



March 2007



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NIEHS Spotlight

Advisory Council Hears NIEHS Updates and New Concepts

By Eddy Ball

The NIEHS National Advisory Environmental Health Sciences Council convened on February 15 in Rodbell Auditorium for a daylong session of reports on NIEHS programs and initiatives. In addition to its usual business, Council voted unanimously to approve Concept Clearance for two new funding mechanisms and heard reports on new developments in global environmental health (GEH) and translational research. The advisors also received an update on extramural research on endocrine disruptors.

NIEHS Associate Director and Director, Office of Translational Research (OTR), Bill Martin, M.D., opened his portion of the meeting with a report on “The Mandate for Effective Translational Medicine and the Special Challenges for Environmental Health Sciences.” Martin explained that at many NIH Institutes and Centers (ICs), researchers tend to focus on outcomes of new therapeutics or diagnostics for a well-defined subset of diseases. The research focus at NIEHS, however, is usually more related to development of tools and discoveries to impact public health policy and prevention.

As a result, OTR has proposed a modified version of the NIH definition of translational research. According to this definition, Martin explained, “Translational research transforms scientific discoveries arising from laboratory, clinical or population studies into clinical or population-based applications to improve health by reducing disease incidence, morbidity and mortality.”

To facilitate translational research at NIEHS, OTR set several objectives for its Office of Technology Transfer (see related Spotlight story) and proposed a new funding mechanism for Concept Clearance. Known as K18, the mechanism would complement existing investigator recruitment efforts by establishing a program of short-term, three-month to one-year, mentored career development awards for established physician-scientists and environmental health basic science investigators.



In a configuration not often seen in Rodbell Conference Center, the Council sat around a group of tables placed in the center of the auditorium with attendees seated on both sides. (Photo courtesy of Steve McCaw)



During the meeting, Council Chair David Schwartz, M.D., center, was flanked at the head of the table by DERT Acting Director Dennis Lang, Ph.D., left, and Deputy Director Sam Wilson, M.D. (Photo courtesy of Steve McCaw)

The program will encourage interdisciplinary research and divergent thinking by immersing researchers in collaborative environments to stimulate a healthy interplay of perspectives. Clinicians who have received funding from the more traditional ICs will bring their bedside orientation to laboratory-based environmental health research. In turn, environmental health basic science researchers will find out what it means to work in a disease-oriented translational program.

In Martin's second report, he told Council members about the NIEHS Global Environment Health Conference held January 10–13 in San Francisco. The conference engaged 45 leading environmental health experts from around the world in an intense work-group exercise to address diseases linked to environmental factors.

Conference organizers charged the work groups with identifying diseases and approaches for research and intervention. Participants also had to pinpoint barriers as well as ways of connecting NIEHS/NIH funded researchers with communities and researchers in the developing world and suggest public and public-private partnerships. By the end of the workshop, the experts had produced white papers listing and rank-ordering research topics and proposed next steps. These reports will serve as an action plan for improving environmental health worldwide.

In another report to the Council, Health Science Administrator Jerry Heindel, Ph.D., surveyed the successes and challenges of extramural research on the human health effects of phthalates and bisphenol A. Endocrine disruptors are the subjects of ongoing controversy among scientists. Even within the Institute, scientists strongly disagree about the health threats these compounds may actually pose. Council Member Dan Liebler, Ph.D., expressed concern that the research so far has produced little in the way of definitive findings.

Following the Council's closed session to consider grant applications, Program Administrator David Balshaw, Ph.D., presented another concept for clearance – a new extramural grant mechanism called "Fusion." Balshaw described Fusion as a funding strategy to enhance "transformative research in the environmental health sciences." He explained that the proposed mechanism would foster a level of interdisciplinary synergy capable of producing "paradigm shifts" by encoding collaboration into a special RO1 grant mechanism.



Duke Geneticist Hunt Willard, Ph.D., addressed a major theme in currently funded research with his lecture on epigenetics. (Photo courtesy of Steve McCaw)

Council Firsts

February's meeting introduced several new elements into the format of Council meetings. Council, for the first time, conducted its review in a full-day session, instead of the customary day-and-a-half session. NIEHS Director David Schwartz, M.D., indicated that future meetings will likely follow the new format as well.

The February meeting also was the first time that some members were able to telecommute to the Council meeting. Because of a rash of airport closings in the northeastern United States, members from New York, Boston and Washington, D.C. attended the meeting by phone and viewed presentations through video feeds, unintentionally putting DERT's paperless initiative to its first test before the Council.

Finally, the advisors heard a presentation on the potential of epigenetic research by Hunt Willard, Ph.D., director of the Institute for Genome Sciences and Policy at Duke University and Vice Chancellor for Genome Sciences at Duke University Medical Center. Willard's talk was the first scientific lecture in what will become a series that the Council will hear in upcoming meetings.

Balshaw said that paradigm shifts occur when science and imagination converge, often by accident, to see phenomena in surprisingly new and unconventional ways. According to Balshaw, the Fusion program will encourage this kind of transformational research by using a new Multiple Principal Investigator (PI) RO1 grant mechanism to include at least two PIs from distinctly different disciplines in a single project funded over a five-year period. Because the investigators will see their common goal from different disciplinary perspectives, Fusion grants will encourage animated dialogue across disciplines and lead to a more creative, non-traditional approach to problem solving.

When Council approves Concept of Clearance, proposals enter a “holding pattern,” a period when they are contingent upon funding and subject to reassessment at upcoming Council meetings. Implementation begins only after further review.

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During his report on DIR accomplishments, Acting Scientific Director Perry Blackshear, M.D., twice asked council members to encourage their friends and relatives to apply for his job. (Photo courtesy of Steve McCaw)

Technology Transfer – The Institute’s Million Dollar Baby

By Eddy Ball

NIEHS convened a meeting on January 26 in Rodbell Auditorium to familiarize scientists with the technology transfer process and introduce impending changes in NIH rules and procedures governing it. William Martin, M.D., director of the Office of Translational Research, opened the meeting by encouraging audience participation. “We want this to be a dialogue,” he said. “Technology transfer should always be seen as a work in progress. We’re here to talk about ways to make the process work for you.”

Joining Martin was John Penta, Ph.D., and three NIH technology transfer specialists from the Bethesda campus, including Director Lili M. Portilla and NIEHS Technology Transfer Advisor Peg Koelble, [Office of Technology Transfer and Development, National Heart, Lung and Blood Institute](#), and Senior Technology Licensing Specialist Susan S. Rucker, J.D., [NIH Office of Technology Transfer \(OTT\)](#), each of whom delivered presentations and took questions from the audience.



Rucker, left, and Martin listened as Deputy Scientific Director Bill Schrader, Ph.D., talked about changes in the technology transfer process. (Photo by Eddy Ball)

Technology transfer refers to the transmission of intellectual property to individuals, commercial organizations and academic institutions in the non-government sector and the protection of patented technology and methodology from unlicensed use. It is also the process that intramural scientists use to exchange research materials, such as samples and laboratory animals, with collaborators at other agencies and institutions.

In his remarks, Penta underscored the importance of technology transfer to the scientists in the audience. “In the past five years,” he noted, “NIEHS has made over 1.3 million dollars from licensing patented inventions. Four hundred thousand dollars of that went back to the scientists responsible for the patents.” Understanding the process, he continued, can help scientists get the recognition, patent protection and compensation they deserve for their original ideas.

Focusing on Material Transfer Agreement (MTA) issues, Portilla presented an overview of “Transfer of Human Samples at the NIH.” She explained that a special MTA policy work group at NIH is in the midst of formulating new policies to govern the transfer and exchange of human samples in order to maintain patient confidentiality in laboratory studies.

Until the new policies are published, Portilla advised investigators to execute MTAs for all transfers of human tissue to or from NIEHS. Investigators should collect samples according to an Institutional Review Board-approved protocol and secure informed consent for transfer. In addition, Cooperative Research and Development Agreements between collaborators should specify sample transfer procedures and conditions of use.

In her presentation on “Working with OTT – Just the Basics,” Rucker focused on the protection of intellectual property and the role of Employee Invention Reports (EIRs). According to Rucker, investigators should complete EIRs carefully, providing specific documentation of date of conception for inventions and making certain they submit patent applications prior to a publication or public presentation of results. “In the past,” she warned the audience, “we’ve lost patent battles because the invention wasn’t [adequately] documented.”



Biologist Joel Abramowitz, Ph.D., sought advice from Penta about transferring specimens to a collaborator. (Photo by Eddy Ball)

Goals for Technology Transfer

During the February 15 meeting of the National Advisory Environmental Health Sciences Council, Martin emphasized the critical role of technology transfer (TT) in the Institute’s overall translational research effort. He also set five major goals for the NIEHS Office of Technology Transfer:

- Increase coordination and planning with other institutes and centers
- Increase customer service and access to information for NIEHS investigators (and senior leadership)
- Improve the Institute’s TT web site to provide up-to-date forms and information about the necessary steps in completing TT
- Increase participation among stakeholders with a series of town hall meetings
- Develop metrics of performance for analyzing TT at the Institute

Along with urging careful attention to documenting inventions, Rucker encouraged would-be inventors to work closely with the technology licensing specialists assigned to them, keeping the specialists up to date on progress with the invention during the patent application process. Once the licensing negotiations begin, however, inventors should resign themselves to being kept at arm's length because of conflict of interest concerns.

Rucker cautioned attendees that “scientists often have unrealistic expectations” about how much they should receive for licensing their inventions. To make technology that benefits the public available, NIH often accepts less than top dollar for licensing agreements. “There is [also] a statutory cap on how much the scientist can receive,” she explained.

As the meeting concluded, Martin announced that his office is in the process of developing a comprehensive Web site to help scientists with filling out forms correctly and processing their agreements and requests.

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UMBC President Speaks on Minorities in Science

By Eddy Ball

On February 20, a capacity audience gathered to hear Freeman Hrabowski, Ph.D., deliver the Institute's keynote Black History Month address at an event sponsored jointly by the RTP Chapter of Blacks in Government and the NIEHS Diversity Council. Hrabowski is the president of the University of Maryland-Baltimore County (UMBC) and a leader in efforts to increase the representation of minorities and women in the sciences. He spoke on “Beating the Odds: Preparing Minorities for Research Careers in Health Sciences.”

In his opening remarks, NIEHS Director David Schwartz, M.D., described the celebration's keynote speaker as “an incredibly accomplished educator” whose leadership has made UMBC the single most important American undergraduate institution in producing African-American students who go on to get doctoral degrees in science. Hrabowski's recent honors include election to the American Academy of Arts and Sciences, the U.S. Presidential Award for Excellence in Science, Mathematics and Engineering Mentoring, and honorary degrees from Princeton and Duke.

Hrabowski, Schwartz observed, is also a thinker who looks at problems globally. In addition to his work at the post-secondary level, he has also written two books on parenting and early education for minority children and is currently a consultant on projects in the Baltimore schools funded by the National Science Foundation.



Hrabowski told the audience, “My line to my students in science... is ‘if you’re going to do science, you have to marry the work. It cannot be a part-time lover.’” (Photo courtesy of Steve McCaw)



Many of the people in the audience were women who chose careers in science. Pictured from left to right are IRTA Pre-doctoral Fellow Monica High, Contract Laboratory Technician Jessica Martin and Laboratory of Experimental Pathology Biologist Eli Ney. (Photo courtesy of Steve McCaw)

Hrabowski opened his talk by referring to the comments of Harvard Professor of African-American Studies Henry Louis Gates, Jr. regarding progress for African-Americans since the assassination of Martin Luther King, Jr. in 1968. Gates noted that while the black middle class has tripled since 1968 to 17 percent of the African-American population, the proportion of black children below the poverty line (35 percent) has remained constant. “There are now two classes in black America,” Hrabowski observed, “the black middle class and the larger black underclass.”

As the country undergoes demographic change in the first half of this century, Hrabowski continued, people of color — the fastest growing population — are the very people who are getting the least amount of education at a time when the country will need more scientists, doctors and engineers. In the inner cities, an estimated 50 to 70 percent of children do not finish high school. While the percentage of blacks with college degrees reflects the proportion of blacks in the middle class, 17 percent, African-Americans represent only two to three percent of people with doctoral degrees.

According to Hrabowski, the most pressing concern for the educational and scientific communities is how to convince female and minority students to make a commitment to pursue careers in science and become consumed by “the nobility of the work.” The solution involves role modeling and mentoring. “It takes a scientist to produce a scientist,” he said. “People gravitate to people like themselves [and] everybody needs support.”

Getting through the first two years of a science curriculum and taking “ownership” of the commitment to science are difficult for any young person, Hrabowski explained, and 60 to 70 percent of students who begin as science and engineering majors change their majors by the end of their sophomore year. “It’s an American story, and the same thing happens with Ph.D.s.”

Minorities can find “this road to be particularly lonely” without support and people like themselves to emulate. For a long time, whites accepted the racial status quo in education and society, before they began to recognize the disparities that existed. Now, young African-Americans and Hispanics, women as well as men, need the opportunity to envision themselves in the role of the black or Hispanic professor, doctor or engineer who is teaching their classes.

Parents and public school educators must also do their part, Hrabowski argued. Public schools need higher standards for elementary and middle school teachers in math and science. Comparing the motivation of people of color from other countries to American minority students, Hrabowski pointed to the importance of family, community and school expectations of excellence and the involvement of parents in the schoolwork of their children.



NIEHS Deputy Director Sam Wilson, M.D., and Schwartz listened with interest to Hrabowski’s challenge to the NIEHS and the scientific community in general. (Photo courtesy of Steve McCaw)



Following the presentation, Hrabowski joined Director of Education and Biomedical Research Development Marian Johnson-Thompson, Ph.D., and Biomedical Engineer Kennita Johnson, Ph.D. Johnson is an alumna of the Meyerhoff Scholarship Program headquartered at UMBC. (Photo courtesy of Steve McCaw)

As Hrabowski came to the end of his talk, he addressed the executive officers in the audience. “My challenge to NIEHS is that you look critically at self and tradition. Ask the question, ‘How do we continue to pull in more people who have not been represented in this group?’” Diversity, he added, does not just mean color or race. Institutions, such as NIEHS, also need to strive for socioeconomic diversity.

(Learn more about this dynamic speaker’s achievements in improving minority representation in science by reading the MiSciNet article [“Fulfilling the Expectation of Excellence” by Clinton Parks.](#))

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Olden Urges Fourth and Fifth Graders to Dream

By Eddy Ball

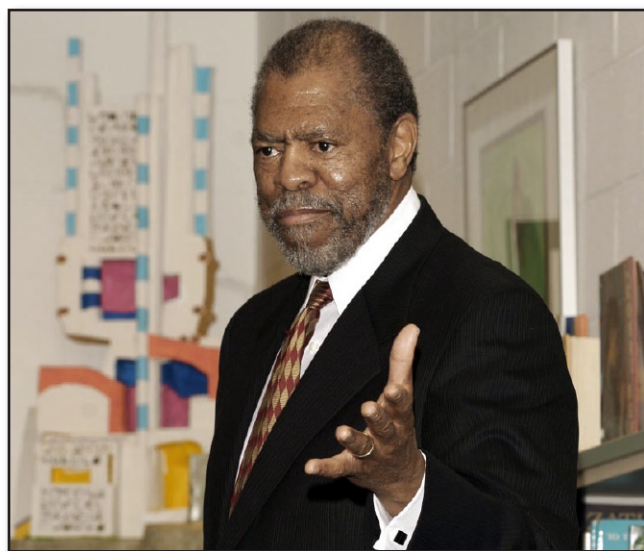
On February 5, NIEHS Director Emeritus Kenneth Olden, Ph.D., spoke to approximately 120 fourth- and fifth-grade students at Club Boulevard Humanities Magnet Elementary School. Olden’s 90-minute talk and question-and-answer session were part of the Durham school’s celebration of Black History Month.

Gathered in the school’s media center, the students listened attentively as Olden described his childhood on his family’s small farm in rural East Tennessee. Olden’s family had few resources, but they had a deep respect for education and believed that it would help the five children get ahead in life.

Olden and his brothers and sisters walked six miles each day to a small segregated rural school. It was there that one of his teachers convinced him that determination and hard work were the keys to success. “‘By golly!’ my teacher always said, ‘you boys and girls can become anything you want,’” Olden recalled. “‘And I believe that. If you want something badly enough, you can eventually make it happen.’”

When he was old enough to work in town, he became “a shoe shine boy with a dream,” saving enough money to pay for his first year at Knoxville College. Every summer after that, he worked to pay for the next year’s room, board and tuition — as a dishwasher, cook, farm worker and construction laborer.

All of the five children in the Olden family finished high school, which was quite unusual at the time in that community. Olden was the only one in his family and, for many years, the only one in his community to finish college.



“It happened because I paid attention to my teachers when they told me to read and sit down and behave,” Olden told the students at Club Boulevard. (Photo courtesy of Steve McCaw)



The 10- and 11-year-old students listened closely to Olden and stayed on their best behavior as he described his journey from a sharecropper’s farm near Newport, Tenn. to the director’s office on the NIEHS campus in RTP. (Photo courtesy of Steve McCaw)

After graduating in a high school class of 11 students, Olden began college determined to go to medical school, even when that meant swallowing his pride and taking remedial courses to make up for deficiencies in his rural education. “I made the decision early,” he recalled. “No matter how hard I had to work, no matter how much time I had to spend reading and re-reading my assignments, I was not going to be denied an education.”

In 1959 an opportunity to be one of the first two African-Americans to attend the undergraduate school of the University of Tennessee exposed him to laboratory research and changed the course of his life. Instead of settling for a rural medical practice, Olden decided to pursue a career where “I could [potentially] affect the lives of hundreds of millions of people.”

After graduation, his pursuit took him to the University of Michigan for a master’s degree, Temple University for a doctorate in cell physiology and biochemistry, and Harvard University for postdoctoral work. With his advanced degrees, Olden went to work in cancer research at the National Cancer Institute and Howard University Cancer Center before being appointed as director of NIEHS in 1991.

When he began his talk, Olden showed the students a photo and story from the Newport, Tenn. newspaper about his great-grandmother, Augusta Foster, who was born into slavery in 1855. Foster lived with the family when Olden was a child, and the contrast between her experiences and his taught him an important lesson about making the most of new opportunities in a changing world. As he reached the end of his talk, Olden reflected on the much different prospects Foster faced four generations ago. “How could my great-grandmother ever have imagined what would happen in my lifetime?” he asked.

After the talk, Olden took questions from the audience. Many of the students were interested in the scientist’s own children, and several wanted to know more about the famous people he has known — presidents, senators, performers and, especially, Hillary Clinton.

Others were intrigued by Olden’s cancer research and asked questions about chemotherapy and its side effects. One boy’s question about how to get ahead brought a telling response from Olden: “If you can dream it, you can do it.”

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Olden talked with Club Boulevard Principal Micah Copeland, left, and John Peterson of NIEHS prior to the talk. Peterson’s wife, Jo Anne, sponsored Olden’s talk at the school. (Photo courtesy of Steve McCaw)



Club Boulevard Humanities Magnet Elementary School sits in a quiet, older neighborhood in north Durham. (Photo courtesy of Steve McCaw)

RTP Chapter of Blacks in Government Holds Black History Month Luncheon

By Robin Arnette

On February 15, the Research Triangle Park Chapter of Blacks in Government (BIG) held its sixth annual EPA Legacy Luncheon at the Radisson Hotel Research Triangle Park. This year's theme was "From Slavery to Freedom: The Story of Africans in the Americas." The guest speaker, Irving L. Joyner, J.D., professor of law at North Carolina Central University (NCCU) School of Law, discussed the strides that African-Americans have made, but also stressed that there's more to do.

Chapter president Veronica Godfrey, biologist and program officer in the Laboratory of Pharmacology and Chemistry at NIEHS, opened the program with a welcome address and led the participants in singing James Weldon Johnson's "Lift Every Voice and Sing." After the invocation by EPA employee Vonda Dowe, approximately 60 attendees enjoyed a buffet-style lunch.

Annette Rice, Ph.D., second vice president for Region IV of BIG and a research stem cell biologist working in the Laboratory of Reproductive and Developmental Toxicology at NIEHS, introduced Joyner. Several special guests also attended the luncheon. They included Joe L. Dudley, Sr., CEO of Dudley Products, Inc., Willie Bailey, vice president of Training at Dudley, Steve Middleton, Ph.D., professor of history at NCCU, and Norwood Dennis, area director of Civil Rights at EPA.

Joyner chronicled the plight of African-Americans on a national scale from the end of slavery to the 21st century, and also provided little-known facts about life for people of color living in North Carolina during that time. "During slavery North Carolina had the largest population of free blacks in the country, and during the years of 1865–1880, more blacks served in the North Carolina General Assembly than we do now," he said. When asked about the importance of celebrating black history, he said, "There's always a need to understand, appreciate and celebrate the history of our people. Because it is from that that we get inspiration and motivation to do better. We should have black history everyday rather than one month out of the year."

Joyner's talk was well-received and attendees gave him a standing ovation. Marian Johnson-Thompson, Ph.D., director of Education and Biomedical Research Development at NIEHS, enjoyed the talk. "Dr. Joyner gave a really nice historical overview of the hardships our fore parents overcame and how some of our youth have squandered their efforts," she commented. "It's our responsibility to try to get them back on track. It was a very good message."



NCCU Professor Irving Joyner gave the keynote address at the 2007 EPA Legacy Luncheon. (Photo courtesy of Steve McCaw)



Annette Rice of NIEHS introduced the luncheon's guest speaker. (Photo courtesy of Steve McCaw)

Joan Pakenham, Ph.D., Program Director of the Division of Intramural Research at NIEHS, echoed Johnson-Thompson's sentiments. "We need to empower the young people because we have not overcome" she said. "We have to let them know that we still have work to do."

Near the end of the luncheon, Godfrey presented Joyner and Kim Peterson, immediate past president of the RTP chapter of BIG, with plaques of appreciation. Randy Harrison, vice president of the RTP chapter and a chemist at EPA, provided closing remarks.

Joyner, a native of Brooklyn, New York, has been a Professor of Law at NCCU School of Law since 1982, and served as its Associate Dean from 1984 to 1992. He regularly teaches courses in criminal law, criminal procedure, civil rights, race and the law, professional responsibility and trial practice. Joyner received a B.S. from Long Island University and a J.D. from Rutgers, The State University of New Jersey School of Law in Newark, New Jersey.



BIG RTP Chapter President Veronica Godfrey presented Joyner with a plaque of appreciation. (Photo courtesy of Steve McCaw)

The RTP Chapter of BIG began in 1979 and is comprised of employees from NIEHS, EPA, National Health Statistics/CDC and the State of North Carolina. The chapter sponsors various programs throughout the year such as food and toiletry drives for the needy and oratorical contests for high school students. Although the chapter is heavily involved in public service, its main goals are to promote equity and opportunity for all Americans, particularly for people of color. Rice summed up the group's purpose by saying, "We're in the community, and we're still out there fighting against the discrimination of African-Americans."

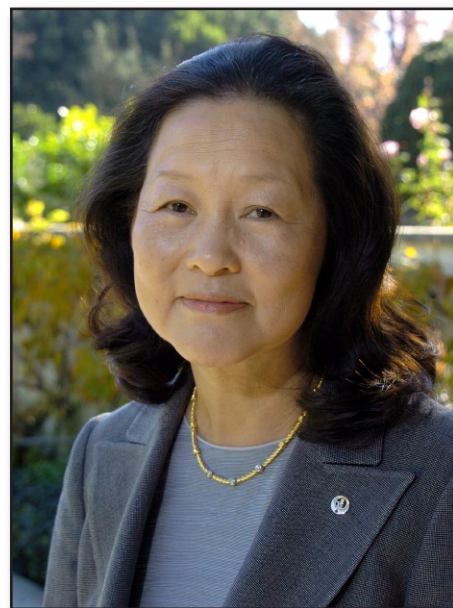
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Upcoming Spirit Lecture by Noted Virologist

By Eddy Ball

On March 20 at 10:00 a.m. in Rodbell Auditorium, Alice Huang, Ph.D., will deliver the sixth lecture in the annual Spirit Lecture Series. Huang is senior councilor for External Relations and faculty associate in Biology at the California Institute of Technology. The NIEHS Diversity Council is sponsoring Huang's lecture, "Beyond the Numbers: Where Are We Going," as part of the Institute's celebration of Women's History Month.

Huang began her career as a microbiologist and eventually became a professor of microbiology and molecular genetics at Harvard Medical School, where she made important discoveries in virology. She has since moved on to a far-ranging career dealing variously with medicine, science and technology policy, science writing and higher education.



2007 Spirit Lecturer Alice Huang (Photo courtesy of the California Institute of Technology)

Huang has received a long list of honors for her scientific and educational contributions. She holds several chairs and sits on boards of major organizations, including the Foundation for Microbiology and the Food and Drug Administration Advisory Committee on Vaccines and Related Biological Products.

Each year since 2002, the NIEHS Spirit Lecture Series has recognized outstanding women who have achieved a balance between the competing aspects of work and family in their lives, thereby becoming better scientists and better members of their families and communities.

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Science Notebook

Cancer Research Pioneer Explores Epigenetic-Environmental Connections

By Eddy Ball

Stephen B. Baylin, M.D., presented the latest talk in the 2006-2007 Distinguished Lecture Series on February 13 in Rodbell Auditorium. Baylin is professor of medicine and oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. The topic of his lecture was “Cancer: The Environment and the Epigenetic Interface.”

In his introduction, lecture host Paul Wade, Ph.D., an investigator in the Laboratory of Molecular Carcinogenesis (LMC), described Baylin as “a true pioneer in his field.” “He has continued to publish at the highest level [throughout his career]...with over 300 peer-reviewed publications.” Wade also credited Baylin’s work as one of the reasons that epigenetics is such an important part of cancer research today.

Baylin began his talk by assuring the audience that “I didn’t put ‘environment’ into the title [of the lecture] gratuitously.” At the center of the epigenetic cancer model is the phenomenon of abnormally prolonged survival responses at the cellular level to such environmental factors as the chronic stresses of aging, acute inflammation and its products, reactive oxygen species, and chronic injury. These prolonged survival responses can trigger the cascade of biological events that lead ultimately to tumorigenesis.



Guest Lecturer Steven Baylin (Photo courtesy of Steve McCaw)

Epigenetics, according to the most widely accepted definition, is the study of sustained heritable alterations in gene expression that are based on factors other than changes in the DNA sequence. While this is a normal process, sometimes the process goes awry, presumably through environmental exposures, and can lead to histone modifications and altered chromatin status. These epigenetic events beget other epigenetic events throughout the multiple layers of memory in the epigenome.

Cancer-related epigenetic changes in gene structure and function can result in the inactivation of genes that otherwise should remain active. Aberrant silencing of genes important to the initiation and progression of tumors affects several groups of genes. These include tumor suppressor genes, developmental transcription factors, tissue remodeling genes, DNA repair genes, cell cycle control genes, anti-apoptotic genes and genes that prevent abnormal activity of developmental pathways in tumors.

Understanding the environmental-epigenetic interface holds promise for translational applications to target metabolic processes in the development and progression of cancer. “One of the important things about research into the environment and epigenetics,” Baylin maintained, “is that many of the things we’re learning here are turning up biomarkers for the earliest stages of not just cancer, but also other diseases, where epigenetic changes are underlying predisposition or risk. I think they are really going to emerge as markers for prevention.”

According to Baylin, the loss of function of genes in tumors, triggering abnormal cellular memory, may be more significantly impacted by epigenetic causes than genetic ones. Epigenetic alterations, in fact, may have pivotal involvement in abnormal clonal expansion of stem and progenitor cells and predisposition to cancer.

“Altered DNA methylation occurs throughout the [cancer progression] process,” Baylin maintained, “...and these changes, the genetic and the epigenetic, start very early in the process and can manifest by the time there are the earliest, pre-invasive changes along this progression cascade.” It is at this point that Baylin sees the involvement of the environment in pre-disposition and where he hopes to identify potential targets for preventive interventions.

In his review of findings by his group and others, Baylin observed that knowledge of the cancer epigenome is advancing rapidly and progress has been made in identifying a group of target genes common to several cancers. However, he cautioned that much



Lecture host Paul Wade (Photo courtesy of Steve McCaw)



Shown in the audience from left to right are NCI Fellow Lamia I. Benbrahim-Tallaa, Ph.D. (on detail to the Environmental Toxicology Program), Laboratory of Reproductive and Developmental Toxicology Fellow Chris Geyer, Ph.D., LMC Microbiologist Bob Langenbach, Ph.D., and LMC Special Volunteer Barbara Burkhardt, Ph.D. (Photo courtesy of Steve McCaw)

remains to be discovered about basic chromatin function, the relationships of adult stem and precursor cells to normal cell renewal, and the origins and progression of human cancers.

Baylin has received a host of accolades for his work, including appointment to the Virginia and D.K. Ludwig Chair in Cancer Research at Johns Hopkins. Among many other honors and appointments during his career, he received the 2004 National Investigator of the Year Award from the NCI Specialized Program of Research Excellence and the 2005 Shubitz Cancer Research Prize from the University of Chicago.

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LPC/ LMT Guest Lecturer on Genomics and Risk Assessment

By Eddy Ball

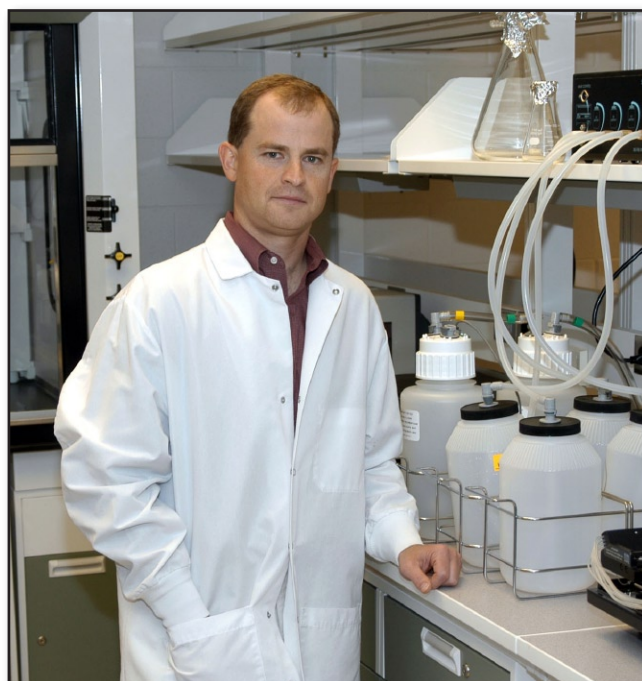
Guest Lecturer Rusty Thomas, Ph.D., spoke to a standing-room-only audience of NIEHS scientists on January 25 in F-193. The talk, sponsored jointly by the Laboratory of Pharmacology and Chemistry (LPC) and the Laboratory of Molecular Toxicology (LMT), addressed an important question, “Chemical Risk Assessment Improvement: Can Genomic Tools Provide More Power?”

Thomas is the Director of the Functional Genomics Research Program and the Gene Expression Core at The Hamner Institutes for Health Sciences in Research Triangle Park. NIEHS Director of the Office of Risk Assessment Research Chris Portier, Ph.D., sponsored the lecture.

In his talk, Thomas reported on The Hamner Institute’s progress in using genomic tools to assess health risks from chemical exposure. “Both the risk assessment community and the toxicology community have really been struggling over the past few years with how to apply these new tools...,” he explained, “and how to get the most out of them in terms of hazard identification, dose response assessment and trying to predict some of the more complex endpoints that we see after chemical exposure.” In response to these challenges, the American Chemistry Council funded a series of projects to examine how best to apply genomic tools to environmental health and risk assessment.

The process of chemical risk assessment can be broken down into a series of steps that include hazard identification and dose response assessment. In the first project, Thomas looked to apply genomic tools to the hazard identification step. Part of the hazard identification stage involves determining which chemicals pose significant risks of causing long-term health effects, such as cancer.

Thomas explained that, currently, the National Toxicology Program (NTP) rodent cancer bioassay is considered by most toxicologists the gold standard for assessing the carcinogenic potential of chemical agents, but each rodent cancer bioassay is extremely expensive, costing from two to four million dollars per chemical.



Guest Lecturer Rusty Thomas (Photo courtesy of The Hamner Institute)

Because of the cost and the length of time involved, investigators have been able to test only about 1,500 of the over 80,000 chemicals on the Environmental Protection Agency's Toxic Substance Control Act inventory.

In his studies, Thomas attempted to identify genomic biomarkers that could predict mouse lung tumor formation in a two-year rodent cancer bioassay after a 90-day exposure. Thomas exposed mice to a diverse set of 13 chemicals previously tested by the NTP. These chemicals included seven lung carcinogens and six non-carcinogens. Thomas was able to predict lung tumor formation with an overall accuracy of nearly 94 percent using gene expression changes in a select group of informative genes. This study suggested that it is possible to predict the long-term health effects of a chemical using the gene expression changes following a short-term exposure.



Automation makes it possible for researchers to screen the full-length gene library quickly to recover large quantities of data. (Photo courtesy of The Hamner Institute)

In the second project, Thomas applied genomic tools in order to understand better the underlying signaling pathways involved in the toxicologic response, using cell-based screens to identify novel modulators of selected signaling pathways. By first constructing luciferase or fluorescent protein reporters to indicate when a particular pathway is turned on, Thomas was able to specify the novel modulators involved. Robotic systems individually screened thousands of full-length genes and small interfering (si) RNA duplexes to identify which genes, when over-expressed or knocked-out inside the cell, alter the signaling of the pathway of interest.

By identifying these novel modulators and performing additional follow-up studies, Thomas is seeking to determine what molecular targets may be involved in the pathway, the overall logic of the cell signaling network, the potential shape of the dose-response curve and the degree to which this response is conserved across species. The Hamner Institute maintains a full-length gene library that contains approximately 15,000 genes and a large inhibitory RNA library that contains synthetic siRNA duplexes that target the known kinases, phosphatases and G-protein coupled receptors.

In the conclusion to his talk, Thomas readily conceded that his work is still in its infancy and that he has yet to fully answer the question posed in the title of his lecture. However, Thomas has seen enough promising data in his preliminary studies to keep working toward his goal — integrating genomic tools into toxicology and chemical risk assessment.

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Guest Lecturer Discusses Health Risks of Flame Retardant Compounds

By Eddy Ball

On February 8, a capacity audience of NIEHS scientists gathered for a guest lecture by former NIEHS scientist Linda S. Birnbaum, Ph.D. Birnbaum spoke on the topic of “Brominated Flame Retardants: What We Know and What We Don’t.”

Birnbaum is currently the director of the Experimental Toxicology Division at the Environmental Protection Agency. She is an internationally recognized authority on the potential health risks posed by the brominated chemical flame retardants that are present in consumer products found in virtually every home and workplace in North America.

The Laboratory of Pharmacology and Chemistry (LPC) and the Laboratory of Molecular Toxicology jointly sponsored Birnbaum’s presentation. LPC Chemist Tom Burka, Ph.D., hosted the lecture.

Despite successful efforts to ban several kinds of brominated flame retardants (BFRs), the chemicals continue to concern environmental scientists. Products that contain banned BFRs are still in use, and concentrations of these compounds in people are rising sharply. Recent research suggests that “safer” alternatives promoted by the chemical industry may be little better than the banned chemicals.

Many of the BFRs are bio-accumulative and persistent, and function as endocrine disruptors in animals. BFRs are widely dispersed and have been found in animals living in environments where the compounds are not commonly used, such as the Arctic. “We’ve got lots of it in the air,” Birnbaum noted as she described the worldwide distribution of the chemicals and the high levels in indoor environments.

According to Birnbaum, BFRs are very effective in preventing fire and protecting firefighters by reducing the risk of flash-over, the sudden and intense burst of flames from smoldering material that is a major cause of death among first responders. BFRs are present in such products as carpets, upholstery, plastics, styrofoam and wire insulation. Since the introduction of the compounds in the 1970s, manufacturers have used BFRs more widely in the United States than anywhere else in the world, primarily because of the stringent fire regulations in this country.

Birnbaum focused her talk on five of the most widely used BFRs. They include tetrabromobisphenol A (TBBPA), hexabromocyclododecane (HBCD) and three forms of polybrominated diphenyl ethers (PBDEs), known as Penta, Octa and Deca.

All of these brominated compounds cause concern among environmental scientists due to their potential toxicity or mutagenicity in animal studies and their ability to function as endocrine disruptors. However, Birnbaum devoted most of her lecture to reviewing the available information on the more volatile, persistent and potentially more dangerous PBDEs.

Because of the compounds’ persistence and presence in products still in use, Penta and Octa, though no longer produced, are still a concern. New information about Deca, which industry groups have promoted as the “safer” form, suggests that it may in fact break down into Penta and Octa and pose just as much of a health risk.



*EPA Toxicologist Linda Birnbaum
(Photo courtesy of Steve McCaw)*

PBDE levels in human milk are highest in the United States and Canada and are doubling every two to five years. In the very limited sampling performed thus far, scientists have found large inter-individual variation of levels in human milk. Data presented by Birnbaum indicate that five percent of the population, for example, has ten times the mean level, and one percent has 100 times the mean level.

Studies on PBDE exposure in animals suggest that there are potentially significant health effects. Researchers have found a strong association between PBDE levels and disruption in estrogen, androgen and thyroid hormones. The compounds may alter cell signaling, induce enzymes and be toxic to the liver and nervous system, affecting detoxification, cognitive function and development. PBDEs also appear to have additive effects when combined with other toxins.

Birnbaum repeatedly pointed to the significant gaps in the research so far on PBDEs, especially in regard to humans. “If you don’t look,” she lamented, “you don’t find.” Throughout the lecture, Birnbaum emphasized that scientists need to understand better the mechanisms involved, the consequences of inter-individual variability and the roles of the different metabolites of PBDEs.

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Upcoming Distinguished Lecturer

By Eddy Ball

University of Southern California (USC) Distinguished Professor Peter Jones, Ph.D., will deliver the next talk in the 2006-2007 NIEHS Distinguished Lecture Series at 11:00 a.m. on March 13 in Rodbell Auditorium. Jones is director of the USC/Norris Comprehensive Cancer Center and holds the H. Leslie Hoffman and Elaine S. Hoffman Chair in Cancer Research. He will speak on “How the Epigenome Changes in Cancer.”

Jones’ laboratory studies of DNA methylation in human cancer focus on the biochemical mechanisms by which cytosine methylation patterns are changed. His lab is particularly interested in these changes with respect to the cell cycle and seeks to determine how this process is involved in the transformation of human cells. Jones is working to understand fundamental aspects of the control of DNA methylation as it relates to the *de novo* methylation of the promoter regions of tumor suppressor genes. This epigenetic mechanism by which tumor suppressor genes can be inactivated may be an important pathway which contributes to carcinogenesis in a wide variety of tumors.

Laboratory of Molecular Carcinogenesis Chief Trevor Archer, Ph.D., is host of the lecture.

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*Distinguished Guest Lecturer Peter Jones
(Courtesy of the University of Southern California)*

Upcoming LMG Guest Lecturer

By Jan Drake

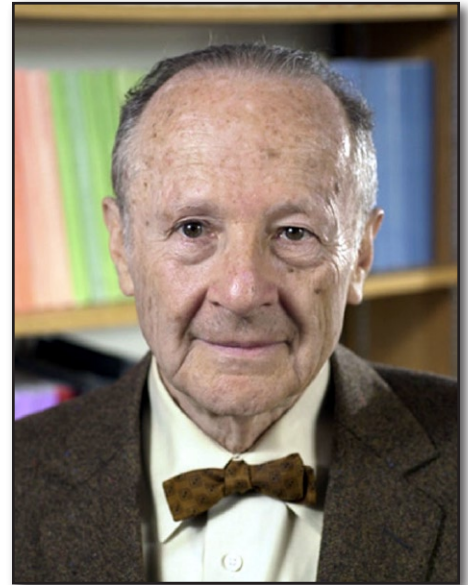
Matthew Meselson, Ph.D., will explore the question “What Maintains Sexual Reproduction?” in a Laboratory of Molecular Genetics (LMG) Trainee Seminar Series Lecture on March 9 at 10:00 a.m. in Rodbell Auditorium. Meselson is the Thomas Dudley Cabot Professor of the Natural Sciences at Harvard University and an adjunct scientist at the Marine Biological Laboratory in Woods Hole, Cape Cod, Mass.

Meselson’s contributions to molecular biology include the development of equilibrium sedimentation of macromolecules in density gradients, the experimental proof of the semi-conservative nature of DNA replication, the demonstration of a break-reunion mechanism of genetic recombination in phage lambda, the discovery of the methylation-based mechanism that protects DNA against restriction enzymes, and the elucidation of DNA mismatch repair.

Meselson’s current research is focused on the evolution and consequences of sex. The objective of his research is to understand why nearly all animals and plants reproduce sexually and why the loss of sexual reproduction usually leads to early extinction. He is studying an asexual rotifer species in an effort to understand why it appears to be an exception.

LMG Fellow Libertad Garcia Villada, Ph.D., is hosting Meselson’s visit.

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*Biologist Matthew Meselson
(Photo courtesy of Harvard University)*



DETR Papers of the Month

By Jerry Phelps

Asthma Exacerbated by Exposure to Florida Red-Tide Toxins

Some of the most deadly and potent natural toxins known are derived from harmful algal blooms known as red tides. The microalgae *Karenia brevis* causes red tides each year throughout the Gulf of Mexico. The organism produces a highly potent toxin called brevetoxin. NIEHS grantee Dan Baden from the University of North Carolina at Wilmington and colleagues report in the journal *Chest* that exposure to brevetoxins exacerbates asthma symptoms in people with physician-diagnosed asthma.

Brevetoxins are sodium channel blockers and may activate histamine leading to immune responses. Previous research in laboratory animals demonstrated that brevetoxins caused airway constriction, a classic symptom of asthma. The new research was conducted in 97 asthmatics who visited a beach for one hour during periods with and without active algal blooms. They carried personal air monitors that were later used to determine the concentration of toxin they were exposed to. All 97 subjects had more difficulty breathing after exposure to brevetoxin, as determined by a questionnaire and by a series of airflow tests.

These findings could have major implications for asthmatics living near beaches in the Gulf of Mexico region since red tides occur frequently there. Future research will focus on more in-depth analysis of susceptible populations and the potential for long-term effects of brevetoxin exposure.

Citation: [Fleming LE, Kirkpatrick B, Backer LC, Bean JA, Wanner A, Reich A, Zaias J, Cheng YS, Pierce R, Naar J, Abraham WM, Baden DG.](#) 2007. Aerosolized red-tide toxins (brevetoxins) and asthma. *Chest* 131(1):187-194.

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Bisphenol-A Alters Fetal Mammary Gland Development in Mice

New work from the laboratory of NIEHS grantee Ana M. Soto at Tufts University School of Medicine illustrates that female mice exposed to bisphenol-A (BPA) *in utero* from days 8 to 18 of fetal development experience alterations in mammary gland development.

Pregnant female mice were given an environmentally relevant dose of BPA daily from gestational days 8 to 18. The mammary glands of the female pups were evaluated on gestational day 18. Results showed that this dose of BPA, which fell within the range of estimated human exposure, sped development of the fat pad and altered collagen localization in the stromal region of the glands. In the mammary epithelium, BPA exposure delayed lumen formation and led to decreases in cell size.

BPA's current uses are as a component in polycarbonate plastic and resins. BPA has been known to leach from plastics that are cleaned with harsh detergents or used to contain acidic or high temperature liquids. The chemical is found in most people who live in developed countries.

BPA activates estrogen receptors, resulting in similar physiological effects to those caused by the body's own naturally occurring estrogens. Other studies have demonstrated that fetal exposure to bisphenol A increased the chances of breast cancer in laboratory rats. Soto's work expands the knowledge of the effects of BPA and suggests that alterations in mammary glands observed at puberty and in adulthood in perinatally exposed mice originate during fetal development.

Citation: [Vandenberg LN, Maffini MV, Wadia PR, Sonnenschein C, Rubin BS, Soto AM.](#) 2007. Exposure to environmentally relevant doses of the xenoestrogen bisphenol-A alters development of the fetal mouse mammary gland. *Endocrinology* 148(1):116-127.

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Urinary Arsenic Levels Correlate with Intelligence Scores

Research findings from the laboratory of NIEHS grantee Allan Smith at the University of California-Berkeley demonstrate adverse effects on children's intellectual function and intelligence associated with urinary arsenic levels.

The study was carried out in West Bengal, India, a region known for high levels of arsenic in ground water. The 351 children in the study were divided into three groups according to high, medium, and low urinary arsenic. The intelligence test results showed a decline of 12 percent for a vocabulary test, 21 percent for an object assembly test, and 13 percent in a picture completion test for the children in the high urinary arsenic group. These findings were similar to another NIEHS-supported arsenic study in neighboring Bangladesh.

Acute neurotoxic effects of arsenic have been well documented and include short-term memory loss and problems in learning and concentration. Children are known to be particularly susceptible to the neurotoxic effects of other metals, especially lead and mercury. Limited evidence from animal studies and earlier studies in children gave some indication that arsenic is associated with neurodevelopmental delays. The current findings need to be confirmed; however, they add to the body of knowledge of the adverse health effects of arsenic in children.

Citation: [von Ehrenstein OS, Poddar S, Yuan Y, Mazumder DG, Eskenazi B, Basu A, Hira-Smith M, Ghosh N, Lahiri S, Haque R, Ghosh A, Kalman D, Das S, Smith AH.](#) 2007. Children's intellectual function in relation to arsenic exposure. *Epidemiology* 18(1):44-51.

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Lead and Mercury Disrupt Neuronal Stem Cells

Groundbreaking research from Mark Noble at the University of Rochester concludes that low levels of diverse environmental agents, namely lead, methylmercury and paraquat, disrupt the normal functioning of progenitor cells within the central nervous system.

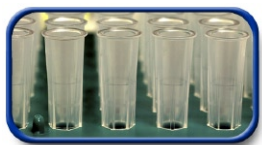
Noble and his colleagues found a previously unknown mechanism by which these agents cause the effects. The agents make the cells more oxidized, which causes the activation of an enzyme known as Fyn kinase, which in turn activates another enzyme called c-Cbl. C-Cbl modifies and degrades protein receptors necessary for cell division and survival. When the receptors are degraded, their downstream signaling pathways are repressed and the cells fail to divide and develop properly.

The work was conducted in cell cultures of glial progenitors, advanced-stage stem cells important for the growth and development and normal functioning of the central nervous system. The cells proved to be exquisitely sensitive to minute levels of the toxicants. The pathway they activate is a normal cellular regulatory pathway; however, according to the authors, "they are just activating it inappropriately."

The discovery of a molecular target that is shared by a variety of compounds may represent a new tool for rapidly screening compounds to determine their potential neurotoxicity. It may also provide insights into how to protect cells from the signaling disruption once exposure has occurred.

Citation: [Li Z, Dong T, Proschel C, Noble M.](#) 2007. Chemically diverse toxicants converge on Fyn and c-Cbl to disrupt precursor cell function. *PLoS Biol* 5(2):e35.

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DIR Papers of the Month

By Eddy Ball

Unique Substrate Specificity of DNA Polymerase Mu

Scientists from the Laboratory of Structural Biology and Laboratory of Molecular Genetics have demonstrated substrate interactions unique to polymerase mu (pol μ), an enzyme involved in a type of DNA repair called nonhomologous DNA end-joining (NHEJ). The NIEHS-funded study appeared in the January 2007 issue of *Nature Structural & Molecular Biology*.

Pol μ is one of four closely related members of the family X DNA polymerases in mammals. These enzymes participate in the repair of double-strand breaks (DSBs) in DNA in order to maintain stability and replicate large genomes. Anomalies in the repair of DSBs can lead to mutations and threaten the viability of an organism. While studies have demonstrated that pol μ associates with end-joining factors *in vitro* and is able to repair gapped intermediates in an NHEJ reaction, the specific substrate interactions of pol μ have not been well understood. Investigators had previously explained structures for the remaining family members, polymerase beta (pol β), polymerase lambda (pol λ) and terminal deoxyribonucleotidyl transferase (TdT).

In this experiment, the research team crystallized the polymerization domain of mouse pol μ and described its structure. The study found substrate interactions and functions that differ from those found in pol β , pol λ and TdT in several notable ways that may prove biologically relevant.

Citation: [Moon AF, Garcia-Diaz M, Bebenek K, Davis BJ, Zhong X, Ramsden DA, Kunkel TA, Pedersen LC.](#) 2007. Structural insight into the substrate specificity of DNA Polymerase μ . *Nat Struct Mol Biol* 14(1):45-53.

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Receptor Regulation in Liver Regeneration

Scientists in the Pharmacogenetics Section of the Laboratory of Reproductive and Developmental Toxicology have demonstrated the therapeutic potential of phenobarbital (PB) treatment in the modulation of liver regeneration. The NIEHS-supported study, published in the January 2007 issue of *The Journal of Pharmacology and Experimental Therapeutics*, investigated the regulation of the enzyme type 1 diiodinase (D1) and thyroid hormone activity in the regenerating mouse liver by constitutive active/androstane receptor (CAR).

Researchers experimented with wild type and CAR-knockout mice following partial hepatectomy (PH) and treatment with PB. Liver injury increased levels of reverse triiodothyronine (rT3), which in turn repressed the expression of key thyroid-regulated genes in the liver. This increase in rT3 may also be involved in a slight decrease in levels of total tetraiodothyronine (T4), the most common thyroid hormone. Treatment with PB normalized rT3 levels and levels of D1 in a CAR-dependent manner, but only in wild type mice.

Thyroid hormone has a well established role in liver regeneration and energy use. These hormones regulate genes involved in the metabolism of sugars and fatty acids. This research demonstrates that PB or other CAR activators may restore normal biosynthesis of thyroid hormones and help the liver regenerate following such events as transplantation, chemical exposure and physical injury or resection.

Citation: [Tien ES, Matsui K, Moore R, Negishi M.](#) 2007. The nuclear receptor constitutively active/androstane receptor regulates type 1 deiodinase and thyroid hormone activity in the regenerating mouse liver. *J Pharmacol Exp Ther* 320(1):307-313.

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Cancer and Organochlorine Insecticides

In a study funded by NIEHS and the National Cancer Institute, epidemiologists investigated the relationship between site-specific cancer incidence and organochlorine (OC) insecticide use among private pesticide applicators, primarily farmers, in Iowa and North Carolina enrolled in the Agricultural Health Study (AHS).

The seven OC chemicals included in the study were aldrin, chlordane, DDT, dieldrin, heptachlor, lindane and toxaphene. The chemicals were widely used in agriculture between the 1940s and 1960s. State and federal regulations banned or limited their use in the 1970s and 1980s because of concerns over their environmental persistence and possible health effects.

The scientists examined data from 25,291 participants who had completed a take-home questionnaire eliciting information on comprehensive exposure to 28 pesticides in addition to the detailed information on 22 pesticides provided during enrollment. The researchers identified cancers through December 31, 2002, using cancer registries from Iowa and North Carolina.

The study, which appeared in print in the February 2007 issue of the *International Journal of Cancer*, did not find any clear relationship between cancer risk and the use of this group of insecticides. The researchers did, however, observe associations among specific chemicals, some of which are supported by previous research and warrant further investigation.

Citation: [Purdue MP, Hoppin JA, Blair A, Dosemeci M, Alavanja MC.](#) 2007. Occupational exposure to organochlorine insecticides and cancer incidence in the Agricultural Health Study. *Int J Cancer* 120(3):642-649.

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Organochlorines and Breast Cancer among African-American Women

A team of researchers that included NIEHS Senior Investigator Matthew Longnecker, M.D., found no significant association between levels of two organochlorines (OCs) in blood and breast cancer risk in a study of African-American women. Their research, funded partially by NIEHS and published in the February 2007 issue of *Cancer Causes and Control*, is the largest case-control study of African-American women to date and the first to examine factors related to tumor status.

The team selected 355 cancer patients and 327 controls from the African-American women participating in the Los Angeles component of the Women's Contraceptive and Reproductive Experiences (CARE) Study, a population-based, case-control study of lifestyle factors and breast cancer risk. Participants provided serum samples, which were analyzed for levels of two common OCs, polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethenes (DDE), the metabolite of the pesticide DDT. The researchers also obtained status in regard to estrogen receptor (ER) and progesterone receptor (PR), p53 and HER-2/*neu* gene over-expression, and chemotherapy.

“This study did not find an increased risk of breast cancer in African-American women from PCBs or DDE at the levels measured in serum, nor was there evidence for effect modification by tumor ER or PR status, or HER-2/*neu* or p53 expression,” the researchers concluded.

Citation: [Gatto NM, Longnecker MP, Press MF, Sullivan-Halley J, McKean-Cowdin R, Bernstein L. 2007. Serum organochlorines and breast cancer: a case-control study among African-American women. Cancer Causes Control 18\(1\):29-39.](#)

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Inside the Institute

NIEHS Challenge Team Brings “Scores of Spores” to the Small Screen

By Eddy Ball

During a lunch-time presentation on February 8, Health Science Administrator Mike Humble, Ph.D., gave his colleagues a behind-the-scenes look at how an NIEHS team played its part in the 2006 Discovery Channel Young Scientist Challenge (DCYSC). Filmed last October at the NIH Clinical Center in Bethesda, highlights of the event were featured in a television special aired last month.

The NIEHS competition was called “Scores of Spores: Mold, Human Health and the Indoor Environment” and featured a welcome and introductory video of NIEHS Director David Schwartz, M.D., discussing health problems linked to exposure to molds. The “Scores of Pores” mold challenge called upon the young scientific investigators to detect evidence of mold in the indoor environment, collect samples, identify the molds and recommend effective remediation for a hypothetical school setting.



After dreaming of an entire house for a set, what the NIEHS team finally ended up with was a small lab. (Photo courtesy of Mike Humble)

Each year since 1999, the Discovery Channel has chosen a theme for the Young Scientist Challenge and contacted a scientific organization to design age-appropriate exercises for the competition. Working with the 2006 theme, “Disease Detectives,” NIEHS, along with three other institutes and the NIH Clinical Center, created hands-on health-related scientific activities linked to such global health concerns as mold, avian flu and obesity.

Working with Arts and Photography, NIEHS scientists created an introductory presentation showing the life cycle of mold, where it is found, the positive and negative aspects of mold, health concerns related to mold, ways to detect it and remediation strategies. The team created special lab books for collecting and recording data, a booklet for each team's final report, a mold identification key with color photographs of the most common indoor molds, and instruction manuals for the sample collection equipment used in the challenge. Along with collection equipment, the young people had access to high-quality microscopes and sealed Petri dish samples to help them identify the molds.

The Discovery Channel describes the Young Scientist Challenge as the nation's premier science contest for students in grades 5-8. Contestants are the 40 middle-school finalists selected from the more than 60,000 students around the United States who participate in science and engineering fairs affiliated with Science Service. Judges select the finalists based on their exceptional performance in oral, visual and written presentations.

The 40 young scientists selected in 2006 aspired to become "America's Top Young Scientist of the Year" and take home a scholarship of \$20,000. Second and third place winners received \$10,000 and \$5,000

The NIEHS Challenge Team

Although Humble and Salo were the main figures at "ground zero" in Bethesda throughout filming, the Challenge Team included many people from DIR, DERT and Arts and Photography who put in a lot of time and hard work making the challenge a success.

DIR: Sam Arbes, D.D.S., Perry Blackshear, M.D., Patricia Chulada, Ph.D., Stephanie London, M.D., David Schwartz, M.D., and Daryl Zeldin, M.D.

DERT: Liam O'Fallon

Arts and Photography: Paul Cacioppo, John Maruca and Steve McCaw

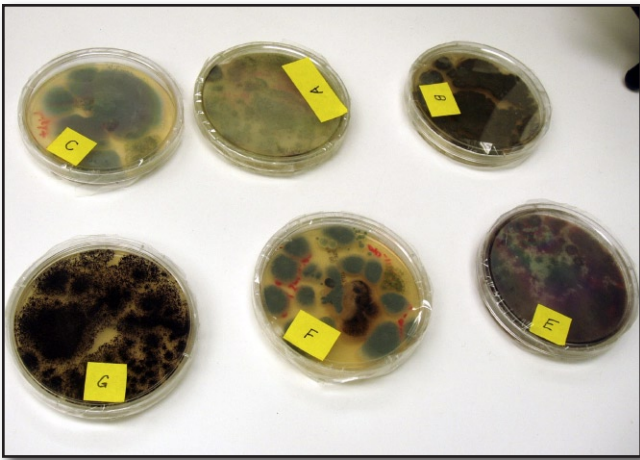
In addition, many other NIEHS employees and contractors helped out when the team needed supplies, equipment and goodies for the students. When it came to making the project happen, Humble noted, "Everybody went to bat for us and helped however they could."



While the kids ran their experiments, the Discovery crew filmed from the other side of the bench. NIEHS Team Member Pat Chulada, left, looked on during one of the scenes. (Photo courtesy of Mike Humble)



Space was always at a premium during filming. Here the Discovery crew maneuvers in for a shot over the heads of the young researchers. (Photo courtesy of Mike Humble)



Some of the samples the kids collected were “mock mold,” but thanks to Pat Chulada’s New Orleans connections, the mold in these Petri dishes was very real. (Photo courtesy of Mike Humble)



Parents were excluded from the competition and filming, but they joined their children at a reception and banquet afterwards. (Photo courtesy of Mike Humble)

scholarships, and the remaining finalists got \$500 scholarships for completing the competition. All finalists received an all-expense-paid trip to Washington, D.C., event shirt, \$50 gift certificate, DCYSC medal and plaques. In addition, DCYSC awarded 15 additional prizes, such as a week in Space Camp or at the National Zoo, for other team and individual accomplishments.

According to Humble, the competition wasn’t nearly as much about accuracy as about scientific problem solving, communication and team work. Identifying molds is a challenge even for experts, and some of the sites used “mock mold” created by NIEHS scientists. After the teams completed their challenge activities, they presented their results and recommendations to the NIEHS scientists and judges.



Humble, the team’s skeletal mascot, “Bones,” Chulada and Salo were eager to head back to RTP after an exhausting weekend of activities and filming. (Photo courtesy of Mike Humble)

As much fun as the team had, Humble quickly dispelled any illusions about the glitz and glamour of working in TV. In the course of putting the NIEHS challenge together, he recalled, the team dealt with shifting expectations and false starts, while struggling to finish the project on time. Once the filming began, Humble and Laboratory of Respiratory Biology Fellow Paivi Salo, Ph.D., spent long, nerve-racking days under hot lights in crowded working conditions.

“We were told initially that ‘the sky was the limit’ in the creation and construction of our challenge” Humble explained, “but in the end we found ourselves in one bay of a lab.” Still, despite all the difficulties he faced throughout the process, Humble thoroughly enjoyed the experience of working with the Discovery Channel crews. “This has got to be one of the highlights of my career here,” he admitted, and he speculated, only partly in jest, about moving into TV production full-time one day.

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Tony Drake Retires from NIEHS Facilities Engineering Branch

By Eddy Ball

On February 2, Pipe Fitter Tony Drake retired from NIEHS after 33 years of government service. Drake began his career with the Institute in 1973 as a plumber in the Office of Facilities Engineering. His work has taken him outdoors and between floors, installing and repairing the utilities that keep the Institute operating.

Drake began work when NIEHS was still temporarily headquartered on the North Campus in Building 6 and moved to the South Campus when the new facility opened nine years later. For much of his career at South Campus, Drake worked out of the 102 building where the Facilities Engineering Branch has its offices, store rooms and shops.

For 12 years (1984-1996) Drake worked a shift schedule as a utilities systems repairer-operator in the main building, but he returned to the Facilities Engineering Branch where he finished his NIEHS service as a pipe fitter. “I kinda got tired of the shift work,” he commented, “so I came back over here, and that’s where I’ve been ever since.”

Moving on the next phase of his life, Drake said he will miss many things about his job at NIEHS. “I’ve enjoyed everybody here, and I hate to leave,” he observed. “I’ve met a lot of people and made a lot of friends. It’s been a wonderful place to work.” The Institute has recognized Drake for his quality work over the years, and his job has taken him to nearly every part of the operation, giving him a chance to meet nearly everyone at NIEHS.

However, Drake said he won’t miss the three hours he spent commuting every day in recent years. Although the Garner native lived during most of his NIEHS career in his hometown and in Apex, he and his wife, Kay, moved to their dream house on Lake Gaston a few years ago. Since then, Drake has driven 168 miles getting to and from work each day, dealing with the traffic on I-85 and spending increasing amounts of money for gasoline and maintenance.

After four days of getting used to staying at home for a change, Drake, his wife and their two Labrador Retrievers took to the road for a series of trips in their motor home across the North American Continent. They traveled first to the North Carolina Coast to join his brother- and sister-in-law and then wound their way toward Florida by way of Charleston and Savannah, before driving west across the panhandle, through Alabama and Mississippi to Louisiana, and then back to Lake Gaston.



In his final week at NIEHS, Drake was outdoors working on his backhoe in search of buried utility lines. (Photo courtesy of Steve McCaw)



Drake (center) posed with some of his many friends and well-wishers at the Facilities Engineering Branch. (Photo courtesy of Steve McCaw)

The Drakes intend to return to the road after a short break at home. Drake wants to drive north into Canada, spend some time in Nova Scotia and then make his way through Canada to Alaska. On the return trip east, the couple plans to take the northern route back across the United States before making their way back home.

In between their travels, Drake and his wife will visit their daughter, an attorney, and her family who live in Clayton. Drake plans to stay busy working around the house and at a part-time job to build up his Social Security earnings. He also has some quiet time scheduled on his porch overlooking the lake, and he'll almost certainly work in a little fishing time as well.

When he departed NIEHS for this more leisurely phase in his life, Drake offered some words of encouragement to his friends at NIEHS. "Keep up the good work that's been going on around here," he said. "Everybody just needs to hang in there, and their time will come too."

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Alexandra Heinloth Leaves NIEHS to Work in the Private Sector

By Eddy Ball

On January 26, friends and colleagues packed into Rall D-250 to offer their best wishes to Alexandra Heinloth, M.D., who left NIEHS after working at the Institute as a fellow for the past six years. Heinloth was an investigator in the Laboratory of Molecular Toxicology of the Environmental Toxicology Program. In January, she accepted a position in clinical research at i3 Statprobe in Cary, a division of United Health Group, and assumed her new duties in February.

A native of Germany, Heinloth received her medical degree in 1998 from the University of Würzburg, which was founded in 1402 and is known in Bavaria as Julius-Maximilians Universität. She interrupted her residency in internal medicine at the university hospital in 2000 to pursue basic research training as a post-doctoral fellow at NIEHS. In 2006, she accepted an offer of a visiting research fellowship.

During her tenure at NIEHS, she worked under the direction of Senior Scientist Rick Paules, Ph.D., whom she described as "an excellent mentor." They collaborated in several programs sponsored by the former National Center for Toxicogenomics (NCT). She was part of the NIEHS Microarray Group, developing the technology used to monitor the expression of thousands of genes and analyze expression patterns.

She also worked with the Growth Control and Cancer Group in the Laboratory of Environmental Carcinogenesis and Mutagenesis. While at NIEHS, she co-authored 14 peer-reviewed studies and participated in numerous conferences and other professional development activities. "The Institute's emphasis on helping fellows publish in peer-reviewed journals was a real plus," she said. "With the encouragement of Rick [Paules] and my other colleagues at NCT and NTP [National Toxicology Program], I was able to develop my CV [curriculum vitae] while I was here."



*Research Fellow Alexandra Heinloth, M.D.
(Photo courtesy of Steve McCaw)*

As an NCT researcher, Heinloth participated in studies with the ToxPath Team, whose mission was to design and conduct seminal studies that provide definition to and stimulate development in the field of toxicogenomics. The team integrated global “omics” approaches into conventional studies of toxicity and disease processes. An important part of her duties with NCT involved monitoring the conduct of NCT programmatic studies outsourced to contract laboratories.

Heinloth will combine her training in medicine with her NIEHS laboratory research experience in her new position. i3 Statprobe is a full-service, global clinical research organization that is therapeutically focused on oncology, central nervous system disorders, endocrinology, and respiratory and infectious disease. As a part of i3 Statprobe, Heinloth will participate in clinical research and serve as a medical writer.

As much as she appreciated her educational experiences at NIEHS, Heinloth is ready for her new work. “I’m looking forward to utilizing more of my medical training in clinical research,” she explained. “I certainly wouldn’t rule out returning to NIEHS one day — it’s been a wonderful experience — but for now I want to do more translational research.”

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Calendar of Upcoming Events

- **March 1** in Rall F193, 10:30 – 11:30 — Seminar with Max Costa, Ph.D., speaking on “Epigenetic Mechanisms of Nickel Carcinogenesis”
- **March 7** in Rodbell C, 3:30 – 4:30 — Seminar with Tyrone Hayes, Ph.D., speaking on “From Silent Spring to Silent Night: The Connection between Pesticides, Amphibian Declines and Cancer”
- **March 8** in Rodbell, 8:30 AM – 3:30 PM — 2007 Environmental Stewardship Initiative Meeting featuring William G. Ross, Jr., NC DENR
- **March 9** in Rodbell, 10:00 – 11:30 — LMG Special Seminar Series with Matt Meselson, Ph.D., speaking on “What Maintains Sexual Reproduction?”
- **March 13** in Rodbell, 11:00 – 12:30 — Distinguished Lecture Seminar Series with Peter Jones, Ph.D., speaking on “How the Epigenome Changes in Cancer”
- **March 14 (off campus event)** in the Toxicology Building on the NCSU Centennial Campus, 8:30 AM. – 5:00 PM — Randy L. Rose Memorial Symposium: Human Metabolic Interactions of Environmental Chemicals. To register, contact [Dr. Ernest Hodgson](#).
- **March 14 (off campus event)** in Jones Auditorium, Meredith College, at 7:00 PM — Center for Women and Science Community Outreach Lecture with Judy Norsigian, Executive Director of *Our Bodies-Our Selves*, speaking on “Stem Cell Research and the Implications for Women’s Health.” [RSVP and Information](#)
- **March 16** in Rodbell, 9:00 – 10:00 — Director’s Weekly Seminar (speaker to be announced)

- **March 20** in Rodbell, 10:30 — Spirit Lecture Series featuring Alice Huang, Ph.D.
- **March 20 (off campus event)** in 408 Mary Ellen Jones Building, UNC-CH, at 11:00 — Biochemistry and Biophysics Lecture with John Cidlowski, Ph.D., speaking on “Glucocorticoids: New Mechanisms for Generating Tissue Specific Actions of Steroid”
- **March 20 (off campus event)** in 1102 Mary Ellen Jones Building, UNC-CH, at 4:00 — Pharmacology Lecture with James Putney, Ph.D., speaking on “Molecular Basis of Capacitative Calcium Entry”
- **March 20 (off campus event)** in Women’s Center, Duke West Campus, 5:15 – 7:00 PM — Graduate and Professional Women’s Network screens the film [“Made in Thailand”](#) about women workers; [RSVP and Food Preference](#)
- **March 21** in Nottingham 201, 10:00 – 12:00 — Marketplace 2007 Small Business Regional Planning Meeting
- **March 21** in Rall D350, 12:00 – 1:00 — LMG Seminar Series with Sue Jinks-Robertson, Ph.D., speaking on “Genome Stability and the 3 r’s in Yeast”
- **March 21** in Rodbell C, 2:00 – 3:30 — Mayumi Case, Raleigh Ki-Akido, speaking on “Self Defense for Women Using Mind/Body Coordination”
- **March 26 and 27** in Rodbell, 9:00 AM – 5:00 PM — Board of Scientific Counselors Review of LMC and Former NCT

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