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NIEHS Spotlight

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Virtual Environmental Training for Latin American Women

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Science Notebook

UNC Researcher Discusses Causes and Treatment of Cystic Fibrosis

NIEHS opened its 2008–2009 Distinguished Lecture Series on September 8 with a seminar about cystic fibrosis (CF), an inherited chronic disease that causes mucus to clog the lungs and other organs of the body. Richard Boucher, M.D., a specialist in the field of pulmonary pathophysiology, presented "Cystic Fibrosis: A Failure of Lung Defense Against the Environment." ...read more

Environmental Cardiology Grantees Meet

Air pollution researchers funded by grants from NIEHS and the Environmental Protection Agency (EPA) attended a full-day workshop September 3 in Rodbell Auditorium. They gathered to share the results of their studies on the effects of particulate matter (PM) on cardiovascular disease (CVD) and to speculate on future directions. ...read more

Meeting Explores Genetic Susceptibility to Cardiopulmonary Disease

Health Science Administrators from the NIEHS Division of Extramural Research and Training (DERT) joined their grantees, NIEHS intramural investigators and other experts in the fields of genetics and air pollution on September 4 and 5 for a meeting on genetic susceptibility to the health effects of air pollution exposure. ....read more

NIEHS Spotlight

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NRDC Scientist Gives Labor Day Seminar

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The September 15 town hall meeting, "Your Home, Your Health, Your Voice," was about empowerment for individuals dealing with environmental exposures , and it was held appropriately in a monument to empowerment during extreme adversity, the Underground Railroad Freedom Center in Cincinnati, Ohio. ...read more

Johnson-Thompson Retires

On September 30, microbiologist Marian Johnson-Thompson, Ph.D., began a well-deserved hiatus from her work as a researcher, science educator, mentor, advocate for women and minorities in science when she retired from the NIEHS after 16 years of service. ....read more

Upcoming Symposium on Children and the Built Environment

The Children's Environmental Health Institute announced that it is accepting registrations for the Fifth Biennial Scientific Symposium to be held at the historic Barr Mansion in Austin, Texas October 30-31. ...read more

Science Notebook

High Levels of Pesticides and Endocrine Disruptors in Pregnant Women in the Netherlands

In an NIEHS-led study published online September 4 in the journal *Environmental Research*, a team of American and European researchers reported finding high levels of organophosphorous (OP) pesticides and some suspected endocrine disrupting compounds including bisphenol A (BPA) and phthalates, in pregnant women and their offspring in the Generation R Study in the Netherlands. ...read more

NTP Holds Meeting on High-Throughput Screening

The National Toxicology Program (NTP) took an important step forward in the development of a more rigorous and comprehensive high-throughput screening program for toxicology studies by hosting a Request for Information (RFI) meeting September 11 – 12 in Rodbell Auditorium at NIEHS. ...read more

Upcoming Distinguished Lecturers Tom Ellenberger and C. Ronald Kahn

The NIEHS 2008 – 2009 Distinguished Lecture Series features two talks during October. On October 14, Tom Ellenberger, D.V.M., Ph.D., will explore the topic of "Structural Biology of DNA End Joining." Later in the month on October 28, C. Ronald Kahn, M.D., will deliver the 2008 Falk Lecture titled "Public-Policy Issues of Diabetes and Obesity." ...read more

Inside the Institute

NIEHS Honors Long-Time Director

Although he's officially a retiree now, Director Emeritus and Principal Investigator Ken Olden, Ph.D., will still be going into the office regularly after he moves to New York for his next challenge in public health. ...read more

Tennant Looks Forward to New Adventures

With 42 years of government service to his credit, Principal Investigator Ray Tennant, Ph.D., bid farewell to friends and colleagues at his retirement party on the afternoon of August 30 in Rall Building F193. ...read more

Event Celebrates Johnson-Thompson's Career

Marian Johnson-Thompson, Ph.D., served as NIEHS director of Education and Biomedical Research from 1994, when she was recruited by former Director Ken Olden, Ph.D. On September 22, people from NIEHS, the greater scientific community and her family filled Rodbell Auditorium to celebrate her career. The retirement ceremony was organized by friends at NIEHS and moderated by NIEHS Acting Deputy Director Bill Suk, Ph.D. ...read more

Seminar Examines Aging and Arthritis

One of North Carolina's leading authorities on the public health implications of arthritis was the guest lecturer at a seminar sponsored by the NIEHS Disability Advocacy Committee (DAC) on September 9 in the Rall Building D-250 conference room. ...read more

Extramural Research

Extramural Update

With concept clearance approval by the NIEHS National Advisory Environmental Health Sciences Council on September 9, a Division of Extramural Research and Training (DERT) workgroup prepares to implement the Partnerships for Environmental Public Health (PEPH) program. The program is an important step as NIEHS establishes a sustainable commitment to the environmental public health community. ...read more

Extramural Papers of the Month

- Arsenic and Type 2 Diabetes
- Connection Between Built Environment and Obesity
- p53 Inhibits Cell Growth as well as Cell Proliferation
- The Ah Receptor is Essential for Mediating an Anti-Inflammatory Effect

Intramural Research

Intramural Papers of the Month

- DEPs Involved in a Novel Blood-Brain Barrier Signaling Pathway
- Loss of Estrogen Receptor-Alpha Affects Bone
- NELF Enhances Gene Expression
- The Role of Genetics in Heart Rate and Heart Rate Variability

Calendar of Upcoming Events

- **October 3**, in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, speaker and topic T.B.A.
- **October 6 (Offsite Event)**, at the Radisson Hotel in RTP. 8;30 – 5:00 — Fall Meeting of the Genetics and Environmental Mutagenesis Society (GEMS)
- **October 7 – 9 (Offsite Event)**, at the Hyatt Regency Hotel in Chicago — 2008 International Environmental Nanotechnology Conference: Applications and Implications, sponsored by the U.S. Environmental Protection Agency
- **October 9**, in Rodbell Auditorium, 1:00 – 2:00 — LSB Seminar Series, featuring Graham Walker, Ph.D., speaking on "Dealing with DNA Problems: Template Lesions and Replication Blocks"
- **October 14**, in Rodbell Auditorium, 11:00 – 12:00 — Distinguished Lecture Series with Tom Ellenberger, D.V.M., Ph.D., speaking on "Chemical Genetics of DNA Repair Pathways"
- **October 16 – 17 (Offsite Event)** at the Sheraton Chapel Hill Hotel — Worker Education and Training Program Workshop on "Implications for Safety and Health Training in a Green Economy"
- **October 17**, in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, speaker and topic T.B.A
- **October 23**, in Rodbell Auditorium, 12:00 – 5:00 — North Carolina Chapter of the Society of Toxicology Fall Meeting, "Pharmaceuticals and Personal Care Products in the Environment"
- **October 28**, in Rodbell Auditorium, 11:00 – 12:00 — Distinguished Lecture Series, "Public-Policy Issues of Diabetes and Obesity" by C. Ronald Kahn, M.D.
- **October 30**, in Rodbell Auditorium, 8:30 – 2:30 — Outstanding New Environmental Scientist (ONES) grantee lectures
- **October 30 – 31 (Offsite Event)** at the Barr Mansion in Austin, Texas — Fifth Biennial Scientific Symposium sponsored by the Children's Environmental Health Institute of Texas
- **October 31**, in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, speaker and topic T.B.A
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Council Meets in Public Session

By Eddy Ball

Members of the NIEHS National Advisory Environmental Health Sciences Council met in public session on September 9 in Rodbell Auditorium. The group heard reports during the morning and approved unanimously a concept clearance for the Partnerships for Environmental Public Health program (see related story) before entering closed session to consider grant applications.

With a panoramic image of the Institute on the screen behind him, Wilson outlined his action plan for the Council members, who responded with expressions of confidence in the ability of NIEHS leadership to move forward. (Photo courtesy of Steve McCaw)

The meeting began with the report by Acting Director Sam Wilson, M.D., who opened his presentation with an update on the Institute's Corrective Action Plan (CAP) and developments since the Council's last meeting in May. During the summer, NIEHS staff completed the CAP, which was approved by NIH Director Elias Zerhouni, M.D., and took actions necessary to begin to realize its short- and long-range goals. Wilson explained that NIEHS management plans to prepare quarterly progress reports and will update Council on the latest status at upcoming meetings.

Blackshear, standing, told the audience that DIR is recruiting talent in the areas of stem cell research, reproductive epidemiology and crystallography. Seated beside him were, left, NIEHS Director of Science Policy and Planning Joyce Martin, J.D., and Hrynkow, right. (Photo courtesy of Steve McCaw)

During his report, Wilson reflected on the Institute's management challenge, "to propel NIEHS forward to a renewed future," and its overall scientific challenge, "to produce high quality information for high quality decisions" as the basis for regulatory measures to protect human health. "No one else does quite what we do," he told the audience, as he pointed to the extent to which regulatory agencies depend on studies by NIEHS and the National Toxicology Program for solid evidence of danger to human health.

As Wilson recounted the highlights of the past four months, he observed the unexpected death of Colin Chignell, Ph.D., the retirement of key investigators including Director Emeritus Ken Olden, Ph.D., and the honorary degree awarded Allen Wilcox, M.D., Ph.D., by the University of Bergen. He also noted that progress was being made in the selection of a new director for NIEHS from the 22 applications received in response the advertisement of the position.

Acting Scientific Director Perry Blackshear, M.D., D.Phil., made an impromptu presentation on the impact of the recent retirements and departures on the NIEHS Division of Intramural Research (DIR). He said that DIR has a strategy for filling three tenure-track investigator positions in the coming year.

Following updates by NIEHS Acting Deputy Director Bill Suk, Ph.D., NIEHS Associate Director Sharon Hrynkow, Ph.D., and NIEHS Acting Director of the Division of Extramural Research and Training (DERT) Dennis Lang, Ph.D., Council turned to the business of considering a concept clearance for the NIEHS Partnerships for Environmental Public Health (PEPH) program.

Presenting the PEPH program's plans for implementation, DERT Susceptibility and Population Health Branch Chief Gwen Collman, Ph.D., offered Council her definition of environmental public health (see text box). She said that the November 2007 Request for Information, a workshop held June 30 - July 1 on the responses, and follow-up activities involving stakeholders and the DERT working group resulted in several goals.

Prominent among them are reassessing current programs and exploring new avenues of research to "make a synergistic program" to address comprehensively emerging and future environmental public health needs over the next decade. Collman explained that the PEPH program would also emphasize involvement of stakeholders during every step of the process, development of an evaluation component with appropriate metrics for every component, and increased education and training at every level.

The PEPH concept clearance was well received by Council members, who gave DERT the go-ahead to begin implementing the integrated program and, as Council liaison Stefani Hines commented, take "a beautifully written document" and "move from a concept to a vision."

Collman, shown above at the PEPH workshop earlier this summer, explained how the integrated program will facilitate translation. "Ultimately, the community members themselves will use this information to work within their own structures to try to enact public health change," she said. (Photo courtesy of Steve McCaw)

Member Altaf Wani, Ph.D., of The Ohio State University, pondered Collman's report on the PEPH program. Like his colleagues, including Kate Dixon, Ph.D., right, he voted to approve the concept clearance. (Photo courtesy of Steve McCaw)

A Working Definition of Environmental Public Health — Science to Action

Asked at earlier meetings about the meaning of "environmental public health," Collman was prepared at the concept clearance to offer the following definition that incorporates Wilson's commitment "to produce high quality information for high quality decisions" in the context of environmental public health:

"Environmental public health is the science of conducting and translating research into action to address environmental exposures and health risks of concern to the public. We see this being accomplished through the dissemination of science-based or research-generated information about environmental risks and diseases to community members and other stakeholders who have a need for the information to enact change in the spheres of influence that they have. By fostering partnerships between and among community residents and organizations, researchers and these other stakeholders in the process, we believe vital information about the linkages between exposure and disease can be used to promote health and reduce disease among populations at the highest risk."

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NIEHS Invests $21.25 Million to Find Environmental Causes of Parkinson's Disease

By Robin Mackar

On September 16, NIEHS announced that it will award three new grants totaling $21.25 million over a five-year period to study how environmental factors contribute to the cause, prevention and treatment of Parkinson's disease and other related disorders.

Parkinson's disease is a neurodegenerative disorder that affects nerve cells, or neurons, in several parts of the brain, including neurons that use the chemical messenger dopamine to control muscle movement. More than one million Americans suffer from Parkinson's disease, with approximately 60,000 new cases reported each year. The average age of onset is 60 years, although people have been diagnosed much younger.

The five-year grants are being awarded as part of the NIEHS' Centers for Neurodegeneration Science (CNS) announcement issued in 2007. The CNS program builds on the previous successes of the NIEHS Collaborative Centers for Parkinson's Disease Environmental Research. Each center has assembled an interdisciplinary team of investigators that are working on several tightly connected research projects related to Parkinson's disease.

"Given the growing body of literature that is identifying environmental stressors such as pesticides as risk factors for Parkinson's disease, it is more important than ever that we bring clinical and basic scientists together to clarify the causes of this disease," said Cindy Lawler, Ph.D., program administrator at NIEHS. "These new centers will bring us one step closer to new prevention and treatment strategies."

The three grantees include:

- **Gary Miller, Ph.D., Emory University, Atlanta** — Parkinson's disease (PD) has been linked to pesticide exposure, mitochondrial damage, and altered storage of the neurotransmitter dopamine. Miller and his team will be looking at how environmental and genetic factors interact to alter these functions in dopamine neurons. Identifying these mechanisms could lead to new therapeutic targets. In addition, the Emory team will be attempting to develop new biomarkers in the blood that will help identify people that may be at risk for developing Parkinson's disease.

- **Marie-Françoise Chesselet, M.D., Ph.D., University of California, Los Angeles** — The researchers at UCLA have previously shown associations between high levels of exposure to specific environmental pesticides and Parkinson's disease and will build on this knowledge to determine the mechanisms of action that may be causing this association. They will use an integrated, multidisciplinary approach to identify additional agricultural pesticides that are disrupting similar molecular pathways, and determine whether these also increase the risk of Parkinson's. Their work is expected to shed light on the pathological processes involved in sporadic Parkinson's disease, the most frequent form of the disorder, and could have public health implications for precautions in the use of some pesticides.

- **Stuart Lipton, M.D., Ph.D., Burnham Institute for Medical Research, La Jolla, Calif.** — Investigators at the Burnham Institute will explore how environmental toxicants may contribute to Parkinson's disease by producing free radical stress that mimics or enhances the effects of known genetic mutations. The focus will be on those proteins known to be related to Parkinson's disease, including parkin, DJ-1 and PINK1, with the goal of determining how chemical reactions that donate extra electrons lead to damaging modifications of these proteins. The clinical implications of these processes will be explored through biomarker development efforts and a screen to identify new lead compounds that can preserve protein function by reducing free radical stress.

"The UCLA and Emory CNS grants will extend the exciting lines of research previously supported by NIEHS through the Collaborative Centers for Parkinson's Disease Environmental Research, while the Burnham Institute grant will bring an important new perspective to research on gene-environment interplay in Parkinson's disease," said Dennis Lang, Ph.D., acting director of the NIEHS Division of Extramural Research and Training.

"As a patient advocacy group, we are thrilled to see that NIEHS is continuing its research investment in this disease," said Amy Rick, chief executive officer of the Parkinson's Action Network (PAN).

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

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NTP Finalizes Report on Bisphenol A

By Robin Mackar

Current human exposure to bisphenol A (BPA), a chemical used in many polycarbonate plastics and epoxy resins, is of "some concern" for effects on development of the prostate gland and brain and for behavioral effects in fetuses, infants and children, according to a final report released on September 3 by the National Toxicology Program (NTP).

The report provides the NTP's current opinion on BPA's potential to cause harm to human reproduction or development. The conclusions are based primarily on a broad body of research involving numerous laboratory animal studies. The report is part of a lengthy review of the scientific literature on BPA and takes into consideration public and peer review comments received on an earlier draft report.

"There remains considerable uncertainty whether the changes seen in the animal studies are directly applicable to humans, and whether they would result in clear adverse health effects," said NTP Associate Director John Bucher, Ph.D. "But we have concluded that the possibility that BPA may affect human development cannot be dismissed."

The NTP Center for the Evaluation of Risks to Human Reproduction (CERHR) conducted the BPA evaluation. About the impact that these findings may have on consumers, CERHR Director Michael Shelby, Ph.D., said, "Unfortunately, it is very difficult to offer advice on how the public should respond to this information."

"More research is clearly needed to understand exactly how these findings relate to human health and development, but at this point we can't dismiss the possibility that the effects we're seeing in animals may occur in humans," Shelby continued. "If parents are concerned, they can make the personal choice to reduce exposures of their infants and children to BPA."

The NTP, an interagency federal research program headquartered at NIEHS, uses a five-level scale ranging from negligible to serious, with "some concern" being the midpoint (see graphic below).

"We are expressing this level of concern because we see developmental changes occurring in some animal studies at BPA exposure levels similar to those experienced by humans," Bucher said.

The report also expresses "minimal concern" that BPA exposure will affect development of the mammary gland or accelerate puberty in females. The NTP expressed "negligible concern" that exposure of pregnant woman to BPA will result in fetal or neonatal mortality, birth defects or reduced birth weight and growth in their offspring.

The NTP also expressed "negligible concern" that exposure to BPA causes reproductive effects in non-occupationally exposed adults and "minimal concern" for workers exposed to higher levels in occupational settings.

"The literature on experimental animal studies is large and filled with many conflicting findings. There are a number of remaining uncertainties in the scientific information on BPA," said Bucher. The report discusses many of the uncertainties, including the very limited data from studies in humans and the difficulty in relating the often subtle developmental endpoints in animal studies to human health risks.

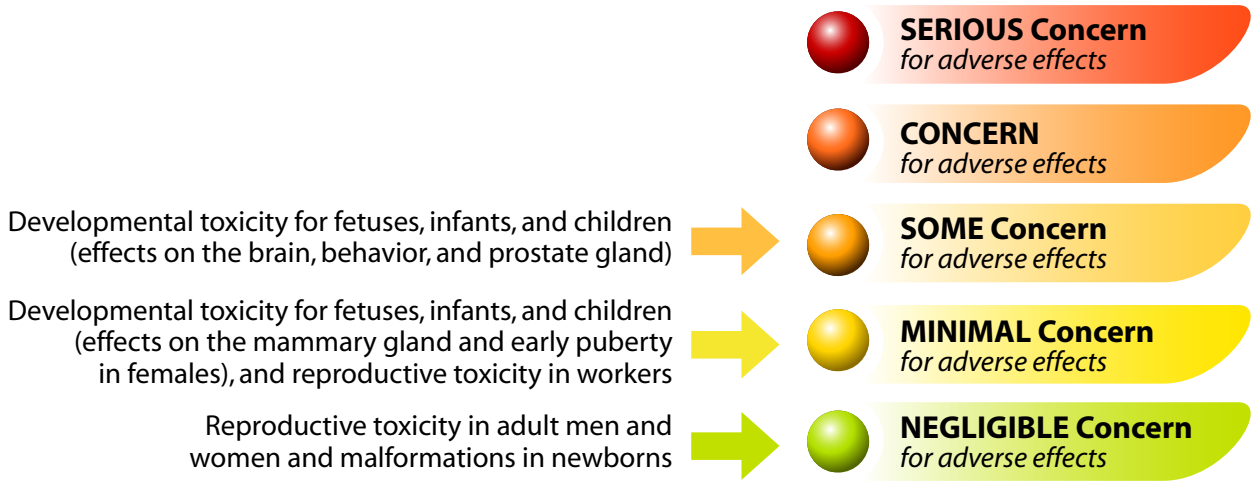
The CERHR follows a formal process for review and evaluation of nominated chemicals that includes convening panels of scientific experts to review the world's scientific literature on the chemical being studied, along with a peer review process with numerous opportunities for public input.

CERHR publishes monographs that assess the evidence that environmental chemicals, physical substances, or mixtures cause adverse effects on reproduction and development and provide opinion on whether these substances are hazardous for humans. Other agencies, such as the US Food and Drug Administration (FDA), apply this science in carrying out their regulatory responsibilities and in accordance with their statutory authority.

In August, FDA released a "Draft Assessment of Bisphenol A for Use in Food Contact Applications" for peer review and public comment. The FDA held a public meeting of its BPA subcommittee of the FDA Science Board on September 16 to discuss this FDA draft assessment.

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

NTP conclusions regarding the possibilities that human development or reproduction might be adversely affected by exposure to bisphenol A. The NTP uses a five-level scale of concern:



Virtual Environmental Training for Latin American Women

By Eddy Ball

During a three-day workshop held September 3-5 in Washington, DC, a group of scientists, health professionals and educators met to discuss and plan a new virtual training program module for Hispanic women in the environmental health sciences. The 35 participants, who included two NIEHS postdoctoral fellows, represented organizations in the United States and more than a dozen Latin American nations — as well as a range of international groups.

Among her many other honors, Roses was reappointed in January 2008 to a five-year term as World Health Organization Regional Director for the Americas. (Photo courtesy of PAHO)

To lay the groundwork for a training module on AIDS and environmental health, the workshop built on a successful generic pilot program discussed at a Leadership and Gender Symposium for Latinas held December 3, 2007 in Bethesda and co-chaired by NIEHS Associate Director Sharon Hrynkow, Ph.D., and National Institute on Drug Abuse Director Nora Volkow, M.D.

NIEHS teamed up with the Pan American Health Organization (PAHO), Facultad Latinoamericana de Ciencias Sociales (FLACSO), United Nations Educational, Scientific and Cultural Organization (UNESCO) for Latin America and the Caribbean (LAC), and National Institute of Allergy and Infectious Diseases (NIAID) to convene the most recent discussion. In her opening remarks, PAHO Director Mirta Roses, M.D., pointed out why leadership and gender training for women scientists in LAC is so important.

The workshop was one of several events Hrynkow discussed during her report at the September 9 meeting of the NIEHS National Advisory Environmental Health Sciences Council. (Photo courtesy of Steve McCaw)

"Women in Latin America do not enjoy the same social status as men," Roses noted. "At the same time, the relatively poorer health status of women in Latin America remains a problem. Women suffer gender-based violence, high rates of maternal mortality and morbidity and the disproportionate burden of mental illness. As scientists, women are a critical part of the solution, so we must empower them to engage and to overcome antiquated notions of their proper roles."

In her opening comments, Hrynkow, co-chair of the meeting, welcomed NIAID and PAHO as new partners, while recognizing the importance of contributions from the Fogarty International Center, NIEHS, NIDA, NIH Office of Aids Research and UNESCO in creating, enabling and implementing the pilot. Hrynkow also

provided historical perspectives on the genesis of the program, noting the original goal of training great leaders as well as great scientists. She noted as well the clear window of opportunity at this point in time to advance women's leadership training on global health challenges.

Alicia Aleman, M.D., an OB/GYN in Uruguay who trained in the United States on a Fogarty fellowship, provided her perspective as a "graduate" of the pilot training program. Her comments focused on the value of the virtual community of women scientists created by the program and the benefits of having mentors available via the Internet with whom she could share experience and thoughts in real-time. According to Aleman, there is a critical shortage of qualified mentors in many countries, and the use of the Internet to create mentor relationships was invaluable as she made critical career path and scientific decisions.

The workshop focused on two health challenges facing Latin America — the growing AIDS epidemic and the burden of ill health due to environmental conditions. Concurrent sessions examined the pilot curriculum and teaching strategies with a view toward adapting them to meet the needs of the women scientists working on AIDS, environmental health and related issues, such as water quality and sanitation.

The enthusiasm of participants for this unique training program and its next steps was palpable. NIEHS post-doctoral fellows Karina Rodriguez, Ph.D., originally from Peru, and Danielle Duma, Ph.D., a native of Brazil, participated in the meeting to share their perspectives as potential end-users.

NIEHS and partner agencies in the PAHO meeting will begin to work with the Organization of American States' Inter-American Commission of Women to consider support for the further elaboration of the curricula and the launch of the next phase of the program.

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Rodriguez is an Intramural Research Training Award (IRTA) Fellow in the NIEHS Receptor Biology Group headed by Principal Investigator Ken Korach, Ph.D. (Photo courtesy of Steve McCaw)

Duma is a visiting fellow in the NIEHS Molecular Endocrinology Group headed by Principal Investigator John Cidlowski, Ph.D. (Photo courtesy of Steve McCaw)

NIEHS Distinguished Lecturers Honored

By Eddy Ball

On September 29 during an award ceremony at the White House, Duke University investigator Robert Lefkowitz, M.D., and Baylor College of Medicine researcher Bert O'Malley, M.D., received the 2007 National Medal of Science in the biological sciences, the nation's highest award for science and engineering. Lefkowitz spoke at the 2008 Rodbell Lecture at NIEHS on May 5, and O'Malley delivered the May 2007 Distinguished Lecture, as reported in the June 2007 issue of the *Environmental Factor*.

A top honor for two NIEHS distinguished lecturers (Photo courtesy of the National Science Foundation)

Lefkowitz and O'Malley were among eight scientists in the biological sciences, chemistry, engineering and physical sciences who were honored for what the National Science Foundation (NSF), which administers the award, describes as "pioneering scientific research that has led to a better understanding of the world around us as well as to innovations and technologies that give the United States its global economic edge."

Lefkowitz is the James B. Duke Professor of Medicine and Biochemistry at Duke University Medical School and an investigator with the Howard Hughes Medical Institute (HHMI). He was honored for his research into understanding the largest, most important and most therapeutically accessible receptor system that controls the body's response to drugs and hormones.

National Medal of Science Laureate Robert Lefkowitz (Photo courtesy of Steve McCaw)

O'Malley is a professor and chairman of the Department of Molecular and Cellular Biology at the Baylor College of Medicine. The Medal of Science recognizes his work on the molecular mechanisms of steroid hormone action and hormone receptors and coactivators, which has had a profound impact on our knowledge of steroid hormones in normal development and in diseases.

Since its establishment by Congress in 1959, the nation has honored 441 distinguished scientists and engineers with the medal. The NSF is currently accepting nominations through December 5, 2008 for the 2009 National Medal of Science, which will be awarded next fall.

Nation Medal of Science Laureate Bert O'Malley (Photo courtesy of Steve McCaw)

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NRDC Scientist Gives Labor Day Seminar

By Robin Arnette

Throughout this country's history women have taken the lead in social reform issues, most notably the suffrage movement and the Equal Pay Act of 1963. A recent Labor Day seminar held at NIEHS expounded the role that women have played in other areas such as public health, environmental justice and workplace safety. On August 28 in Rodbell Auditorium, Jennifer Sass, Ph.D., a senior environmental scientist from the Natural Resources Defense Council (NRDC), presented "Occupational Safety, Public Health and Environmental Protection: The Historical Role of Women in Making the Connection."

Sass, who is also an NIEHS Public Interest partner, said she feels passionately about the Institute and its ability to make a difference with solid scientific studies. (Photo courtesy of Steve McCaw).

The seminar was sponsored by AFGE Local 2923, the union at NIEHS, and the NIEHS Diversity Council. AFGE president, Bill Jirles, gave a brief history of the Labor Day holiday and introduced the speaker.

Sass said that during the mid-1800s and early 1900s, women were shut out of academic institutions, workplaces and unions. As a result many middle-class women wanted an opportunity to contribute to society by devoting their lives to social service.

The audience filled Rodbell A and included NIEHS Deputy Associate Director for Management Chris Long, above, and Acting Director Sam Wilson, M.D. (Photo courtesy of Steve McCaw)

To fill this need, according to Sass, women established institutions called settlement houses in working-class and poor neighborhoods. One of these activists, Jane Addams, started Hull House, the most famous settlement house, in Chicago in 1889. The women of Hull House and other settlement houses offered health care, hygiene education, basic education and childcare, but they also addressed issues involving crowded and unsafe conditions in the textile and garment industries, which employed large numbers of women and children.

Sass explained that in 1909 the women of Hull House documented a strike in which almost 20,000 New York City garment workers walked out in protest, but it wasn't until the Triangle Shirtwaist Factory fire in 1911 that real advances were made. Sass said, "There had been many fires in the building and throughout the garment district because of the hot machinery and all of the textiles lying around. Most of the 146 people who died that day were women. Management kept the doors and fire escapes locked, so a lot of them jumped out of windows."

Sass said that one of the people who observed the fire that day was Frances Perkins. President Roosevelt later appointed Perkins secretary of labor (1933–1945), and she was responsible for several important pieces of legislation including The National Labor Relations Act in 1935, which permitted workers to form unions and bargain collectively and The Fair Labor Standards Act in 1938, which established a minimum wage of 40 cents per hour.

Jirles, above, pondered a question from the audience as he moderated the question and answer session that followed Sass's talk. (Photo courtesy of Steve McCaw)

Other key members of Hull House included Florence Kelley, who was appointed to the Illinois Bureau of Labor Statistics in 1892 and documented child labor in the state. Alice Hamilton was the first industrial physician in North America, and in 1934, published *Industrial Toxicology*, detailing the health effects of occupational exposures to chromium, lead, mercury, beryllium, radiation and other industrial poisons.

These female pioneers laid the groundwork for today's women to continue the tradition and spirit of Hull House. One good example is Margaret Seminario, director of Safety and Health for the AFL-CIO since 1977. Seminario has been involved in the passage of numerous OSHA rules involving respiratory protection, hazardous waste operations and many others.

Despite the advances in understanding the connection between environmental health and work-life, much remains to be done. Sass said the budget cuts in Washington have resulted in federal agencies running out of money to do in-house science. As a result, the science that comes to these agencies is from industry or corporations looking to promote their products.

Sass concluded her seminar with an impassioned plea to NIEHS scientists to become vocal partners in protecting the nation's citizens. She stated, "We can't stay silent when scientists working in the interest of polluters and their contractors maintain controversies and doubt over the evidence. Even though you do so much already, I'm here to ask you to not just generate the data, but to speak out for it."

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NIEHS and University of Cincinnati Host Environmental Health Town Hall Meeting

By Eddy Ball

The September 15 town hall meeting, "Your Home, Your Health, Your Voice," was about empowerment for individuals dealing with environmental exposures, and it was held appropriately in a monument to empowerment during extreme adversity, the Underground Railroad Freedom Center in Cincinnati, Ohio. The meeting was jointly sponsored by NIEHS and the University of Cincinnati (UC) Center for Environmental Genetics (CEG). The event featured talks by experts at UC to help residents understand better the exposures they face each day and to offer practical ideas about how individuals can improve aspects of their health related to those exposures.

Martin, right foreground, and Schelp, on her left in dark jacket, joined participants as they listened to the keynote speakers. (Photo courtesy of the University of Cincinnati)

Welcoming attendees to the day-long event were CEG Director Shuk-mei Ho, Ph.D., NIEHS Acting Director Sam Wilson, M.D., and Ohio State Rep. Steven Driehaus. In his comments, Wilson talked about the value of community engagement by scientists.

"Town hall meetings are important to share views and understand where real needs are on the academic side and from community groups," Wilson said. "The potential benefit is enormous."

Wilson underscored the NIEHS commitment to producing the solid science to underpin good policy and regulatory efforts to impact environmental public health. He spoke against the backdrop of a wall of quilts celebrating the struggles of slaves seeking freedom through the Underground Railroad. (Photo courtesy of the University of Cincinnati)

The speakers from CEG, who are some of the leading researchers in the environmental health sciences, focused on hazards in the home, including exposures to lead, plastics, second-hand smoke, mold and traffic exhaust. Attendees learned how to recognize potentially harmful exposures, prevent them when possible and find help to correct them if necessary.

"This was a unique opportunity for the Greater Cincinnati community and others throughout the region because this will be the only NIEHS town hall meeting of this kind in 2008," said Elizabeth Kopras, CEG junior research associate and meeting coordinator. "Attendees had the opportunity to have direct input on the decision-making process for how NIEHS allocates its funding opportunities for the upcoming fiscal year — as well leave the meeting better equipped to protect their health and the health of their loved ones."

Accompanying Wilson to the meeting were NIEHS Director of Science Policy and Planning Joyce Martin, J.D., and John Schelp, special assistant to the director. Schelp also helps coordinate the NIEHS Public Interest Partners group, a national forum for community advocacy.

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Following their introductory remarks, from left to right, Driehaus, Ho and Wilson pose in front of a mural featuring scenes from the Underground Railroad. (Photo courtesy of the University of Cincinnati)

Johnson-Thompson Retires

By Eddy Ball

On September 30, microbiologist Marian Johnson-Thompson, Ph.D., began a well-deserved hiatus from her work as a researcher, science educator, mentor, advocate for women and minorities in science when she retired from the NIEHS after 16 years of service (see related story). Her immediate plans include enjoying time with her family and pursuing other interests as she decides where next to put her talents and energy to work.

During her career at NIEHS, Johnson-Thompson served as director of Education and Biomedical Research Development in the Office of the Director. In that role, she was responsible for identifying the environmental health research and training needs of underserved populations and organizing programs and partnerships to address them. She was particularly interested in the unique biomedical research needs of women of color and the potential they have for reducing health disparities.

As the Institute's lead person for science education collaborations with schools, universities and organizations on the local and national levels, Johnson-Thompson developed programs that included the Bridging Education, Science and Technology (BEST) Program, the extramural K-12 Environmental Health Science Education program and the Advanced Research Cooperation in Environmental Health (ARCH) program. In the course of these efforts and with individual mentoring, she helped thousands of young people discover the joy and magic of science and pursue scientific careers in high schools, colleges and universities, graduate schools and professional programs throughout the United States.

One of the things young people have heard at programs organized by Johnson-Thompson at NIEHS and elsewhere is an admonition to follow their dreams. "Do what you love," she says, "and the money will follow." (Photo courtesy of Steve McCaw)

Johnson-Thompson also chaired the NIEHS Institutional Review Board for protection of human subjects. At the national level, she served as a member of the NIH Human Subjects Research Advisory Committee and the Trans-NIH Human Microbiome Working Group.

Prior to joining NIEHS in 1992, Johnson-Thompson was Professor of Biology at the University of the District of Columbia (UDC) and Adjunct Professor of Pharmacology at Georgetown University Medical School. A Florida native, she received her post-secondary education in Washington, D.C., at Howard University, where she earned a B.S. and M.S. in microbiology, and Georgetown University, where she received a Ph.D. in molecular virology.

Currently a professor emerita of Biology and Environmental Science at UDC, Johnson-Thompson also holds an appointment as adjunct professor in the Department of Maternal and Child Health in the University of North Carolina School of Public Health in Chapel Hill.

Johnson-Thompson's research at Georgetown and UDC addressed the molecular basis of multi-drug resistance in breast cancer cells. In recognition of her contributions in microbiology, she was elected as a fellow of the American Academy of Microbiology in 1998 and of the American Association for the Advancement of Science (AAAS) in 2004.

An active and life member of Delta Sigma Theta Sorority, Inc,. she maintains her affioiation with the Federal City Alumnae Chapter in Washington, D.C., but also works locally with the Durham Alumnae Chapter. Johnson-Thompson is involved with several boards and organizations, and she has been honored many times for her contributions to science education, including being named Myerhoff Mentor of the Year by the Myerhoff Scholars at the University of Maryland, Baltimore County.

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Upcoming Symposium on Children and the Built Environment

By Rosemarie Ramos, Ph.D.

The Children's Environmental Health Institute announced that it is accepting registrations for the Fifth Biennial Scientific Symposium to be held at the historic Barr Mansion in Austin, Texas October 30-31. The title of this year's symposium is "Blueprint for Children's Health and the Built Environment." NIEHS is a Platinum sponsor of the event.

The program will include keynote talks by Phil Landrigan, M.D., an NIEHS Children's Environmental Health Center grantee, and Donald Mattison, M.D., chief of the Obstetric and Pediatric Pharmacology Research Branch at the NIH National Institute of Child Health and Human Development in Bethesda, Md. Howard Frumpkin, M.D., director of the National Center for Environmental Health at the Centers for Disease Control and Prevention, and other leading authorities in environmental public health and children's health will chair panels on major questions related to the topic.

The mission of the Children's Environmental Health Institute is to support initiatives to improve children's health with an emphasis on their microenvironment. The organization seeks to improve children's health by supporting collaborative efforts in scientific research, environmental education and public policy that identify, develop and promote practices to accurately assess and manage environmental health risks to children.

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

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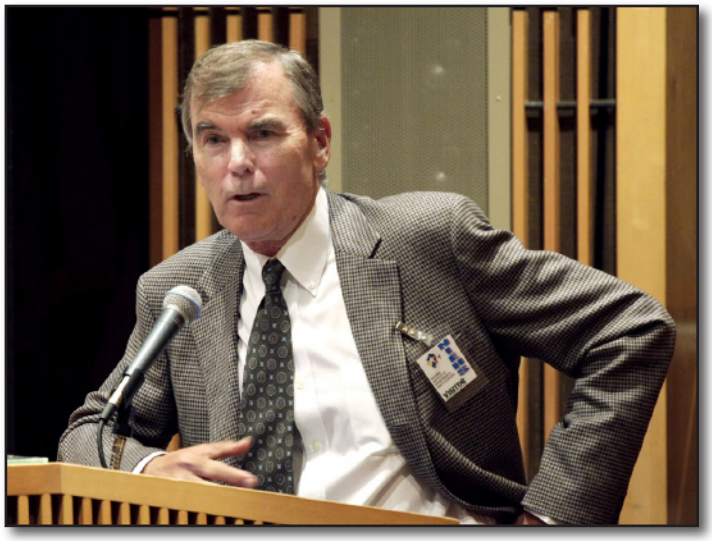
Science Notebook

UNC Researcher Discusses Causes and Treatment of Cystic Fibrosis

By Robin Arnette

NIEHS opened its 2008–2009 Distinguished Lecture Series on September 8 with a seminar about cystic fibrosis (CF), an inherited chronic disease that causes mucus to clog the lungs and other organs of the body. Richard Boucher, M.D., a specialist in the field of pulmonary pathophysiology, presented "Cystic Fibrosis: A Failure of Lung Defense Against the Environment." James Putney Jr., Ph.D., a principal investigator in the NIEHS Laboratory of Signal Transduction, hosted the talk in Rodbell Auditorium.



Boucher conceded that treatment of adults with CF is not very effective, but he noted that preventive therapy beginning at birth can reduce mortality. (Photo courtesy of Steve McCaw)

Boucher is a William R. Kenan Professor of Medicine at the University of North Carolina at Chapel Hill (UNC-CH), director of the Cystic Fibrosis/Pulmonary Treatment and Research Center, and co-director of the Gene Therapy Center, both at UNC-CH. He said that CF was really a failure of the lung's defenses against outside invaders, and specifically, a breakdown of the two-phase system of mechanical clearance. He explained what occurs in normal lungs first. "Bacteria or viruses come into contact with a mucus layer that is designed to trap material and move it away from the airway surface," Boucher said. "They then encounter a watery pericellular environment that provides enough lubricant activity for the mucus — which contains the microbes — to move out of the lung effectively."

The audience included scientists from the Laboratory of Respiratory Biology, including Matrix Biology Group Principal Investigator Stavros Garantziotis, M.D., center foreground. (Photo courtesy of Steve McCaw)

Boucher said that the pericellular layer contains cilia, hair-like cellular projections that move the mucus, but for them to work properly the mucus layer has to be well-hydrated and the airway epithelial cells have to secrete mucus glycoproteins called mucins. Boucher said that hydration is more important in mechanical clearance than cilia or mucins. He pointed out that because salt on the airway surface osmotically determines the amount of water, the lungs modulate hydration by absorbing salt. The lungs then use two mechanisms to secrete chloride and water to the surface — a calcium-activated channel mechanism and a cystic fibrosis transmembrane conductance regulator (CFTR)-chloride channel mechanism.

In CF patients, however, the CFTR protein is mutated. Since CFTR can't enter the plasma membrane in a CF patient's lungs, chloride and water can't be secreted, which leads to unrestrained absorption of salt from the surface. As a result, the mucus layer becomes more concentrated, and together with mucins, forms mucus plaques that stick to airway surfaces and obstruct airflow.

Boucher said these plaques contain 10^7 or 10^8 bacteria/ml of mucus, and that the biofilms the bacteria exist in prevent neutrophils or antimicrobial drugs from reaching the organisms and killing them. He explained, "This resistance leads to a chronic infection in CF patients. When CF kids get their first *Pseudomonas* infection during the first few months of life, they never eradicate it."

Boucher's topic also appealed to investigators with related interests in reproduction and development, such as Research Fellow Boris Risek, Ph.D., above, of the Androgen Biology Group. (Photo courtesy of Steve McCaw)

To examine how much liquid hydration occurs in normal and CF epithelial cells and how it is controlled, Boucher used a lung epithelial cell culture system developed by one of his collaborators. The system mimicked *in vivo* cells by displaying a counterclockwise rotational movement when liquid was present. Boucher's team determined that the airway surface liquid (ASL) compartment in normal cells had a height of 7.5–8 microns of liquid, which was about the height of the extended cilia. This height was maintained through the CFTR protein by the regulated release of ATP and its product adenosine, in a dual, redundant mechanism for hydrating the airway surface. In contrast, without a functioning CFTR, CF patients have to rely on the ATP system since the adenosine pathway needs CFTR. "ATP release gives CF patients enough fluid on the surface to move mucus, but this amount is less than normal," Boucher stated.

Following the talk, Boucher and Putney, right, took questions from the audience. (Photo courtesy of Steve McCaw)

Boucher added that his and other CF investigators' work have yielded two promising therapies for CF sufferers — inhaling a hypertonic saline solution that draws water to the airway surface or taking a drug that turns off sodium absorption and initiates chloride secretion. Several studies have indicated that CF patients participating in either of these regimens increase their lung function and reduce the number of respiratory tract exacerbations.

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Environmental Cardiology Grantees Meet

By Eddy Ball

Air pollution researchers funded by grants from NIEHS and the Environmental Protection Agency (EPA) attended a full-day workshop September 3 in Rodbell Auditorium. They gathered to share the results of their studies on the effects of particulate matter (PM) on cardiovascular disease (CVD) and to speculate on future directions.

For several of the grantees and attendees, the meeting also served as a preliminary to the two-day Global Variability in Response to Air Pollution meeting held September 4 – 5 in Chapel Hill (see related story).

The meeting represented the fifth in a series of meetings on the cardiovascular effects of air pollution exposure that began in 2001. The 2002 meeting in Durham formed the basis for a request for applications (RFA) in 2003. This latest meeting was organized by NIEHS Division of Extramural Research and Training (DERT) Cellular, Organ and Systems Pathobiology Branch Health Science Administrator Srikanth Nadadur, Ph.D., DERT Acting Deputy Director Pat Mastin, Ph.D., and their colleagues at EPA. Representing EPA were Dan Costa, Sc.D., David Diaz-Sanchez, Ph.D., and Bob Devlin, Ph.D. EPA organizing committee members Stacy Katz and Gail Robarge were also in attendance.

Nadadur, shown during the final discussion session, administers grants in the areas of cardiovascular health, nanotoxicology, and pulmonary pathobiology. (Photo courtesy of Steve McCaw)

In his welcoming remarks, NIEHS Acting Deputy Director Bill Suk, Ph.D., praised the Institute's "long-standing relationship with EPA" in synergistic efforts to improve the health of vulnerable populations. He described the meeting as "a fine example of how two organizations with similar missions, although with different cultures, can come together to establish a program… [that] gives us a better understanding of the link between exposure, in this case particulate matter and air pollution, and disease."

Mastin opened the meeting with an overview of the rationale for developing the network of 12 NIEHS and EPA grants that has supported the research over the past five years. "The idea for the RFA came about because at the time — and I think it still holds true — the epidemiological data linking cardiovascular disease to air pollution was robust and getting more robust," he explained. The information on the mechanisms [by which] air pollution could cause or contribute to cardiovascular disease, [however], was far less established." He pointed to a grantee meeting in 2004 at the University of Louisville, "where I think the term environmental cardiology may have been born."

"One of the things we'd like to get out of this [workshop]," Costa told grantees, "is whether it's time to start thinking about developing another RFA to explore this issue from a different angle." (Photo courtesy of Steve McCaw)

The meeting was organized into three sessions on vascular and endothelial function, biochemical/pathophysiological mechanisms of cardiac effects and cardiovascular disease susceptibility, and a

wrap-up session on future directions and plans. The three subject-themed sessions reserved 45 minutes for participants to view and discuss groups of five to eight posters on each session's theme, followed by hour-long informal moderated discussions by panels of the study authors.

The final panel on future directions and plans pulled together findings and attempted to address the implications of the question posed at the beginning of the session by Nadadur — "Where are we after four years?" As the discussion made clear, there are still questions that the researchers cannot answer definitively.

Some of those questions concern whether the effects of air pollution on CVD are direct or indirect, whether experiments could be standardized in future collaborative and centers studies, and how best to integrate mechanistic and genetic research in future investigations. Additional issues include questions about which specific mechanisms, such as oxidative stress and inflammation, seem to be most important in terms of effects on CVD, whether there is a consensus yet about markers, and how much progress has been made toward finding an ideal disease model for studying air pollution-induced CVD.

One thing that the panelists all agreed upon was the important contribution the research has made in changing the discourse on air pollution and CVD. "I think we've answered the question of biologic plausibility that PM [particulate matter] can kill," Devlin concluded. While that represents a significant accomplishment, he acknowledged "we have a long way to go" in understanding the mechanisms.

NIEHS grantee Mark Frampton, M.D., right, is shown here at the Chapel Hill meeting September 4 -5. Frampton presented his University of Rochester group's findings on platelet and leukocyte activation by ultrafine carbon particles at both meetings. (Photo courtesy of Steve McCaw)

Diaz-Sanchez listened as grantees explored standardization before commenting on the variability of particle composition in the same kind of exposure. "There's diesel" he noted, "and then there's diesel." (Photo courtesy of Steve McCaw)

As University of Louisville biochemist Aruni Bhatnagar, Ph.D., explained, the evidence from studies by the grantees has led to widespread acceptance that particulate matter does have a negative impact on cardiovascular health. (Photo courtesy of Steve McCaw)

"PM affects a very, very small portion of the population," Devlin remarked. "The reason we care about it is because a very large percent of the population is exposed." (Photo courtesy of Steve McCaw)

Meeting Explores Genetic Susceptibility to Cardiopulmonary Disease

By Eddy Ball

Health Science Administrators from the NIEHS Division of Extramural Research and Training (DERT) joined their grantees, NIEHS intramural investigators and other experts in the fields of genetics and air pollution on September 4 and 5 for a meeting on genetic susceptibility to the health effects of air pollution exposure. Titled "Global Variability in Response to Air Pollution: Approaches to Translation of Cardiopulmonary Animal Disease Models," the meeting featured 12 thirty-minute talks and four panel sessions at the Sheraton Hotel in Chapel Hill, N.C.

McAlister summarized the background of the workshop. (Photo courtesy of Steve McCaw)

As NIEHS Health Science Administrator Kimberly McAllister, Ph.D., explained in her opening remarks, the meeting was a follow-up to a one-day workshop held exactly a year earlier on September 4, 2007 in conjunction with the International Society of Environmental Epidemiology annual meeting in Mexico City.

"There was a real need," McAllister told the participants, "to have a workshop to bring together the mouse modelers and comparative biologists with the human geneticists and epidemiologists to try to stimulate translation.… We're hoping to foster collaboration among all of you and to think about better integration and interdisciplinary research in the field."

Meeting organizers divided the agenda into five parts, which moved sequentially from an overview of current understanding, through three sessions on investigational approaches, to an exploration in the final session of future needs and implementation. Each of the five sessions was chaired by a DERT staff member with related research and administrative interests — Acting Deputy Director Pat Mastin, Ph.D., Health Science Administrators McAllister, Sri Nadadur, Ph.D., and Kimberly Gray, Ph.D., and Susceptibility and Population Health Branch Chief Gwen Collman, Ph.D.

After meeting with environmental cardiology grantees the previous day (see related story), Mastin chaired the workshop's key overview talks. (Photo courtesy of Steve McCaw)

NIEHS Laboratory of Respiratory Biology Principal Investigator Steven Kleeberger, Ph.D., gave the first presentation of the Gene Susceptibility of Cardiopulmonary Diseases session with a talk on "Identification of Genetic Loci Associated with Pulmonary Effects in Animal and/or Human Studies" and also participated as a panelist for the session. Epidemiology Branch Principal Investigator Stephanie London, M.D., Dr.P.H., was a panelist for the Genetics to G x E (Gene and Environment) Interactions and Methods session and joined Biostatistics Branch Chief Clare Weinberg, Ph.D., on the Implementation session panel.

The presenters and panelists were a mix of bench scientists involved in human and animal studies, clinical researchers, biostatisticians and epidemiologists, and the meeting format encouraged a productive exchange of what were at times strongly opposed viewpoints about how best to blend current approaches into an integrated systems biology model. There was lively debate about the relative merits and limitations of candidate gene studies compared to unbiased genome-wide association studies, as well as discussion of the strengths and weaknesses of knockout and transgenic models of rodents.

Behind the differences of opinion, however, there was a celebration of diversity articulated by NIEHS grantee Ivan Rusyn, M.D., Ph.D., during his talk in the final investigational approach session. "I think it's wonderful that we're in one room talking together," he said as he proceeded to underscore the importance of bioinformatics in efforts to understand genetic interactions in the biological pathways of disease and the limitations of individual single nucleotide polymorphism (SNP) studies.

During the final panel session, discussion turned to ways NIEHS could encourage optimal collaboration of scientists from different disciplines with the remarks of Harvard School of Public Health Professor Marianne Wessling-Resnick, Ph.D. Wessling-Resnick is the current principal investigator for an NIH Roadmap Program in Interdisciplinary Training in Genetics and Complex Diseases, who feels strongly that such collaborations should lead to truly transformative scientific approaches. Modifying the review of training grants, she suggested, could motivate applicants to include truly cross-disciplinary components into their proposals.

To illustrate what she considers optimal collaboration, Wessling-Resnick compared the various terms used to describe cross-disciplinary approaches to children at play. As opposed to a multi-disciplinary approach of parallel research or an inter-disciplinary approach with shared tools, Wessling-Resnick described the most fruitful cross-disciplinary approach as *trans*-disciplinary — when investigators merge their tools in an effort to develop a genuinely new integrated approach.

Kleeberger began the subject-matter sessions by delivering the workshop charge. In the closing session, he also challenged participants to consider comparative genomics studies. (Photo courtesy of Steve McCaw)

University of Southern California Professor Frank Gilliland, M.D., Ph.D., smiled as he recalled some of the unexpected pitfalls in his work to develop a system-level approach to studying the effects of air pollution. (Photo courtesy of Steve McCaw)

London, left, and Rusyn were outspoken about animal models and computational needs during the final panel discussions of the meeting. (Photo courtesy of Steve McCaw)

University of Pittsburgh Visiting Professor George Leikauf, Ph.D., center, argued for fostering more trans-disciplinary training. "When we're training to be narrow," he said, "we attract people who think narrow." (Photo courtesy of Steve McCaw)

Wessling-Resnick pointed to the benefits of trans-disciplinary approaches. "What you really want to stimulate is growth that brings investigators together and creates new scientific endeavor," she said. (Photo courtesy of Steve McCaw)

Wrapping up the workshop, Collman summarized the needs expressed by grantees, most requiring additional funding. She thanked attendees for the input and quipped, "A workshop always ends on the money note." (Photo courtesy of Steve McCaw)

University of Cincinnati Professor Grace LeMasters, Ph.D., above, was adamant about training investigators to look at "the big picture" of cardiopulmonary disease and "really reach across organs… [to] extend a system to other systems." (Photo courtesy of Steve McCaw)

An animated Joel Schwartz, Ph.D., principal investigator on NIEHS grants at Harvard University, weighed in on the computational challenges of trying to scan epigenetic modifications. (Photo courtesy of Steve McCaw)

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High Levels of Pesticides and Endocrine Disruptors in Pregnant Women in the Netherlands

By Dixie-Ann Sawin

In an NIEHS-led study published online September 4 in the journal *Environmental Research*, a team of American and European researchers reported finding high levels of organophosphorous (OP) pesticides and some suspected endocrine disrupting compounds including bisphenol A (BPA) and phthalates, in pregnant women and their offspring in the Generation R Study in the Netherlands. The study is a population-based birth cohort study.

NIEHS Postdoctoral Fellow and lead author Xibiao Ye (Photo courtesy of Steve McCaw)

The investigators analyzed urine specimens of 100 pregnant women selected from the cohort and found relatively high levels of OP and some phthalates, but similar levels of BPA compared to data from studies of pregnant women elsewhere in the world. Because of the surprisingly high levels, as well as the birth outcome and follow-up information in the study of an environmentally exposed population, the researchers concluded that the Generation R study "provides an opportunity to efficiently address questions regarding the reproductive and development effects of prenatal exposures."

The lead author of the paper, Postdoctoral Fellow Xibiao Ye, Ph.D., is a member of the NIEHS Biomarker-based Epidemiology Group, which is headed by co-author and Principal Investigator Matthew Longnecker, M.D., Sc.D. The Biomarker-based Epidemiology Group focuses on health effects of early exposure to background levels of environmental contaminants.

Corresponding author and Biomarker-based Epidemiology Group Head Matthew Longnecker (Photo Courtesy of Steve McCaw)

The study builds upon growing concern about the impact of low-level exposures to these compounds in the general population and, particularly, among pregnant women. The extensive use of OP pesticides increases exposure for humans primarily through food. BPA is used in the manufacturing of plastics and epoxy resins, and human exposure comes from food in containers lined with BPA and from some dental sealants. Phthalates are commonly included in cosmetics and polyvinyl chloride plastics.

Animal studies have shown that these pollutants can affect brain and reproductive development. The effects on the human population, however, are not clear.

The Generation R study, which includes 9778 participants, is led by scientists at Erasmus University. The study addresses four primary areas — growth and physical development, behavioral and cognitive development, childhood diseases and health, and health care for pregnant women and children.

The researchers analyzed the levels of 6 dialkyl phosphate (DAP) metabolites of OP pesticides, a specific metabolite of the widely used pesticide chloropyrifos, TCPy, BPA and fourteen phthalate metabolites in single urine samples from a subset of 100 of the Generation R pregnant women who were enrolled after February 2004 and had a live birth. They then compared the results to data on pregnant women in three US studies and studies from elsewhere in the world.

Their measurements indicated that the subjects from the Generation R study had higher-level exposure to OP pesticides and some phthalates, but BPA levels were similar to the populations in other studies. The choice of metabolites to study was based on the ability to compare to data from available studies. However, the investigators caution about the possible use of these as biomarkers of exposure because they can also reflect direct exposure to metabolites. They also state that it may be necessary to make additional measurements across the entire pregnancy in order to identify critical time periods of exposure.

This study is, nevertheless, the first report of biological monitoring of these specific pollutants in a general population in the Netherlands and can serve as a building block for further investigation of the effects of OP pesticides, BPA and phthalates on human health.

Citation: Ye X, Pierik FH, Hauser R, Duty S, Angerer J, Park MM, Burdorf A, Hofman A, Jaddoe VW, Mackenbach JP, Steegers EA, Tiemeier H, Longnecker MP. 2008. Urinary metabolite concentrations of organophosphorous pesticides, bisphenol A, and phthalates among pregnant women in Rotterdam, the Netherlands: The Generation R study. Environ Res [Epub ahead of print].

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

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NTP Holds Meeting on High-Throughput Screening

By Eddy Ball

The National Toxicology Program (NTP) took an important step forward in the development of a more rigorous and comprehensive high-throughput screening program for toxicology studies by hosting a Request for Information (RFI) meeting September 11 – 12 in Rodbell Auditorium at NIEHS.

The well-attended meeting brought together scientists from assay-development companies, government and universities to provide the NTP with information on how to identify and select critical cellular toxicity pathways to be evaluated by cell-based high-throughput screens. The NTP also solicited recommendations on particularly informative molecular targets within these pathways for both cell-based and biochemical assays.

At the end of his opening remarks, Tice asked attendees to join him in a few minutes of silence to acknowledge the anniversary of the tragic events of seven years earlier on September 11. (Photo courtesy of Steve McCaw)

The meeting featured 26 twenty-minute presentations on methodology, novel targets and pathway identification and was chaired by NTP Toxicologist Kristine Witt, who is involved in assay selection and study design for the NTP's High Throughput Screening (HTS) Initiative. According to event organizer Denise Lasko, more than 130 individuals registered for the meeting, including presenters, NTP, NIEHS and Environmental Protection Agency (EPA) scientists, and other scientists and individuals with interests in HTS and computational toxicology.

Witt, foreground, was a gracious chair and moderator, who also made sure speakers stayed within their allotted 20 minutes. (Photo courtesy of Steve McCaw)

On hand to introduce the meeting and provide clarification was Raymond Tice, Ph.D., deputy director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), acting chief of the NTP Biomolecular Screening Branch and HTS Initiative coordinator.

As Tice explained, the meeting is intended to address one of the short-term goals of the 2005 NTP Roadmap for the 21st Century to identify or develop rapid, mechanism-based predictive screening assays for use in toxicity determinations. He said that the event should also be viewed within the context of the 2007 National Academy of Sciences report Toxicity Testing in the 21st Century: A Vision and a Strategy.

Among the mixed audience from industry, academia and government were NTP scientists, such as Biologist Rachel Frawley, center foreground, and members of the computational toxicology community, including UNC researcher and NIEHS grantee Ivan Rusyn, M.D., Ph.D., seated to the left near the wall. (Photo courtesy of Steve McCaw)

During this same period of time, the NIEHS/NTP, EPA ToxCast Program and National Human Genome Research Institute explored ways to coordinate their work on alternative methodologies. "As a result of this publication and our own interests and efforts," Tice continued, "we put together a Memorandum of Understanding (MOU) in February 2008… on high-throughput screening toxicity pathway profiling and biological interpretation of findings."

As part of the MOU, the interagency consortium, also known as Tox21, set up four focus groups with representatives from each of the three organizations as co-chairs. The RFI meeting is intended to identify information for the first of the groups, Pathways and Assays, whose goal, Tice maintained, is "to identify key toxicity pathways and suitable assays for those pathways, including bio-transformation and evaluating assay reliability."

Over the day and a half of presentations, speakers addressed one or more of the informational needs outlined in the July 7, 2008 announcement of the meeting:

- Identification and selection of critical cellular pathways involved in toxicity and associated with disease outcome
- Assays that can be used to measure the activity of a compound on a target within a critical pathway
- Ways to select the best targets within pathways and networks

- Assays, technologies or methods for identifying compounds that are relevant only after metabolic activation
- New technologies or technologies under development that can help expand and more carefully characterize the findings from initial screens.

The next step, which Tice reminded the audience will take some time, is for the Assays and Pathways focus group to decide what test methods should be recommended to the NIH Chemical Genomics Center for further validation.

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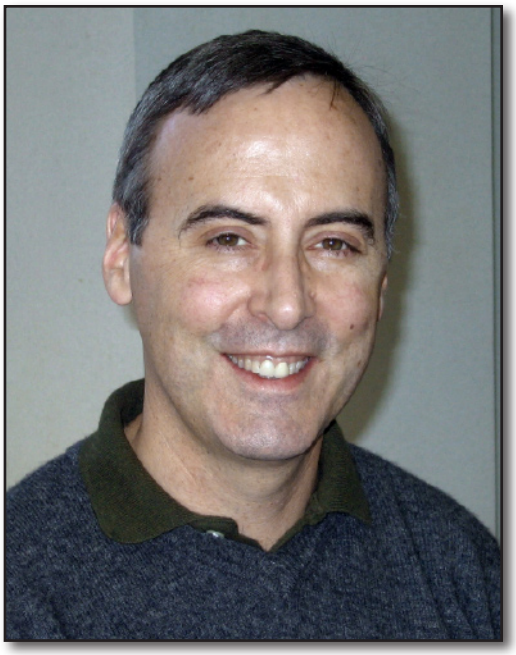
Upcoming Distinguished Lecturers Tom Ellenberger and C. Ronald Kahn

By Eddy Ball

The NIEHS 2008 – 2009 Distinguished Lecture Series features two talks during October. On October 14, Tom Ellenberger, D.V.M., Ph.D., will explore the topic of "Structural Biology of DNA End Joining." Later in the month on October 28, C. Ronald Kahn, M.D., will deliver the 2008 Falk Lecture titled "Public-Policy Issues of Diabetes and Obesity." Both talks will begin at 11:00 in Rodbell Auditorium.



Ellenberger will present the distinguished lecture on October 14. (Photo courtesy of Washington University School of Medicine)

Ellenberger is Wittcoff Professor and head of the Department of Biochemistry and Molecular Biophysics at Washington University School of Medicine. His research focuses on the structures and mechanisms of enzymes that repair chemical modifications of DNA in order to understand the molecular basis for DNA substrate selection and to identify the physical interactions that coordinate multistep repair processes.

Kahn is the Mary K. Iacocca Professor and director of the Joslin Diabetes Center at Harvard University. His principal research interests are understanding the molecular mechanism of action and of insulin and related growth factors at a molecular level and defining at a molecular and physiologic level the defects that underlie human diabetes mellitus.

NIEHS DNA Replication Fidelity Group Staff Scientist Kasia Bebenek, Ph.D., will host the Ellenberger lecture. Kahn's Falk Lecture will be hosted by Bill Schrader, Ph.D., NIEHS deputy scientific director and principal of the Androgen Biology Group.

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Extramural Update

Partnerships for Environmental Public Health Program Takes Shape

With concept clearance approval by the NIEHS National Advisory Environmental Health Sciences Council on September 9 (see related story), a Division of Extramural Research and Training (DERT) workgroup prepares to implement the Partnerships for Environmental Public Health (PEPH) program. The program is an important step as NIEHS establishes a sustainable commitment to the environmental public health community.

The PEPH program will provide a structure to coordinate and support a variety of research and dissemination activities to bring scientists, community members, educators, health care providers, public health officials and policy makers together in the shared goal of advancing the impact of science-based inquiries of environmental health threats of concern to communities on the local, regional and national levels. Initiatives under the umbrella of PEPH will be designed to provide grant support in five major categories — research, communication and dissemination, training and education, evaluation and coordination.

During the past year, DERT gathered and analyzed information from the extramural community to develop the next phase of the NIEHS programs in environmental public health. The DERT workgroup released a Request for Information in October, 2007 and received 120 responses from interested parties, which are available in executive summary on the PEPH website.

In June 2008, the workgroup convened a workshop of thought leaders from the fields of public health, environmental justice, community-based research, communication and advocacy to help develop the framework for a new program. The DERT workgroup also announced and awarded supplements to 17 existing grants to continue work in this area while a coordinated, ten-year program is established.

A hallmark of this program is that communities will be actively engaged in all stages of the research, dissemination and evaluation. Emphasis will be placed on robust research to investigate linkages between exposure and disease, as well as research and evaluation to improve the theories, methods and implementation strategies for working with communities to address their environmental health concerns. The program will emphasize both scientific advances and development of practical materials for use in communities, with a focus on translating research findings into tools, materials and resources that can be used by a variety of audiences to prevent, reduce, or eliminate adverse health outcomes caused by environmental exposures.

The PEPH program has set four major goals:

1) Strategically coordinate and integrate the various new and existing initiatives that involve communities and scientists working together on contemporary issues in environmental public health research.

2) Develop and evaluate strategies to communicate environmental public health messages to a diversity of audiences.

3) Create and provide materials to increase awareness and literacy about environmental health risks.

4) Evaluate program contributions to the advancement of environmental public health.

NIEHS intends to provide multiple ways for researchers and communities to obtain support for innovative and creative activities to protect the health of groups that are disadvantaged by exposure to occupational or environmental hazards. As part of this strategy, NIEHS will work in coordination and partnership with NIH and federal partners. By adding training and career development in environmental public health and research in communication and dissemination strategies to translate environmental health research results to a wide variety of stakeholders, NIEHS will continue to provide strong support for increasing science and health literacy and promoting prevention strategies to protect human health.

For more information, contact: Mr. Liam O'Fallon at ofallon@niehs.nih.gov.

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Extramural Papers of the Month

By Jerry Phelps

Arsenic and Type 2 Diabetes

New research findings from the National Health and Nutrition Examination Survey (NHANES) suggest that exposure to levels of arsenic commonly found in drinking water may be a risk factor for type 2 diabetes — suggesting that millions of Americans may be at increased risk.

Data on the nearly 800 participants in the study for which urinary arsenic concentrations were available, indicated that urine levels of arsenic were significantly associated with the prevalence of type 2 diabetes. After splitting the subjects into 5 groups based on the level of arsenic in their urine, the researchers determined that those in the highest category were more than three and one-half times more likely to have diabetes.

Inorganic arsenic in drinking water at concentrations higher than 100 parts per million has been linked to type 2 diabetes in countries where drinking water is commonly contaminated with high levels of arsenic. The U.S. drinking water standard is currently 10 parts per million. However, the researchers estimate that about 13 million Americans live in areas where public water systems exceed the EPA standard for arsenic and this number does not included private wells and water systems.

Animal studies have shown that arsenic affects the production of glucose, insulin secretion and can cause insulin resistance.

Citation: Navas-Acien A, Silbergeld EK, Pastor-Barriuso R, Guallar E. 2008. Arsenic exposure and prevalence of type 2 diabetes in US adults. JAMA 300(7):814-822.

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Connection Between Built Environment and Obesity

People living in neighborhoods with a high density of fast food restaurants, few sidewalks and no parks are more likely to be part of the estimated 34 percent of the U.S. population aged 20 years or more who are obese, according to NIEHS-supported research by the Oregon Research Institute. In contrast, people living in neighborhoods with higher mixed-land use, high street connectivity, better access to public transportation and more green and open spaces are more likely to engage in some form of neighborhood-based walking program.

This study focused on the baby boom population aged 50-75, which will become the major demographic group in healthcare utilization in the next 20 years. Finding and ameliorating built environment limitations on physical activity are important in keeping this population healthy and reducing the health care burden.

The research findings point to access to unhealthy food and lack of accessibility to spaces for exercise as contributing factors for the rise in obesity. The researchers point out that zoning and development policies need to be altered to enable people to lead healthier lifestyles.

The researchers examined 120 neighborhoods in Portland, Oregon. More than 1,200 residents in these neighborhoods completed questionnaires providing basic demographic data along with information on exercise and eating habits.

Citation: Li F, Harmer PA, Cardinal BJ, Bosworth M, Acock A, Johnson-Shelton D, Moore JM. 2008. Built environment, adiposity, and physical activity in adults aged 50-75. Am J Prev Med 35(1):38-46.

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p53 Inhibits Cell Growth as well as Cell Proliferation

New research findings by NIEHS grantees indicate that the tumor suppressor gene p53 is involved in regulating the growth of cells as well as the proliferation of cells. The fact that p53 targets genes inhibiting cell proliferation genes had long been known, but its targets for inhibiting cellular growth have not.

The p53 protein acts in the cell nucleus to control the expression of other genes whose products can inhibit the abnormal cell proliferation and growth characteristic of cancer. The researchers discovered that two p53 target genes, known as Sestrin1 and Sestrin2, provide an important link between p53 and a protein kinase called mTOR, a central regulator of cell size. mTOR is the target for the immunosuppressive drug rapamycin, which was recently shown to have anti-cancer activity.

The major tumor suppressor p53 can either inhibit cell proliferation and cell growth or induce cell death. Its different functions are mediated through numerous target genes and depend on the extent of damage to the cell. More than half of all human cancers are either missing p53 expression or express a defective version of the protein. Understanding the mechanisms by which p53 suppresses tumors may lead to the development of new cancer preventives and chemotherapeutic agents.

Citation: Budanov AV, Karin M. 2008. p53 target genes sestrin1 and sestrin2 connect genotoxic stress and mTOR signaling. Cell 134(3):451-460.

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The Ah Receptor is Essential for Mediating an Anti-Inflammatory Effect

A research team made up of NIEHS grantees from the University of Rochester and the University of California, Davis has discovered a potentially new role for the Ah receptor in treating inflammatory or immunologic disorders. This research adds new information on the diverse functions of the receptor, including xenobiotic metabolism, involvement in proper blood vessel formation and now immune responses.

The team happened upon this discovery while investigating a low-molecular-weight compound with potent anti-inflammatory activity known as VAF347. The compound is a drug candidate that inhibits allergic lung inflammation. The team demonstrated that VAF347 interacts with the Ah receptor, resulting in stimulation of its signaling pathway. Additional experiments in Ah receptor-deficient mice confirmed the connection. These mice are resistant to the compound's ability to block allergic lung inflammation. The data indicate that the Ah receptor protein is an important target of VAF347 and is important in mediating the anti-inflammatory effects of the compound.

Although the importance of the Ah receptor in mediating the toxicity of various organic compounds is well known, this finding suggests that harnessing the biological activity of the receptor for therapeutic purposes is possible and suggests a new tool for the treatment of inflammatory and immunologic disorders.

Citation: Lawrence BP, Denison MS, Novak H, Vorderstrasse BA, Harrer N, Neruda W, Reichel C, Woisetschläger M. 2008. Activation of the aryl hydrocarbon receptor is essential for mediating the anti-inflammatory effects of a novel low-molecular-weight compound. Blood 112(4):1158-1165.

(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

DEPs Involved in a Novel Blood-Brain Barrier Signaling Pathway

Scientists from NIEHS, the University of Minnesota and Virginia Commonwealth University Medical Campus demonstrated that diesel exhaust particles (DEPs) alter blood-brain barrier function through oxidative stress and proinflammatory cytokine production. It is the first study to show this interaction and an important finding since DEPs are the main particulate component of urban air pollution worldwide.

DEPs have a carbon core with heavy hydrocarbons and hydrated sulfuric acid. Polycyclic aromatic hydrocarbons are adsorbed to the particles. Researchers knew that once DEPs enter the body through inhalation they could travel to all tissues. This research team wanted to understand the specific effects in the central nervous system (CNS).

When brain capillaries isolated from rats were exposed to DEPs, a signaling pathway involving NADPH oxidase and tumor necrosis factor alpha was activated. This pathway signaled increased expression of P-glycoprotein, a major blood-brain barrier drug efflux transporter for therapeutic drugs.

The results reveal a novel blood-brain barrier signaling pathway turned on by urban air pollutants that could affect pharmacotherapy for a number of CNS diseases.

Citation: Hartz AM, Bauer B, Block ML, Hong JS, Miller DS. 2008. Diesel exhaust particles induce oxidative stress, proinflammatory signaling, and P-glycoprotein up-regulation at the blood-brain barrier. FASEB J 22(8):2723-2733.

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Loss of Estrogen Receptor-Alpha Affects Bone

An interdisciplinary team of researchers from NIEHS and several other institutions determined that a homozygous disruption of the estrogen receptor-alpha (ER-α) affected bone growth, mineral content and structure. Interestingly, this loss did not affect periosteal circumference. The periosteum is a dense membrane composed of fibrous connective tissue that lines the surface of bone. The study attempted to provide insight into the roles of androgen and estrogen on male and female subjects and was a follow-up analysis of the first individual described to have a germ line loss of function mutation of the ER-α gene.

The team wanted to determine the impact of a loss of function mutation in the ER-α gene on histomorphometry, bone volumetric density, bone geometry and skeletal growth, and ER-α heterozygosity on spine density and adult height in an extended pedigree. The researchers evaluated the kindred of the mutant patient for the study and measured vital signs, height and weight. In addition to giving blood for ER-α carrier status, subjects had areal spine bone mineral density (aBMD) measurements using x-ray absorptiometry (DXA).

The data suggested that a disruption of ER-α resulted in a host of physical skeletal abnormalities, including increased osteopenia and periosteal expansion and decreased epiphyseal closure. ER-α heterozygosity did not appear to impair the skeleton. The team also found that both estrogen and androgen can contribute to bone growth, mineral content and skeletal structural integrity.

Citation: Smith EP, Specker B, Bachrach BE, Kimbro KS, Li XJ, Young MF, Fedarko NS, Abuzzahab MJ, Frank GR, Cohen RM, Lubahn DB, Korach KS. 2008. Impact on bone of an estrogen receptor-alpha gene loss of function mutation. J Clin Endocrinol Metab 93(8):3088-3096.

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NELF Enhances Gene Expression

The transcription regulatory complex, Negative Elongation Factor (NELF), affects many rapidly inducible genes involved in cellular responses to stimuli, according to scientists at NIEHS and Pennsylvania State University. NELF induces RNA polymerase II (Pol II) to stall during early transcription elongation and represses expression of several genes, including *Drosophila Hsp 70*, mammalian proto-oncogene *junB* and HIV RNA. This research identifies a novel role for stalled Pol II in regulating gene expression.

The researchers wanted to determine all of the genes that NELF targeted in *Drosophila* and used microarray analysis of S2 cells depleted of NELF in their studies. NELF RNAi indicated that the majority of target genes exhibited decreased expression levels while far fewer genes were, like *Hsp 70*, up-regulated by NELF-depletion.

The presence of a stalled Pol II at down-regulated genes enhanced gene expression by maintaining a permissive chromatin architecture near the promoter-proximal region. In addition, a loss of Pol II stalling resulted in an increase in nucleosome occupancy and a decrease in histone H3 lysine 4 trimethylation, an epigenetic mark of transcription activity.

Future studies will examine how stalled Pol II affects local nucleosome architecture and promoter accessibility.

Citation: Gilchrist DA, Nechaev S, Lee C, Ghosh SK, Collins JB, Li L, Gilmour DS, Adelman K. 2008. NELF-mediate stalling of Pol II can enhance gene expression by blocking promoter-proximal nucleosome assembly. Genes Dev 22(14):1921-1933.

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The Role of Genetics in Heart Rate and Heart Rate Variability

Recent studies suggest that there is a strong genetic component in the regulation of resting heart rate (HR) and heart rate variability (HRV) in quiescent mice. The investigation, performed by researchers from NIEHS and the Genomics Institute of the Novartis Research Foundation, provides the basis for investigating the precise interaction between genotype and the underlying mechanism associated with murine heart regulation.

Prior to this study, several other peer-reviewed journal articles suggested that genetics were important in HR and HRV, so the investigators examined 30 inbred strains and 29 recombinant inbred (RI) strains of mice during periods of rest using electrocardiograms (ECG) to measure HR and HRV and performed interval mapping to associate chromosomal regions with HR and HRV differences. Pulmonary function was also measured. Differences in HR and HRV were observed between strains; however, in the majority of the strains a continuous distribution of HR and HRV was observed, which implied that HR and HRV regulation is a complex trait and is influenced by multiple genes.

To determine which chromosomal regions were responsible for variations in the phenotypes, a quantitative trait locus (QTL) analysis was performed. QTLs were found on chromosome 2, 4, 5, 6 and 14.

Significant differences in HR, HRV and pulmonary function were found between strains, which indicated a strong genetic component to the regulation of these phenotypes.

Citation: Howden R, Liu E, Miller-DeGraff L, Keener HL, Walker C, Clark JA, Myers PH, Rouse DS, Wiltshire T, Kleeberger SR. 2008. The genetic contribution to heart rate and heart rate variability in quiescent mice. Am J Physiol Heart Circ Physiol 295(1):H59-68.

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Inside the Institute

NIEHS Honors Long-Time Director

By Eddy Ball

Although he's officially a retiree now, Director Emeritus and Principal Investigator Ken Olden, Ph.D., will still be going into the office regularly after he moves to New York for his next challenge in public health. On August 30, Olden's friends and colleagues from throughout the Institute flocked to the Rall Building B200 Conference Room during a lunchtime party to offer him their best wishes with his new position and say farewell to the man who led NIEHS for 14 years.

Olden decided to end his 23-year career with NIH this summer when he accepted an offer to become the dean of the new school of public health at the City University of New York (CUNY) — the first school of public health at CUNY and the first such program designed with an urban focus. Olden, who will work from the Hunter College campus, has made a three-year commitment to the challenge of creating the program and making it a sustainable part of the CUNY system.

Acting Director Sam Wilson, M.D., praised Olden's contributions to the environmental health sciences and presented him with a plaque in recognition of his service to the NIH and NIEHS. Wilson was one of several senior staffers in attendance who were recruited by Olden when he was director of NIEHS.

Olden spoke briefly of his excitement about being on the front lines of an emerging paradigm in public health education. He also assured his friends and colleagues that he would see them soon. He and his wife, Sandie White, Ph.D., plan to keep their home in North Carolina and to return there regularly. Olden said, "I'm sure I'll be back on campus frequently to visit and take advantage of the library."

With the formalities behind them, well-wishers mingled and enjoyed sandwiches and snacks before making their way back to their labs and offices. Afterwards, with his hands full of official and personal gifts, the former director walked along the C-module mall, saying goodbye to the people he met along the way, and then left the NIEHS campus to begin the next phase of his long career in science.

Olden, center, shared a laugh with colleagues, left to right, Allen Deary, Ph.D., Anne Sassaman, Ph.D., and Ray Tennant, Ph.D., standing. Seated to Tennant's right is fellow cancer investigator Trevor Archer, Ph.D. (Photo by Eddy Ball)

With the speeches out of the way, people began to take advantage of the refreshments. (Photo by Eddy Ball)

Former Scientific Director Lutz Birnbaumer, Ph.D., left, and Wilson, center, were recruited by NIEHS during Olden's tenure as director. (Photo by Eddy Ball)

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Tennant Looks Forward to New Adventures

By Eddy Ball

With 42 years of government service to his credit, Principal Investigator Ray Tennant, Ph.D., bid farewell to friends and colleagues at his retirement party on the afternoon of August 30 in Rall Building F193. The room, which was the venue of many lectures that Tennant gave or attended during his 28 years at NIEHS, was filled to capacity and then some as well-wishers talked, snacked and watched a slide show of Tennant's career and some of his extracurricular adventures.

Tennant's adventures have included what colleague John Pritchard, Ph.D., described as "jumping out of perfectly good airplanes" and fishing excursions throughout the United States. Claiming, like poet Robert Frost, that he still has "promises to keep and miles to go before I sleep," Tennant told the people at his retirement party that he looks forward to the freedom of pensioned unemployment.

"Except for the people here, I'm not sorry to be leaving," he said. "Now I'll do whatever I want to do."

Tennant's federal service began with a 14-year stint at the Oakridge National Laboratory before he joined NIEHS in 1980. During Tennant's career at NIEHS, he worked with the National Toxicology Program, served as a lab chief Laboratory of Molecular Toxicology's Cancer Biology Group and headed the National Center for Toxicogenomics from its inception in 2000 to 2006. His special research interests lay in the field of skin tumor development. Along with several of his colleagues who came to wish him well in retirement, Tennant worked at the leading edge of omics methodologies and experimental and computational toxicology.

Now that he's free of work commitments, Tennant plans to indulge his passion for the outdoors and new adventures. He will leave soon for his ultimate fishing trip — along the dark and sometimes dangerous waters of the Amazon River.

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High above the ground below, Tennant prepared to abandon his seat on "a perfectly good airplane" and gamble that his equipment would work. (Photo courtesy of Ray Tennant)

Tennant fell in tandem before opening his parachute. (Photo courtesy of Ray Tennant)

It was clearly a thumbs-up day for Tennant, as he posed with family members after a successful jump that left him physically intact and ready for more adventures. (Photo courtesy of Ray Tennant)

Event Celebrates Johnson-Thompson's Career

By Eddy Ball

Marian Johnson-Thompson, Ph.D., served as NIEHS director of Education and Biomedical Research from 1994 (see related story), when she was recruited by former Director Ken Olden, Ph.D. On September 22, people from NIEHS, the greater scientific community and her family filled Rodbell Auditorium to celebrate her career. The retirement ceremony was organized by friends at NIEHS and moderated by NIEHS Acting Deputy Director Bill Suk, Ph.D.

Colleagues Annette Rice, left, and Veronica Godfrey set the tone for the celebration with their bittersweet mix of joy and humor about the good times they've shared with Johnson-Thompson — and their loss now that she won't be as much a part of their working lives. (Photo courtesy of Steve McCaw)

As a collage of photos from Johnson-Thompson's years at NIEHS filled the screens in the auditorium, speaker after speaker praised her accomplishments as a microbiologist, educator, patient and human rights advocate, trusted advisor, friend and sorority sister. Several speakers praised Johnson-Thompson's tenacity in the defense of what she felt was right and her ability to disagree with colleagues on the NIEHS Institutional Review Board (IRB) without taking things personally.

One speaker, longtime friend Sandie White, Ph.D., lauded Johnson-Thompson for "fighting the good fight." Another, NIH colleague Kay Johnson Graham, Ph.D. observed that Johnson-Thompson's mission to expand science education opportunities for minorities and underserved populations demonstrated her commitment to genuine equality of opportunity.

Suk, holding the standard retirement-gift photo of the Institute, served as master of ceremonies at the event. (Photo courtesy of Steve McCaw)

The final speaker at the ceremony, NIEHS Acting Director Sam Wilson, M.D., described Johnson-Thompson as "one of the closest advisors to me" and the many planning meetings they had together over the years. Wilson credited her with inspiring some of the most effective and innovative education and recruitment programs anywhere.

Well-wishers presented the retiree with personal gifts and mementos. Colleague Sharon Beard gave her a collage of photos from their work together, NIEHS Acting Clinical Director Darryl Zeldin, M.D., presented a plaque on behalf of the IRB, and Suk gave Johnson-Thompson a vase on behalf of colleagues at the Institute. Wilson presented her with a panoramic photo of the Institute signed by friends and colleagues.

Closing out the program, Johnson-Thompson talked of the challenges and rewards of her work at NIEHS. She was visibly moved by the words of her friends and colleagues, and her voice quivered with emotion as she thanked the audience and offered them her best wishes.

Sandie White, Ph.D., reflected on her memories of working with Johnson-Thompson early in their respective careers at Howard University and the University of the District of Columbia in the late 1970s. After she and husband Ken Olden, Ph.D., moved to North Carolina, Olden recruited Johnson-Thompson. (Photo courtesy of Steve McCaw)

Wilson, above, laughed as he remembered some of the lighter moments of the past 14 years. He was the final speaker before the honoree herself took the podium to thank the audience for helping to make her experiences at NIEHS so rewarding. (Photo courtesy of Steve McCaw)

Johnson-Thompson, center, posed with friends James Copeland of the U.S. Environmental Protection Agency, left, and Kay Johnson Graham, minority outreach coordinator in the NIH Office of Equal Opportunity and Diversity Management. (Photo courtesy of Steve McCaw)

Along with joining in the fun, Zeldin praised his colleague for her leadership of the IRB and dedication to the protection of human subjects' rights and privacy. (Photo courtesy of Steve McCaw)

Durham Alumnae Chapter of Delta Sigma Theta sisters Joan Packenham, Ph.D., left, and Sharon Beard have been important partners with Johnson-Thompson in their service to community and science education. (Photo courtesy of Steve McCaw)

Holding the flowers she received earlier, the guest of honor posed with events coordinator and friend Elliott Gilmer, who was in charge of set-up, computer-projection and sound support for the many meetings Johnson-Thompson organized at NIEHS. (Photo courtesy of Steve McCaw)

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Seminar Examines Aging and Arthritis

By Eddy Ball

One of North Carolina's leading authorities on the public health implications of arthritis was the guest lecturer at a seminar sponsored by the NIEHS Disability Advocacy Committee (DAC) on September 9 in the Rall Building D-250 conference room. Hosted by DAC Chair Alicia Moore, the talk by University of North Carolina (UNC) Professor Leigh Callahan, Ph.D., was titled "Aging and Arthritis – Quality of Life and Issues Related to Disability." Callahan's presentation explored the public health implications of the disease, possible links to environmental exposures and ways to help prevent onset or ameliorate symptoms.

Callahan described recent efforts to increase awareness of arthritis as "a movement forward for getting people thinking about the public health impact." (Photo courtesy of Steve McCaw)

One of the 90 UNC specialists who donate their time as part of the university's Carolina Speakers program, Callahan is an associate professor of Medicine, Orthopaedics and Social Medicine at the UNC Thurston Arthritis Research Center. She has more than 20 years of experience in arthritis and health outcomes research, and served as an arthritis epidemiologist with the Centers for Disease Control and Prevention (CDC) prior to joining UNC. She spoke about what was until recently an underappreciated cause of disability. Callahan also took questions from an audience of some 20 NIEHS staffers on topics ranging from the possible contribution of hormones to the merits of alternative treatments.

As Callahan explained, arthritis is a public health concern that, in its more than 100 forms, affects more than 46.1 million adults in the United States — a number expected to increase to more than 67 million by 2030 as the population ages. Arthritis can significantly limit activity and impact quality of life, Callahan told the audience, "and it is the leading cause of partial or total disability for adults." According to the Arthritis Foundation, she added, the costs associated with arthritis total more than $128 billion each year.

DAC chair Alicia Moore presented Callahan with a certificate of appreciation at the end of the seminar. (Photo courtesy of Steve McCaw)

Turning to the geographical distribution of arthritis, Callahan said that the varying rates in different parts of the country are probably related to obesity rates. However, she also observed that recent research, such as the Johnson County Osteoarthritis Project conducted by colleagues of hers at the Thurston Research Center, turned up possible links to environmental exposures that merit further investigation.

Selenium, for example, may be protective, and investigators in the Johnson County studies have observed associations of higher blood levels of lead with osteoarthritis biomarkers and knee severity. Callahan noted that there was also some suspicion that mercury, arsenic and cadmium may have an influence on disease severity.

Callahan pointed to non-modifiable risk factors for disease, including gender, age and genetic predisposition, and socioeconomic factors associated with higher rates of disease in certain groups and communities. She noted that the modifiable risk factors — sports and occupational joint injuries, infection, joint-straining occupations and, especially, excess weight — offer individuals ways to potentially influence disease onset, symptom severity and impact on quality of life.

According to Callahan, one study found that a weight loss of just 5.1 kilograms was associated with a reduction in risk of developing osteoarthritis over a ten-year period. Losing weight can also help people who already have arthritis, she added, because obesity leads to greater limitations and more rapid disease progression. She said that the risk of developing arthritis makes even more compelling the CDC recommendation of dietary changes and moderate intensity exercise for 30 minutes three times per week to help control weight gain.

Callahan concluded her presentation by acknowledging that Americans are beginning to pay more attention to arthritis with such policy forums and initiatives as Healthy People 2010, the National Arthritis Action Plan, the NC Arthritis Action Plan 2001 and the Bone and Joint Decade Proclamation.

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