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March 2008

NIEHS Spotlight

Wilson Updates Council on NIEHS Developments and Challenges

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Trans-Agency Agreement to Transform Environmental Health Protection

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NCCU Chancellor Speaks at Black History Month Celebration

Most Americans know that February is Black History Month, but many don't realize the origins of the observance. That's why the employees of the Research Triangle Park (RTP) campus of the Environmental Protection Agency (EPA) sponsored "Carter G. Woodson and the Origins of Multiculturalism," one of several events held to celebrate the contributions of African Americans to the nation's culture and history. ....read more

Science Notebook

Researcher Warns about Pregnancy and Weight Gain

Nutritional epidemiologist Anna Maria Siega-Riz, Ph.D., had good reason to sound alarmed when she talked about pregnancy and weight gain during her February 1 Frontiers of Environmental Sciences lecture in Rodbell Auditorium. According to the University of North Carolina at Chapel Hill professor, overweight and obese women, as well as women who gain too much weight during their pregnancies, may be endangering their own health — and the health of their children. ...read more

Increased Allergen Levels in Homes Linked to Asthma

Not all asthma sufferers have respiratory allergies, but the ones who do must be wary of certain "triggers" that initiate asthma attacks. The results of new research may help the millions of Americans who fall into this category. ...read more

Methods Determine Estrogenization Effects in Infants

Some studies suggest that adults who consume foods rich in soy protein receive several health benefits such as healthy bones and a decreased risk of breast or prostate cancer, although research investigating diets rich in soy are in progress. However, soy isoflavones are weak estrogens and their affect on newborns, especially in regard to breast and genital development, is less established. ....read more

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Plan Expedites Alternatives to Animal Testing

A new plan to further reduce, refine and replace the use of animals in research and regulatory testing, commonly referred to as the *3Rs*, was unveiled at a symposium February 5 in Bethesda, Md. marking the 10-year anniversary of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). ...read more

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NIEHS to Celebrate Women in Science with March Events

As part of its observance of Women's History Month, NIEHS plans a series of talks featuring women scientists during March.

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Science Notebook

Superfund Program Helps Train Mexico's Environmental Scientists

Thanks to Hugo Alonso Zúñiga Hernández — and other young scientists like him — what now looks like a moonscape in the Mexican state of Sonora may one day again live up to the meaning of its name in the Opata language, the "Place of Corn." ...read more

UC-San Diego Superfund Researcher Honored with Gillette Award

Former Superfund Basic Research Program (SBRP) scientist Kathy Senekeo-Effenberger, who worked in the laboratory of Pharmacologist Robert Tukey, Ph.D., at the University of California-San Diego (UC-San Diego), was awarded the James R. Gillette Drug Metabolism Best Paper of 2007. ...read more

Upcoming Distinguished Lecture Features Kathryn Horwitz

The 2007-2008 NIEHS Distinguished Lecture Series continues at 11:00 a.m. March 11 with a talk by Kathryn Horwitz, Ph.D., on "Hormonal Regulation of Breast Cancer: Stem Cells and Metastasis." ...read more

Inside the Institute

Institute Celebrates China Day

By the time the China Day celebration on February 12 got underway, the NIEHS Cafeteria was packed with employees, contractors and relatives drawn to the event by the promise of good food and entertainment. All who attended, including NIEHS Acting Director Sam Wilson, M.D., who introduced the event, seemed completely satisfied with the quality of both. ...read more

Family Health Seminar on Loss and Grieving

Clinical associate Edna Ballard has had ample opportunity to see the various ways that individuals face loss and express their grief. In the course of her work at the Joseph and Kathleen Bryan Alzheimer's Research Center, she became convinced that no one has the right or the ability to judge the appropriateness or quality of anyone else's response. ...read more

Schwartz Accepts Research Position in Denver

Former NIEHS Director David Schwartz, M.D., will end his three-year tenure with the Institute in May to assume a research position with the National Jewish Medical and Research Center (NJMRC) in Denver, Colorado. ....read more

Extramural Research

Extramural Update

The NIEHS appropriation for fiscal year 2008 provides for an overall budget for grants amounting to one percent more than 2007 funding. This is significantly less than the cost of inflation and will result in continued austerity in the grants budget. Below we have outlined the steps the Division of Extramural Research and Training will be taking in this fiscal year to meet the requirements set out by NIH. ...read more

Extramural Papers of the Month

- New *In Vitro* Test May Replace Some Animal Testing
- Early-life Exposure to Lead Causes Alzheimer's Like Changes in Older Monkeys
- Oxidative Stress Marker Identified in Stroke Victims
- Lipoic Acid Supplementation Inhibits Lesion Development in Mice

Intramural Research

Intramural Papers of the Month

- Atopic Asthma Risks to Women in the Agricultural Health Study
- Nicotinamide Involvement in Hormone-Mediated Transcription
- Crystallization of the Type II Dihydrofolate Reductase Complex
- The Roles of XRCC1 and Pol β in Repair of SSBs

Calendar of Upcoming Events

- **March 3** in Rodbell Auditorium, 2:00 – 3:00 — Frontiers in Environmental Sciences Lecture Series, featuring Devra Davis, Ph.D., speaking on “The Need to Revitalize Toxicology: Lessons from the Secret History of the War on Cancer”

- **March 4** in Rodbell Auditorium A, 1:30 – 2:30 — Seminar on “Disability and Social Justice” with David Resnik, J.D., Ph.D.

- **March 4 - 6 (Offsite Event)** at the U.S. Geological Survey National Center in Reston, Va., 8:00 – 5:00 — GeoHealth I: Building Bridges Across the Geological and Health Sciences

- **March 6** in Rodbell Auditorium AB, 8:00 – 4:00 — Science Teachers Workshop

- **March 6** in Rodbell Auditorium C, 11:00 – 12:00 — Seminar on “Procreative Responsibility and the Ethics of Stem Cell Research” with Anne Drapkin Lyerly, MD

- **March 7** in Rodbell Auditorium, 9:00 – 10:00 — Spirit Lecture/Frontiers in Environmental Sciences Lecture Series on “Application of Omics-Based Tools and Microarrays to Optimize Bioremediation,” featuring Lisa Alvarez-Cohen, Ph.D., Topic TBA

- **March 10** in Rodbell Auditorium, 10:00 – 11:00 — Women’s History Month Presentations by RAISE Project Directors Stephanie Pincus, M.D., and Florence Haseltine, M.D., Ph.D.

- **March 10** in Rodbell Auditorium, 2:00 – 4:00 — International Women’s Day Panel Discussion with NIEHS Scientists Maria Kadiiska, M.D., Ph.D.; Harriet Kinyamu, Ph.D.; Xiaoling Li, Ph.D.; and Ivana Yang, Ph.D.

- **March 11** in Rodbell Auditorium, 11:00 – 12:00 — Distinguished Lecture Series with Kathryn Horwitz, Ph.D., speaking on “Hormonal Regulation of Breast Cancer: Stem Cells and Metastasis ”

- **March 14 -18 (Offsite Event)** in Philadelphia, Penn., 8:00 – 5:00 — American Academy of Allergy, Asthma & Immunology Annual Meeting

- **March 14** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, featuring a talk by Deborah A. Cory-Slechta, Ph.D., “Multiple Hit Models of Neurotoxicity: Clarifying the Contribution of Neurotoxicants to Human Diseases and Disorders”

- **March 25** in Rodbell Auditorium, 8:00 – 4:00 — NC Environmental Stewardship Initiative Participants Meeting

- **March 27 - 30 (Offsite Event)** in Istanbul, Turkey 8:00 – 5:00 — 3rd Euro-Asian Conference on Hazardous Waste & Human Health

- **March 27** in Rodbell Auditorium AB, 8:00 – 4:00 — Science Teachers Workshop

- **March 28** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series talk on “Environmental Science and Social Responsibility” by JoAnn Burkholder, Ph.D

- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Wilson Updates Council on NIEHS Developments and Challenges

By Eddy Ball

As he began his report at the 123rd regular meeting of the National Advisory Environmental Health Sciences Council February 19 in Rodbell Auditorium, NIEHS Acting Director Sam Wilson, M.D., greeted members with his characteristic low key humor. "These past several months here at the Institute have been very eventful and very involved," Wilson said in reference to the series of news-making events and major new initiatives underway since the group's last meeting in September.

Wilson reinforced his opening statement about the NIEHS mission several times during the meeting. "I think our institute has an important role in prevention," he said. (Photo courtesy of Steve McCaw)

Wilson also introduced a motif that would inform his report and surface several times during the day's discussions. "The general theme of our work here at NIEHS is research excellence in pursuit of disease prevention and better health," he began. "Our Institute [addresses] real world, human health problems related to environmental exposures and environmental triggers in human disease."

Wilson's report touched on leadership changes and several new developments and meeting highlights. He introduced the new editor-in-chief of *Environmental Health Perspectives*, Hugh Tilson, Ph.D., who spoke about his first two months on the job.

Council member Ken Ramos, Ph.D., was a discussant on the Concept Clearance proposal presented by NIEHS Health Science Administrator Kim Gray, Ph.D., on Children's Environmental Health. The proposal passed unanimously. (Photo courtesy of Steve McCaw)

Wilson then related the Institute's activities with the trans-NIH Gene-Environment Interaction and Epigenomics initiatives, the Superfund Basic Research Program anniversary symposium, alternate toxicity testing employing "robo-tox" high-throughput screening methods (see related story) and the Institute of Medicine's transportation and health workshop.

However, Wilson devoted most of his report to the topics of congressional appropriations to NIEHS and proposed modifications to the peer review process for grantees in the environmental health sciences.

Although appropriations increased slightly for fiscal year 2008, Wilson explained, the overall NIH budget remains flat. The President's Budget for 2008 continues funding at the 2008 level, signaling an effective decrease in funding due to inflation. Moreover, two separately funded programs operated by NIEHS, the Superfund Basic Research Program and the Worker Education Training Program, actually experienced reductions.

According to Wilson, when the budget is adjusted for inflation, using what is called the Biomedical Research and Development Price Index, a picture emerges of a significant and continuing decline in NIH resources. "Compared with the appropriation in 2003," he observed, "the spending power that we have across the NIH is down by more than ten percent."

Until this year, Wilson said, NIEHS "has been able to accommodate for the decrease in spending power by discontinuing a number of capacity-building programs… [making it] possible for us to continue pretty much with business as usual." This year, however, "the budget is extremely tight and certainly much tighter than it's been any time in my experience here at the Institute."

Wilson then turned to the topic of peer review by the NIH Center for Scientific Review (CSR) and described an innovative pilot effort by the CSR that could help assure that toxicology and environmental health research applications will get reviewed by researchers who are more familiar with these areas. For June 2008 submissions, grant proposals that had been assigned to diverse disease or organ-based study sections can go to a pilot Special Emphasis Panel (SEP), called Systemic Injury by Environmental Exposure, resulting in what Wilson called an enhanced "clustering of our proposals."

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NIEHS Associate Director Sharon Hrynkow, Ph.D., addressed Council for the first time and outlined her role in the Institute's top management circle. (Photo courtesy of Steve McCaw)

NIEHS Acting Deputy Director Bill Suk, Ph.D., right, spoke with Kate Dixon, Ph.D., center, and John Essigman, Ph.D., during the morning break — a welcome venue for informal interaction. (Photo courtesy of Steve McCaw)

Council welcomed two new members at the February meeting. Pictured above is Nsedu Obot-Witherspoon, executive director of the Children's Environmental Health Network and chair of the NIEHS Public Interest Partners Group. (Photo courtesy of Steve McCaw)

After the report by Acting Scientific Director Perry Blackshear, M.D., Ph.D., Council member George Leikauf, Ph.D., expressed his appreciation for Blackshear's leadership during a period of transition for the Division of Intramural Research. (Photo courtesy of Steve McCaw)

Trans-Agency Agreement to Transform Environmental Health Protection

By Robin Mackar and Eddy Ball

Recent advances in science and technology now make it possible to improve how scientists evaluate the health risks posed by chemicals found in the environment. During a press teleconference on February 14, NIH Director Elias A. Zerhouni, M.D., and NIEHS Acting Director Sam Wilson, M.D., joined with leading scientists from NIEHS, the National Human Genome Research Institute (NHGRI) and the U.S. Environmental Protection Agency (EPA) to announce a new collaborative agreement intended to take advantage of new technologies and shift the protocol for toxicity assessments from laboratory animal studies to more cell- based tests.

The concept behind this agreement was highlighted in paper published as the Policy Forum of the Feb. 15, 2008 issue of the journal *Science*. The article was jointly authored by NHGRI Director Francis Collins, M.D., Ph.D., Assistant Administrator of EPA's Office of Research and Development George Gray, Ph.D., and John Bucher, Ph.D., associate director of the National Toxicology Program (NTP), which is headquartered at NIEHS.

NIEHS and NHGRI signed a five-year Memorandum of Understanding (MOU) with the EPA to use the NIH Chemical Genomics Center's (NCGC) high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals. This new, trans-agency collaboration is anticipated to generate data more relevant to humans; expand the number of chemicals that are tested; and reduce the time, money and number of animals involved in testing. Full implementation of the anticipated paradigm shift in toxicity testing will require validation of the new approaches, a substantial effort that could consume many years.

The MOU builds on the experimental toxicology expertise of the NTP, the quantitative high-throughput screening technology at NCGC, managed by NHGRI, and the computational toxicology capabilities at the EPA's recently formed National Center for Computational Toxicology (NCCT).

The Agreement in Context

The MOU and the plans articulated in the *Science* article provide a framework to implement the long-range vision outlined in the 2007 National Research Council (NRC) report, Toxicity Testing in the 21st Century: A Vision and a Strategy, which proposed a collaborative effort across the toxicology community to rely less on animal studies and more on *in vitro* tests using human cells and cellular components to identify chemicals with toxic effects. Importantly, the strategy calls for improvements in dose-response research, which will help predict toxicity at exposures that humans may encounter.

Data collection to determine chemical toxicity currently relies heavily on whole-animal tests. The growing number of new chemicals, adding to a backlog of thousands that have yet to be thoroughly assessed, high testing costs and public unease with animal testing led to the search for alternate toxicology testing methods. Quantitative high-throughput screening (qHTS), developed at NCGC, increases the rate at which chemicals are tested, and profiles compounds over a wide range of concentrations.

These qualities make the new qHTS technology ideal for toxicology testing, with the potential for advancing the goal of more accurate and timely public health decisions. According to the Science article, the screening of >100,000 per day with HTS performed on automated platforms is routine in drug discovery. NHGRI has posted photos and videos of automated equipment at the NCGC facility.

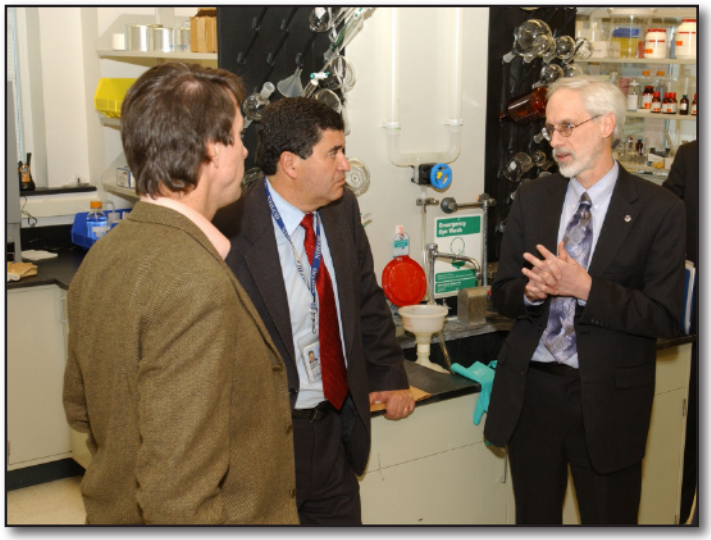
By pooling resources and forming a working partnership, the agreement overcomes the resource limitations of a single agency, builds on existing expertise and avoids the need to create a new administrative and support structure for the effort.

The agreement addresses opportunities for coordination in four basic areas related to achieving the toxicant testing goals: identification of toxicity pathways; selection of chemicals for testing; analysis and interpretation of data; and outreach to scientific and regulatory communities. The collective budget is yet to be determined.

"The experimental and computational expertise required to transform toxicology is an enormous undertaking and too great for any of our existing organizations to accomplish alone," added. Bucher. "This collaborative approach allows us to draw on our individual strengths and establishes a long-term, multiple U.S. federal agency commitment."
NTP will contribute thousands of compounds for testing. NTP's animal toxicology expertise will be utilized, along with a large database of the chemicals' effects on animals, with which the new cell-based data will be compared.

Wilson, left, sat beside Collins during the press conference. He said of the collaboration, "The NTP's expertise in toxicology and its large database of chemical effects in animals will play critical roles in evaluating the high throughput testing process." (Photo courtesy of Maggie Bartlett and NHGRI)

"A central component of federal effort will explore the use of high-throughput screening assays in toxicology," Collins explained. "Such assays allow for the testing of thousands to hundreds of thousands of chemicals a day to determine their possible toxic effect." NCGC is part of a larger Molecular Libraries Imaging Program within the NIH Roadmap for Medical Research. It was designed to advance research on molecules from which most medicines marketed today are derived.

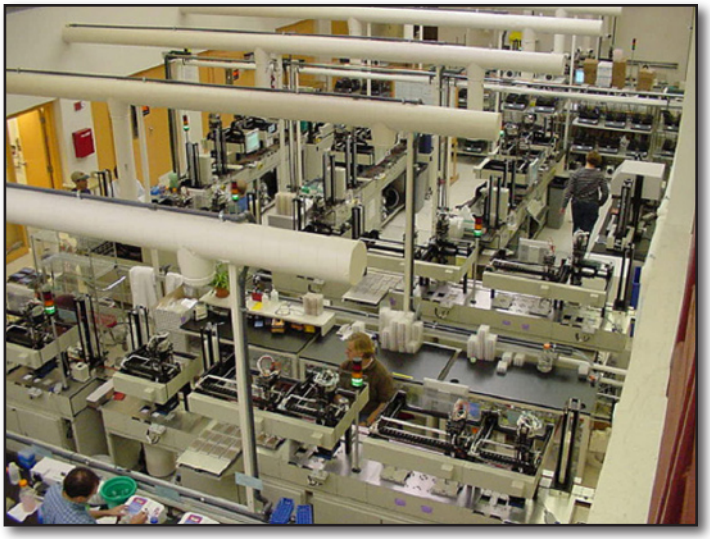


During a tour of the NCGC facility, Bucher, right, talked with Zerhouni, center, and Austin. (Photo courtesy of Maggie Bartlett and NHGRI)

"As our detailed research strategy continues to develop, we will welcome the participation of other federal partners, as well as interested public and private sector organizations, to make this vision of 21st century toxicology a reality" Gray observed.
The EPA's engagement in this collaboration is part of its ToxCast™ program—an initiative launched in 2007 to integrate advances in computers, genomics and cellular biology into the agency's chemical toxicity evaluation procedures.

Also participating in the press conference were Robert Kavlock, Ph.D., director of the National Center for Computational Toxicology (NCCT), Office of Research and Development, EPA, Christopher Austin, director of the NIH Chemical Genomics Center, and Raymond Tice, Ph.D., acting chief of the NTP Biomolecular Screening Branch.

Housed at the NIH Chemical Genomics Center, these Kalypsys robots perform precision plate handling for high throughput screening. (Photo courtesy of NHGRI)



In what will become a more common sight in the future, researchers work at an NHGRI-supported large-scale sequencing center at the Broad Institute of the Massachusetts Institute of Technology and Harvard University. (Photo courtesy of NHGRI)

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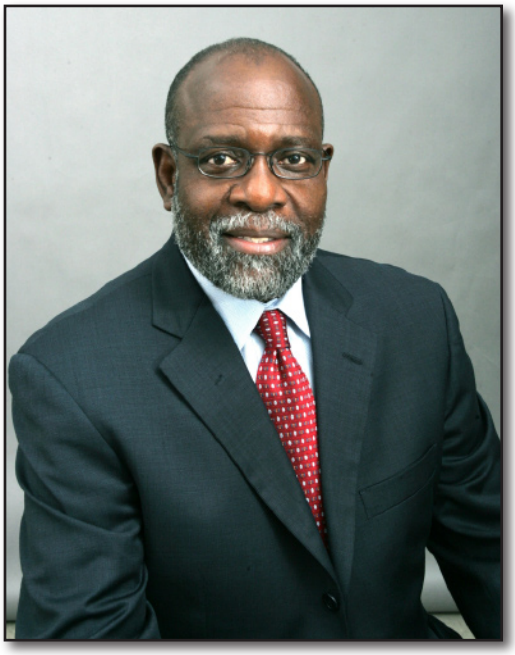
NCCU Chancellor Speaks at Black History Month Celebration

By Robin Arnette

Most Americans know that February is Black History Month, but many don't realize the origins of the observance. That's why the employees of the Research Triangle Park (RTP) campus of the Environmental Protection Agency (EPA) sponsored "Carter G. Woodson and the Origins of Multiculturalism," one of several events held to celebrate the contributions of African Americans to the nation's culture and history. Employees from the EPA, the NIEHS, as well as members of the general public, gathered at the EPA Auditorium on February 12 to hear Charles Nelms, Ph.D., deliver the keynote address.



NCCU Chancellor Charles Nelms (Photo courtesy of North Carolina Central University and Mihi Bell)

Nelms is the tenth Chancellor of North Carolina Central University in Durham, North Carolina, one of the 16 four-year institutions of higher learning in the University of North Carolina system. As an experienced university administrator, Nelms considers promoting multiculturalism part of his job. According to him, a university campus is a microcosm of the larger world community, and multiculturalism, which he defined as the preservation of different cultures or cultural identities within a state or nation, is essential to a university's health and to society at large.

Nelms stressed the importance of learning about Carter G. Woodson, Ph.D., the founder of the study of black history and multiculturalism. "It doesn't matter if you are black, white, Asian, Latino, male or female because

it's all part of the history we need to understand," he explained. "We're really not talking about black history; we're talking about American history."

Nelms then treated the audience to what he called "adult story hour" by relaying his childhood memories of growing up on a farm outside of Crawfordsville, Arkansas. "I grew up in the Delta region of Arkansas, the poorest most racially segregated area in the U.S.," he said. "Since the school year was organized around the harvesting and planting season, you're looking at a person who never attended school longer than 4.5 months out of the year."

Fortunately, Nelms' parents stressed the importance of education for him and his 10 brothers and sisters. Even though his mother and father had little formal schooling, they knew that education was the great equalizer and the key to a better life. They encouraged all of their children to aim high. "My mother told me I could be anything that I wanted to be, so when I got to Indiana University, and I was having difficulty with statistics, they told me I should drop the course; I didn't," Nelms stated. "Because my mother had already convinced me of my potential, I chose to believe my mother."

Nelms went on to earn a bachelor's degree from the University of Arkansas at Pine Bluff and master's and doctoral degrees from Indiana University. He served with distinction as chancellor of the University of Michigan at Flint and Indiana University at Richmond; he also held several teaching and administrative positions at colleges and universities throughout the U.S.

Nelms said he tells his students that they are more than their SAT and GRE scores because the educational system hasn't developed a test that can measure motivation, persistence and hard work. Indeed, Nelms is a walking example of what a person may achieve despite hardships.

He closed his talk by encouraging the audience to leave the world better than they found it. His three keys to changing the world included the following precepts.

1. Educate yourself about the issues, and the way to do that is to study *all* history.
2. Educate your children by exposing them to art, literature, mathematics and science. Teach your children how to read, and they will develop a love for it.
3. Share your talents and resources with someone else.

A Quick Black History Month Quiz

Nelms recounted that as a seventh-grader, he won a contest at his school's annual Negro History Week observances, now known as Black History Month. The contest tested the students' knowledge of black history, and he won by answering the following questions. Do you know the answers?

Q: Who was the first African American to win a Nobel Peace Prize? What year did he or she win it, and what was it for?

A: Ralph Bunche, Ph.D., won the Nobel Peace Prize in 1950 for negotiating the Palestine peace agreement between the Arab states and Israel.

Historian and civil rights activist Carter G. Woodson (1875-1950), shown here as a young man, developed Negro History Week in 1926. (Photo courtesy of Special Collections and University Archives, W.E.B. Du Bois Library, University of Massachusetts Amherst)

Nelms said, “I had a few choices after growing up in Arkansas. I could have been angry, but that wouldn’t have changed the world. We should live our lives so that our children will tell their children that we not only stood for something, but we worked to make it happen.”

Our Friends Across the Lake: The EPA-RTP Black History Month Celebration Organizing Committee

Employees representing various offices within the EPA were responsible for organizing this year’s event. Several of them spoke during the program:

- Wanda Pemberton, Office of Administration & Resources Management (OARM)
- Steve Van Horn, OARM
- Lillian Bradley, Office of Air Quality Planning and Standards (OAQPS)
- Ron Evans, OAQPS

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Plan Expedites Alternatives to Animal Testing

By Robin Mackar

A new plan to further reduce, refine and replace the use of animals in research and regulatory testing, commonly referred to as the *3Rs*, was unveiled at a symposium February 5 in Bethesda, Md. marking the 10-year anniversary of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). A cornerstone of the federal government’s five-year plan is the formation of partnerships with industry and other national and international stakeholders to achieve measurable progress.

Stokes is also an Assistant Surgeon General in the U.S. Public Health Service Commissioned Corps. (Photo courtesy of Steve McCaw)

NIEHS is one of the fifteen federal regulatory and research agencies that make up ICCVAM. One of the speakers at the symposium was William Stokes, D.V.M., director of the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).

“We’ve made great progress in the past decade, and with the help of our partners we can do even more to increase the pace of developing and introducing alternative methods,” he said of the group’s accomplishments. “By incorporating recent advances in science and technology, new alternative test methods can be developed that will benefit animal welfare by reducing, refining and replacing animal

use, and that will benefit public health by ensuring continued or improved protection of human and animal health and the environment."

Stokes was one of nearly 200 scientists, public attendees, advocates, media representatives and invited guests participating in a scientific symposium. ICCVAM is a permanent interagency committee composed of representatives from agencies which use, generate or disseminate toxicological information.

"ICCVAM has a proven track record of thoroughly reviewing test methods and has established an excellent blueprint for advancing the *3Rs*, and for advancing the health and safety of our nation as well," said Marilyn Wind, Ph.D., deputy associate executive director of the Consumer Product Safety Commission and the chair of ICCVAM.

ICCVAM does not conduct research itself. Instead, the committee promotes the development, validation and regulatory acceptance of scientifically sound new, revised and alternative testing methods brought forth by government and industry labs that protect human and animal health and the environment. Based its evaluation of new methods, ICCVAM makes recommendations about their usefulness to federal regulatory agencies.

Traditionally, chemicals, consumer products, medical devices and new drugs are tested on animals to predict toxicity on humans. Alternative test methods are those that accomplish one or more of the *3Rs* so animals experience less pain and distress, or replace animals with non-animal systems.

Stokes highlighted some of the progress made since ICCVAM was formed, including the evaluation of more than 185 test methods since its inception in 1997. Many of these methods need further development and validation before they are ready for regulatory consideration. However, several are now in widespread use around the world for routine safety testing, resulting in notable reduction and refinement of animal use.

Stokes said ICCVAM will emphasize the use of new technologies to develop predictive systems that would be less reliant or not at all reliant on animals. Technologies touted by the National Research Council and the NTP, including high throughput screening techniques that can screen large numbers of potentially hazardous chemicals at one time and toxicogenomics, for example, will be studied and incorporated where they can to provide more accurate and timely public health decisions.

A high priority for ICCVAM, Stokes added, will be to focus on evaluating alternatives to test methods that use a large number of animals or that can involve significant pain and stress, including safety tests for ocular (eye) injuries, dermal (skin) damage, acute poisoning and tests for biologics such as vaccines. Additional priorities include safety tests to determine if products and chemicals may cause other adverse health effects such as cancer, birth defects, infertility and allergic responses.

The five-year plan was developed over a 12-month period with multiple opportunities for input, including a public Town Meeting held in June 2006. The NICEATM-ICCVAM Five-Year Plan is available online.

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Bioethicist Addresses Issues of Responsibility for Health

By Eddy Ball

NIEHS Bioethicist David Resnik, J.D., Ph.D., presented his latest contribution to the on-going discourse about health policy and spending priorities in the United States with his January 31 talk in Rodbell Auditorium. In his presentation on "Responsibility for Health: Personal, Social, and Environmental," Resnik explored the strengths and weaknesses of opposing arguments about who is responsible for health. He also argued that government could improve its efforts in health promotion and prevention of disease by addressing environmental and regulatory issues and realigning spending priorities.

NIEHS Bioethicist David Resnik (Photo courtesy of Steve McCaw)

According to Resnik, the conflict between ways of looking at responsibility for health has increased because of advances in medicine and public health that have changed the kinds of disease that threaten health and well being in industrialized nations. Today, six of the top ten causes of disease and illness can be traced to lifestyle choices, such as smoking, unhealthy eating and substance abuse, which together are estimated to cost Americans $188 billion per year. According to Resnik, these kinds of lifestyle-related diseases raise important bottom-line questions that impact society as a whole: "Who's responsible for these diseases? Who should have to pay?"

Unlike the infectious diseases of the past, diseases caused by lifestyle choices can be seen as the responsibility of the individuals who are "making a personal choice" to harm themselves, rather than as a collective burden all should share. People with a strong "libertarian" orientation justify assigning the responsibility of health to individuals by arguments of utility, fairness, autonomy and the individual's moral responsibility. Resnik summarized the libertarian argument, "If you make people pay for their lifestyle choices, then they are going to change their behavior."

Advocates with a more "socialist" perspective counter with arguments that question the fairness and effectiveness of shaming and other punitive strategies, such as taxes and higher insurance costs, to discourage people from making life-style choices linked to preventable disease. These people disagree with what they consider an overly simplistic definition of free will and point to genetic and social factors that influence addictions, obesity and sexual behavior. As Resnik noted, "The problem with [the libertarian] argument is figuring out [just] how responsible someone is."

The extreme libertarian position on personal responsibility, Resnik continued, also runs opposite to society's perception of medicine as humanitarian and compassionate rather than judgmental and punitive. He gave several examples, including a drunk driver in a single vehicle accident and an alcoholic who needs a liver transplant. The drunk driver and the alcoholic have made negative lifestyle choices, to be sure, but, Resnik asked, "Should doctors withhold treatment because an individual made a personal choice that endangered his life?… Should doctors be assessing the moral character of their patients?… It doesn't seem that's what medicine is about at all."

Resnik's analysis of the arguments over social responsibility have led him to favor a balance between personal and social responsibility and re-direction of health spending. "Some social responses [such as health education and well being programs] can encourage personal responsibility," he explained. "And only government has the resources and motivation that are necessary for some situations." According to Resnik, much of what government can do, such as controlling pollution, regulating food and drug safety, and sanitation, will help everyone, as opposed to the few who benefit from technological advances in patient care.

By re-aligning spending to channel more resources into health promotion, prevention and regulation, Resnik concluded, government can get more benefit from the health dollar. We need to ask ourselves the big question, Resnik argued: "How much health is the $2.1 trillion [spent annually on health care] actually getting us?"

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Theologian Challenges Audience at MLK Observation

By Eddy Ball

Theologian and ethicist James Seymour, D.Min., addressed a capacity audience in Rodbell Auditorium during the NIEHS Martin Luther King, Jr. Birthday Observation January 30. Seymour's talk, "The Seamstress and the Scholar Who Changed America," was sponsored by the NIEHS Diversity Council and the Research Triangle Park Chapter of Blacks In Government (BIG). Seymour used the stories of Montgomery Fair Department Store seamstress Rosa Parks and religious scholar Martin Luther King, Jr. to spur his audience to moral action.

"There are times when the immoral thing to do is to obey an unjust law," Seymour said of King's and Park's civil disobedience. "Just because something is legal doesn't necessarily mean that it's moral." (Photo courtesy of Steve McCaw)

The event opened with welcoming remarks by Acting Director Sam Wilson, M.D., who spoke of King's impact on the scientist's own life and elaborated on the event's theme, "A Day on, Not a Day Off." Wilson said of the minister and social activist, "Martin Luther King represented the kind of commitment to ideals and to courage that has always been an inspiration for me" and a model for efforts to effect change in today's world.

After a short film on the Martin Luther King, Jr. National Memorial, which followed Wilson's introduction, U.S. Department of Agriculture employee and BIG member Gloria Chance introduced the keynote speaker. She described Seymour as a "friend and almost like family, …a missionary at heart" and an important moral and ethical model for his students.

Seymour, who is chair of the Department of Religion at St. Augustine College in Raleigh, N.C., has spent his entire life involved in cross-cultural and interracial settings. Along with his academic duties, he also serves as executive director of the nonprofit Accumulated Resources of Kindred Spirits (ARKS), which provides resources to humanitarian, educational and religious projects in America, Africa and India.

Wilson underscored the value of the MLK observance. "I think it's incredibly important for all of us to have events like this to celebrate Martin Luther King, his contributions to the American way of life and his contributions to all of us." (Photo courtesy of Steve McCaw)

The speaker referred to his nearly 30-year association with this transcontinental ministry, especially his experiences in several African countries, several times to illustrate "some of the things that Dr. King taught us and things we need to renew in thinking during days like this." Seymour's narrative of the lives and Parks and King was organized around four essential "life" questions that can stimulate an individual's understanding of self and help guide behavior:

- What do you want, or what is your vision?
- What is your passion, or how badly do you want it?
- What are you willing to sacrifice to get what you want?
- What do you do with what you achieve, or what is your moral obligation to give back to those who are coming behind you?

As Seymour told the stories of Parks and King, people who found themselves thrust into the center of the important events of their time, he provided answers to the four questions in their lives, with an emphasis on the last two. Parks, he explained, was willing to sacrifice her freedom and her livelihood by going to jail: "When she remained seated, that simple decision eventually led to the end of institutionalized segregation in the South." Leading a movement that changed America, King was arrested 25 times, faced vicious dogs, was brutally beaten by police and opponents at least twice, and made the ultimate sacrifice by laying down his life for his pursuit of social justice and equality for his brothers and sisters.

Building a Bridge of Understanding

Seymour teaches a course at St. Augustine's titled "Suffering, Perseverance and Hope: Three Themes of the African and African-American Experience." In 2005, he taught a seminar based on that course at the Pan African Christian College in Nairobi, Kenya, a nation that experienced tribal violence following what many outside monitors considered a stolen election. Despite that violence and the genocide elsewhere in the continent he knows and loves so well, Seymour is convinced that non-violent protest and moral action can bring change to the nations of Africa.

Seymour began his lecture as he does his courses with a song, "Lift Every Voice and Sing," written by the civil rights activist and author James Weldon Johnson (1871-1938). The words, Seymour observed, reflect the themes of suffering, perseverance and hope for Africans and African Americans alike:

Lift ev'ry voice and sing,
Till earth and heaven ring.
Ring with the harmonies of Liberty;
Let our rejoicing rise,
High as the list'ning skies,
Let it resound loud as the rolling sea.

Sing a song full of the faith that the dark
Past has taught us,
Sing a song full of the hope that the
Present has brought us;
Facing the rising sun of our new day begun,
Let us march on till victory is won.

"Where there is crisis today [in African nations]," Seymour contended, "the church and people of faith are standing up and trying to make a difference."

Describing King's ideology, based on the New Testament, and methodology, modeled on the nonviolent civil disobedience practiced so successfully by Mahatma Gandhi, Seymour said of the activist, "The Golden Rule made perfect sense to Martin Luther King, Jr." According to the speaker, one of the movement's greatest obstacles to overcome, as King articulated in the famous "Letter from Birmingham Jail," was the "appalling silence of good people." Addressing the audience directly, Seymour admonished, "You can't do everything…, [but] the one option you don't have is to do nothing" when encountering injustice.

Following his talk, Seymour was presented with a poster of the event by NIEHS Diversity Council Vice-Chair Brad Collins. BIG Chapter President Veronica Godfrey made closing remarks.

NIEHS Chemist Beby Jayaram, Ph.D., read over "Lift Every Voice and Sign" as Seymour recited the song and related its lyrics to themes in African and African-American experience. (Photo courtesy of Steve McCaw)

The speaker's words engaged many in the audience, such as NIEHS Chief of Staff Ebony Bookman, Ph.D., shown here. (Photo courtesy of Steve McCaw)

After giving Seymour an event poster, Collins opened the floor for questions. People in the audience asked about the current situation in Kenya and issues that members of the African-American Community are facing. (Photo courtesy of Steve McCaw)

Godfrey thanked Seymour for "challenging us as a community to be better among ourselves and with ourselves" and Wilson for joining the audience for the event. (Photo courtesy of Steve McCaw)

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NIEHS to Celebrate Women in Science with March Events

By Eddy Ball

As part of its observance of Women's History Month, NIEHS plans a series of talks featuring women scientists during March. Events will include the seventh annual Spirit Lecture, jointly sponsored by the NIEHS Frontiers of Environmental Sciences (FES) Lecture Series, three additional FES Lectures by women scientists, talks by and a celebration of International Women's Day featuring four foreign-born women scientists who work in labs at NIEHS.

There will also be a presentation by the director of the Recognition of the Achievements of Women In Science, Medicine, and Engineering (RAISE) Project, an effort to increase the status of professional women, a program of the Society for Women's Health Research.

The events are part of NIEHS' strategic effort to consider gender issues, one of the priorities of Acting Director Samuel Wilson, M.D. Associate Director Sharon Hrynkow, Ph.D., led the development of this program, working closely with NIEHS counterparts Molly Vallant, biologist and Diversity Council member, and Associate Director Christopher Portier, Ph.D. Many others, including Veterinary Medical Officer Darlene Dixon, D.V.M., Executive Assistant to the Acting Director Angie Sanders and the NIEHS Spirit Lecture Committee contributed to the enterprise.

The NIEHS Office of the Director, NIEHS Diversity Council, and FES lecture series are sponsors of this series. The Foundation for NIH, the United Nations Foundation and the Society for Women's Health Research provided support for networking receptions held in conjunction with several of the events.

Events include:

March 3, 2:00 — 3:00 p.m. in Rodbell Auditorium: FES Lecture by **Devra L. Davis, Ph.D.**, on "The Need to Revitalize Toxicology: Lessons from the Secret History of the War on Cancer" Davis is the director of the Center for Environmental Oncology and professor of Epidemiology at the University of Pittsburgh Graduate School of Public Health (UPMC). The talk is hosted by Wilson.

March 7, 9:00 — 10:00 a.m., in Rodbell Auditorium: Seventh annual Spirit Lecture, co-sponsored by the FES Lecture Series, by **Lisa Alvarez-Cohen, Ph.D.**, on "Application of Omics-Based Tools and Microarrays to Optimize Bioremediation." Alvarez-Cohen holds the Fred and Claire Sauer Chair in Environmental Engineering and serves as Chair of the Engineering Faculty at the University of California at Berkeley. The lecture is hosted by Portier.

Hrynkow said that the NIEHS International Women's Day is an opportunity to recognize great science as well as challenges overcome. (Photo courtesy of Steve McCaw)

Vallant is active in the Diversity Council and chair of the Spirit Lecture Committee. (Photo courtesy of Steve McCaw)

March 10, 10:00 – 11:00 a.m., in Rodbell Auditorium:
"RAISE-ing the Status of Women in Science," a presentation by RAISE Project Director **Stephanie Pincus, M.D.**, with a discussion led by **Florence Haseltine, M.D., Ph.D.**, director, Center for Population Research, National Institute of Child Health and Human Development. This event is hosted by Hrynkow.

March 10, 2:00 – 4:00 p.m., in Rodbell Auditorium:
International Women's Day, a panel discussion by four foreign-born women scientists at NIEHS moderated by Dixon and Vallant: Laboratory of Pharmacology and Chemistry Staff Scientist **Maria Kadiiska, M.D., Ph.D.**; Laboratory of Molecular Carcinogenesis Staff Scientist **Harriet Kinyamu, Ph.D.**; Mammalian Aging Group Leader **Xiaoling Li, Ph.D.**; and Laboratory of Respiratory Biology Staff Scientist **Ivana Yang, Ph.D.** Hosted by Hrynkow.

March 14, 9:00 — 10:00 a.m., in Rodbell Auditorium:
FES Lecture on "Multiple Hit Models of Neurotoxicity: Clarifying the Contribution of Neurotoxicants to Human Diseases and Disorders" by **Deborah A. Cory-Slechta, Ph.D.**, Professor, Department of Environmental Medicine at the University of Rochester School of Medicine and Dentistry. Hosted by Portier.

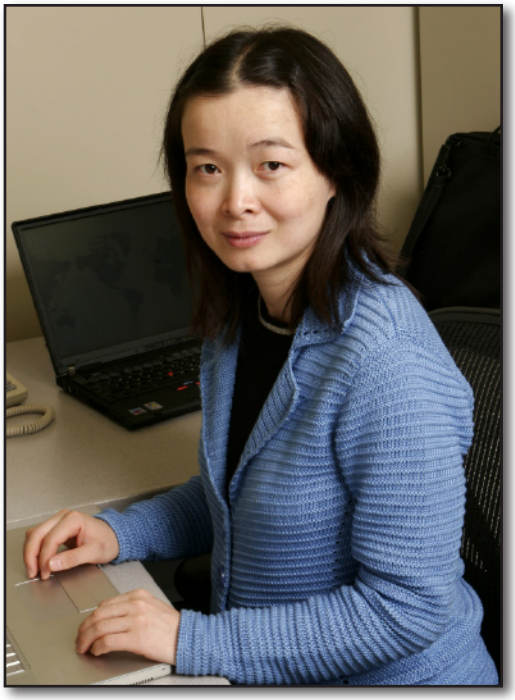
March 28, 9:00 — 10:00 a.m., in Rodbell Auditorium:
FES Lecture on "Environmental Science and Social Responsibility" by **JoAnn Burkholder, Ph.D.** Burkholder is a professor of Aquatic Ecology and Toxic Dinoflagellates at the Center for Applied Aquatic Ecology, North Carolina State University. The lecture host is David Resnik, J.D., Ph.D.

Dixon is an advisor to the Office Scientific Director representing the interests of women scientists at NIEHS. (Photo courtesy of Steve McCaw)

Panelist Kadiiska laughed as she described her circuitous route from Bulgaria to Research Triangle Park. (Photo courtesy of Steve McCaw)

Attending high school and college in Virginia during the siege of Sarajevo, Panelist Yang was unable to contact her family for long stretches of time. (Photo courtesy of Steve McCaw)

Panelist Kinyamu was intrigued by Kadiiska's account of why she left her position in pediatrics to pursue a degree in toxicology. (Photo courtesy of Steve McCaw)



Panelist Li's group at NIEHS is trying to unravel the secrets of aging. (Photo courtesy of Steve McCaw)

March 3 FES Lecturer Devra Davis (Photo courtesy of the University of Pittsburgh Cancer Institute)

Lisa Alverez-Cohen will give the Spirit Lecture as part of the FES Lecture Series. (Photo courtesy of the University of California Berkeley)

Pincus, above, and her fellow director Haseltine are nationally known for their tireless advocacy for the recognition of women's achievements in science. (Photo courtesy of RAISE)

Haseltine is a center director at NICHD and a founding board member of the Society for Women's Health Research. (Photo courtesy of RAISE)

March 14 FES Lecturer Deborah Cory-Slechta (Photo courtesy of the University of Rochester School of Medicine and Dentistry)

March 28 FES Lecturer JoAnn Burkholder closes out an event-packed Women's History Month. (Photo courtesy of North Carolina State University)

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Science Notebook

Researcher Warns about Pregnancy and Weight Gain

By Eddy Ball

Nutritional epidemiologist Anna Maria Siega-Riz, Ph.D., had good reason to sound alarmed when she talked about pregnancy and weight gain during her February 1 Frontiers of Environmental Sciences lecture in Rodbell Auditorium. According to the University of North Carolina at Chapel Hill professor, overweight and obese women, as well as women who gain too much weight during their pregnancies, may be endangering their own health — and the health of their children.

Before her talk began, Siega-Riz, left, talked over logistics with the lecture host, NIEHS Fellow Rose Ramos, Ph.D. (Photo courtesy of Steve McCaw)

In her talk, "Maternal Obesity — The Number One Problem Facing Prenatal Care Providers in the New Millennium," Siega-Riz presented a preponderance of evidence that these women have a significantly greater risk of suffering from metabolic syndrome-related diseases, of bearing children with birth defects, such as spina bifida, and of giving birth to babies who will experience problems with their own health.

More women are overweight and obese worldwide, and more of them are gaining excessive weight during pregnancy. Compounding the problem, Siega-Riz added, is the complacency of many pregnant women and, even more disturbing, their health care providers.

Investigator Olga Basso, Ph.D., who has major research interests in the field of reproductive epidemiology, had several questions about the speaker's findings on the incidence of diabetes in overweight mothers. (Photo courtesy of Steve McCaw)

"Maternal obesity is not unique to the United States," Siega-Riz said as she began her lecture. "It is occurring globally." Many developing countries are facing the same problems as the United States, with obesity rates between 20 and 30 percent. Not only are rates increasing, Siega-Riz noted, but obesity is also emerging as a health disparity issue due to its greater prevalence among minority women.

According to Siega-Riz, in the United States about a third of women are overweight and 10 to 15 percent are obese. The majority of pregnant women are gaining 21 to 40 pounds during pregnancy, and since the 1990s, there has been a 30 percent increase in the number of women who gain 40 or more pounds. "Only about a third of women are gaining weight within the targeted weight-gain recommendations," she said. In addition to the significant health problems that obesity contributes to on its own, such as diabetes and cardiovascular disease, Siega-Riz pointed to studies suggesting that about 25 percent of problems with fecundity and fertility are due to obesity.

Maternal overweight and obesity have been associated with a dramatic increase in risk for gestational diabetes, gestational hypertension, pre-eclampsia, caesarian delivery, fetal death and birth defects. The effects of overweight and obesity persist beyond childbirth and include post-partum weight retention, post-partum anemia related to the higher rate of caesarian sections, shorter duration of breast feeding and persistent glucose intolerance. Moreover, with excessive weight gain, a woman is also more likely to find herself in a higher weight classification at twelve months postpartum than she was at conception, putting her at even greater risk for complications in a subsequent pregnancy.

Because of these trends, physicians are seeing a growing number of pregnant women weighing as much as 300 pounds. "Quite frankly, they don't know how to manage them," Siega-Riz observed. One study found that 33 percent of subjects reported receiving no advice on gestational weight gain from their providers. The few intervention studies thus far have failed to show promising results and have found poor rates of compliance with interventions on the part of physicians and pregnant women.

As she and her colleagues strive to close the gaps in research on gestational weight gain, Siega-Riz continues to push for translation of this research through education and policy change. She currently serves a member of the Institute of Medicine's (IOM) Committee to Reexamine IOM Pregnancy Weight Guidelines. In 2004, she served on the IOM's Committee to Review the WIC Food Packages. As result of the recommendations from this committee, the USDA made the first major changes to the food packages since WIC's inception 30 years ago. In November 2007, the March of Dimes recognized her distinguished achievements in research, education and clinical services in the field of maternal-fetal nutrition with the Agnes Higgins Award.

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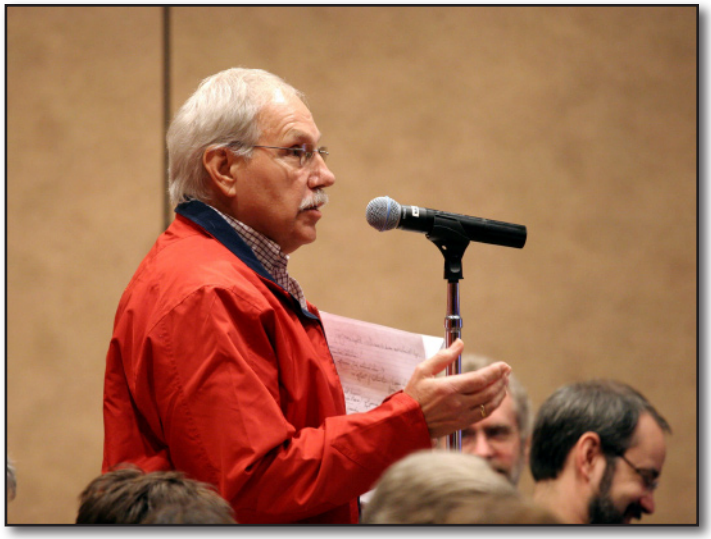

Health Scientist Administrator Jerry Heindel, Ph.D., asked Siega-Riz about the problems of physician and patient compliance with efforts to encourage pregnant women to control weight gain. (Photo courtesy of Steve McCaw)

Siega-Riz enjoyed a little comic relief when a questioner confused a study she reported on with one she actually performed. (Photo courtesy of Steve McCaw)

Increased Allergen Levels in Homes Linked to Asthma

By Robin Arnette

Not all asthma sufferers have respiratory allergies, but the ones who do must be wary of certain "triggers" that initiate asthma attacks. The results of new research may help the millions of Americans who fall into this category.

The findings of a national survey suggest that asthmatics with allergies may alleviate symptoms by reducing allergen exposures inside their homes. The work was carried out by investigators at the National Institute of Environmental Health Sciences (NIEHS), the University of Iowa, Rho Inc. and the Constella Group.

"Indoor allergen exposures are of great importance in relation to asthma because most people spend a majority of their time indoors, especially at home," said Darryl Zeldin, M.D., a senior investigator in the Laboratory of Respiratory Biology at the NIEHS and senior author on the paper.

The outcome of the investigation, published online and available in the March issue of the *Journal of Allergy & Clinical Immunology*, reveals that exposure to multiple indoor allergens was common in U.S. households, with 52 percent having at least six detectable allergens and 46 percent having three or more allergens at increased levels. The indoor allergens studied included those from dog, cat, mouse, cockroach, dust mite, and the fungus *Alternaria*.

The researchers used data from the National Survey of Lead and Allergens in Housing (NSLAH) to examine factors that contribute to high allergen levels in homes and to determine whether elevated household allergen levels were associated with occupants' asthma status. The NSLAH, which was the first study to characterize how allergen exposures vary in homes at the national level, surveyed the homes of nearly 2500 individuals in 75 locations throughout the U.S. The survey was jointly funded by the NIEHS and the U.S. Department of Housing and Urban Development.

The researchers reported that several factors contributed to the increased concentrations of allergens. Types and levels of allergens were influenced by sociodemographic factors, including race, income and type of home, as well as by apparent sources of allergens, such as presence of pets and pests. The study also showed that homes with children were less likely to have high allergen levels. The authors noted that this finding may not be surprising since homes with children may be cleaned more frequently than homes without children. Regular household cleaning is a simple, yet effective, regimen that helps to reduce the overall exposure burden.

Lead Author and Postdoctoral Fellow Päivi Salo of the Environmental Cardiopulmonary Disease Group (Photo courtesy of Steve McCaw)

Zeldin is the NIEHS acting clinical director, a senior investigator and head of the Environmental Cardiopulmonary Disease Group at NIEHS. (Photo courtesy of Steve McCaw

According lead researcher and NIEHS Postdoctoral Fellow Päivi Salo, Ph.D., the study provides useful information to asthma patients. "Our results highlight the importance of exposure reduction as a fundamental part of asthma management," she said. "Although homes cannot be made allergen free, asthmatics that have allergies may need to do better job in reducing allergen levels in their homes in order to improve asthma control."

While several studies have demonstrated that exposure to allergens aggravates asthma symptoms, this investigation is the first to provide information on total allergen burden in U.S. homes and how it relates to asthma. "This study confirms that indoor allergens play a major role in asthma," Zeldin stated.

Salo and her co-authors, however, point out that more research is needed to understand the complex relationships between genetic and environmental factors that cause asthma. "Although reducing allergen levels in the home may not prevent individuals from developing asthma, reducing exposure levels is crucial for those whose asthma is allergic in nature." Zeldin concluded.

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Sam Arbes, Ph.D., who is now a researcher with Rho Inc., was formerly a staff scientist in the Environmental Cardiopulmonary Disease Group. (Photo courtesy of Steve McCaw)

Methods Determine Estrogenization Effects in Infants

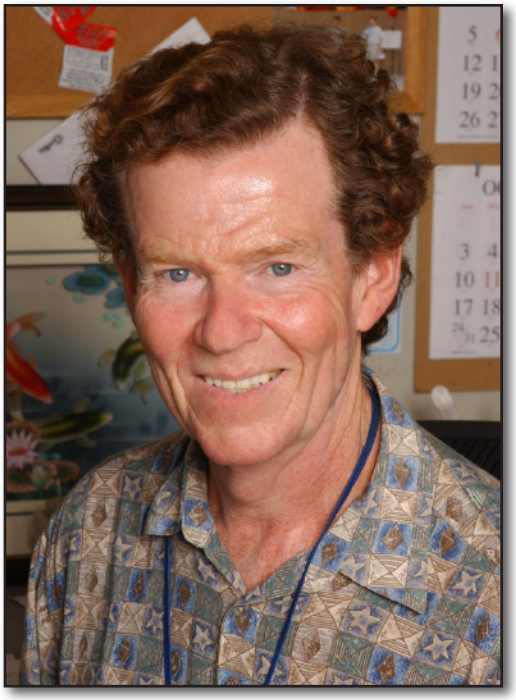
By Robin Arnette

Some studies suggest that adults who consume foods rich in soy protein receive several health benefits such as healthy bones and a decreased risk of breast or prostate cancer, although research investigating diets rich in soy are in progress. However, soy isoflavones are weak estrogens and their affect on newborns, especially in regard to breast and genital development, is less established. In a pilot study to develop methods for investigating estrogen's effects in infants, researchers used several examination methods on babies who were fed breast milk, cow milk or soy formula. The team determined that measurement of breast tissue and characterization of vaginal wall cells could be used to evaluate the effects of estrogen exposure.

The team was comprised of investigators from the NIEHS Epidemiology Branch, Children's Hospital of Philadelphia, Children's Hospital Medical Center in Cincinnati, Westat, Inc. and Social & Scientific Systems, Inc. The study, titled "Pilot Studies of Estrogen-Related Physical Findings in Infants," appears in the March issue of *Environmental Health Perspectives*.

Lead author Judy Bernbaum is a pediatrician and investigator in the NIEHS-funded Soy Estrogens and Development (SEAD) Project. (Photo courtesy of Steve McCaw)

According to Walter Rogan, M.D., principal investigator in the Epidemiology Branch at the NIEHS and corresponding author of the paper, the research attempted to address the hypothesis that compounds found in food or pollutant chemicals may have hormonal consequences in humans, such as undescended testicles or early puberty. "This study was an attempt to develop simple, reproducible methods for assessing whether a child exhibited effects consistent with estrogen exposure using physical examination and simple lab tests," Rogan explained.



Rogan is lead researcher in the SEAD project, which evolved from a 2004 review, "Isoflavones in Soy Infant Formula: A Review of Evidence for Endocrine and Other Activity in Infants," authored by Rogan and former NIEHS Postdoctoral Fellow Aimin Chen. (Photo courtesy of Steve McCaw)

Seventy-two children, 37 boys and 35 girls, from birth to six months of age, were divided into three groups. Each group was fed breast milk, soy formula or cow milk formula. The researchers measured breast adipose tissue, breast buds and testicular volume. They also observed breast and genital development and collected vaginal wall cells and information on vaginal discharge.

The team was aware that physical effects in newborns could be a response to the mother's estrogen, so they "looked at characteristics that exhibited declines from younger to older children," said Judy Bernbaum, M.D., director of the Neonatal Follow Up Program at the Children's Hospital of Philadelphia and lead author of the study.

The investigators reported that most of the infants from all three groups retained palpable adipose breast tissue at six months, but they did not observe a postnatal increase in breast bud size in males or females. Testicular volume occurred within the range reported in other studies, but because of a possible peak in testosterone at two months, further research with more frequent exams was warranted.

In all three groups, the maximal amount of breast tissue occurred in newborns and decreased in older children, but external genitalia showed few differences by age. In newborn girls vaginal wall cells were responsive to maternal estrogen and lost that effect by one month. However, the team was unable to determine whether cells after this period responded to estrogen produced by the infant or the estrogen in the soy formula.

Although the team was encouraged that the measurement of breast tissue and vaginal wall cells was a dependable test of estrogen exposure, Rogan stressed that the study was too small to have reliable findings about differences in feeding methods. He said, "None of the differences we observed between feeding groups were statistically significant, which is what we expected from this small study."

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Superfund Program Helps Train Mexico's Environmental Scientists

By Eddy Ball

Thanks to Hugo Alonso Zúñiga Hernández — and other young scientists like him — what now looks like a moonscape in the Mexican state of Sonora may one day again live up to the meaning of its name in the Opata language, the "Place of Corn." Zúñiga Hernández is the latest of 23 bright young exchange students, doctoral candidates and visiting scholars who have returned home to Mexican universities following training in the Mexican Exchange Scientist Program at The University of Arizona's (UA) U.S.-Mexico Binational Center for Environment Sciences and Toxicology, which is part of the Outreach Core funded by the Superfund Basic Research Program (SBRP).

A student at the Universidad de Sonora (UNISON), Zúñiga Hernández spent four months as a Training, Internships, Exchanges, and Scholarships (TIES) Fellow in the UA Department of Soil, Water and Environmental Science, studying advanced techniques of phytostabilization for soils around former copper mines in Sonora. Zúñiga Hernández' field work, which started in February, involves the enrichment of depleted topsoil and the growth of plants to revitalize nutrients and stabilize soils with extensive environmental contaminants.

Mining of copper and other minerals has gone on for centuries in the border state, and resurgence in mining is anticipated due to increased demand and drastically higher prices for the commodity. At arid and semi-arid sites, the materials left over after the process of separating the valuable fraction from the worthless fraction of an ore, known as mine tailings, are prone to wind dispersion and water erosion. According to Zúñiga Hernández, these pollutants pose a health threat, especially for children in nearby communities and for sensitive riparian or wildlife refuge areas. Successful stabilization of such sites offers an economical approach to containing mining wastes and developing these wastes back into soil-like materials that can support normal vegetation.

Working with the UA team headed by Raina Maier, Ph.D., Zúñiga Hernández studied methods for the establishment of a vegetation cover using native

The Binational Centers

Trainees' studies in the Mexican Exchange Scientist Program range across the engineering, environmental and biological sciences — including arsenic biotransformation, perchlorate removal and remediation, genetics, environmental toxicology, acid mine drainage, genomic analysis of arsenic and human cells, and characterization of morpho-functional alterations induced by mercuric chloride on a kidney cell line. The trainees typically participate in one of the Center's Collaborative Research Projects.

Center Activities include:

Training Fellowships: Scholarships are available for Mexican graduate students to enhance their capacity in environmental science, engineering, and toxicology.

Specialized Workshops: Workshops for graduate students, environmental professionals, and University faculty interested in topics ranging from bioremediation of environmental contaminants to harmful impacts of heavy metals in children.

Collaborative Projects: The projects address common environmental contamination problems within the Border region:

- Arsenic and Health - Diabetes and Breast Cancer
- Long-Term Effects of Heavy Metals on Children's Health
- Landfill Leachate Plumes - Characterization, Natural Attenuation, and Bioremediation
- Mine Tailings – Characterization, Phytostabilization and Phytoremediation

plants to minimize dispersion and erosion processes. Organic matter amendment up to 15 percent by mass may be required, depending on the extent of pH, metal and microbial community stress that exists in a given site. Successful mine tailings re-vegetation with a goal of minimizing amendment addition will involve tailoring the compost rate to optimize nutrients and microbial supplements and to re-establish the correct pH at a site.

Binational Center Trainee Hugo Alonso Zúñiga Hernández (Photo courtesy of the Binational Center and Denise Moreno Ramirez)

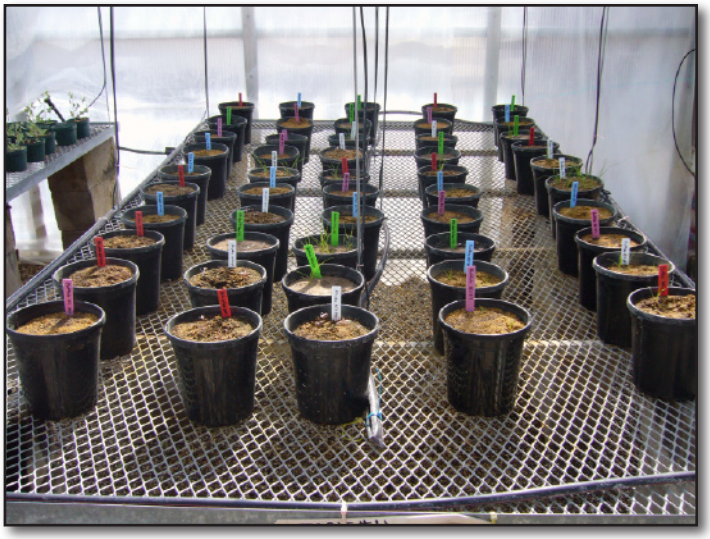
Funded collaboratively by the SBRP, the U.S. Environmental Protection Agency (EPA), which administers a $1.46 million special appropriation from Congress, USAID, and Mexico's Science and Education Ministry (CONACyT), the Binational Center is a component of the UA SBRP Outreach Core headed James A. Field, Ph.D., and UA SBRP director A. Jay Gandolfi, Ph.D. A prime example of the NIEHS Strategic Plan goal of developing a global health program, the Binational Center partners with UA scientists from six colleges and Mexican scientists from 11 different universities and research institutes to promote technology and information transfer between the two countries by training the next generation of environmental scientists in the border region.

The challenge for Zúñiga Hernández and other young environmental scientists is to restore vegetation on moonscapes like one in Nacozari de Garcia, Sonora. The two women are, left, UNISON geologist Margarita De la O-Villanuevaa and EPA Grants Officer Emily Pimentel. (Photo courtesy of the Binational Center and Denise Moreno Ramirez)

The Center is also involved in community-based Outreach Projects to educate and empower residents living along the U.S.-Mexico border, which has been impacted with the growth of manufacturing, increase in trade, and rise in populations due to the North American Free Trade Agreement (NAFTA). The Center's goals are to increase public awareness of the risks associated with common occurring contaminants in the Border region, such as arsenic and heavy metals, and to provide information about and assistance with remedial measures.

According to the Center's website, the exchange program is based on a premise of building human capital, as advocated by such social science scholars and economists as the Brazilian Paulo Friere and American Gary Becker. Center literature describes this basis as "an alternative to the old paradigm in which the developed country 'provides solutions' to the emerging country… [a] paradigm that has repeatedly failed and has created a vicious cycle and waste of resources."

Before experiments could begin, students performed the hard work of collect soil samples for phytostabilization greenhouse trials. Zúñiga Hernández, right, worked with UASBRP students using a tarp to remove samples. (Photo courtesy of the Binational Center and Denise Moreno Ramirez)



Using soils from the Nacozari tailings, researchers search for the optimum compost percentage for the site. (Photo courtesy of the Binational Center and Denise Moreno Ramirez)

Program staff includes UA SBRP Research Translation Core Coordinator Monica Ramirez, left, and UA SBRP Outreach Core and U.S.-Mexico Binational Center Coordinator Denise Moreno Ramirez. (Photo courtesy of the Binational Center and Denise Moreno Ramirez)

Binational Center Co-Director James Field, Ph.D., left, is shown with Jay Gandolfi, Ph.D., UA SBRP director and Binational Center co-director. (Photo courtesy of the Binational Center and Denise Moreno Ramirez)

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UC-San Diego Superfund Researcher Honored with Gillette Award

By Melissa Fabiano

Former Superfund Basic Research Program (SBRP) scientist Kathy Senekeo-Effenberger, who worked in the laboratory of Pharmacologist Robert Tukey, Ph.D., at the University of California-San Diego (UC-San Diego), was awarded the James R. Gillette Drug Metabolism Best Paper of 2007. The award was presented by the Awards Selection Committee of the Drug Metabolism Division of the American Society of Pharmacology and Experimental Therapeutics (ASPET).

Co-authors Kathy Senekeo-Effenberger, left, and Jessica Bonzo, right (Photo courtesy of Kathy Senekeo-Effenberger)

Effenberger was lead author on the paper, "Expression of the human UGT1 locus in transgenic mice by 4-chloro-6-(2,3-xylidino)-2-pyrimidinylthioactetic acid (WY-14643) and implications on drug metabolism through peroxisome proliferator-activated receptor α activation," which was published in the ASPET journal *Drug Metabolism and Disposition*.

The Gillette Award is presented annually to authors of the two best papers published in *Drug Metabolism and Disposition* in the broad areas of drug metabolism and pharmacokinetics and disposition. The award honors the late NIH Pharmacologist James R. Gillette, Ph.D., a scholar and scientist who demonstrated excellence in research. During his scientific career, Gillette published more than 300 papers and chapters, and co-edited seven books. He was considered a visionary and significant contributor to the field of drug metabolism and pharmacokinetics.

Effenberger's research supports the lab's examination of the role of nuclear receptors and cellular signaling events that regulate cytochrome P450 (*CYP*) and UDP-glucuronosyltransferase (*UGT*) genes. The Gillette Best Paper of 2007 focused on previous lab reports that demonstrated the *in vivo* control in animals of human *UGT1A* gene expression by xenobiotics, in addition to novel regulatory events that control expression of the human *UGT1* locus. The animal models developed will allow researchers to understand the role of proteins in xenobiotic metabolism, and the potential mechanisms of adverse drug-drug interactions.

Jessica Bonzo, Ph.D., was Effenberger's colleague and a co-author of the paper. Bonzo, a UC-San Diego graduate, funded by the SBRP, now works for the National Cancer Institute Center for Cancer Research in Bethesda, Maryland in the Laboratory of Metabolism with laboratory chief Frank Gonzalez, Ph.D.

"This research article was the culmination of the effort of many people to characterize, in as much detail as possible, the influence of a widely used class of hyperlipidemia drugs on one of the major drug metabolizing enzyme families," Bonzo said. "It was a surprise to everyone involved in this effort…Kathy is very deserving as first author to be recognized for all her hard work. The paper only shows a small portion of the numerous animal studies Kathy performed in order to characterize this regulatory mechanism."

As part of this prestigious award, Effenberger will present her group's research at the Experimental Biology Meeting in San Diego, California (April 4-9, 2008) on Sunday April 6th at the Drug Metabolism Division's platform session on Biotransformation and Drug Transport.

Currently, Effenberger is working for the clinical stage biopharmaceutical company Mpex Pharmaceuticals, which is involved in the development of new therapies to combat the growing issue of antibiotic resistance to gram-negative bacteria. In her work there, she hopes to expand her understanding of the risks associated with chemicals that are related to human health and the environment. She adds, "I would also like to gain experience and be involved with risk assessment, risk communication, and, ultimately, help in developing regulations and shaping public policies that will ensure [that] we can continue to protect and preserve our health and environment."

At the UC-San Diego Tukey Laboratory work continues to further characterize the cellular events that will lead to the regulation of the *UGT1* locus. According to Effenberger, work continues on the recently developed *Ugt1* null mouse model and its implementation to create a humanized *UGT1* mouse model, which should help examine the regulation and role of human *UGT1A* proteins in vivo.

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Upcoming Distinguished Lecture Features Kathryn Horwitz

By Eddy Ball

The 2007-2008 NIEHS Distinguished Lecture Series continues at 11:00 a.m. March 11 with a talk by Kathryn Horwitz, Ph.D., on "Hormonal Regulation of Breast Cancer: Stem Cells and Metastasis." Horwitz' talk will take place in Rodbell Auditorium and be hosted by John Cidlowski, Ph.D., supervisory biologist and head of the Molecular Endocrinology Group of the NIEHS Laboratory of Signal Transduction.

Distinguished Lecturer Kathryn Horwitz (Photo Courtesy of Kathryn Horwitz and the University of Colorado Health Science Center)

Horwitz is the University Distinguished Professor of Hormones and Breast Cancer at the University of Colorado Health Science Center in Denver. Horwitz oversees a laboratory of 15 collaborating investigators performing research in breast cancer that ranges from basic molecular biology of receptor action in transcription to cell and tumor biology, the role of hormones in metastasis, and translational studies. As a leading National Foundation for Cancer Research project director, she is committed to understanding the role that sex hormones play in the development and progression of breast cancer-and to finding better long-term treatments to fight this devastating disease, which is the most common cancer in women.

The NIEH Distinguished Lecture Series does not have a speaker scheduled in April. The series will continue May 5 with the annual Rodbell Lecture.

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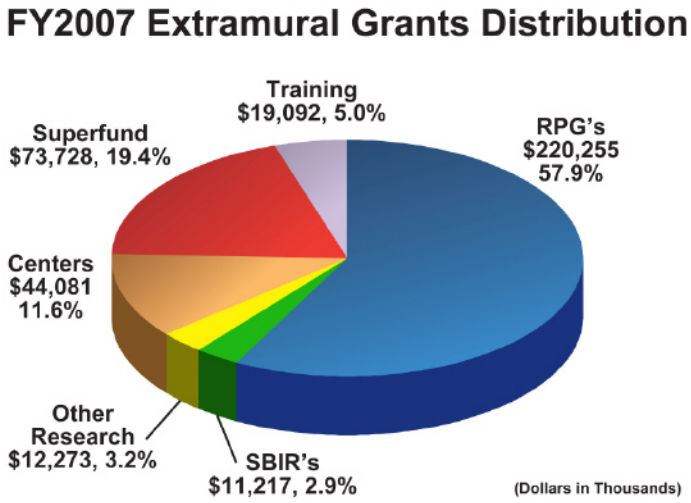
Extramural Update: NIEHS FY 2008 Extramural Budget

By Dennis Lang

The NIEHS appropriation for fiscal year 2008 provides for an overall budget for grants amounting to one percent more than 2007 funding. This is significantly less than the cost of inflation and will result in continued austerity in the grants budget. Below we have outlined the steps the Division of Extramural Research and Training will be taking in this fiscal year to meet the requirements set out by NIH.



In order to fund as many research grants as possible, it is necessary to continue the moratorium on the submission of new P01s and to carefully prescreen applications requesting direct costs in excess of $500,000. Despite these efforts the overall success rate is expected to be lower than in recent years.

To maintain our emphasis on investigator initiated research, the NIEHS does not intend to release new initiatives beyond those already announced. As programs begun under past Request for Applications approach the end of their project periods, they will be evaluated to determine whether the programs should be continued, and if so, in what format. Some programs may be discontinued. Extramural management and staff will determine whether funds freed up by the discontinuation of a program will be used to create new initiatives or to increase the number of EITHER investigator-initiated OR unsolicited research projects to be paid.

The NIH budget strategy requires that the average cost for research grants may not increase by more than 1% of the 2007 funded level. Therefore, additional budgetary reductions will be necessary as described below:

- **Competing Awards:** Budget reductions will be necessary in order to meet NIH funding guidelines; however, the extent of these reductions and how they will be applied will be determined after taking into consideration the average cost of competing RPGs (research project grants) as well as the availability of funds.

  The funding period may be adjusted based on percentile ranking, type of research and new investigator status of the applicant.

  These guidelines do not necessarily apply to applications funded in response to an RFA.

- **Noncompeting Awards:** All non-competing continuation awards, including those initiated through solicitations will be funded at 98% of the committed level for Fiscal Year 2008 that is reflected on the Fiscal Year 2007 Notice of Grant Award. Future years will be adjusted as well. See: NOT-OD-08-036.

We realize these reductions will cause additional hardship for our grantees and regret their necessity. Please know we are doing the best we can in a difficult situation.

(Dennis Lang, Ph.D., is the interim director of the NIEHS Division of Extramural Research and Training)

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Extramural Papers of the Month

By Jerry Phelps

New *In Vitro* Test May Replace Some Animal Testing

NIEHS-supported scientists have developed a new *in vitro* screening tool that may reduce the number of animals needed in drug testing. The test system consists of two glass slides — one containing 1,080 individual human cell cultures encapsulated in collagen or other matrices and the other coated with P450 metabolic enzymes.

The product was developed by Jonathan Dordick and Douglas Clark of Solidus Biosciences in part through a Small Business Innovative Research Grant from NIEHS. The cell culture slide, known as the DataChip, has been tested with human bladder, liver, kidney, heart, skin, or lung cells. The enzyme containing slide is called the MetaChip. When the two slides are sandwiched together and incubated, they mimic the body's reaction to compounds. If the cells stop growing, appear sick or die, it's an indication that a toxin is present.

While the investigators don't think their product will replace the use of live laboratory animals in drug testing, they do think that it could reduce the total number of animals used to in bringing new products to the marketplace and provide a more rapid screening tool for weeding out highly toxic or unpromising compounds.

Citation: Lee MY, Kumar RA, Sukumaran SM, Hogg MG, Clark DS, Dordick JS.. 2008. Three-dimensional cellular microarray for high-throughput toxicology assays. Proc Natl Acad Sci U S A 105(1):59-63.

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Early-life Exposure to Lead Causes Alzheimer's Like Changes in Older Monkeys

Alzheimer's-like symptoms were seen in a group of older long-tailed macaque monkeys given low levels of lead in infant formula during the first 400 days of life at a non-NIH facility. The findings suggest that Alzheimer's disease is influenced by early-life exposures to environmental triggers. NIEHS grantees and intramural scientists collaborated on the study.

The monkeys' blood lead levels at the end of the exposure period were in the range of 19-26 micrograms/deciliter and resembled the levels seen in many inner city children. After they had reached adulthood, their blood lead levels were the same as the control group, indicating that any significant exposure was confined to the developmental and adolescent periods. No health problems were found in any of the monkeys during the 23-year study.

The researchers discovered amyloid protein plaques differences and changes in gene expression in the lead-exposed monkeys. All of the adult monkeys were found to have amyloid plaques, but the lead-exposed group's plaques were more numerous and more dense. Expression of Alzheimer's specific genes (APP and BACE1) was elevated in the lead-exposed monkeys. These effects were accompanied by higher levels of DNA oxidation and decreased DNA methyl-transferase activity, suggesting epigenetic influences on the expression of the Alzheimer's disease-related genes.

Citation: Wu J, Basha MR, Brock B, Cox DP, Cardozo-Pelaez F, McPherson CA, Harry J, Rice DC, Maloney B, Chen D, Lahiri DK, Zawia NH.. 2008. Alzheimer's disease (AD)-like pathology in aged monkeys after infantile exposure to environmental metal lead (Pb): evidence for a developmental origin and environmental link for AD. J Neurosci 28(1):3-9.

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Oxidative Stress Marker Identified in Stroke Victims

New research supported in part by NIEHS has revealed a possible biomarker that may be useful in determining the effectiveness of antioxidant therapies used to treat stroke victims. Laboratory studies show that oxidative stress is a major contributing factor to brain injuries resulting from the restriction of blood flow caused by stroke. To date, however, a useful biomarker has not been available.

The group hypothesized that F2-isoprostanes, which are products of neuronal cell arachidonic acid peroxidation during stroke, might be good candidates for a marker. They performed a case control study of 52 stroke patients and 27 controls. Twenty-five of the stroke patients had received the clot busting drug tissue plasminogen activator (tPA). The researchers measured antioxidant dietary intake by a questionnaire.

The study showed that F2-isoprostanes were indeed elevated in the plasma of stroke victims within the first 8 hours of the appearance of symptoms but not at 24 hours or later time points. They also found a correlation between F2-isoprostanes and matrix metalloproteinase 9 (MMP9) in tPA-treated stroke patients — confirming earlier findings that oxidative stress may be an early stimulus for MMP activation and blood-brain barrier injury. While the findings need to be confirmed in large studies, they do offer a new research opportunity in the treatment of stroke.

Citation: Kelly PJ, Morrow JD, Ning M, Koroshetz W, Lo EH, Terry E, Milne GL, Hubbard J, Lee H, Stevenson E, Lederer M, Furie KL. 2008. Oxidative stress and matrix metalloproteinase-9 in acute ischemic stroke: the Biomarker Evaluation for Antioxidant Therapies in Stroke (BEAT-Stroke) study. Stroke 39(1):100-104.

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Lipoic Acid Supplementation Inhibits Lesion Development in Mice

NIEHS-supported research has determined that dietary supplementation with alpha-lipoic acid (ALA) reduces the formation of fatty plaques in two mouse models of atherosclerosis.

Atherosclerosis and its associated vascular complications are the principal cause of cardiovascular and cerebrovascular diseases (CVDs) leading to heart attacks and stroke. These diseases represent the principal cause of death in Western civilizations, accounting for more than 40% of all deaths. According to the American Heart Association, almost 62 million Americans suffer from CVDs, which have been the number one killer in the U.S. for more than nine decades.

ALA is a naturally occurring compound that appears to be useful in treating conditions associated with oxidative stress. It has been safely used for more than 30 years in Europe to prevent and treat complications associated with diabetes and cataracts.

Mice were fed diets containing either normal or high amounts of fat and cholesterol with or without 0.2 percent ALA. The animals receiving the supplementation had significantly reduced numbers of aortic lesions, 40 percent less body weight gain, and lower serum triglyceride levels. The supplementation also reduced the expression of aortic adhesion molecules and proinflammatory cytokines. The authors conclude that ALA "may be a useful adjunct in the prevention and treatment of atherosclerotic vascular diseases."

Citation: Zhang WJ, Bird KE, McMillen TS, LeBoeuf RC, Hagen TM, Frei B.. 2008. Dietary alpha-lipoic acid supplementation inhibits atherosclerotic lesion development in apolipoprotein E-deficient and apolipoprotein E/low-density lipoprotein receptor-deficient mice. Circulation 117(3):421-428.

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Intramural Papers of the Month

By Robin Arnette

Atopic Asthma Risks to Women in the Agricultural Health Study

A team of researchers from the NIEHS, the National Institute for Occupational Safety and Health and the National Cancer Institute (NCI) determined that pesticides may contribute to atopic asthma, which is defined as asthma symptoms produced upon exposure to an environmental antigen. The results, generated from the 25,814 women who provided information on asthma status as part of the Agricultural Health Study, were published in the January 1 issue of the *American Journal of Respiratory and Critical Care Medicine*. The study was funded by the Intramural Research Program of the National Institutes of Health, the NIEHS and the NCI.

Farm women who spent their childhood on farms had a lower incidence of allergic asthma. There was additional protection for those women who grew up on farms and currently work with animals; however, women who did not grow up on farms had a higher risk if they currently worked with animals. Farm women who applied pesticides had a 50 percent increased risk of allergic asthma. Women who used parathion, phorate or coumaphos, among the most potent organophosphate pesticides, had a two-fold increased risk of atopic asthma. Pesticides were not associated with non-allergic asthma.

The study is significant because it is the largest sample of farm women evaluated for asthma.

Citation: Hoppin JA, Umbach DM, London SJ, Henneberger PK, Kullman GJ, Alavanja MCR, Sandler DP. 2008. Pesticides and atopic and nonatopic asthma among farm women in the Agricultural Health Study. Am J Respir Crit Care Med 177(1):11-18.

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Nicotinamide Involvement in Hormone-Mediated Transcription

In a study funded by the Intramural Research Program of the NIH and NIEHS and published in the January issue of *Molecular and Cellular Biology*, investigators from the NIEHS Laboratory of Molecular Carcinogenesis reported that nicotinamide (NAM) uncouples promoter chromatin remodeling from the transcription preinitiation complex (PIC) assembly. This finding suggests that NAM blocks the regulation of a pathway that links the chromatin remodeling function with activation of gene expression.

The researchers wanted to know whether the sirtuin family of deacetylases, homologues of the yeast SIR2 family of deacetylases that require NAD as a co-substrate, was involved in progesterone receptor (PR)-mediated transcription. They monitored the effects of a sirtuin inhibitor, NAM, on PR-mediated transcription in T47D breast cancer cells using hormone treatments, siRNA knockdowns and ChIP assays.

Treating cells with NAM prior to hormone treatment suppressed hormone-dependent activation of PR- and glucocorticoid (GR)-regulated genes in a dose-dependent manner. Unexpectedly, an siRNA knockdown of SIRT1 and PARP1, two NAM sensitive proteins closely linked to transcription and gene regulation, determined that NAM inhibition occurred independently of these two factors. The ChIP data demonstrated that NAM inhibition of PR-regulated transcription occurred at the level of PIC formation which implied that the assembly of the basal transcription machinery was being disrupted.

The results of the research provide more information on the complexity of gene regulation.

Citation: Aoyagi S, Archer TK. 2008. Nicotinamide uncouples hormone-dependent chromatin remodeling from transcription complex assembly. Mol Cell Biol 28(1):30-39.

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Crystallization of the Type II Dihydrofolate Reductase Complex

In the December 2007 issue of *Biochemistry*, scientists from the NIEHS and the University of Tennessee presented the first crystallographic data that explains how the Type II dihydrofolate reductase (DHFR) enzyme, with structurally similar binding sites, accommodates both the NADP+ cofactor and the dihydrofolate (DHF) substrate.

DHFR confers resistance to bacterial DHFR-targeted antifolate drugs and therefore plays an important role in the treatment of pathogenic and neoplastic diseases. DHFR, one of the smallest enzymes able to self-assemble, forms a homotetramer with its active site occurring within a central pore in the tetramer. The crystal structure provided several pieces of information about how the DHFR•DHF•$NADP^+$ complex works, but a few of the important findings included the following conclusions: (1) two equivalent isoleucine residues bind structurally similar regions of the nicotinamide and pteridine rings and stabilize a catalytically-favorable interaction; (2) two pairs of residues, tyrosine 69 and glutamine 67, are hydrogen-bonded and provide a “clamp” which holds the rings in place during hydride transfer; and (3) the ternary complex explains how the enzyme retains activity even after massive mutations.

This study is the first to provide functional data on the DHFR•DHF•$NADP^+$ enzyme which may lead to the development of inhibitors that can target Type II DHFR.

Citation: Krahn JM, Jackson MR, DeRose EF, Howell EE, London RE. 2007. Crystal structure of a type II dihydrofolate reductase catalytic ternary complex. Biochemistry 46(51):14878-14888.

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The Roles of XRCC1 and Pol β in Repair of SSBs

Scientists from the NIEHS Laboratory of Structural Biology and the Laboratory of Molecular Carcinogenesis examined the scientific literature pertaining to the roles of X-ray cross-complementing group 1 (XRCC1) and DNA polymerase ß (pol ß) in protecting cells against DNA single-strand breaks (SSBs). The journal review article was published in the January issue of *Cell Research* and represented a thorough analysis of the research that had been performed to date on the topic.

The 70-kDa XRCC1 has no known enzymatic activity, but physically interacts with other proteins known to be involved in SSB and base excision repair (BER). The 39-kDa pol ß contributes both polymerase and end-tailoring lyase activity to the predominant single-nucleotide BER pathway. Mouse cell lines that lacked XRCC1 and pol ß (*XRCC1*$^{-/-}$ and pol *ß*$^{-/-}$, respectively) were especially hypersensitive to damage caused by the alkylating agent methyl methanesulfonate (MMS). Data from the comet assay, a technique that detects DNA damage in individual cells using electrophoresis, demonstrated elevated levels of SSBs, and diminished repair in XRCC1- and pol ß-deficient cells following exposure to MMS.

The BRCT I domain of XRCC1 specifically interacts with activated poly (ADP-ribose) polymerase 1 (PARP-1) that is bound to damaged DNA. Since inhibition of PARP activity enhanced MMS-induced cell killing in *XRCC1*$^{-/-}$ cells, the authors concluded that PARP activation played a role in the modulation of cytotoxicity beyond recruitment of XRCC1 to sites of DNA damage.

Citation: Horton JK, Watson M, Stefanick DF, Shaughnessy DT, Taylor JA, Wilson SH. 2008. XRCC1 and DNA polymerase beta in cellular protection against cytotoxic DNA single-strand breaks. Cell Res 18(1):48-63.

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Inside the Institute

Institute Celebrates China Day

By Eddy Ball

By the time the China Day celebration on February 12 got underway, the NIEHS Cafeteria was packed with employees, contractors and relatives drawn to the event by the promise of good food and entertainment. All who attended, including NIEHS Acting Director Sam Wilson, M.D., who introduced the event, seemed completely satisfied with the quality of both.

Sponsored by the NIEHS Diversity Council and organized by the Council's China Day Organizing Committee (see text box), China Day celebrated the fifteen-day Chinese New Year holiday. On hand to ring in the Year of the Rat, which began with the New Moon on February 8, were a Chinese opera dancer, two classical vocalists and a master demonstrating the martial/spiritual movement art of Taiji or Tai Chi. There were also posters and booths showcasing the art, crafts, clothing and calligraphy of China — along with plenty of Chinese food and publicity for the upcoming Beijing 2008 Olympics.

China Day began with an introduction of Wilson by Master of Ceremonies and NIEHS Staff Scientist Leping Li, Ph.D. Along with his welcome to employees and guests, Wilson also reassured the audience about the entertainment. "Just in case any of you are on pins and needles about this program, [which] lists 'solo baritone' as the first event," he quipped, "I'm not going to sing."

Li and many in the audience were visibly moved by the quality of the performances and deeply affected by their memories of their homeland and cultural traditions. Li reminisced about the festive middle days of the New Year celebration in China, which he likened to Halloween, "but without the tricks." People gave out treats as families visited one another. Seeing and hearing the performers, Li remarked several times, made him "feel like I'm back in China in the 1980s."

Following the performance, people visited the displays and flocked to the buffet. A few minutes after the performances ended, the line of people waiting to serve themselves already stretched to the entrance of the cafeteria.

The China Day Organizing Committee

Chair

Yang Cao, Ph.D.

Vice Chairs

Hui Hu, Linda Yu,
Shuang Shuang Dai, Ph.D.

Members

Ding Ding,
Xiaoqing Chang,
Jianying Li,
Jianjun Gao, Ph.D.,
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Hao Wu, Ph.D.
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Lianming Wang,
Jianxin Shen,
Yuan Wang, Ph.D.,
Honglei Chen, Ph.D.,
Leping Li, Ph.D.
Zhongjing Wang, Ph.D.

Wilson, who has known Li for nearly 18 years, was impressed with the emcee's colorful traditional attire. (Photo by Eddy Ball)

Opera dancer Yi Lu warmed up in the NIEHS Cafeteria, stretching and practicing leg lifts for her first number. (Photo by Eddy Ball)

The food was plentiful at the long buffet, shown here before the performances got underway — a calm before the storm of hungry people. (Photo by Eddy Ball)

NIEHS Microbiologist Julius Thigpen, Ph.D., attended in appreciation of Chinese culture. (Photo by Eddy Ball)

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Family Health Seminar on Loss and Grieving

By Eddy Ball

Clinical associate Edna Ballard has had ample opportunity to see the various ways that individuals face loss and express their grief. In the course of her work at the Joseph and Kathleen Bryan Alzheimer's Research Center, she became convinced that no one has the right or the ability to judge the appropriateness or quality of anyone else's response.

Among the many faces of loss and grief, Ballard observed, is miscarriage, which outsiders often do not fully understand. "The worst thing you can tell a grieving woman is that 'You can always have another one,'" she said. (Photo courtesy of Steve McCaw)

On February13, Ballard shared some of what she has learned in a talk in the NIEHS Executive Conference Room titled "The Many Faces of Loss, Grief and Bereavement: Finding Your Way Back to Normal." NIEHS Biologist Alicia Moore, chair of the Diversity Council Disability Advocacy Committee (DAC), hosted the event, which is part of the Family Health Transitions Seminar Series sponsored by DAC and the NIEHS Office of Management.

Ballard opened her talk by emphasizing the many different kinds of loss and the impact on an individual and his or her family, caregivers, friends, supervisors and colleagues. The topic has received even more attention, she noted, with the graying of the Baby Boomer generation and the increase in the numbers of seniors, as well as the number of people who find themselves assuming the role of caregiver.

As this photo of lecture host Alicia Moore indicates, Ballard's account of loss, grief and bereavement also included some self-effacing humor. (Photo courtesy of Steve McCaw)

"Grieving is not only related to loss because of a death," she told the audience. "The list is very long. It could be loss of a relationship, even the loss of dreams, loss of the illusion of safety, the loss of a younger self, the loss of independence. Grief is extremely powerful; it can catch you totally unprepared and knock you off balance."

Grief is a natural reaction to loss, Ballard continued, and "It can't be hurried." Part of coping with this inner pain and turmoil is "the sharing of grief outside oneself" or bereavement. Affected by such factors and culture, gender and the circumstances surrounding the loss, bereavement and mourning rituals are healthy and necessary responses to loss. Individuals who try to assume the roles of what Ballard called "Macho Man," "Competitor" or "Protector" can rob themselves of this much needed outlet for their grief by trying to suppress the emotion and avoid mourning.

Ballard had tips for the persons who face loss and for those who are affected by the losses of others. In the face of loss, she said, people should take care of themselves and defer major decisions, such as moving or selling a

house, and instead set short-term, quickly achievable goals and look to the future by making long-term plans for life after a loss. Friends and colleagues can help those who have a loss by being patient and fully present, offering specific kinds of help and, most importantly, listening and allowing the person to fully express feelings.

Ballard argued that different individuals may need to mourn in different ways and may need different amounts of time to return to what she called "the new normal." Talking about stages of grief and standards of behavior in mourning, she said, "We need to be ok with a person who takes a really short time to get over grief or with a person who takes a much longer time."

"There is no right or wrong way to grieve," Ballard asserted. Her advice to the audience was straightforward: "Do what works for you" to deal with grief.

Ballard is the author of a 1990 book, Managing Grief and Bereavement. She referred several times to her work with Alzheimer's patients during her talk in the intimate setting of the Executive Conference Room. (Photo courtesy of Steve McCaw)

Ballard's talk introduced the topics of loss and grieving in the Family Health Transitions Seminar Series. On February 20, Barbara Keyworth of the NIEHS Employee Assistance Program spoke on "Loneliness from Loss." A third seminar, "Coping with Childhood Grief," is scheduled for March 12, 1:30 – 3:00 p.m., also in the Executive Conference Room.

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Schwartz Accepts Research Position in Denver

By Eddy Ball

Former NIEHS Director David Schwartz, M.D., will end his three-year tenure with the Institute in May to assume a research position with the National Jewish Medical and Research Center (NJMRC) in Denver, Colorado. In his new position, Schwartz will serve as director of the Pulmonary and Critical Care Division and lead a new Center for Genetics and Therapeutics. He replaces Acting Head Kevin Brown, M.D.

Schwartz became the fourth director of the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program in May, 2005, succeeding Ken Olden, Ph.D. Schwartz oversaw several new initiatives while serving as director, including the five-year Strategic Plan, start-up of

Former NIEHS Director David Schwartz (Photo courtesy of Steve McCaw)

NIH Roadmap Initiatives on epigenetics and gene-environment interaction, and the soon-to-be opened Clinical Research Center on the Institute's Research Triangle Park campus.

Before joining NIEHS, Schwartz was the director of the Pulmonary, Allergy, and Critical Care Division and vice chair of research in the Department of Medicine at Duke University. At Duke, Schwartz was an NIEHS grantee and played a principal role in developing three interdisciplinary centers in environmental health sciences, environmental genomics and environmental asthma.

Schwartz has authored more than 150 peer-reviewed research papers, 38 book chapters and a textbook. He has served on numerous editorial boards and scientific review committees including, most recently, the NIH/National Heart Lung and Blood Institute's Innovative Grant Program Review Committee and the Veterans Administration Merit Review Board. He is a member of the American Society for Clinical Investigation and the Association of American Physicians and the recipient of many awards. The American Thoracic Society presented Schwartz with a Scientific Accomplishment Award in 2003.

In a statement released on February 8 after Schwartz tendered his resignation, NIH Director Elias Zerhouni, M.D., said, "He is one of the world's leading researchers in pulmonary medicine, and I have the utmost respect for his scientific abilities and his scientific vision for the future of environmental health research. Dr. Schwartz's new position will enable him to further that vision, while providing him more opportunities to conduct research and care for patients."

According to NJMRC, Schwartz' new position will also involve overseeing work funded by NIH grants to physicians in the Pulmonary and Critical Care Division. The division is highly respected among physicians and scientists in the pulmonary and critical care communities. It recently assumed responsibility for the intensive care unit and hospitalist care at nearby HealthOne Rose Medical Center.

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