



Environmental Factor

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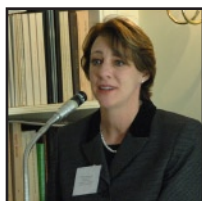
NIEHS Spotlight



Superfund Basic Research Program Anniversary

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acknowledge the program's many laurels — and look forward to new challenges. ...[read more](#)



Leadership and Gender Symposium for Latinas

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was the site of a symposium focused on the needs of women in science. ...[read more](#)



NTP Board of Scientific Counselors Meets

With an observation that "this is a very active time in this field of ours," NIEHS/NTP Acting Director Sam Wilson, M.D., opened the fall 2007 meeting of the

NTP Board of Scientific Counselors (BSC) on December 6 in Rodbell Auditorium.[read more](#)



Former Postdoc Awarded Cancer Scholarship

Less than eight months after completing her postdoctoral fellowship at NIEHS, molecular geneticist Francesca Storici, Ph.D., became one of 29 researchers

selected as Georgia Cancer Coalition Distinguished Cancer Scholars for 2008. ...[read more](#)

Science Notebook



Translesion DNA Synthesis Uses Specialized Polymerases

On December 11, Errol C. Friedberg, M.D., delivered a seminar about DNA damage and repair to a near capacity audience in Rodbell Auditorium.

The seminar, titled "Specialized DNA Polymerases in Higher Organisms: Insights from the Polk [polymerase kappa] Knock-Out Mouse," was part of the NIEHS Distinguished Lecture Series. ...[read more](#)



Study Links Gene Expression Changes in Babies and Arsenic Exposure

In a study made possible by NIEHS extramural funding, a team of researchers from the Massachusetts

Institute of Technology (MIT) and Thailand's Chulabhorn Research Institute (CRI) have identified for the first time a highly predictive biomarker gene set for prenatal arsenic exposure. ...[read more](#)



Superfund Looks to Its Future

After two days of sharing the excitement of their science and recounting the accomplishments of the Superfund Basic Research Program (SBRP), on December 5 attendees at

the twenty-year anniversary celebration were confronted with the mass of unfinished business still to address and the challenges the program is sure to face in the future.[read more](#)

NIEHS Spotlight



Environmental Justice Grantees Meet in Boston

It may have been cold and overcast in Boston during the December 10-12 gathering of grantees in the NIEHS Environmental Justice

Research Program, but the atmosphere indoors was anything but gloomy. ...[read more](#)



Bucher Announces NTP Realignment

During his report to the National Toxicology Program (NTP) Board of Scientific Counselors on December 6, NTP Associate Director

John Bucher, Ph.D., presented an update on the realignment of the program within the NIEHS Division of Intramural Research. ...[read more](#)



NIEHS Kicks Off Transportation and Health Workshop

In spite of the bad luck associated with its ordinal designation, Workshop 13 in the Institute of Medicine's (IOM) ongoing Roundtable on Environmental Health

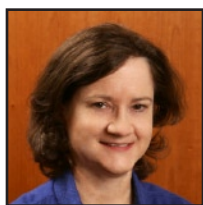
Sciences, Research and Medicine may turn out to be its luckiest so far.[read more](#)



Jayes Accepts Duke Research Position

It won't be much consolation for her colleagues in the NIEHS Trainees Assembly (NTA) who will miss her energy and dedication to her fellow

trainees. But the loss of Friederike Jayes, D.V.M., Ph.D., for NIEHS will be a gain for students at Duke University Medical Center. ...[read more](#)

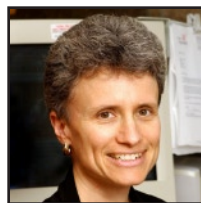


Noteworthy Developments

In the closing months of 2007, NIEHS Health Science Administrator Cindy Lawler, Ph.D., was named to a new Interagency Autism Coordinating Committee, and NIEHS postdoctoral alumna and pharmacologist Julianne Hall, Ph.D., returned to

RTP to assume a position as a research investigator at the Hamner Institutes, formerly CIIT.[read more](#)

Science Notebook



Higher BMI Worsens Ozone Effect

A new study published in *Inhalation Toxicology* and co-authored by two NIEHS researchers, Stephanie

London, M.D., and Grace Kissling, Ph.D., provides the first evidence that people with higher body mass index (BMI) may have a greater response to ozone exposure than leaner people. ...[read more](#)



Low Dose Arsenic Can Be an Endocrine Disruptor

The U.S. drinking water supply contains several naturally occurring contaminants, such as potassium, arsenic, manganese and radium,

as well as a number of organic contaminants including chlorination by-products and groundwater contaminants. ...[read more](#)



Upcoming Distinguished Lecture Features Richard A. Flavell

The 2007-2008 NIEHS Distinguished Lecture Series continues at 11:00 a.m. on January 8 with a talk by

Richard A. Flavell, Ph.D., on "Innate and Adaptive Immunity." ...[read more](#)

Inside the Institute



NIEHS Holds Awards Day

On December 13, NIEHS honored employees at the Director's Annual Honor Awards Ceremony in Rodbell Auditorium. The event was chaired by

Director of Education and Biomedical

Research Development Marian Johnson-Thompson, Ph.D. ...[read more](#)



Diversity Council Hosts Native American Heritage Concert

True to tradition, the NIEHS Diversity Council gave NIEHS employees and contractors something a little different when it presented a concert in the

NIEHS cafeteria by R. Carlos Nakai and Keola Beamer in celebration of Native American Heritage Month November 30. ...[read more](#)



Institute Celebrates the Season

Members of the NIEHS community, who put their best efforts into advancing science during the rest of the year, are also accomplished at ushering in the solstice season.

During the weeks leading up to the two-day holiday, the festive season gives contractors and employees an opportunity to show off their goofy ties, silly sweaters, and ridiculous hats and to decorate office doors with wrapping paper, ribbon and bows.[read more](#)



Clinical Research Unit Takes Shape

The factory-built modular units that will make up the new Clinical Research Center arrived right on schedule in early December, and

workers started placing the units and connecting them together to create a structure resembling the artist's rendition posted on the NIEHS web site.[read more](#)

Extramural Research

Extramural Update

The Superfund Basic Research Program (SBRP) announced that Roxanne Karimi, Ph.D., of Dartmouth College is the recipient of the tenth annual Karen Wetterhahn Memorial Award. The award was presented on December 4th, 2007 at the SBRP 20th Anniversary Annual Meeting in Durham, N.C., by NIEHS Division of Extramural Research and Training Acting Director Dennis Lang, Ph.D. ...[read more](#)

Extramural Papers of the Month

- [Beyond the Human Genome Sequence: Scientists Map "Silenced Genes"](#)
- [Bisphenol A Effects on ER \$\beta\$ Expression: Implications in Prostate Cancer](#)
- [Regular Use of NSAIDS May Reduce the Risk of Parkinson's Disease](#)

Intramural Research

Intramural Papers of the Month

- [Genes in Blood Can Predict Harmful Levels of Acetaminophen](#)
- [DNA Polymerase Gamma Mutant Causes Enhanced Oxidative Stress](#)
- [Regulatory Roles of Two Retinoid-related Orphan Receptor Isoforms](#)
- [Glucocorticoid Receptor Isoforms Regulate Bone Cell Apoptosis](#)

Calendar of Upcoming Events

- **January 8** in Rodbell Auditorium, 11:00 – 12:00 — Distinguished Lecture Series with Richard Flavell, Ph.D., speaking on “Innate and Adaptive Immunity”
- **January 8** in Rall F-193, 2:00 – 3:00 — Featuring William G. Thilly, Sc.D., presenting a seminar on “Fetal-juvenile stem cells and the origins of oncomutations in humans”
- **January 9** in Rodbell Auditorium, 2:30 – 4:30 — NTP Biomolecular Screening Branch Seminar on “Identifying Toxicity Pathways: linking genes, pathways and disease,” with Chris Portier, Ph.D.
- **January 14** in Executive Conference Room, 2:00 – 4:00 — Durham Careers in Life Sciences Meeting, chaired by Marian Johnson-Thompson, Ph.D.
- **January 16 - 18 (Off-site event)** at the Ronald Reagan Building and International Trade Center in Washington, DC. — Climate Change: Science and Solutions
- **January 16 (Off-site event)** in the EPA Auditorium, 10:00 – 11:30 — Martin Luther King, Jr. Observation, featuring Bennett College President Julianne Malveaux, Ph.D.
- **January 18** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, featuring Fred Wright, Ph.D., topic TBA
- **January 18** in Rodbell Auditorium, 1:00 – 1:30 — Tae Kwon Do Demonstration by Team White Tiger
- **January 24** in Rall F-193, 1:00 – 2:00 — Laboratory of Structural Biology Seminar Series, with Eric C. Greene, Ph.D., speaking on “Visualizing DNA repair proteins in action”
- **January 25** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, featuring Rita Colwell, Ph.D., topic TBA
- **January 31** in Rodbell Auditorium C, 11:00 – 12:00 — Seminar on “Responsibility for health: personal, social, and environmental,” with David B. Resnik, Ph.D., J.D.
- **February 1** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, featuring Anna Maria Siega-Riz, Ph.D., topic TBA
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Superfund Basic Research Program Anniversary

By Eddy Ball

For pioneers in the [NIEHS Superfund Basic Research Program \(SBRP\)](#), the twenty year anniversary celebration December 1-3 was a time to acknowledge the program's many laurels — and look forward to new challenges. Grantees, students, administrators and friends of SBRP gathered on the Duke University Campus at the Washington Duke Inn for a full agenda of partnership reaffirmation, presentations by outstanding researchers, poster sessions, science sessions and a colloquium on the program's visions for the future ([see related Science Notebook story](#)), chaired by SBRP Acting Director Claudia Thompson, Ph.D.

Aptly titled “20 Years of Success and a Vision for the Future,” the event drew more than 350 attendees, one-third of them postdoctoral fellows and students. SBRP was authorized by Congress in 1986 at a time when images of the fiery Cuyahoga River and the Love Canal disaster still resonated in the American consciousness, and it officially began operations in 1987 — administering a network of university grants designed to seek solutions to the complex health and environmental issues associated with the nation's hazardous waste sites.

One of the program's most loyal supporters in Washington since his first term began in 1987, North Carolina's Fourth District Representative David Price, Ph.D., joined NIEHS Acting Director Sam Wilson, M.D., in opening remarks underscoring the enormous contributions of SBRP to the nation's environmental health.

Wilson and Price both described the program as the “crown jewel” of environmental programs. “There aren't any programs that achieve what the Superfund Basic Research Program achieves...

[from] on-the-ground impact on human health to fundamental production of knowledge,” Wilson observed. In his remarks, Price called SBRP “one of our most productive federal research programs” and underscored the relevance of SBRP research to the country's efforts to ensure homeland security.



Wilson, left, welcomed Price to the podium. Wilson described the congressman as “a good friend” of NIEHS and the Environmental Protection Agency. (Photo courtesy of Steve McCaw)



Thompson, left, who is currently leading the SBRP, introduced founding director Suk, who spoke on the importance of partnerships to the Superfund effort. (Photo courtesy of Steve McCaw)

Present at the meeting were several NIEHS people who were involved in the program from the beginning, including Acting Deputy Director Bill Suk, Ph.D., who was SBRP's first director. He was joined by Chip Hughes, the program director who established the SBRP Worker Education Training Program, and Anne Sassaman, Ph.D., director emeritus of the Division of Extramural Research and Training, which oversees the program's administrative staff.

Throughout the meeting's sessions, the program emphasized several major themes of SBRP:

Partnerships: SBRP fosters partnerships among research institutions, the public and private sectors and agencies with interests in Superfund sites. At the meeting, Partnerships Session speakers included Susan Bodine, J.D., assistant administrator of the U. S. Environmental Protection Agency Office of Solid Waste and Emergency Response, and Henry Falk, M.D., director of the Centers for Disease Control and Prevention Center for Environmental Health.

"Trans-Disciplinary" Approaches: Suk suggested replacing the term "interdisciplinary" with "trans-disciplinary" as a more accurate description of the kind of collaborative research that SBRP encourages. SBRP investigations do more than cross the divisions between disciplines in an area of science; they routinely bridge the even greater chasms between realms of science, such as those separating the pursuit of knowledge in the biological, geo-physical, ecological, engineering and social sciences.

Nurturing the Next Generation: The 120 postdoctoral fellows and graduate students in attendance were a major presence at the event. There were special student events, such as the pre-meeting social and student mixer, poster sessions and receptions and meals that encouraged interaction among students, grant administrators and SBRP center directors. Student presentations constituted 40 to 60 percent of the four science sessions, and among the meeting highlights was the presentation of student awards ([see Extramural Update](#)).

Poet-Scientist Sandra Steingraber on "Living Downstream"

Born in 1959 in Peoria, Ill., biologist Sandra Steingraber, Ph.D., grew up on the banks of the Illinois, down stream from Rockford, Ill., a hazardous waste site located atop an aquifer. She is a survivor of bladder cancer, which she described as "the quintessential environmental cancer," as well as the adopted child of a mother who has survived breast and bone cancer and a father who developed Lewy Body Dementia when Steingraber was still a teenager. In her keynote presentation at the SBRP anniversary meeting, she explained that she learned the hard way that "families have a lot more than genes in common" and, as a woman who became pregnant in her late thirties, that "I am a habitat" for my unborn child.

Steingraber, who is now a Distinguished Visiting Scholar at Ithaca College in upstate New York, holds a master's degree in English literature and a doctorate in biology. She has combined her two loves — of the word and the human organism — into an ecological crusade for bottom-up public advocacy. She is on a mission to combat what she terms "the cultural amnesia about Superfund" and describes herself as a "cancer abolitionist." By emphasizing that "every data point is a human life," Steingraber is out to stem "sin by silence" with a challenge to the very concept of acceptable levels of contamination in environmental regulation.

Along with her books, *Post Diagnosis*, a poetry collection, *Having Faith*, an account of her pregnancy with her daughter, Faith, and *Living Downstream: An Ecologist Looks at Cancer and the Environment*, Steingraber works in the tradition of Rachael Carson to channel grass roots concerns into scientific investigation. With the support of the [Breast Cancer Fund](#), she authored a reader-friendly review of research on breast cancer risk, *The Falling Age of Puberty in U.S. Girls: What We Know, What We Need to Know*, which is available free in hardcover and as a [download](#).

The SBRP pioneers deserve to look back on the past 20 years with pride. In the two decades of SBRP, the program has supported researchers who have published more than 8,290 papers, received more than 65 patents on methods and technology, pioneered new assessment methodologies, contributed to mediation at more than 200 sites and trained hazardous material first responders nationwide.

Just as importantly, it has laid the foundation for the research teams that will carry on the good work in the decades to come.



Key players in Superfund partnerships speaking at the meeting included, left to right, Thompson, Wilson, Suk, Hughes, Bodine and Falk. (Photo courtesy of Steve McCaw)



NIEHS Director Emeritus Ken Olden, Ph.D., spoke at the meeting and took the opportunity to catch up with a long-time friend, former NIEHS employee “Captain” Dave Mineo. Olden was director during the early years of SBRP up to his retirement in 2005. (Photo courtesy of Steve McCaw)



Writer and biologist Steingraber’s talk was titled “We All Live Downstream: An Ecologist’s Perspective on Toxic Waste and Environmental Human Rights.” She is shown talking with a student in the audience. (Photo courtesy of Steve McCaw)



University of California at Davis entomologist Bruce Hammock, right, talked with a student at the mixer luncheon. In his presentation, Hammock reflected on the value of students to the SBRP: “Perhaps the most important contribution of SBRP is its support for training the next generation of environmental scientists.” (Photo courtesy of Steve McCaw)

Leadership and Gender Symposium for Latinas

By Eddy Ball

The picturesque Lawton Chiles International “Stone House” at the Fogarty International Center (FIC) on the NIH campus in Bethesda, Md., was the site of a symposium focused on the needs of women in science. The December 3 meeting was co-chaired by NIEHS Associate Director Sharon Hrynkow, Ph.D., and National Institute on Drug Abuse (NIDA) Director Nora Volkow, M.D. The symposium was titled “Leadership and Gender Training for Women in the Health Sciences in Latin America: Taking Stock of Lessons Learned from a Pilot Program, and Ways Forward.”

The event brought together 50 representatives from 14 NIH institutes and centers, multi-national organizations, and private groups, academic leaders, government officials, and women scientists from Latin America and the Caribbean. Joining NIEHS and NIDA in sponsoring this meeting were the NIH Office of Research on Women’s Health (ORWH) and the Office of AIDS Research.

The symposium was a follow-up to two colloquia convened by FIC in partnership with NIEHS, NIH/ORWH and the Canadian Institutes of Health Research in 2003 and 2004 when Hrynkow was serving at FIC. Its focus was the assessment of a two-year pilot leadership-training program developed by the Institute of Gender Studies, Facultad Latinoamericana de Ciencias Sociales (FLACSO), Argentina.

In her opening remarks, Hrynkow noted the reasons for such a program. “Women scientists in poorer countries told us that they needed mentors,” she explained, “and that they wanted training on both how to become effective leaders and how to consider gender issues as part of their own research efforts.” Latin America was selected as the site for the pilot because of the number of NIH-trained women who had returned home to the region.

When Volkow addressed the group, she pointed to her own Latina heritage and described the value of having women scientists in top positions. “Women simply gravitate towards women leaders,” she observed, “so it is critical to position women at the top.” Seeing women in leadership roles, she continued, also has a positive effect on males in the organization.



Hrynkow’s interest in the role of gender was also evident in her December 14 Frontiers of Environmental Sciences Lecture at NIEHS, “A Conversation on Gender, Equity and Environmental Health.” (Photo courtesy of Michael Spencer, NIH)



Volkow, whose family has roots in Mexico, still works in her own lab. It is a fertile training ground for women scientists. (Photo courtesy of Michael Spencer, NIH)



The meeting gave trainees, including Chair of the NIH Visiting Fellows Committee Elizabeth Rex, Ph.D., left, an opportunity to network with successful Latina scientists, such as Cauce. (Photo courtesy of Michael Spencer; NIH)



Bonder, who was on stage for much of the event, took advantage of being a part of the audience to enjoy a well-deserved break. (Photo courtesy of Michael Spencer; NIH)

The keynote talk was presented by FLASCO Institute of Gender Studies Director Gloria Bonder, co-developer of the pilot, an Internet-based program that connects women researchers from across Latin America. Women receive training on leadership skills, negotiation, communication of science and incorporating issues of gender more fully into their own research.

In a test of the pilot, more than 50 women researchers made a six-month commitment of several hours per week to the program. Many of the participants were former NIH intramural postdoctoral fellows or students who had trained in FIC programs at American universities. All had returned to their home countries and were eager to complement their scientific training with gender and leadership training.

Bonder highlighted testimonials from the participants on the success of the pilot. According to one, for the first time it was possible to “do research in my own style.” Others have gone on to such empowering activities as creating day-care centers at their universities, forming networks of emerging scientific leaders within their universities and crafting family-friendly policies for working women in science.

The symposium also included discussion sessions facilitated by Bonder, University of Washington Dean of Arts and Sciences Ana Mari Cauce, Ph.D., and Jose Szapocznik, co-director of the National Hispanic Scientist Network (NHSN) on Drug Abuse. Following a lively exchange of ideas for building on the success

Partners at the Symposium

With her wealth of experience at FIC, Hrynkow is a natural at forming partnership that cross borders and the divisions between disciplines and sectors. Several national and international organization participated in the symposium, including:

- [Pan American Health Organization \(PAHO\)](#)
- [Organization of American States \(OAS\)](#)
- [Inter-American Development Bank](#)
- [Howard Hughes Medical Institute](#)
- [National Hispanic Scientist Network \(NHSN\) on Drug Abuse](#)
- [U.S. Department of State](#)
- [United Nations Educational, Scientific and Cultural Organization \(UNESCO\)](#)

of the pilot, the session reached a consensus on the value of special training “modules” for women scientists working in specific thematic areas. HIV/AIDS was selected as the first theme, and there was interest in NIEHS exploring a second module in the environmental health sciences arena.

As a next step, FLACSO and NHSN agreed to work together to create an expert committee of advisors to adapt the curriculum as needed for the AIDS community. Hrynkow said she was confident that NIEHS will be able to work with partners to develop a curriculum in the field of environmental health sciences, and she is starting to explore options.



Szapocznik, left, posed with University of Miami colleague Hilda Pantin, Ph.D., and National Institute of Allergy and Infectious Diseases Associate Director for Policy and Review Hortencia Hornbeak, Ph.D., right. (Photo courtesy of Michael Spencer, NIH)



Maria Celina Conte, a specialist with the Organization of American States Office of Science and Technology, talked with another participant as the next speaker set up her microphone. (Photo courtesy of Michael Spencer, NIH)

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NTP Board of Scientific Counselors Meets

By Eddy Ball

With an observation that “this is a very active time in this field of ours,” NIEHS/NTP Acting Director Sam Wilson, M.D., opened the fall 2007 meeting of the NTP Board of Scientific Counselors (BSC) on December 6 in Rodbell Auditorium. Wilson’s statement soon became reality for members of the board as they plowed through a packed agenda of reports, two precedent-setting initiatives and seven nominations, including the second one involving a nanoscale element.

The meeting began with an update by NTP Associate Director John Bucher, Ph.D., who discussed NTP realignment ([see related story](#)) within the NIEHS Division of Intramural Research, an upcoming



In his opening remarks, Wilson reminded the Board of recent media interest in NTP studies and renewed public concern about lead in imported toys and products. (Photo courtesy of Steve McCaw)

celebration of the 10-year anniversary of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) on February 5, 2008, and a workshop on *in vitro* approaches and humane endpoints for acute chemical safety testing on February 6 and 7.

Bucher acknowledged special recognition of several NTP staff. In 2006, Susan Elmore, D.V.M., and others from NTP were recognized for the year's best paper by the Society of Toxicologic Pathology. Senior toxicologist Ron Melnick, Ph.D. received the 2007 David P. Rall Award for Advocacy in Public Health at the American Public Health Association's 135th Annual Meeting in November. Bucher also noted the contribution of geneticist Frank Johnson, Ph.D. and the recent paper in *Nature* describing NIEHS/NTP efforts toward identifying single-nucleotide polymorphism maps of 15 commonly used laboratory murine strains.

ICCVAM and the NTP Interagency Center for the Evaluation of Alternative Methods (NICEATM) in response to request from the U.S. House and Senate Appropriations Committees have developed a five-year plan to advance alternative test methods of high scientific quality to better protect human health, animal health and the environment. As an example of the potential of this kind of toxicity pathway analysis, Bucher pointed to the development of four *in vitro* alternatives to ocular testing. "If positive findings are coming up in these *in vitro* tests, there is no need to go on to a rabbit eye test," he said.

In the first of two reports on initiatives that involve new directions in NTP studies, Dori Germolec, Ph.D., NTP immunology discipline leader, outlined plans for studying mold. The study will use pooled specimens of several fresh isolates of mold species on different building materials to mimic "real-life exposure" to whole organisms in rodent toxicology studies. As Germolec explained, the proposed study design "is a very significant departure from the traditional NTP study, where we're using a very well characterized compound and have a very good idea of the metabolites and where they go in the tissues."

In his report on nominations for the Center for the Evaluation of Risks to Human Reproduction (CERHR), Director Michael Shelby, Ph.D., described the nominations of low-level exposures to lead and cadmium proposed for expert panel evaluation.



Bucher, left, and Chair Gail McCarver, M.D., listened as the Board approved nominations for aminopyridines, 2-methoxy-4-nitroaniline, nanoscale gold, 2'2''-dithiobisbenzanilide, pentaethylenhexamine and the phthalate initiative. (Photo courtesy of Steve McCaw)

Moving Day in Chicago – Radiofrequency Radiation Studies to Begin Soon

During his report, Bucher showed slides of workers moving 21 reverberation chambers from flatbed trucks through the sidewalk into a sub-basement area at the Illinois Institute of Technology Research Institute in Chicago. The chambers, which were built in Switzerland and carried by sea to the United States, are being installed as part of NTP studies of exposure to radiofrequency radiation from cellular phones and other wireless communications devices.

According to Bucher, the thermal pilot studies are set to begin in February 2008, with the perinatal pre-chronic studies anticipated to start in the summer and chronic studies in 2009. The overall objective of these studies is to determine the potential toxic and/or carcinogenic effects of exposure to cellular phone radiofrequency emissions in laboratory animals. The Federal Communication Commission and others will use this information to determine the adequacy of current guidelines for protecting against potential adverse effects of chronic exposure. The current FCC exposure limits are designed to protect against acute injury from thermal effects of radiofrequency radiation.

As Shelby noted, “This is the first time the BSC is being asked to provide input on whether there is sufficient concern and scientific data to warrant CERHR conducting an evaluation for a particular nominated substance.”

The lead nomination, Shelby noted, also marks the first evaluation by CERHR of a known developmental toxicant, and study results could support the first use of reproductive toxicity to revise occupational exposure limits downward. The current Recommended Exposure Limit is four times that considered elevated in children and applies to all workers, even women of childbearing age.

The board’s responses to reviews on the mold and proposed CERHR evaluations were overwhelmingly positive. The board also approved NTP recommendations for all study nominations except for the compound diethyl phthalate. The board also unanimously approved the recommendations on the findings and conclusions for the six draft NTP Technical Reports presented by Nancy Kerkvliet, Ph.D., chair of the board’s Technical Reports Review Subcommittee. The meeting concluded with a progress report by Bucher on implementation of the NTP Workshop and Retreat Recommendations.



“Many uncertainties remain,” Germolec noted as she told the Board that of an estimated 1.5 million species of fungi, only approximately 80 thousand have been described. (Photo courtesy of Steve McCaw)



Noting the rising incidence of “sick building” syndrome, BSC member Vernon Walker, D.V.M., Ph.D., described mold as “a significant public health issue.” (Photo courtesy of Steve McCaw)

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Former Postdoc Awarded Cancer Scholarship

By Eddy Ball

Less than eight months after completing her postdoctoral fellowship at NIEHS, molecular geneticist Francesca Storici, Ph.D., became one of 29 researchers selected as Georgia Cancer Coalition Distinguished Cancer Scholars for 2008. As a scholarship winner, Storici, now an assistant professor at the Georgia Institute of Technology School of Biology, will receive \$50,000 in Coalition funding annually for the next five years.

“The award is an honor and provides very good support as I am setting up my lab here at Georgia Tech,” Storici said after the announcement. “It will be a great help in recruiting students and acquiring specialized equipment for my research.”

Storici attended the University of Trieste in Italy, where she qualified as a biologist and earned a Ph.D. in molecular genetics from the International School for Advanced Studies. She worked at the International Center for Genetic Engineering and Biotechnology there under the direction of Carlo Buschi, Ph.D., in the Yeast Molecular Genetics Group.

From 1999 to April 2007, she held positions as a visiting and then research fellow in the Chromosome Stability Group of the Laboratory of Molecular Genetics, headed by Mike Resnick, Ph.D. Just before joining the School of Biology at Georgia Tech, Storici conducted a few months internship as research assistant professor at the Gene Therapy Center of the University of North Carolina at Chapel Hill, directed by Jude Samulski, Ph.D.

“NIEHS was an incredibly exciting opportunity and a journey of professional growth for me. It’s an experience I could never have had in Italy and one that has influenced me profoundly,” Storici said of her fellowships at the Institute. “Mike, Dmitry [Gordinin, Ph.D.], and my other colleagues there helped me learn how to be a scientist and helped me keep in mind that there is always more to learn.”

In her work at NIEHS and in her own lab at Georgia Tech, Storici uses the yeast *Saccharomyces cerevisiae* model organism and mammalian cells to trace the molecular mechanisms involved in the repair of broken DNA. A focus of her research is studying the mechanisms by which RNA can directly record itself into the DNA genome, following the discovery of RNA-templated DNA repair when still at NIEHS, work recently published and pod cast in *Nature*. Her objectives are directed also toward developing more effective and safe technologies of genome modification as unique tools for structure/function studies as well as for medical and industrial applications.

A major accomplishment during her tenure at NIEHS was Storici’s development of one of the most powerful approaches for targeted genome correction with synthetic oligonucleotides, known as *delitto perfetto*, Italian for “perfect murder.” Storici named the approach after the Italian title of Alfred Hitchcock’s film, “Dial M for Murder,” because the approach provides *in vivo* selection for almost any chromosomal modification and leaves no trace of the material used at the “scene” of the targeted mutation. Storici, who is known among colleagues for her sense of humor, also noticed that yeast mutated using *delitto perfetto* showed an uncanny resemblance to the corpulent director.



Storici is shown in her office at Georgia Tech. According to her mentor, Mike Resnick, Storici is an “exceptional and highly motivated scientist who was a wonderful person to have in the lab.” (Photo courtesy of Francesca Storici and Georgia Institute of Technology)

them to the extent that our funding allows.” Wilson also expressed his conviction “that community-based approaches have an important role to play in the entire environmental health research enterprise.”

During plenary sessions, workshops and an evening poster session, grantees devoted their time to learning from one another and sharing their accomplishments in environmental sciences, especially with regard to exposure monitoring, capacity building, and the development of cooperatives to increase awareness of environmental and occupational health. Participants also discussed larger trends in CBPR and EJ, planned for the future, and considered ways in which they could build upon their successes over the past years.

In a session exploring ways to continue their work beyond the funding period, grantees who recently completed four years of NIEHS support as part of the EJ Program presented project highlights and shared strategies for sustaining their activities. These projects included the [Work Environment Justice Partnership for Brazilian Immigrants in Massachusetts](#), [Communities Organized against Asthma and Lead \(COAL\)](#), and the [Healthy Homes and Community for High Point Families](#).

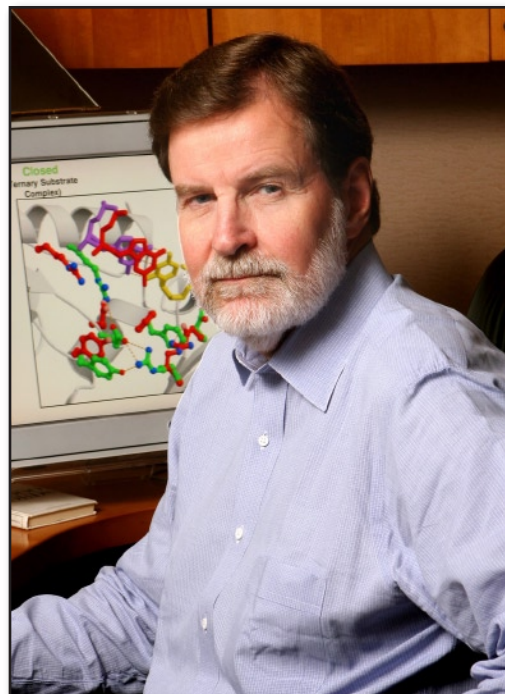
Meeting organizers took advantage of the December 11 lunch break and a Tuesday afternoon session to discuss the recently released [Request for Information \(RFI\) on the Partnerships for Environmental Public Health program](#) that the NIEHS is developing. Meeting participants shared their ideas and engaged in rich dialogue about future opportunities in environmental public health.

As the meeting came to a close December 12, an exhausted O’Fallon evaluated the busy three days in Boston. “This was an excellent meeting,” he said. “These meetings are instrumental in promoting a positive environment in which our grantees can learn from one another and explore new collaborations with colleagues from around the country.”

According to O’Fallon, the interactions among attendees at the meeting and the quality of their presentations show how far the program has come since it was established in 1994. “It is exciting to see such productive interactions and collaborative projects among community groups, researchers and healthcare providers,” he added. “These projects demonstrate the value of developing partnerships to address the impact of environmental exposures on public health.”

NIEHS Community-Based Research and Environmental Justice program grants are administered by the [Susceptibility and Population Health Branch \(SPHB\)](#) under the direction of Branch Chief Gwen Collman, Ph.D. The meeting was hosted by the [Silent Spring Institute](#).

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Wilson describes NIEHS as an umbrella — with ample room for the kind of basic bench research he performs so admirably in his own lab, as well as the participatory and activist research conducted by grantees at the Boston meeting. (Photo courtesy of Steve McCaw)

Bucher Announces NTP Realignment

By Eddy Ball

During his report to the National Toxicology Program (NTP) Board of Scientific Counselors on December 6 (see related [Spotlight story](#)), NTP Associate Director John Bucher, Ph.D., presented an update on the realignment of the program within the NIEHS Division of Intramural Research. These changes are being implemented in order to give a clearer identity to the activities, staff and resources associated with the NTP.

According to Bucher, “This realignment provides greater transparency to the NTP budget as well as clarifies our physical location, capabilities and mission. Our traditional testing and assessment activities are strong, but now we have an organizational scaffold to accelerate fulfillment of our goals in the NTP Roadmap and building new programs.”

The realignment was completed on October 28, 2007, with staff assignments to a newly designated program office and five branches. New appointments included Deputy Program Director for Policy Mary Wolfe, Ph.D., and Deputy Program Director for Science Nigel Walker, Ph.D.

- **Program Office** is comprised of the Office of Liaison, Policy and Review, also headed by Wolfe; Office of Nomination and Selection, directed by Scott Masten, Ph.D.; Report on Carcinogens, under Bill Jameson, Ph.D.; the NTP Interagency Center for the Evaluation of Alternative Methods (NICEATM), headed by Bill Stokes, Ph.D.; and the Center for the Evaluation of Risks to Human Reproduction (CERHR), under Mike Shelby, Ph.D.
- **Toxicology Branch**, headed by Acting Director Paul Foster, Ph.D., brings together all of the toxicology efforts within NTP, with a renewed emphasis on integrating toxicology studies with toxicokinetics and toxicogenomics. Significant activities include directing interagency agreements with the Food and Drug Administration’s National Center for Toxicological Research and the Center for Disease Control and Prevention’s National Institute for Occupational Safety and Health.
- **Cellular and Molecular Pathology Branch**, headed by Robert Sills, D.V.M., Ph.D., provides support for NTP pathology and program archives and support for pathology investigations by intramural researchers. One of this group’s many current projects is compiling an atlas of non-neoplastic lesions in rodents.



The bulk of Bucher’s report to the NTP Board of Scientific Counselors was devoted to realignment of the NTP within the Division of Intramural Research. (Photo courtesy of Steve McCaw)



Foster, left, and Jameson listened as Bucher described their roles in the realigned NTP. Both scientists addressed the Board later in the meeting. (Photo courtesy of Steve McCaw)

- **Program Operations Branch**, headed by Acting Chief Cynthia Smith, Ph.D., provides oversight for activities that support NTP research and testing, including chemistry activities, studies related to absorption, distribution, metabolism, and excretion (ADME), quality assurance, maintenance and development of data capture and retrieval systems, the central data repository, and the NTP web site.
- **Host Susceptibility Branch**, headed by Acting Chief Jef French, Ph.D., is responsible for planning, conducting and analyzing assessments of chemical toxicity in multiple murine strains. Another function of this group is putting together collaborations that will foster an interaction among the NTP, intramural and extramural investigators, and potential public-private partnerships to examine the genetic basis of response to environmental exposures and the clinical manifestations of resulting disease states.
- **Bio-molecular Screening Branch**, headed by Acting Chief Ray Tice, Ph.D., is charged with implementing the portion of the NTP Roadmap related to development of high- and medium-throughput screening activities. This branch works cooperatively with the Environmental Protection Agency's ToxCast program and the NIH Chemical Genomics Center to identify and evaluate in vitro and cell based high-throughput assays as tools useful for screening and prioritizing chemicals for toxicity testing. This branch also carries out NTP automated screening of *C. elegans* performed at NIEHS by the WormTox Group headed by Jonathan Freedman, Ph.D.

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NIEHS Kicks Off Transportation and Health Workshop

By Eddy Ball



In spite of the bad luck associated with its ordinal designation, Workshop 13 in the Institute of Medicine's (IOM) ongoing Roundtable on Environmental Health Sciences, Research and Medicine may turn out to be its luckiest so far. According to NIEHS Acting Director Sam Wilson, M.D., who opened the meeting with a plenary presentation, the November 29 – 30 workshop in Washington, D.C., “Environmental Health, Energy and Transportation: Bringing Health to the Fuel Mixture,” set important precedents for upcoming meetings in the series.

“[Workshop 13](#) was the first time [in this series] that representatives from the transportation and energy sectors met with colleagues in the environmental health arena,” Wilson observed. “As our nation moves forward with new energy policies and strategies, such dialogue is essential. We should consider the health implications of our fuel choices up front as we move ahead in the energy arena,” he added.



Wilson developed the theme that “human health is fundamentally linked to the economy,” both as an economic incentive to growing the economy and as a consequence of the energy usage fueling that economy. (Photo courtesy of Steve McCaw)



Wirth's talk emphasized an important consideration for policy makers: "The history of our relationship with automobiles and petroleum provides textbook examples of unintended consequences – choices that seemed right at the time and turned out badly over the long run." (Photo courtesy of the United Nations Foundation)

Wilson's opening presentation, "Healthy People, Healthy Economy: Integrating Human Health and Emerging Alternative Fuels," set the stage for the two-day event that brought together national and international experts on a range of subjects that bear on efforts to craft a viable energy and transportation plan for the future.

In the course of the two full days of presentations and discussion which followed, the workshop featured five sessions on different aspects of the issues involved in transportation, conventional and alternative fuels, and health. Topics ranged from engine parameters, health effects of fuel components, additives and exhaust gases to the advantages and potential health threats of alternative fuels, such as ethanol and biodiesel.

Workshop 13 was also the first meeting that the United Nations Foundation (UNF), represented by UNF President and former U.S. Senator Timothy Wirth and Senior Vice President Melinda Kimble, participated in and supported financially. Wirth challenged the audience to consider how to move research from the laboratory into the policy arena. His comments, based on his many years of experience in Congress and as Under Secretary of State for Global Affairs, spurred the participants to re-examine their preconceptions about alternative energy sources, as well as the global implications of this country's energy policies.

Organizers maintained that the environmental sciences will play a major role in the cross-disciplinary research needed for developing new technologies and better understanding the behavioral, dietary and genetic factors

A Congregation of Stakeholders in the Future of Energy, Transportation and Health

As the institute with arguably the broadest perspective of any in the NIH family, NIEHS was poised to play an important role in getting specialists from disparate areas talking and communicating with one another. Along with Wilson and Hrynkow, the Institute was represented by Associate Director for Risk Assessment Chris Portier, Ph.D., Assistant to the Deputy Director Sally Tinkle, Ph.D., Office of Planning Health Scientist Administrator Sheila Newton, Ph.D., *EHP* News Editor Kimberly Thigpen Tart, and Program Analyst Mary Gant.

Transportation and energy spokespeople at the workshop included representatives of petroleum producer Exxon Mobil, the Argonne National Laboratories, Lawrence Berkely Laboratory and the American Petroleum Institute. They interacted with federal health and regulatory officials from the Centers for Disease Control and the U.S. Environmental Protection Agency, as well as health and policy specialists from around the world.

Specialists in public health, such as Goldman, occupational health and the environmental health sciences, such as NIEHS grantee Grace LeMasters, Ph.D., came from university and non-profits throughout the United States. Along with Wirth and Gray, European, Canadian and Brazilian researchers offered international and global environmental health perspectives on the issues.

For the first time, a sister institute, the National Institute on Child Health and Human Development, joined NIEHS at the Roundtable as a core supporter.

involved. With its experience in the health effects of aromatics, respiratory diseases, particulates from exhaust, the synergy of components in mixtures, exposure biology and monitoring, environmental justice issues, global environmental health, high-throughput *in vitro* methodologies and other related issues, NIEHS is in unique position to make a major contribution to the workshop series.

“We were also grateful to have U.S. Ambassador to the European Union C. Boyden Gray, J.D., at the workshop,” said Sharon Hrynkow, Ph.D., NIEHS associate director and one of the organizers of the workshop. Gray, who served as White House Counsel under President George H.W. Bush, is an ardent spokesperson for removal of the aromatic fraction from gasoline formulations. His talk, “A History of Fuel Development: Lead, MTBE and Benzene,” focused on the largely unintended consequences of efforts to improve gasoline as a fuel.

By breaching the communications gap between these interest groups and increasing the international focus of the series, Workshop 13 furthered the major goal of the IOM series significantly by fostering dialogue among parties from the academic, industrial, and federal research perspectives on sensitive and difficult environmental health issues.

According to Hrynkow, this is the kind of dialogue that promises to help the country make more informed policy decisions about how to deal with significant health threats associated with transportation exhausts, which are also the source of 25 percent of the greenhouse gases produced by Americans each year.

The meeting concluded with a Panel Discussion that endeavored to define “Criteria to Determine Potential Costs and Benefits of Fuels,” moderated by Johns Hopkins Bloomberg School of Public Health Professor Lynn Goldman, M.D.

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Jayes Accepts Duke Research Position

By Eddy Ball

It won't be much consolation for her colleagues in the NIEHS Trainees Assembly (NTA) who will miss her energy and dedication to her fellow trainees. But the loss of Friederike Jayes, D.V.M., Ph.D., for NIEHS will be a gain for students at Duke University Medical Center. Jayes will begin work there on January 7 as a senior research associate in the Department of Obstetrics and Gynecology (OB/GYN).

“There's never really been a certain job category out there that I could look for, certainly not as a traditional PI [Principal Investigator],” Jayes said of her search. “I've always tried to find a bigger group where I can fit in and contribute as part of a team.... It [my new position] is not officially a tenure-track position yet, but hopefully it will lead into one.”

In her new position, Jayes will work with a group of investigators headed by [Phyllis C. Leppert, M.D., Ph.D.](#), the department vice chair for research and former chief of the Reproductive Science Branch at the National Institute of Child Health and Human Development (NICHD).



“This is a very stimulating atmosphere,” Jayes said of NIEHS. “People are really very easy to meet here after a seminar or anywhere.” (Photo courtesy of Steve McCaw)

Jayes will be studying the molecular biology of reproduction and working on the etiology of uterine fibroids and the development of new medical treatments for these extremely common benign tumors in women of reproductive age.

Jayes got to know her new supervisor during the course of her research with the Receptor Biology Group in the NIEHS Laboratory of Reproductive and Developmental Biology headed by Ken Korach, Ph.D., and with the Laboratory of Women's Health headed by Barbara Davis, V.M.D, Ph.D. Jayes worked with Davis during the time the group chief served as principal investigator of the [Fibroid Growth Study](#).

When Jayes learned of Leppert's retirement from NICHHD and return to Duke, where she got her M.D., Jayes began the networking and "listening around" that ultimately landed her the position. Leppert's motivation for coming back to Duke was to strengthen the basic research component in the OB/GYN department, and Jayes felt being a part of Leppert's group would be a good career match and offer her an opportunity to make a contribution.

"[I realized that] many clinical people don't have the time to fit basic research into their rotations in OB/GYN and saw a potential for someone like me to help support the research program and also to help medical students understand the value of basic research," Jayes explained. "I've been interacting with her [Leppert] for over a year now, which motivated her to find a place for me in the group she is building at Duke. I've been exposed to many different aspects of reproductive physiology and felt that a broad range of experience was one of the strengths I could offer her."

Jayes came to NIEHS in 2002 after earning a doctorate at North Carolina State University in physiology. She completed her D.V.M. at the German University of Giessen, which is officially known as the Justus-Liebig-Universität Gießen, before she made a permanent move to the United States in 1988.

As she was wrapping up her tenure at the Institute, Jayes paused to reflect on her experience as a postdoc at NIEHS. "It's a really conducive environment for developing personally and scientifically. I've been very fortunate both times, with Barbara Davis' group and with Ken Korach's group, to be a part of teams that are very supportive and really interact well with each other."

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Noteworthy Developments

By Eddy Ball

In the closing months of 2007, NIEHS Health Science Administrator Cindy Lawler, Ph.D., was named to a new Interagency Autism Coordinating Committee, and NIEHS postdoctoral alumna and pharmacologist Julianne Hall, Ph.D., returned to RTP to assume a position as a research investigator at the Hamner Institutes, formerly CIIT.



Jayes was active in the NTA and served as chairperson of the 2007 NIEHS Career Fair Committee. She is shown queuing up a PowerPoint presentation for the event's guest speaker, Preston MacDougall, Ph.D. (Photo courtesy of Steve McCaw)

Seeking public comment on the expert panel review of bisphenol A, the National Toxicology Program (NTP) made the final version of the report available November 26.

- **Cindy Lawler** — Health and Human Services (HHS) Secretary Mike Leavitt announced November 27 that Lawler will be one of the 19 members of the [Interagency Autism Coordinating Committee](#) authorized under the Combating Autism Act of 2006. This planning and advisory group is chaired by Thomas R. Insel, M.D., director of the National Institute of Mental Health (NIMH).



*NIEHS Scientific Program Director Cindy Lawler
(Photo courtesy of Steve McCaw)*

In addition to Lawler and Insel, the 13 federal members include NIH Director Elias Zerhouni, M.D., and directors of three other NIH institutes. Other federal members represent various other offices and branches of HHS, including the Centers for Medicare and Medicaid Services, Department of Education, Centers for Disease Control and Prevention, Administration for Children and Families, Substance Abuse and Mental Health Services Administration, HHS Office of Disability, and Health Resources and Services Administration. Six non-federal members are officials in autism advocacy groups and private sector specialists.

Lawler is scientific program director of the Cellular, Organs, and Systems Pathobiology Branch in the NIEHS Division of Extramural Research and Training. Among her responsibilities is administering the grant which supports the NIEHS/EPA-funded Childhood Autism Risks from Genetics and the Environment programs.

- **Julianne Hall** — On November 28, [Hamner Institutes for Health Sciences](#) President and CEO William F. Greenlee, Ph.D., announced that Hall has joined the organization as a research investigator for the Division of Computational Biology. Hall was a postdoctoral fellow in the Laboratory for Reproductive Development and Toxicology Receptor Biology Group headed by Ken Korach, Ph.D. After leaving NIEHS, Hall was a research scientist and pharmacology junior faculty member at Duke University and, most recently, at Elon University.

Hall, who received her doctorate from Duke University, has been involved with breast cancer research for more than a decade. She is a member of the American Society for Biochemistry and Molecular Biology (ASBMB), the Federation of American Societies for Experimental Biology (FASEB), the Endocrine Society and Women in Endocrinology. At Hamner, Hall will work in molecular pharmacology as part of the Institutes' emerging cancer biology program focused on the development of novel therapeutic approaches for the detection and treatment of breast and other cancers.

- **Bisphenol A** — In a November 30 *Federal Register* [notice](#), the NTP Center for the Evaluation of Risks to Human Reproduction (CERHR) announced the availability of the [expert panel report on bisphenol A \(BPA\)](#). The notice invited the public to submit comments on the report, which is an evaluation of the reproductive and developmental toxicity of BPA conducted by an independent, 12-member expert panel composed of scientists from the public and private sectors convened by CERHR.

Comments should be received by January 25, 2008. Comments on the expert panel report and any other correspondence should be sent to CERHR Director Michael Shelby, Ph.D., by mail at NIEHS, P.O. Box 12233, MD EC-32, Research Triangle Park, NC 27709, by fax to (919) 316-4511, or by [e-mail](#).

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Science Notebook

Translesion DNA Synthesis Uses Specialized Polymerases

By Robin Arnette

On December 11, Errol C. Friedberg, M.D., delivered a seminar about DNA damage and repair to a near capacity audience in Rodbell Auditorium. The seminar, titled “Specialized DNA Polymerases in Higher Organisms: Insights from the Polk [polymerase kappa] Knock-Out Mouse,” was part of the NIEHS Distinguished Lecture Series. Principal investigator Tom Kunkel, Ph.D., and Fellow Zachary Pursell, Ph.D., of the Laboratory of Molecular Genetics hosted the event.

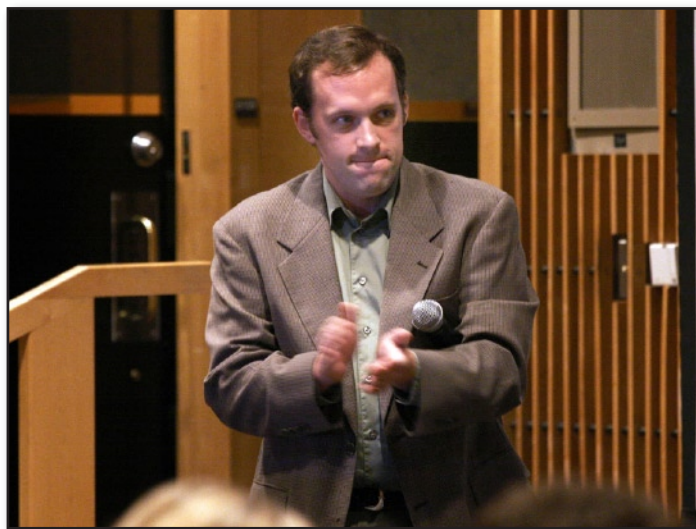
[Friedberg](#), holder of the Senator Betty and Dr. Andy Andujar Distinguished Chair in Pathology, is also professor and chairman of the Department of Pathology at the University of Texas Southwestern Medical Center in Dallas, Texas. His research focuses on understanding the molecular mechanism of DNA repair and mutagenesis in eukaryotes and the roles these processes play in cancer.

Friedberg prefaced his talk by providing background on how organisms handle molecular damage that halts DNA replication. “Through eons of evolution, cells have relied upon a variety of DNA damage tolerance mechanisms,” he said. “Lesions that were not repaired or removed from the genome were, in fact, tolerated so that important phenomena like replication and transcription could continue past a bulky DNA template lesion.” Friedberg emphasized that repair would occur somewhere down the line, but how these tolerance mechanisms worked remained a mystery until about 10 years ago.

That was when a new class of enzymes—Friedberg prefers to call them specialized polymerases—was discovered. A specialized polymerase differs from a high fidelity polymerase in that a specialized polymerase allows an open and solvent-accessible active site that can tolerate lots of lesions. In contrast the tight structure of a high fidelity polymerase permits the DNA duplex to fit snugly into its active site.



Friedberg began his talk by describing DNA damage as the “scourge of all living organisms.” (Photo courtesy of Steve McCaw)



Co-host Pursell introduced the lecturer, taking care to pronounce the tongue twister in the speaker’s alma mater, the University of the Witwatersrand. Following the question-and-answer session, Pursell showed his enthusiasm over Friedberg’s talk. (Photo courtesy of Steve McCaw)

Specialized polymerases are involved in translesion DNA synthesis (TLS), one of the tolerance mechanisms Friedberg is interested in, and research from several labs has demonstrated that multiple polymerases, such as Rev1 protein, polymerase iota (Pol ι) and polymerase eta (Pol η), work together during this process. “When the replication machinery is arrested, a polymerase switch is believed to occur,” Friedberg explained. “Rev1 will incorporate one or, at most, two cytosine residues, irrespective of what the nucleotide structure of the template strand is, but if a thymine dimer is present, Pol η incorporates a small number of nucleotides which allows bypass of the arresting lesion.”

Friedberg’s work may suggest that specific specialized polymerases evolved to bypass particular lesions during TLS. He and colleagues determined that Pol κ , a newly discovered specialized polymerase, bypasses bulky polycyclic or multiple-ring adducts on DNA. The experiments compared cells from normal mice and cells from a strain of knock-out mice that lacked Pol κ (pol κ ^{-/-}). Benzpyrene—a five-ring aromatic hydrocarbon mutagen found in coal tar, cigarette smoke, jet fuel exhaust and charcoal-broiled meats—served as the lesion.

In collaboration with a group from the Weitzman Institute in Israel, Friedberg and his colleagues generated a plasmid that had a benzpyrene adduct on the template strand in the middle of a gap and a control gap plasmid without a lesion. They transfected the plasmids into cells, recovered colonies and measured TLS by comparing the efficiency of gap repair in each. In normal cells, with Pol κ present, efficient bypass occurred across the benzpyrene adduct, but in pol κ ^{-/-} cells, the efficiency decreased significantly. Adding Pol κ back into these mutant cells fully restored bypass efficiency of benzpyrene.

Other research groups have reported that Pol κ may also be involved in nucleotide excision repair and spermatogenesis. Although more work is needed to completely uncover all of Pol κ ’s physiological duties, Friedberg anticipated more important discoveries about this specialized polymerase. “Some of these may turn out to be very interesting,” he said.

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Kunkel, Pursell’s mentor and lecture co-host, helps field questions from the audience. (Photo courtesy of Steve McCaw)



Among the postdoctoral fellows captivated by Friedberg’s research findings was Visiting Fellow Wataru Nakai, Ph.D., of the Laboratory of Molecular Genetics Chromosome Stability Group. (Photo courtesy of Steve McCaw)

Study Links Gene Expression Changes in Babies and Arsenic Exposure

By Eddy Ball

In a study made possible by NIEHS extramural funding, a team of researchers from the Massachusetts Institute of Technology (MIT) and Thailand's Chulabhorn Research Institute (CRI) have identified for the first time a highly predictive biomarker gene set for prenatal arsenic exposure. According to the authors, who published the study in the journal *PLoS Genetics*, the results of the study clearly demonstrated "that prenatal exposure in humans results in measurable phenotypic responses in the newborn."

Results of earlier rodent studies, the authors note, suggest that "*in utero* arsenic exposure may result in epigenetic changes that persist through the life of the organism, ultimately impacting health status." Duke University researcher Randy Jirtle, Ph.D., has compared the genome to computer software due to the similarities between how it influences gene expression within the genome and the way software controls the efficient operation of computer hardware.

Arsenic contamination is a health concern worldwide with millions exposed to levels that exceed the World Health Organization (WHO) safety standard of 10 parts per billion (ppb). The element was classified as a Group 1 carcinogen by the International Agency for Research on Cancer and has been implicated in such diseases as vascular disorders and diabetes.

The research was led by Mathuros Ruchirawat, Ph.D., director of the CRI Laboratory of Environmental Toxicology in Bangkok, working with Leona Samson, Ph.D., director of the MIT Center for Environmental Health Sciences and the American Cancer Society professor in the departments of Biological Engineering and Biology. Rebecca Fry, Ph.D., a research scientist at the MIT Environmental Health Sciences Center, was lead author of the [study](#).

The investigators recruited 32 healthy, pregnant women between the ages of 20 and 40 for the study. Twenty three of the women lived in the Ron Pibul District of southern Thailand in villages that had been classified as high-level arsenic contaminated areas as a result of extensive tin mining from the 1960's to 1980's. Levels of arsenic in groundwater in the area are as much as 50 times the WHO standard. Women with toenail arsenic levels representing exposure below the WHO limit of 10ppb served as a control group.

During the subjects' pregnancies, the Chulabhorn investigators collected toenail samples, which were analyzed for total arsenic concentrations that reflect past exposures. After delivery of the women's children, a sample of newborn cord blood was collected for microarray analysis of gene expression. The researchers then performed data analysis to identify genes that showed modulated expression as a result of prenatal exposure and also to determine transcription factor binding sites and molecular interactions.



Shown in her Bangkok office, CRI Vice President for Research Mathuros Ruchirawat, Ph.D., posed at her computer as colleague Panida Navasumrit, Ph.D., an investigator in the CRI Laboratory of Environmental Toxicology, joined her for this photograph. (Photo courtesy of CRI)



Lead author Rebecca Fry wrote that "the genome-wide changes associated with prenatal arsenic exposure are robust, [and] arsenic-modulated networks represent numerous biological processes." (Photo courtesy of MIT)

Microarray analysis identified approximately 450 genes that were differentially expressed between the two populations, 90 percent of them showing an increase in expression level. The MIT investigators were able to isolate three arsenic-associated gene expression signatures and found that even the smallest set, which included eleven genes, showed 83 percent accuracy in predicting prenatal arsenic exposure. The eleven genes fall into gene ontology categories related to cell growth and death, stress and immune response, and inflammation.

“We were looking to see whether we could have figured out [from gene expression screening] that these babies were exposed *in utero*,” Samson explained. “The answer was a resounding ‘yes.’”

The government is aware of the arsenic contamination and, according to Fry, has provided alternative water sources to the affected villages in the Ron Pibul District.

The research was supported by NIEHS Division of Extramural Research and Training grants funding the MIT Center for Environmental Health Sciences and the development of *in vitro* alternative toxicity and carcinogenicity testing employing microarray and bioinformatics analysis. The grants are administered by Program Administrator Les Reinlib, Ph.D., and Acting Deputy Director Bill Suk Ph.D., who is on detail from his position as director of the Superfund Basic Research Program. In his work as part of the NIEHS global environmental health effort, Suk has collaborated with the Chulabhorn Research Institute.

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Superfund Looks to Its Future

By Eddy Ball

After two days of sharing the excitement of their science and recounting the accomplishments of the [Superfund Basic Research Program \(SBRP\)](#), on December 5 attendees at the twenty-year anniversary celebration (see [Spotlight story](#)) were confronted with the mass of unfinished business still to address and the challenges the program is sure to face in the future.

Titled “Colloquium: Visions for the Future,” the session included four presentations and a panel discussion. The session was chaired by SBRP Acting Director Claudia Thompson and moderated by University of Arizona pharmacologist Jay Gandolfi, Ph.D., and Texas A & M University geneticist Richard Finnell, Ph.D.



Corresponding author Leona Samson is the principal investigator for the two grants that funded the study. (Photo courtesy of MIT)



Moderators Gandolfi, left, and Finnell shared a laugh during the panel session. One outcome of the Colloquium for Finnell was his new awareness that “maybe we need to now add the epigenome” to his research approach. (Photo courtesy of Steve McCaw)

Johns Hopkins University Bloomberg School of Public Health Professor Lynn Goldman, M.D., opened the colloquium with a grim assessment of the globalization of hazardous wastes in a presentation sparked by the question “What Are the Lessons for Public Health?” Beginning what she described as “one of the most challenging talks I’ve given in a while,” Goldman enumerated a host of new challenges brought about by an increasing reliance on developing countries for processing the world’s wastes.

Goldman challenged the United States to adopt a regulatory system similar to the European Union’s, which requires the same kind of authorization for chemicals that is required for pesticides. She also called for dramatic expansion of the “standard suite of [hazardous chemical] candidates” that are studied and a stronger commitment to the public’s right to know. “If it’s in our bodies,” she argued, “I think we need to understand it.”

NIEHS grantee Randy Jirtle, Ph.D., a professor of radiation oncology at Duke University, offered an introduction to “Epigenetics: The New Genetics of Toxicology” to support his contention that the future of toxicology rests with an epigenetic approach utilizing high-throughput screening of human cell lines. Offering an overview of the differences in imprinting and epigenetic responses between species, Jirtle urged his audience to bear in mind that “a mouse is not a human.”

Quoting Alexander Pope’s “Essay on Man,” Jirtle argued that in toxicology, as in philosophy, “The proper study of mankind is man.” However, Jirtle’s human-centric approach to toxicology did not go unchallenged during the question-and-answer session, as a more traditional toxicologist in the audience echoed some of the issues that persist in relation to alternative testing and countered that “a cell is not an organism” either.

In a presentation titled “Systems Biology Approach to Optimizing Bioremediation,” University of Massachusetts at Amherst microbiologist Derek Lovley, Ph.D., reported on his group’s progress with *in situ* groundwater bioremediation using several species of the anaerobic bacteria *Geobacter*. Lovley’s lab has demonstrated that *Geobacter* species can break down contaminants such as acetate and uranium VI in groundwater and that the organisms show promise for use in the anaerobic degradation of polycyclic aromatic hydrocarbons — as well as in the conversion of waste matter to electricity.



Lovley, left, watched as Goldman responded to a comment from the audience. “What about all the other things that are involved in these waste sites?” she asked as she called for expanding the list of usual suspects looked for at hazardous waste sites. (Photo courtesy of Steve McCaw)



Jirtle, right, used the software/hardware analogy to illustrate the role of the role of epigenetics in regulating expression of the genome as Wiesner looked on. (Photo courtesy of Steve McCaw)

Lovley's systems approach utilizes sequence genomics, gene expression studies, proteomics and *in silico* modeling to predict optimal methods for use at Department of Energy, Department of Interior and Department of Defense hazardous waste sites. Coupled with hydrological and geophysical models, the approach promises to advance bioremediation and maximize resources available for cleaning hazardous waste sites.

The final presentation, by Duke University Professor of Civil and Environmental Engineering Mark Wiesner, Ph.D., focused on "Research Needs in Evaluating Nanomaterial Risks: The Fullerene Example." As his experiments with the nano carbon C₆₀ demonstrate, the more research that is performed with nanomaterials, the more questions arise about how these microscopic particles interact with the human organism.

There are so many factors that influence nanomaterial behavior, he argued, that "the idea of putting all things that are small in the same box doesn't make any sense." Established risk parameters, he also noted, do not seem to work for nanoparticles. Until the new physics of nanoparticles is better understood, scientists will not understand how much of a threat, if any, they actually pose to public health.



Like others in the audience, Suk appeared to have plenty to ponder during the three and a half hour Colloquium. The presentations reinforced the urgency of the global environmental health threat posed by inadequately regulated hazardous waste disposal. (Photo courtesy of Steve McCaw)



When the meeting concluded, the "heavy lifters" posed for the camera. Shown left to right, the event organizers are contract audiovisual specialist Justine Crane of MDB, Ahlmark, Thompson, MDB Technical Writer Maureen Avakian, SBRP Program Analyst Beth Anderson and Program Administrator Heather Henry, Ph.D. (Photo courtesy of Steve McCaw)

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Higher BMI Worsens Ozone Effect

By Robin Mackar

A new study published in *Inhalation Toxicology* and co-authored by two NIEHS researchers, Stephanie London, M.D., and Grace Kissling, Ph.D., provides the first evidence that people with higher body mass index (BMI) may have a greater response to ozone exposure than leaner people. Ozone is formed in the atmosphere in the presence of sunlight from pollutants emitted from vehicles and other sources.

Researchers at the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health, the University of North Carolina (UNC) at Chapel Hill and the U.S. Environmental Protection Agency (EPA) analyzed data on young (18–35 years), healthy, non-smoking men and women to see if BMI — a measure of the amount of fat a person has calculated by the ratio of height to weight — had an effect on lung response to acute ozone exposure.

“It has been known for a long time that in response to short-term exposure to ozone lung function tends to temporarily drop in many people. There has recently been interest in why some people’s lung function drops more than others. “Age and perhaps genetics, as well as diet may play a role,” said London, an NIEHS researcher and co-author. “We were intrigued by recent mouse studies that showed that obesity increases lung responses to ozone and wanted to see whether this applied in humans.”

To examine the question of whether higher body mass index influences ozone responses in humans, the investigators took advantage of an earlier study led by [Milan J. Hazucha and colleagues](#) at the Center for Environmental Medicine, Asthma and Lung Biology/UNC and the USEPA Human Studies Facility in Chapel Hill, N.C.

The study determined BMI in 197 subjects who had been exposed to ozone for 90 minutes, during which they alternated 20 minutes of exercise with 10 minutes of rest. The subjects’ lung capacity and function were tested immediately before and after the exposure period using spirometry, a basic lung function test that measures the speed and volume of air breathed out of the lungs.

In general, the higher the BMI, the greater the ozone response, providing one more reason why maintaining a healthy body weight is important to good health. When subjects were put into categories of body fatness defined by the US Centers for Disease Control based on their BMI, the ozone-related drops in lung function, particularly the forced expiratory volume in one second (FEV1), were lowest in underweight people (BMI less than 18.5), greater in normal weight people (BMI 18.5 to 25) and greatest in overweight individuals (BMI above 25).

“It’s notable that these results came out of a study that was done in a population of predominantly normal weight individuals,” said London. “This suggests that these effects may be even more important in the general population where there are large proportions of overweight and obese individuals.” An estimated two-thirds of U.S. adults are overweight or obese, with a BMI greater than 25, according to [CDC](#).



*NIEHS Epidemiology Branch Senior Investigator Stephanie London
(Photo courtesy of Steve McCaw)*

The physiologic mechanisms responsible for the decline in lung function after ozone exposure with increasing BMI are not clear, although the authors suggest that perhaps circulatory hormones and other inflammatory factors may play a role. These factors have been shown to affect airway hyper-responsiveness and inflammation in animal models.

The authors note that the study was limited by the small number of obese individuals (the subjects had not been selected with a study of BMI in mind) and by having only one measure of a person's body fat. Future studies of the effects of obesity on ozone response, they say, should include a targeted pool of obese and lower weight subjects, as well as measures of central adiposity such as waist circumference, given that fat deposited centrally may have a greater influence on an individual's respiratory response to ozone.

The study was supported by U.S. EPA Cooperative Agreement CR824915 and CR829522 and in part by the Division of Intramural Research, NIEHS, NIH, HHS.

Reference: [Bennett WD, Hazucha MJ, Folinsbee LJ, Bromberg PA, Kissling GE, London SJ. 2007. Acute Pulmonary Function Response to Ozone in Young Adults as a Function of Body Mass Index. Inhal Toxicol 19 \(14\): 1147-1154.](#)

[Hazucha, M. J., Folinsbee, L. J., and Bromberg, P. A. 2003. Distribution and reproducibility of spirometric response by gender and age. J. Appl. Physiol. 95:1917-1925.](#)

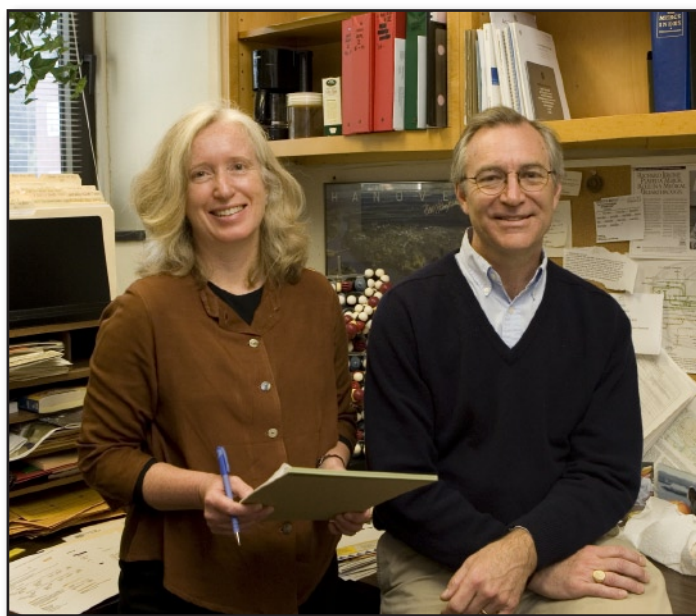
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Low Dose Arsenic Can Be an Endocrine Disruptor

By Robin Arnette

The U.S. drinking water supply contains several naturally occurring contaminants, such as potassium, arsenic, manganese and radium, as well as a number of organic contaminants including chlorination by-products and groundwater contaminants. The federal government established acceptable limits of these substances to protect the health and well-being of its citizens. But in a new Superfund study, researchers at Dartmouth Medical School have discovered that even low levels of one of these contaminants—arsenic—can disrupt hormone pathways that are involved in normal human development.

The corresponding author of the study, [Joshua W. Hamilton, Ph.D.](#), is director of the [Center for Environmental Health Sciences at Dartmouth](#) and a professor in the Department of Pharmacology and Toxicology at Dartmouth Medical School. The article appeared in the October 26 online edition of [Environmental Health Perspectives](#).



Hamilton, right, is shown with the study's lead author, a colleague in the Department of Pharmacology and Toxicology at Dartmouth College Medical School, Jennifer Davey. (Photo courtesy of Joseph Mehling, Dartmouth College)

Hamilton and his colleagues knew from their previous work that low levels of arsenic prevented the ability of steroid hormone receptors (SR) to bind molecules of hormone in whole animal models and in cell culture. This disruption occurred in several SRs, including glucocorticoid, androgen, progesterone, mineralcorticoid and estrogen. The team wanted to know if the same was true for the retinoic acid (RA) receptor (RAR) and the thyroid hormone (TH) receptor (TR), two members of the nuclear hormone receptor super-family that are essential for normal vertebrate development.

They used two lines of experimentation to study the effects of arsenic on receptor-mediated gene transcription. In one approach, they constructed artificial RAR response elements or TR response elements and transfected them into cell lines. Human embryonic NT2 cells received the RAR construct and rat pituitary GH3 cells received the TR construct. The cells were then treated with low, non-cytotoxic doses (0.01–5.0 μM) of sodium arsenite for 24 hours, in the presence or absence of RA or TH, respectively. In both cases, arsenic suppressed RAR- and TR-dependent gene transcription.

In the second approach, the team used frog tail shrinkage or resorption as an example of the hormone-dependent developmental transition that amphibians experience to study the effects of arsenic on TR. Frog tail shrinkage is tightly controlled by TH through TR, so they measured the area of the tail fin over a four-day period in the presence or absence of varying doses of arsenic (0.1–4.0 μM). The TH-dependent tail shrinkage was inhibited by arsenic in a dose-dependent manner.

The study concluded that low dose arsenic prevented TH from functioning and metamorphosis did not occur. These findings are important because the TH spike in amphibians during metamorphosis is analogous to the TH spike in plasma levels in humans during the perinatal period. Thus, inhibiting TH action in humans could potentially lead to birth defects in arsenic-exposed populations in the U.S. and in many parts of the world.

“The two most important implications of this work with respect to possible human health effects are that human embryonic, neonatal and childhood development is critically dependent on the proper regulation of key developmental processes by thyroid hormone, retinoic acid hormone, and other hormones,” Hamilton explained, “and that these endocrine disrupting effects were observed at or below the current U.S. and WHO arsenic drinking water standard of 10 ppb.”

Hamilton’s research was funded by NIEHS through the [Superfund Basic Research Program \(SBRP\)](#) and is a great example of the collaborative effort that SBRP grantees play in addressing the challenges of environmental contamination. “The opportunity to regularly interact with many other researchers doing complementary research on other mechanisms of arsenic’s actions as a toxicant on the one hand, and on endocrine disruption by other chemicals on the other,” he says, “has provided us with important and timely insights that have been directly applied to our own research.”

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Upcoming Distinguished Lecture Features Richard A. Flavell

By Eddy Ball

The 2007-2008 NIEHS Distinguished Lecture Series continues at 11:00 a.m. on January 8 with a talk by Richard A. Flavell, Ph.D., on “Innate and Adaptive Immunity.” Flavell’s talk will take place in Rodbell Auditorium and be hosted by Donald Cook, Ph.D., head of the Immunogenetics Group in the NIEHS Laboratory of Respiratory Biology.

Flavell is Sterling Professor and Chairman of the Department of Immunobiology at the Yale University of School of Medicine. He is also a professor of Molecular, Cellular and Developmental Biology and an investigator with the Howard Hughes Medical Institute.

His lab’s research is focused on several basic research topics in the field of immunity. He is interested in the molecular basis of the activation and differentiation of T-lymphocytes, and his team is working to elucidate the mechanisms of CD4 T cell differentiation to effector cells. The lab integrates the molecular approaches that the investigators use to understand molecular mechanisms of differentiation and death into the study of critical autoimmune diseases and their relationship to toll-like receptors (TLR).



*Distinguished lecturer Richard Flavell
(Photo courtesy of Yale University)*

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Extramural Update

Karimi Honored with Superfund’s 2007 Karen Wetterhahn Memorial Award

The Superfund Basic Research Program (SBRP) announced that Roxanne Karimi, Ph.D., of Dartmouth College is the recipient of the tenth annual [Karen Wetterhahn Memorial Award](#). The award was presented on December 4th, 2007 at the SBRP 20th Anniversary Annual Meeting in Durham, N.C., by NIEHS Division of Extramural Research and Training Acting Director Dennis Lang, Ph.D.

Each year, the SBRP presents this award to an outstanding scholar to pay tribute to the life and scientific accomplishments of Karen E. Wetterhahn, Ph.D., Professor of Chemistry, the Albert Bradley Third Century Professor in the Sciences, and former director of the SBRP at Dartmouth College. Wetterhahn died in 1997 as the result of an accidental



Karimi presented her study, titled “The Ecophysiology of Metal Accumulation in Aquatic Food Webs.” In May 2007, National Public Radio featured [a related study](#) by her team on the program “Science Friday.” (Photo courtesy of Steve McCaw)



Lang, left, and Superfund Technical Information Specialist Kathy Ahlmark applauded past winners of the Wetterhahn Award prior to Karimi's presentation. (Photo courtesy of Steve McCaw)

exposure to dimethylmercury. She played an integral role in the administration of the sciences at Dartmouth and co-founded Dartmouth's Women in Science Project (WISP), which is aimed at increasing the number of women majoring and taking courses in the sciences, including mathematics and engineering.

An acknowledged international expert on the effects of heavy metals on biological systems and a dedicated teacher and mentor, Wetterhahn was a leader in conducting research on how metals initiate cancer and other metal-induced human diseases at the molecular level. She fostered links between biology, chemistry, environmental studies, engineering and medical science, insisting that "the life sciences are interdisciplinary."

According to the nominating committee, Karimi exhibits characteristics worthy of a Karen Wetterhahn Memorial Awardee. She has been active in the WISP program, has mentored several undergraduate women in her lab, and has also been active in promoting the participation of underrepresented groups in the sciences.

Karimi completed her Ph.D. at Dartmouth College in the spring of 2007, and is now working in a postdoctoral fellowship in the Marine Sciences Center at Stony Brook University. Karimi's SBRP research focused on the accumulation and cycling of heavy metals within freshwater organisms, food webs and ecosystems. Her research has also revealed that, contrary to the

Superfund Poster Awards

Grantees and students displayed 154 poster abstracts at the anniversary meeting. In addition to Karimi, four students were honored as winners for their entries in the poster session, two for each of the evening sessions. Winners will receive a check for \$250 in honor of their accomplishment.

- Elizabeth Oesterling, University of Kentucky, as lead author of "Benzo[a]pyrene-Induced Vascular Endothelial Adhesion Molecule Expression Can Be Reduced by Selective Flavonoid Treatment"
- Bryan Clark, Duke University, as lead author of "Investigation of PAH Adaptation in Atlantic Killifish (*Fundulus heteroclitus*) Using Morpholino Gene Knockdown"
- Karen Wovkulich, Columbia University, as lead author of "Mobilization of Arsenic from Contaminated Sediments for Improved Remediation"
- Courtney Kozul, Dartmouth College, as lead author of "Chronic Low-dose Arsenic Exposure Alters Key Regulators of Innate Immune Response *in vivo*"



On the final morning of the meeting, Superfund Acting Director Claudia Thompson, Ph.D., congratulated Brian Clark on his poster session award. (Photo courtesy of Steve McCaw)

prevailing conventional wisdom, free-swimming fish who feed in open waters, what is known as the pelagic zone, actually accumulate more mercury than those feeding on food webs of the sediments in the lowest levels of a body of water, or the benthic zone.

Karimi's current postdoctoral research at Stony Brook University examines pairwise, metal-metal and metal-nutrient interactions and their effects on metal accumulation and efflux in marine organisms. For example, essential metals, namely selenium, while potentially toxic at relatively high concentrations, can have protective effects against mercury accumulation and toxicity.

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Extramural Papers of the Month

By Jerry Phelps

Beyond the Human Genome Sequence: Scientists Map "Silenced Genes"

NIEHS supported researches have identified and mapped a set of about 200 genes that are turned off or silenced and are believed to play a profound role in people's health. This work marks an important step in studying how the environment interacts with genes to help determine why some people get sick and others don't.

Usually, people inherit two alleles or copies of genes, one from each parent. Typically, both copies are active, but if one copy of a gene becomes mutated and quits working properly, often the other copy can compensate. Genetic imprinting turns off or silences the backup copy. Molecular signals, such as DNA methylation, imprint the copy from the other parent to be silent. Until now, only about 40 human imprinted genes had been identified.

The research team reported that many of the newly found imprinted genes are in regions of chromosomes already linked to the development of obesity, diabetes, cancer and some other major diseases — including several cancers and, possibly, epilepsy and bipolar disorder.

Previous research has indicated that imprinted genes accounted for only about 1 percent of the human genome. While scientists must double-check that the newly identified ones are truly silenced, the new map matches that tally.

Citation: Luedi PP, Dietrich FS, Weidman JR, Bosko JM, Jirtle RL, Hartemink AJ. 2007. Computational and experimental identification of novel human imprinted genes. *Genome Res* (12):1723-1730.

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Bisphenol A Effects on ER β Expression: Implications in Prostate Cancer

Bisphenol A causes down regulation of gene expression for estrogen receptor β (ER β) and likely regulates cell proliferation in prostate cancer, according to new research from NIEHS grantees at the University of Cincinnati.

Prostate adenocarcinomas are dependent on the androgen receptor for growth and progression. Current therapies are aimed at repressing androgen receptor activity; however, androgen receptor activity can be reactivated through somatic mutations that form mutant receptors. These altered receptors can be activated by alternative ligands including bisphenol A, an endocrine disrupting chemical that is found in many plastics.

Using a prostate cancer cell line containing mutant androgen receptors and employing DNA microarray analysis, the researchers were able to show that bisphenol A dramatically reduced ER β expression. Since ER β functions to antagonize the androgen receptor function and androgen receptor-dependent cell proliferation, decreasing its expression could likely lead to growth of prostate tumors. Future research in this laboratory will focus on the contribution of ER β on the bisphenol A-induced proliferative response.

Citation: [Hess-Wilson JK, Webb SL, Daly HK, Leung YK, Boldison J, Comstock CE, Sartor MA, Ho SM, Knudsen KE. 2007. Unique bisphenol A transcriptome in prostate cancer: novel effects on ER beta expression that correspond to androgen receptor mutation status. Environ Health Perspect 115\(11\):1646-1653.](#)

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Regular Use of NSAIDS May Reduce the Risk of Parkinson's Disease

Over-the-counter nonsteroidal anti-inflammatory agents (NSAIDS) reduce the risk of Parkinson's disease (PD) by a little more than half among regular users of these common drugs, according to new NIEHS-supported epidemiologic research. Using as few as two pills per week for as little as one month lowered a person's risk of the disease by 20 percent.

Neuroinflammatory markers, such as the presence of microglia, immune cells within the central nervous system and increased levels of proinflammatory cytokines, are frequently found in the brains and cerebrospinal fluids of PD patients. However, the link between anti-inflammatory agents and Parkinson's in humans remains uncertain, although there is a body of evidence in laboratory animal models of PD that NSAIDS exert a protective effect.

The study participants included 579 men and women, about half of whom had PD. A stronger protective effect was seen for regular users of non-aspirin anti-inflammatory agents. Only 44 percent of non-aspirin users who had taken the drugs regularly for more than 24 months developed Parkinson's. Interestingly, a protective effect for regular aspirin use was only seen in women — reducing their risk by about 40 percent.

Future research by this and other research teams will be focused on trying to determine the exact mechanism by which anti-inflammatory drugs exert this effect.

Citation: [Wahner AD, Bronstein JM, Bordelon YM, Ritz B. 2007. Nonsteroidal anti-inflammatory drugs may protect against Parkinson disease. Neurology 69\(19\):1836-1842.](#)

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Intramural Papers of the Month

By Robin Arnette

Genes in Blood Can Predict Harmful Levels of Acetaminophen

A new study, published in a recent issue of *PNAS* and funded by the NIH and the NIEHS, reports that gene expression data obtained from blood cells can predict harmful levels of acetaminophen exposure.

Millions of people around the world use acetaminophen to reduce fever and relieve pain, but too much of it or heavy prolonged use may lead to acetaminophen intoxication and eventually severe liver damage. With this information in mind, the team set out to determine whether gene expression patterns derived from blood cells could indicate levels of acetaminophen exposure.

Researchers used a rat model to generate a training data set consisting of genomic, clinical chemistry, histopathology and hematology data. They then determined the gene sets that would act as indicators of subtoxic/nontoxic and toxic dose levels of acetaminophen and used microarray analysis to screen thousands of genes simultaneously. Genetic markers derived from a rat blood test data set indicated from several prediction methodologies that the level of accuracy was 88.9–95.8 percent. After determining the human gene orthologs, they found that the blood from overdose victims contained different patterns of expression from the cluster of indicator genes.

This work represents a possible first step in the development of a diagnostic test that can identify patients who are at risk of an acetaminophen overdose.

Citation: Bushel PR, Heinloth AN, Li J, Huang L, Chou JW, Boorman GA, Malarkey DE, Houle CD, Ward SM, Wilson RE, et al. 2007. Blood gene expression signatures predict exposure levels. *PNAS* 104(46):18211-18216.

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DNA Polymerase Gamma Mutant Causes Enhanced Oxidative Stress

NIEHS scientists have found a biochemical link that explains the enhanced oxidative stress and DNA mutagenesis that occurs in patients suffering from progressive external ophthalmoplegia (PEO) with Parkinson symptoms. The research was funded by NIEHS and published in *Human Molecular Genetics*.

Previous work had demonstrated that the DNA polymerase gamma (pol γ) present in these patients carried a tyrosine to cysteine mutation (Y955C) that, in turn, induced replication stalling and DNA deletions. Because these patients also develop Parkinson symptoms, and animal models show enhanced incorporation of 7,8-dihydro-8-oxo-2'-deoxyguanosine (8-oxo-dG), a common oxidative lesion into mitochondrial DNA, the team wanted to determine why the Y955C pol γ allowed more 8-oxo-dG in DNA and oxidative stress.

They performed DNA polymerase reactions with both wild type and mutant polymerases and then developed molecular models with 8-oxo-dG in the active site and the incorporation of different dNTPs.

The results indicated that the Y955C pol γ was more likely to insert the 8-oxo-dG lesion instead of the normal nucleotide dGTP. Once the 8-oxo-dG was present in DNA, the Y955C pol γ was also more likely to incorporate a dATP opposite this lesion which results in a mutation. The research explains why these PEO patients present phenotypes normally associated with oxidative stress and Parkinson disease.

Citation: [Graziewicz MA, Bienstock RJ, Copeland WC](#). 2007. The DNA polymerase γ Y955C disease variant associated with PEO and parkinsonism mediates the incorporation and translesion synthesis opposite 7,8-dihydro-8-oxo-2'-deoxyguanosine. *Hum Mol Genet* 16(22):2729-2739.

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Regulatory Roles of Two Retinoid-related Orphan Receptor Isoforms

In a study funded by NIEHS and the Clinical Nutrition Research Unit Center and published in *Physiological Genomics*, researchers reported that retinoid-related orphan receptors alpha (ROR α) and gamma (ROR γ), expressed in the liver, have multiple physiological roles — including regulating the genes encoding several phase I and phase II enzymes, such as cytochrome P450.

The researchers had previously shown that ROR α and ROR γ were coexpressed in a variety of tissues including fat, kidney and liver. The team set out to identify their physiological roles in liver and, in addition, wanted to determine whether these two receptors exhibited redundant functions as has been shown for several other nuclear receptors. They used ROR α -deficient *staggerer* (sg) (ROR $\alpha^{sg/sg}$) mice, ROR $\gamma^{-/-}$ mice and ROR $\alpha^{sg/sg}$ ROR $\gamma^{-/-}$ double knockout mice and microarray analysis to compare the gene expression profiles from the livers of these mice to those of wild-type mice.

Gene expression analysis indicated that some liver genes were specifically regulated by either ROR α or ROR γ , while other genes were regulated by both receptors indicating functional redundancy. Most importantly, lack of ROR α and ROR γ affected the expression of phase I and phase II enzymes, suggesting these receptors play a role in the regulation of metabolic homeostasis.

Citation: [Kang HS, Angers M, Beak JY, Wu X, Gimble JM, Wada T, Xie W, Collins JB, Grissom SF, Jetten AM](#). 2007. Gene expression profiling reveals a regulatory role for ROR α and ROR γ in phase I and phase II metabolism. *Physiol Genomics* 31(2):281-294.

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Glucocorticoid Receptor Isoforms Regulate Bone Cell Apoptosis

A newly published study found that the glucocorticoid receptor D (GR-D) isoform, one of eight translational glucocorticoid receptor isoforms, exhibited reduced cell-killing capacity in bone cells while still repressing nuclear factor kappa-beta, which is involved in many inflammatory diseases. This data is important because glucocorticoids — generally prescribed to treat a variety of illnesses such as cancer, inflammation and autoimmune disorders — selectively kill bone cells while protecting other cells such as liver and skin. NIEHS researchers published this data in *Molecular and Cellular Biology*. The work was supported by NIEHS and a division grant from the Department of Medicine, Northwestern University.

Glucocorticoids provide a medical benefit, but patients who use them chronically suffer debilitating and sometimes life-threatening side effects, such as muscle wasting and osteoporosis. To determine the enzymes important in glucocorticoid-induced apoptosis in bone, the team treated human osteoblastic cells U-2 OS with dexamethasone and used small interfering RNA (siRNA) and PCR to determine that granzyme A and caspase-6 were involved. Results from microarray analysis indicated that each GR isoform had a distinct set of glucocorticoid target genes and specific functions.

These findings may lead to the development of safe glucocorticoids that exhibit reduced side effects.

Citation: [Lu NZ](#), [Collins JB](#), [Grissom SF](#), [Cidlowski JA](#). 2007. Selective regulation of bone cell apoptosis by translational isoforms of the glucocorticoid receptor. *Mol Cell Biol* 27(20):7143-7160.

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Inside the Institute

NIEHS Holds Awards Day

By Eddy Ball

On December 13, NIEHS honored employees at the Director's Annual Honor Awards Ceremony in Rodbell Auditorium. The event was chaired by Director of Education and Biomedical Research Development Marian Johnson-Thompson, Ph.D. Handing out awards were Acting Director Sam Wilson, M.D., Acting Deputy Director Bill Suk, Ph.D., Acting Scientific Director Perry Blackshear, M.D., D.Phil., Division of Extramural Research and Training Acting Deputy Director Pat Mastin, Ph.D., and Deputy Associate Director for Management Chris Long.

Program Analyst Diane Crawford, the organizer of the event, had notified the NIH Merit Award and Service Award winners, but there were also three categories of winners that were not announced until the ceremony itself. Unlike the announced winners, the winners in the categories of Unsung Hero, Peer Awards and Fellows Award for Research Excellence Awards could look forward to seeing a very tangible and negotiable acknowledgement of their contribution to the mission of NIEHS.



Johnson-Thompson, at the podium, speaks as the presenters wait their turns: left to right, Suk, Long, Blackshear, Mastin and Wilson. (Photo courtesy of Steve McCaw)

The NIH Merit Award Winners

Individuals

Office of the Director (OD) — Brenda Weiss, Ph.D., Christine Bruske-Flowers, Joyce Daye, Robin Mackar and Eddy Ball, Ph.D.

Division of Extramural (DERT) Research and Training — Annette Kirshner, Ph.D., Jerry Heindel, Ph.D.,

Groups

OD — Lindsay Lloyd, Angie Sanders, Shannon Baker

DERT — Linda Bass, Ph.D., Leroy Worth, Ph.D., Rose Ann McGee, Terry Nesbitt, Ph.D., Gwen Collman, Ph.D., David Balshaw, Ph.D., Daniel Shaughnessy, Ph.D., Lerlita Garcia

Division of Intramural Research (DIR) — William Schrader, Ph.D., Frank Johnson, Ph.D.

DIR — Michelle Hooth, Ph.D., Raj Chhabra, Ph.D., Grace Kissling, Ph.D., Greg Travlos, D.V.M., Nigel Walker, Ph.D., Ron Melnick, Ph.D., Kristine Witt, Brad Collins, Leo T. Burka, Ph.D., Ron Herbert, D.V.M., Ph.D., Charles Alden, Ph.D., Dave Malarkey, D.V.M., Ph.D.

DIR — Lisa Rogers, Cindy Garrard, Nell Boyd, Barbara Curtis

Office of Management — Dona McNeill, Diane L. Crawford, Alma Britton, Richard Sloane, Cynthia Radford

Cross Divisional — William Stokes, D.V.M., Sheila Newton, Ph.D.

Cross Divisional — Christine Bruske-Flowers, Cheryl Thompson, Robin Arnette, Ph.D., Kimberly Thigpen Tart, Sharon Beard, Beth Anderson, Pat Chulada, Ph.D., Donna Byrd, Sharon Hite, Robin Jones

Cross Divisional — Joel Abramowitz, Ph.D., Donna Byrd, Allen Dearry, Ph.D., Stephanie Holmgren, Bill Jirles, Dennis Lang, Ph.D., Dona McNeill, Liam O’Fallon, John E. Schelp, Bill Schrader, Ph.D., Mary Wolfe, Ph.D., Beth Bowden

Cross Divisional — Josee Crowell, Donald Hannah, David Little, Samuel Musulin, Joey Shealey, Terry Wells

The Unsung Hero Awards

Kent Stone, Jennifer Collins, Connie Riley

The Peer Awards

Mitsue Parrish, Page Myers, Nell Boyd

The FARE Awards

Mercedes Arana, Ph.D., Marcelo Bonini, Ph.D., Brian Hawkins, Ph.D., Senyene Hunter, Ph.D., Nobby Kamiya, Ph.D., Gino Limmon, Ph.D., Negin Martin, Ph.D., Stephanie Nick McElhinny, Ph.D., Zac Pursell, Ph.D., Arno Siraki, Ph.D., Paivi Salo, Ph.D., Yong Yang, Ph.D., Meilan Zhao, Ph.D.

Service Awards

30 years — Jan Drake, Ph.D., Renee McCants, Clarence Gibson, Carolyn Milford, John Hong, Ph.D., Michael Shelby, Ph.D., Frank Johnson, Ph.D., Richard Sloane, Lawrence Lazarus, Ph.D., Michael Snell

40 years — Barbara Corbett, Thomas Gray

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Each of the lucky 13 FARE Award winners could bank on a \$1,000 stipend for professional development. Pursell and Arana were also winners in 2006. (Photo courtesy of Steve McCaw)

Diversity Council Hosts Native American Heritage Concert

By Eddy Ball

True to tradition, the NIEHS Diversity Council gave NIEHS employees and contractors something a little different when it presented a concert in the NIEHS cafeteria by R. Carlos Nakai and Keola Beamer in celebration of Native American Heritage Month November 30.

Hosted by EEO Specialist Gerard Roman and attended by nearly 50 people, the performance featured music on the slack key guitar, Native American cedar wood flute and the Hawaiian nose flute, which didn't turn out to be nearly as ridiculous as the term might suggest.



As staff cleaned the cafeteria's serving area in the background, Beamer accompanied his soulful Hawaiian chanting with the mellow sounds of the slack key guitar; an instrument introduced to the islands by the Spanish. (Photo by Eddy Ball)



Nakai, a Navajo-Ute, took a break from his cedar wood flute to treat the audience to a traditional chant with percussion accompaniment. (Photo by Eddy Ball)

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Institute Celebrates the Season

By Eddy Ball

Members of the NIEHS community, who put their best efforts into advancing science during the rest of the year, are also accomplished at ushering in the solstice season. During the weeks leading up to the two-day holiday, the festive season gives contractors and employees an opportunity to show off their goofy ties, silly sweaters, and ridiculous hats and to decorate office doors with wrapping paper, ribbon and bows.

Holiday parties are an important part of the season at NIEHS. Core groups of people in divisions, labs or buildings hold smaller lunches and receptions, and as the big break gets closer, there are two Institute-wide events, the International Day celebration following Awards Day and the Director's Holiday Reception, hosted this year by Acting Director Sam Wilson and Acting Deputy Director Bill Suk.

Luckily, photographers were on hand to record the fun and fellowship.

Down the Hall



Ken Olden's door reflects the holiday spirit in Nottingham Hall. (Photo by Eddy Ball)



As does one at the other end of the hall belonging to Marian Johnson-Thompson. (Photo by Eddy Ball)



It's hard to beat the optimism expressed by these three words on a hat hanging outside the door to Jane Lambert's office. (Photo by Eddy Ball)

Nottingham Gets Down for the Holidays – December 4



When it's time for Office of Management folks to party, Dick Sloan, right, is usually on hand. Dick is joined by Susan Sherron, left, and Tommy Hardy, standing, as they go over the order of entertainment. (Photo courtesy of Dona McNeill)



Like other "local" events, the Nottingham party is a potluck paradise. From left to right, Jennifer Collins, Kelly Powell, Fran Cowans and Tammy Baynor enjoy the holiday fare. (Photo courtesy of Dona McNeill)

Nottingham Gets Down for the Holidays — December 4 (cont'd)



Sporting his holiday tie, Phil Hanson, right, built his plate, as Donna Byrd, foreground, tried to decide where to begin. Celeste Edwards was in the background making difficult choices from among the abundance of goodies. (Photo courtesy of Dona McNeill)



Were Keith Holloway, left, and Sheila Norton talking IT and Policy — or chicken and cake? (Photo courtesy of Dona McNeill)



A'tondra Carree will surely cherish this turkey... uh, chicken... for years to come. Giving gag Secret Santa gifts like this one is one way to clean out the attic — and clutter up someone else's. (Photo courtesy of Dona McNeill)



The luncheon may have begun on a quiet note, but once the sugar started to kick in, the event became loud and exuberant. (Photo courtesy of Dona McNeill)

International Day – December 13



Chris Long may be a little green, but he showed he has the right stuff as he filled in for Marc Hollander as emcee. (Photo courtesy of Steve McCaw)



Dick Sloan put his heart into the NIEHS band with Santa cap, goofy tie and white “Mr. Rogers” sweater, as band mate Doug Bristol joined in. (Photo courtesy of Steve McCaw)



Perry Blackshear enjoyed an opportunity to talk with newcomer Sharon Hrynkow, whose oriental garb reflected the international theme of the event. (Photo courtesy of Steve McCaw)



For some of the small children, the best part of International Day was decorating the tree. (Photo courtesy of Steve McCaw)

International Day – December 13 (cont'd)



*And big kids, such as Dona McNeill, also seemed to enjoy it.
(Photo courtesy of Steve McCaw)*



*Along with the NIEHS Band's repertoire of Christmas tunes, there were professional musicians on hand to entertain the audience.
(Photo courtesy of Steve McCaw)*

Director's Reception – December 17



*Chris (Kringle) Portier made the rounds during the reception.
(Photo by Eddy Ball)*



Framed by the campus lake in the background, Allen Dearry joined Annette Kirschner, left, and Carol Shreffler for an obligatory spot of punch. (Photo by Eddy Ball)

Director's Reception – December 17 (cont'd)



This year Dick Sloane, in white sweater, celebrated his 30th solstice with NIEHS. In the foreground, Rhonda Carroll indulged in the party brew. (Photo courtesy of Steve McCaw)



Dav Robertson, left, and Melissa Chan chatted with Bill Suk. (Photo courtesy of Steve McCaw)



The Director's Reception featured "refreshments," not an all-you-can extravaganza like Nottingham's bash, but keeping the cups filled for guests like Brandon Cuthbertson kept volunteers busy. (Photo courtesy of Steve McCaw)



The event gave Wilson a chance to talk with a number of employees, including Barbara Shane. (Photo courtesy of Steve McCaw)



Durham Chapter Delta Alumnae Sharon Beard, left, and Marian Johnson-Thompson work in different off-campus buildings, but they got to spend some holiday quality time together at the reception. (Photo courtesy of Steve McCaw)



A grateful Wilson posed with Charletta Fowler, the young woman whose extra effort makes each year's reception a success. (Photo courtesy of Steve McCaw)

Clinical Research Unit Takes Shape

By Eddy Ball

The factory-built modular units that will make up the new Clinical Research Center arrived right on schedule in early December, and workers started placing the units and connecting them together to create a structure resembling the [artist's rendition](#) posted on the NIEHS web site.

The former parking lot adjacent to F Module sat idle for months before a flurry of site preparation activity began in earnest earlier in the fall. Construction should not take long, but the management and staffing of the facility are different matters, as the Office of the Scientific Director recruits physicians to staff the unit and works with the Institutional Review Board to approve study proposals.

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A portion of the main road through campus was closed as the modules were trucked in. (Photo courtesy of Steve McCaw and John Maruca)



A powerful crane lifted the units into place. The modules were pre-constructed in Pembroke, NC, fitted together and then taken apart before being trucked to the site. (Photo courtesy of Steve McCaw and John Maruca)



One by one, workers guided the units into place as the larger structure emerged. The units, which measure 15 feet by 77 feet, contain the wiring, walls, insulation, windows and even the office doors and door locks. (Photo courtesy of Steve McCaw and John Maruca)



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