pERK-reactive complex (PERC-160) was restricted to the nuclei and contained phosphorylated ERK1 and 14-3-3 protein. Transglutaminase, a cross-linking enzyme that forms bonds between proteins, was proposed to make the structure extremely stable. Analysis using purified nuclei from rat forebrain demonstrated that ERK1 in the structure was dephosphorylated in response to potassium depolarization, representing abnormal neuronal activity, whereas it was phosphorylated in response to normal synaptic activity. The uncomplexed form of ERK was phosphorylated under both conditions.

The research represents the first evidence that neuronal complexed ERK may use different mechanisms to regulate gene transcription in response to various types of neuronal stimulation.

*Citation:* Lundquist JJ, Dudek SM. 2008. Differential activation of extracellular signal-regulated kinase 1 and a related complex in neuronal nuclei. Brain Cell Biol 35(4-6):267-281.

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# Inside the Institute

## A Fond Farewell to Ben Van Houten

By Eddy Ball

When his friends and colleagues decided to mark the departure of Ben Van Houten to his new position at the University of Pittsburgh, they decided to go all out. The more than 200 people who gathered in the NIEHS Cafeteria on July 30 found a wide range of refreshments lining the central buffet bar, decorations and a carefully planned program of reflection and tribute—along with the kind of roast that has come to characterize farewell parties sponsored by the NIEHS Division of Extramural Affairs (DERT).

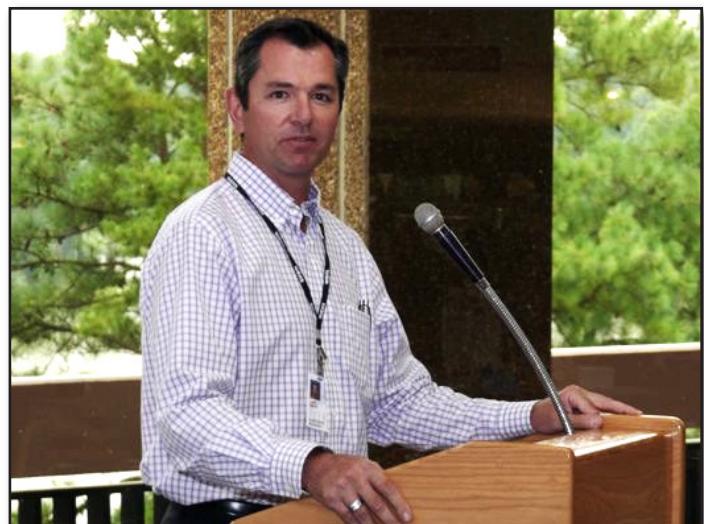
Opening speaker Pat Mastin set the tone for the roasting portion of the event, “Where’s Ben,” with a Vaudeville play on several mispronunciations of Van Houten’s name — pretending that because he’d seen Van Houten so infrequently around DERT, he couldn’t quite remember the name. When he passed the baton to sidekick Jerry Phelps, Phelps showed a series of doctored images and captioned photos. In the course of his routine, Phelps delivered a salvo of one-liners at the expense of Van Houten and the many DERT colleagues caught in his wide-cast net of good-natured ribbing.

The event took on a more serious tone as colleagues looked back on their work with Van Houten over his nine-year career at NIEHS. Former DERT Director Anne Sassaman, reflected on how seamlessly Van Houten had settled into his dual roles at NIEHS to develop a system for evaluating research publications that is now enterprise-wide at NIH. She was followed by Jan Drake, Tom Kunkel, Dennis Lang, Mike Resnick, Rick Paules and Astrid Haugen, a former lab manager in Van Houten’s group and later a fellow analyst in DERT.

Each of the speakers praised Van Houten as a polymath who is accomplished in scientific fields ranging from bibliometric analysis, *C.elegans*, mitochondrial disease and DNA repair to the technical intricacies of omics methodologies and microarray analysis. Several described him as a “star” and a “heavy hitter” in the field of environmental health sciences.



*As well wishers arrived, they joined Lang, center left in blue, Darius Emrani, in yellow, and Annette Kirschner, center in orange print, and others at the well-appointed buffet. (Photo courtesy of John Maruca)*



*Except for that almost imperceptible twinkle in his eye as he took the podium, there's little in this photo of Phelps to indicate the extent of the mischief that would follow as he looked for Ben — and found him — in all the wrong places. (Photo courtesy of John Maruca)*

Like the speakers who preceded him, NIEHS Acting Director Sam Wilson praised Van Houten's work, calling him an "extremely broad individual, but at the same time able to go into depth in his analysis of science in all of his areas of interest." Wilson also paid tribute to his personal friendship with Van Houten and pledged to nurture it despite the physical distance that will separate them.

Van Houten was visibly moved as he referred to his "mixed emotions" about leaving his NIEHS family of friends and colleagues for a "dream come true" at a major medical center. He said he will always be grateful for "how very good NIEHS has been to me and how very much I've learned here." On a lighter note, Van Houten added, "As families go, OK, maybe NIEHS is a little dysfunctional, but a great warm family all the same."



*It didn't take long for Phelps to captivate the audience. Sitting behind Mike Humble, foreground left, are Rose Anne McGee, Martha Barnes, Nishant Shah and Annette Kirschner. (Photo courtesy of Robert Fedic)*



*The jokes came rapid fire, one after another, and the guest of honor, like the rest of the audience, couldn't keep a straight face as he was roasted to the point of well done. (Photo courtesy of Robert Fedic)*



*The speakers who followed Phelps, such as Mike Resnick, above, got a few laughs at Van Houten's expense, but overall their comments focused on their colleague's many contributions to research at NIEHS. (Photo courtesy of Robert Fedic)*



*Wilson, center, joined Van Houten and Leping Li, right. In his comments, Wilson told Van Houten, "I can't say enough in expressing our gratitude for all that you've done." (Photo courtesy of John Maruca)*



*Van Houten was also honored by his trainees and junior associates, such as, left to right, Senyene Hunter, Vijji Panduri and Astrid Haugen. In her tribute, Haugen told her colleague, "Your light is going to shine so brightly it'll blind everybody."* (Photo courtesy of Robert Fedic)



*Visiting Fellow Hong Wang, above, plans to use her K99/R00 grant to follow Van Houten to Pittsburgh.* (Photo courtesy of Robert Fedic)



*As they enjoyed refreshments, Van Houten posed with colleagues from the Laboratory of Structural Biology. Shown left to right are Gerri Wolfe, Bill Beard, Van Houten, Julie Horton and Rajendra Prasad.* (Photo courtesy of Robert Fedic)



*Naturally, the party also featured a very special cake.* (Photo courtesy of Robert Fedic)

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# Science Camp Revamped for Third Successful Year

By Eddy Ball

The Durham Alumnae Chapter of Delta Sigma Theta marked several firsts when its members welcomed students to the third annual Science and Everyday Experiences (SEE) Summer Camp on June 28 at the chapter house in Durham. This year, there were more children and volunteers involved, new activities and an innovative program for parents. In addition, there was a special visitor from Bethesda on hand to help out and observe the program in action — as well as ponder the ways that SEE could work as a model for science enrichment programs elsewhere.



*SEE Campers and organizers posed for a group photo at the start of the third annual SEE Summer Camp. (Photo courtesy of Veronica Godfrey)*

SEE set records this year by engaging 38 Durham Public Schools (DPS) students from grades four through eight through the efforts of some 50 volunteers from the sorority and the Triangle community, including scientists from NIEHS, local schools and universities. Sponsors included [Durham Alumnae](#), NIEHS, Durham Parks and Recreation, Burroughs Wellcome Fund, the Delta Research and Education Foundation, and local businesses.

For the 2008 camp, SEE organizers introduced new hands-on, fun-filled science, mathematics and critical thinking programs for the children. The program, which ran from 8:15 a. m. to 2:30 p.m., began with breakfast followed by a health and fitness warm-up led by NIEHS Technical Information Specialist Shawn Jeter.

Students in grades four through six participated in forensic science activities to solve the CSI-themed “Case of the Missing Play Station,” a curriculum developed by Joan Packenham, Ph.D., co-chair of Durham SEE and director the NIEHS Office of Research Compliance. Participants took prints, analyzed fabric and performed



*Beard welcomed volunteers and students to the third annual SEE Summer Camp, the culmination of months of planning. (Photo courtesy of Veronica Godfrey)*

ink chromatography as they worked to untangle the who-done-it challenge. They also used their own fingerprints to make comprehensive identification cards they could take home for their parents.

For students in grades seven and eight, there were engineering activities developed by Delta member Lauren Davis, Ph.D., professor of Engineering at North Carolina Agricultural and Technical State University, using a computerized application called SimCity to model, build and manage four different cities from infrastructure to operations. The campers had to develop a budget for their cities, calculate the need for such resources as water and plan for the many different situations that real cities must be prepared to face.

A group of Delta members that included NIEHS Director of Biomedical Education Marian Johnson-Thompson, Ph.D., compiled the *Parent Educator Manual*, which served as a companion to the half-day Parent Involvement Workshop. The workshop provided information and hands-on activities for parents and caregivers to effectively engage their children in science and mathematics.

A panel of area educators joined Johnson-Thompson and NIEHS Industrial Hygienist Sharon Beard, chair of Durham SEE, in a series of presentations about the range of educational opportunities for DPS students. Speakers included North Carolina Central University's Josephine Dobbs Clement Early College High School Dean of Students Natasha Godwin, DPS Board of Education member Omega Parker and UNC-CH Math and Science Education Network Assistant Director Diane Affleck.

Kay Johnson Graham, Ph.D., Minority Outreach Coordinator in the NIH Office of Equal Opportunity and Diversity Management, attended the camp in a quasi-official capacity. Graham said later that she'd traveled to Durham specifically to see "the great things that are happening farther down the pipeline of the next generation of scientists and biomedical researchers." While post-secondary opportunities are critical for nurturing future scientists, Graham also recognizes the benefits of programs like SEE, and she considers it an example of effective community-based partnering and "an outstanding model that could be used on the national level."

SEE is part of a year-round sisterhood of science education service in Durham by the women of the Durham Delta Alumnae Chapter. It is the result of a national five-year SEE Initiative, an informal science education project funded by the National Science Foundation and developed by Delta Sigma Theta Sorority, Inc., and the Delta Research and Education Foundation, in partnership with the AAAS Directorate for Education and Human Resources Programs. The Durham Delta Alumnae Chapter is one of only seven chapters that have been recognized on the national level for exemplary SEE program development.



*After breakfast, the campers engaged in a cardio workout led by Jeter that was obviously as much fun as work. (Photo courtesy of Veronica Godfrey)*



*Davis, above, was careful to ensure that all the computers were online for the SimCity activities. (Photo courtesy of Veronica Godfrey)*



Packenham took advantage of the quality help with forensic activities provided by NIEHS scientists Undi Hoffler, Ph.D., above right, Diane Klotz, Ph.D., and Elena Braithwaite, Ph.D. (Photo courtesy of Veronica Godfrey)



Most of the parents shown above in their morning workshop joined their children for activities after lunch. (Photo courtesy of Veronica Godfrey)

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## Health and Wellness Seminar Targets Nutrition

By Eddy Ball

On August 19, NIEHS staffers gathered in Rodbell Auditorium to learn more about the integrative health/natural medicine approach to wellness in a talk on “The Science of Nutrition: How a Healthy Diet Creates a Healthy Future.” Presented by James Winget, D.C., of Raleigh Specific Chiropractic, the presentation focused on the role of nutrition and supplementation as key components of efforts to promote optimal health.

The event was hosted by Health and Fitness Program Manager Stephanie Bullock-Allen of the NIEHS Recreation and Wellness Program. The program consisted of Winget’s talk and complimentary spinal evaluations by members of his staff. Throughout the talk, Winget returned to the question he wanted his audience to ponder as they shopped for groceries and made decisions about meals, “Is it [food choice] about our taste buds or expressing the greatest level of health possible?”

Winget said that green, leafy vegetables should make up the largest percentage of a healthy meal and be consumed raw or lightly steamed to preserve as many of the nutrients as possible. As companion and snack foods, he recommended fruits, preferably organic to reduce pesticide contamination and locally grown and ripened to ensure the highest nutrient content.



Winget, above, pondered a question from the audience about the nutritional value of various kinds of meat. (Photo courtesy of Steve McCaw)

He also recommended lowering consumption of meats and eating only lean meat from free-ranging animals that have not been fed hormone or antibiotic supplements.

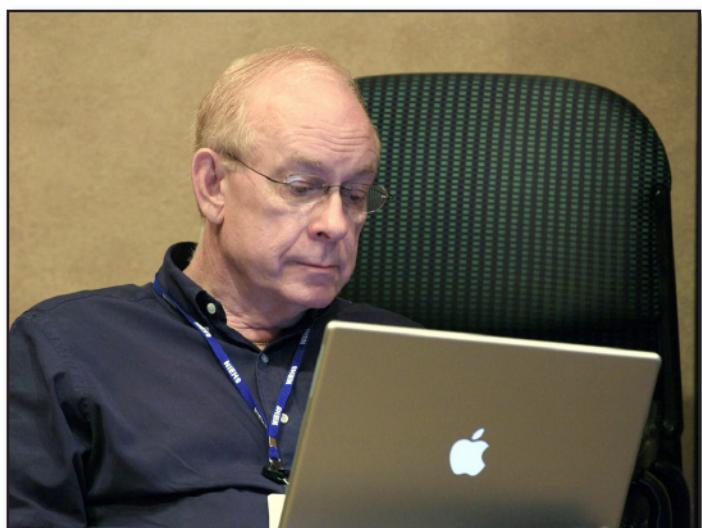
According to Winget, the average American's diet is characterized by foods, such as sugars, white bread, dairy and fried foods, that upset the pH-base balance of the body and the healthy 1:1 balance of omega 3 and omega 6 essential fatty acids. Both, he said, can lead to less than optimal health or disease. Eating foods that are associated with alkalinity and omega 3, such as vegetables and fish, and supplementing omega 3 fats, antioxidants and whole food multivitamins are ways to restore those balances for better health.

As he turned to the subject of probiotics, Winget echoed the naturopathic medicine mantra that health begins in the gut. He explained that the gut's "good bacteria," such lactobacillus and bifidobacter, function to counterbalance potentially pathogenic bacteria in the intestine. He recommended supplementing with probiotics and limiting foods, such as sugars, that help "bad" bacteria proliferate as strategies for balancing gut flora and promoting health.

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NIEHS Research Fellow Jakub Kwintkiewicz, Ph.D., asked several questions during the talk. Kwintkiewicz is a member of the Reproductive Medicine Group. (Photo courtesy of Steve McCaw)



Staff Scientist Jack Bishop, Ph.D., took advantage of his laptop to research probiotics during the talk. (Photo courtesy of Steve McCaw)



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- Director of Communications: Christine Bruske Flowers
- Writer-Editor: Eddy Ball
- Science Editor: Robin Arnette