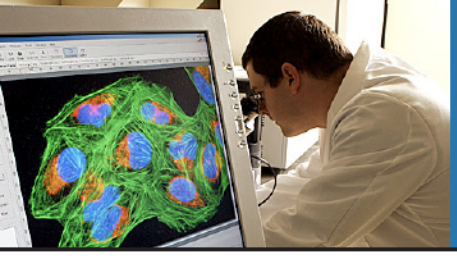

Environmental Factor
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April 2009

NIEHS Spotlight

NIEHS and NTP Formally Welcome Birnbaum as Director

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Autism Panel Releases Strategic Plan

On March 5, the Interagency Autism Coordinating Committee (IACC) released its much-anticipated blueprint for research on autism. ...read more

NIEHS Women at Center Stage in Bethesda

NIEHS leaders Associate Director Sharon Hrynkow, Ph.D., and Director Linda Birnbaum, Ph.D., were featured speakers at the NIH 2009 Women's History Month Observance held in Wilson Hall on the NIH Campus in Bethesda March 12. The event was sponsored by the NIH Office of Equal Opportunity and Diversity Management ...read more

Science Notebook

Transcriptional Control During Embryogenesis

Studies with the common fruit fly (*Drosophila melanogaster*) and sea squirt (*Ciona intestinalis*) are helping to unravel the connection between transcriptional networks and cellular behavior. ...read more

TAC Seminar Explores Y-Family Polymerases

On March 9, the NIEHS Trainee Action Committee (TAC) of the Laboratory of Molecular Genetics welcomed Roger Woodgate, Ph.D., chief of the Laboratory of Genomic Integrity at the National Institute of Child Health and Development. ...read more

First Sister Study Results Reinforce the Importance of Healthy Living

Women who maintain a healthy weight and who have lower perceived stress may be less likely to have chromosome changes associated with aging than obese and stressed women, according to a pilot study that was part of the NIEHS-sponsored Sister Study. ...read more

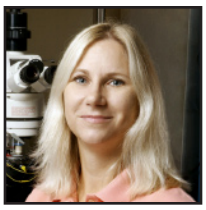
Study Links Maternal Exhaust Exposure to Childhood Asthma

A recent proof-of-principle study, funded in part by NIEHS, reports preliminary evidence of an association between transplacental exposure to traffic-related polycyclic aromatic hydrocarbons (PAHs) and childhood asthma among a cohort in New York City — where more than 25 percent of children are affected by the disease. ...read more

NIEHS Spotlight

Superfund Student Honored at Annual Toxicology Meeting

The NIEHS Superfund Basic Research Program (SBRP) was well represented at this year's Society of Toxicology Annual Meeting March 15–19 in Baltimore, where Dartmouth College Ph.D. candidate and SBRP trainee Courtney Kozul was awarded an impressive four awards in recognition of her research. ...read more



Dudek to Receive A. E. Bennett Research Award

NIEHS Principal Investigator Serena Dudek, Ph.D., will be honored on May 16 by the president of the Society of Biological Psychiatry at the 64th Annual Scientific Convention and Meeting in Vancouver, British Columbia. ...read more

Birnbaum Taps Pritchard as Acting Scientific Director

NIEHS Director Linda Birnbaum, Ph.D., announced the selection of retired NIEHS Principal Investigator John Pritchard, Ph.D., to serve as acting scientific director during a period of comprehensive national searches to fill key leadership positions at the Institute. ....read more

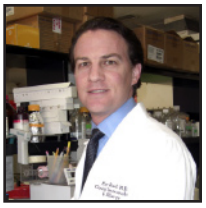
Zeldin Recognized at AAAAI Meeting

Acting Clinical Director Darryl C. Zeldin, M.D., was recognized for his professional accomplishments at the 2009 Annual Meeting of the American Academy of Allergy, Asthma and Immunology (AAAAI), held March 13 – 17 in Washington, D.C. ...read more

Science Notebook

Metabolic Syndrome and Breast Cancer Models

In a new study, funded in part by NIEHS, a collaborative research team reports data supporting the hypothesis that distinct mouse models of breast cancer respond differently to high fat diet and exposure to the endocrine disruptor dioxin and manifest different phenotypes of metabolic syndrome. ...read more



Dietary Broccoli Can Help Protect Against Airway Oxidative Stress

Researchers at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA) and the Environmental Protection Agency (EPA) report that orally administered sulforaphane (SFN) — a compound that is found in cruciferous vegetables and is especially high in broccoli sprouts — can enhance Phase II antioxidant enzyme levels in human airways. ...read more

Nobel Winner Oliver Smithies to Give Rodbell Lecture April 14

Nobel Laureate Oliver Smithies, D.Phil., will deliver the eleventh annual Rodbell Lecture on April 14 at 2:00 p.m. in Rodbell Auditorium. Smithies' seminar, "Turning Pages: From Gels to Genes," is part of the NIEHS 2008–2009 Distinguished Lecture Series. ...read more

This Month in EHP

The April 2009 issue of *Environmental Health Perspectives* is now available on-line, with a feature story on the controversy surrounding health risks related to oil sands development. ...read more

NIEHS Spotlight

NIEHS-Funded Food Allergen Study Highlighted at AAAAI Meeting

Findings of an NIEHS-funded food allergen study, presented by lead author Andrew Liu, M.D., were highlighted in a national press release issued by the American Academy of Allergy, Asthma and Immunology (AAAAI), following the group's 2009 Annual Meeting held March 13–17 in Washington — one of only seven such news alerts issued from the meeting. ....read more

Dearry Represents NIEHS at Ocean Science Public Policy Forum

NIEHS Director of the Office of Environmental Public Health Allen Dearry, Ph.D., was at the speakers' table March 5 when the Consortium for Ocean Leadership held its Annual Policy Forum and reception at the new Capitol Visitor Center on Capitol Hill in Washington. ....read more

Institute Enjoys a Banner Year at SOT

It was a record-setting year at the Society of Toxicology (SOT) 48th Annual Meeting in Baltimore March 15–19 — both for SOT itself and for NIEHS and top-level sponsor the National Toxicology Program (NTP). ...read more

Extramural Research

Extramural Update

NIH announced in a March 10 press release that $1.5 billion is currently available to fund grants for scientific research, construction and improvement of research facilities, and the purchase of scientific equipment. This is the first installment of the $10.4 billion to be provided to NIH as part of the American Recovery and Reinvestment Act of 2009 (ARRA), which was signed into law on February 19. ...read more

Extramural Papers of the Month

- Nanotechnology Delivers – First Report of Targeted Killing of Tumor Cells
- New Genetic Markers Identified for Increased Heart Attack Risk
- Autism Increase Not Due to Better Diagnosis
- Extreme Temperature and Mortality Risk

Intramural Research

Intramural Papers of the Month

- Infants Fed Soy Formula Have High Exposure to Isoflavones
- PXR and CAR are Responsible for Bone Loss in Patients Taking Antiepileptic and Antimicrobial Medications
- The Importance of Pol32 in the Repair of Clustered Lesions
- Protein Kinase Cζ Controls Organic Anion Transporters

Inside the Institute

Assembly Forms to Represent Technical Staff

As far as its organizers know, the first meeting of the Assembly of Laboratory Staff (AoLS) at NIEHS on March 4 may also be the only meeting of an organization of its kind ever anywhere in the NIH network of institutes and centers (ICs). ...read more

Roman Outlines New ADA Amendment

A new amendment to the 1990 Americans with Disabilities Act (ADA) and 1973 Rehabilitation Act went into effect on January 1, 2009 extending coverage of employees with disabling conditions. ....read more

NIEHS Welcomes Japanese Students

On March 9, 16 high school students from the Mizusawa Super Science High School in Iwate, Japan visited NIEHS for an afternoon seminar as part of an ongoing exchange program with the North Carolina School of Science and Mathematics (NCSSM). ...read more

A Belated Retirement Get-Together for Janet Guthrie

A group of about 30 NIEHS employees and retirees gathered February 26 to give longtime NIEHS employee Janet Guthrie a belated retirement party. ....read more

Calendar of Upcoming Events

- **April 2 (offsite event)**, in Love Auditorium at the Levine Science Research Center on the Duke University campus, 4:30–5:30 — Duke M.D./Ph.D. Annual Symposium Keynote Address by Oliver Smithies, D.Phil., discussing "On Being a Scientist for Sixty Years," following a Student Poster Session and Platform Presentations from 1:00 to 4:15

- **April 3 (offsite event)**, in the Searle Center, Room E, on the Duke University campus, 12:00–1:00 — Duke Superfund Basic Research Center Seminar, "Understanding the two faces of mitochondrial energetics with *C. elegans* models of disease and longevity," by Bernard Lemire, Ph.D.,

- **April 6**, in Rodbell Auditorium, 2:00–4:00 — Thank You Ceremony for Samuel Wilson, M.D.

- **April 7**, in Rodbell Auditorium, 10:00–11:00 — "Parkinson's Disease: Etiology, Clinical and Disability Management," a seminar with Honglei Chen, M.D., Ph.D., and Xuemei Huang, M.D., Ph.D.

- **April 7–8 (offsite event)**, in the Sonya Haynes Stone Center, UNC-Chapel Hill — 10th Annual Women's Health Research Conference, with registration required

- **April 7–10 (offsite event)**, in the Natcher Conference Center on the NIH campus in Bethesda, Md. — NanoWeek, featuring review presentations from program directors and extramural investigators on Apr. 7, research presentations and laboratory demonstrations from intramural investigators, and a 2-day joint NIH/IEEE workshop on nanomedicine.

Calendar of Upcoming Events

- **April 10 (offsite event)**, in the Searle Center, Room E, on the Duke University campus, 12:00–1:00 — Duke Superfund Basic Research Center Seminar with Jin-ju Li, Ph.D., speaking on “Diesel-exhaust particles evoke secretion of matrix-metalloproteinase 1 from human airway epithelia in a MEK mitogen-activated kinase dependent manner”

- **April 13 (offsite event)**, EPA Conference Center, 11:30–4:30 — Genetics and Environmental Mutagenesis Society (GEMS) Spring Meeting for 2009, “Genome Architecture: The Role for Copy Number and Structural Variation,” with registration required

- **April 14**, in Rodbell Auditorium, 2:00–3:00 — NIEHS Distinguished Lecture Series Annual Rodbell Lecture with Oliver Smithies, D.Phil., speaking on “Turning Pages: From Gels to Genes”

- **April 16–17 (offsite event)**, at the Hyatt Regency Atlanta — NIH Regional Seminar, covering topics related to NIH Extramural program funding and grants administration

- **April 17 (offsite event)**, in the Searle Center, Room E, on the Duke University campus, 12:00–1:00 — Duke Superfund Basic Research Center Seminar, “Health Disparities: Conceptual and Measurement Issues,” by Jay Kaufman, Ph.D.

- **April 24**, in Rodbell Auditorium, 9:00–10:00 — Frontiers in Environmental Sciences Lecture Series, TBA

- **April 30–May 1 (offsite event)**, at the Millennium Hotel in Cincinnati — Spring 2009 NIEHS WETP Awardee Meeting and Workshop: Local, State and Federal Partnerships for Chemical Preparedness and Response

- View More Events: NIEHS Public Calendar

NIEHS Spotlight

NIEHS and NTP Formally Welcome Birnbaum as Director

By Eddy Ball

NIEHS and the National Toxicology Program (NTP) formally welcomed their new leader, Director Linda Birnbaum, Ph.D., on March 13 with a morning installation ceremony and an "Afternoon of Science" of distinguished lecturers. Guests at the installation ceremony included NIH Acting Director Raynard Kington, M.D., Ph.D., and other NIH officials, U.S. Congressman David Price, Ph.D., NIEHS and NTP advisory and scientific board members, friends, family and Institute employees.

Infusing humor into the solemn oath-taking process, Birnbaum and Kington, right, beamed as they parodied the Obama-Roberts scene at the presidential inauguration, joking about the difficulty of remembering the exact words. (Photo courtesy of Steve McCaw)

The ceremony was held in the Rodbell Auditorium at NIEHS, which was filled to capacity. It was by turns symbolic and inspirational, light-hearted and humorous, and profoundly moving.

The highlight of the day was the formal swearing-in of Birnbaum by Kington. However, as Birnbaum and the other speakers made clear, the ceremony was also deeply infused with symbolism — an event marking the appointment of the first woman and first toxicologist to hold the position of director in the Institute's 43-year history and a reassessment of the direction NIEHS will take in the months and years ahead.

Birnbaum's mother, above, didn't hesitate to show her pride in her daughter's accomplishment with a standing ovation during the swearing-in. As Birnbaum noted, her mother was a strong supporter of her scientific interests during her teenage years. (Photo courtesy of Steve McCaw)

The event was held as the vernal equinox approached, during Women's History Month and just before the annual meeting of the Society of Toxicology. With rain falling heavily outside, Birnbaum observed, "The drought here at NIEHS has ended." As she presented her vision for the Institute, Birnbaum pointed to new opportunities and the significant advances in environmental health science research and translation she hopes NIEHS and NTP will make.

After taking her oath of office, Birnbaum thanked her guests and introduced her family. "It is truly an honor to serve as the Director of the NIEHS and the NTP," she said. "This is a very special day for me, and it's even more special because so many of my family members, friends and colleagues are here to share this occasion with me." Seated in the audience were her mother, husband, David, two daughters, and a host of friends and colleagues from her careers at NIEHS, NTP and the U.S. Environmental Protection Agency.

Birnbaum spoke of her personal quest for equilibrium between the personal and professional —"I try to have some fun everyday" — and her optimism that America today is indeed experiencing the rise of "a national movement for positive and constructive change" in the nation's relationship with the environment. As she reminded the audience that "we all need to make the whole [of NIEHS and public health in general] bigger than the sum of the parts," she reiterated her dedication to comprehensive translational research, "open communication and transparency," and "empowering those who work for me and with me" at what she described as "the world's premier environmental health research organization."

Birnbaum, her husband David, and daughter Lisa had front row seats as speakers praised and reminisced about her career. The Birnbaums obviously enjoyed themselves immensely. (Photo courtesy of Steve McCaw)

"There is no better time than now," Birnbaum said, to tease out "the more subtle actors" in disease processes and discover "more ways to share our science" nationally and globally. In her quest for inclusion, she promised to promote new and renewed relationships with sister institutes and centers at NIH, other governmental agencies, universities, advocates and the general public.

In their remarks, Kington, Price, and master of ceremonies and former NTP Associate Director and *Environmental Health Perspectives* Editor-in-Chief George Lucier, Ph.D., looked to Birnbaum's past and future with comments about her qualifications for her leadership role. They also referred to her ability to balance her roles as a leader, mother, scientist, wife, citizen and grandmother — and the way her infectious humor helps put the gravitas of science and leadership into perspective.

Price discussed his long relationship with Birnbaum and past leaders of NIEHS and NTP. U.S. Representative Bob Etheridge was also scheduled to speak but experienced a death in his family the night before. U.S. Representative Brad Miller and U.S. Senator Richard Burr were represented by staff members. (Photo courtesy of Steve McCaw)

The ceremony concluded with a performance by her daughter, New York actress Lisa Birnbaum. The young performer balanced her statement that "my mom is a role model for women and people everywhere" with a light-hearted little girl's dedication — "This is for you, Mommy." Relying solely on her vocal range, she then delivered an impressive rendition of the theme song from "The Man of La Mancha," inspiring the audience "to dream the impossible dream" — and leaving several in the audience struggling to hold back their tears.

Although the program had listed "Special Music" by Lisa Birnbaum, most people in the audience seemed as surprised as they were moved by her powerful performance. (Photo courtesy of Steve McCaw)

Birnbaum and Kington joined NIH Associate Director for Management Colleen Barros during the reception that followed the installation ceremony. (Photo courtesy of Steve McCaw)

NIEHS Acting Scientific Director John Pritchard, Ph.D., left, and NIEHS Principal Investigator David Miller, Ph.D. — two of the many NIEHS employees at the event — chatted as they enjoyed the refreshments. (Photo courtesy of Steve McCaw)

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Afternoon of Science Showcases Range of NIEHS Research

By Eddy Ball

When NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum chose distinguished lecturers to commemorate her official swearing in on March 13 with an Afternoon of Science, she no doubt chose the high-profile scientists on the basis of their contributions to their fields. However, the scientists who made presentations in the afternoon sessions also represented the work they oversee in their roles as members of advisory/scientific boards at NIEHS and NTP, as well as the comprehensive portfolio of research conducted at the Institute and supported by its extramural grants.

Birnbaum, right, joked about all of LeMasters' titles as she introduced the first speaker of the afternoon. Birnbaum noted that "Grace has a whole series of awards" and an enviable range of research expertise. (Photo courtesy of Steve McCaw)

The talks highlighted what is frequently referred to as the "rainbow" of NIEHS activities — public health-focused extramural grants with directly translatable outcomes; basic mechanistic research conducted in intramural laboratories to enable discovery of interventions to identify, prevent and treat disease and disease processes; and research coordinated by the NTP to provide solid scientific evidence for decisions by regulatory agencies about hazardous compounds.

NIEHS grantee Grace LeMasters, Ph.D., opened the lectures with a talk title "From Neonate to Nanosensor — A 2010 Study Odyssey: The Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS). LeMasters is a member of the NIEHS National Advisory Environmental Health Sciences Council (NAEHSC), which advises the Institute on its overall operations and proposals and is specifically charged with overseeing the NIEHS Division of Extramural Research and Training grants portfolio.

Keene described the post-transcriptional regulation by the ribonome as "a dominant force in coordinating gene expression," noting that there are "two- to three-times as many RNA binding proteins as there are transcripton factors." (Photo courtesy of Steve McCaw)

LeMasters is the principal investigator on NIEHS training and research grants at the University of Cincinnati, where she is a professor of epidemiology. She directs a comprehensive research effort into the effects of genetics and air pollution — especially diesel exhaust particles — on the respiratory health of inner city children. Her group is on the leading edge of developing individual monitors for exposure biology that promise to influence public policy and help prevent asthma and other respiratory diseases.

Following LeMasters was Jack Keene, Ph.D., a professor in the Department of Molecular Genetics and Microbiology at Duke University. He is chair of the NIEHS Division of Intramural Research (DIR) Board of Scientific Counselors, which, working with the NIEHS Office of the Scientific Director, has the primary responsibility for performing regular external reviews of all DIR research programs.

Keene's lecture explored the topic of "Coherent RNA Dynamics in Mammalian Cells." He is a pioneer in the systems biology approach of using advanced proteomics and bioinformatics to understand the post-translational mechanisms of a master regulatory network whose importance is only beginning to be appreciated. The investigations of Keene and others in the field strive to characterize the intense organization and dynamic orchestration of what is called the ribonome, the total cellular complement of RNAs and their regulatory factors, and how that coherence can change with chemical perturbations — with potential implications for preventing and treating disease, especially those linked to cancer and genotoxic responses.

Closing out the Afternoon of Science, Jim Riviere, D.V.M., Ph.D., spoke on "Skin: Barrier or Portal for Entry of Environmental Contaminants?" Riviere is Burroughs Wellcome Distinguished Professor of Pharmacology and director of the Center for Chemical Toxicology Research and Pharmacokinetics in the College of Veterinary Medicine at North Carolina State University. He is a member of the NTP Board of Scientific Counselors (BSC), providing scientific advice to Birnbaum in her role as NTP director and evaluating the scientific merit of the NTP's intramural and collaborative programs. He also sits on the NTP BSC Technical Reports Review Subcommittee.

Riviere said that understanding skin is complicated by the fact that "nearly adjacent surfaces can differ by three or four times in their absorptive capacity." (Photo courtesy of Steve McCaw)

For a rainy Friday afternoon during college basketball's March Madness, the event was well attended. NTP pathologist David Malarkey, D.V.M., Ph.D., above, was one of many NIEHS scientists who made a point to hear the distinguished lecturers. (Photo courtesy of Steve McCaw)

As Riviere explained, the biological roles of skin and the mechanics of dermal absorption are important considerations in classical and alternative toxicological assessment. Whether a dermal exposure to a substance that triggers molecular pathways truly constitutes a risk to human health depends upon how well that substance can cross the stratum corneum — the "bricks and mortar" outer layer of skin cells and lipids — to enter circulation. "People take the skin for granted," Riviere said, but current understanding of absorption through skin and the human and animal models now in use is far from adequate.

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Autism Panel Releases Strategic Plan

By Eddy Ball

On March 5, the Interagency Autism Coordinating Committee (IACC) released its much-anticipated blueprint for research on autism. The federal advisory panel announced the completion of the IACC Strategic Plan for Autism Spectrum Disorder (ASD) Research in a news release on its U.S. Department of Health and Human services web site.

The plan is mandated by the panel's enabling legislation, the Combating Autism Act of 2006. It is the outcome of four scientific workshops to identify research opportunities, expert workgroups to recommend research objectives and solicitation of public input through Requests for Information and town hall meetings — such as a Sacramento Town Hall Meeting, held in May 2008 and organized by NIEHS Health Science Administrator Lawler, Ph.D., and the University of California, Davis Medical Investigation of Neurodevelopmental Disorders (MIND) Institute.

The resulting IACC Strategic Plan reflects a diversity of views and the breadth of research that will be required to address the needs of people with ASD and their families. It is organized around six critically important questions regarding diagnosis, the biology of autism, risk factors, treatments and interventions, services and supports and questions about issues faced by adolescents, adults and seniors with autism and their families. Each question is followed by a brief discussion of what is currently known and what more is needed through research.

Lawler, above, was the initial NIEHS representative on the IACC. She has since been succeeded by NIEHS Director Linda Birnbaum, Ph.D.. (Photo courtesy of Steve McCaw)

NIH Will Use Stimulus Funds to Support Strategic Autism Research

In a press release issued March 24, the National Institute of Mental Health (NIMH) reported that NIH will commit roughly $60 million of American Recovery and Reinvestment Act (ARRA) funds for a new Request for Applications on autism research to meet objectives set forth earlier by the IACC. Approximately $5 million of that commitment will be granted and administered by NIEHS.

Possible topics are included in the grant announcement listing in the NIH Guide. These topics correspond directly to short-term research objectives detailed in the IACC Strategic Plan for Autism Spectrum Disorder Research.

Researchers funded through these new autism grants will be expected to contribute to the National Database for Autism Research (NDAR). NDAR was established to serve the autism research community as a common platform for exchanging data, tools, and research-related information, as well as to serve as a portal to and for the broad autism research community.

The plan includes recommendations for enhancing ASD research and treatment ranging from developing more sophisticated diagnostic tools to improvements in community-based services for children and adults with ASD. The experts offer funding recommendations and strategies for performing complete longitudinal and comprehensive studies of the biological, clinical and developmental profiles of children, identifying genetic and environmental risk factors, and conducting clinical trials of interventions.

Autism is a complex developmental disorder characterized by repetitive behavior and pervasive impairments in language and the ability to relate to others. With a dramatically increasing incidence, autism and related disorders — often grouped together as ASD — constitute a major health concern in the U.S., striking up to one in every 150 children and costing an estimated $35 to $90 billion annually, according to the IACC Strategic Plan.

The IACC will monitor the plan over the next year and incorporate its findings into an updated document for its next annual release in 2010. The IACC is composed of several different Department of Health and Human Services agencies including the National Institutes of Health, Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, and U.S. Department of Education.

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NIEHS Women at Center Stage in Bethesda

By Eddy Ball

NIEHS leaders Associate Director Sharon Hrynkow, Ph.D., and Director Linda Birnbaum, Ph.D., were featured speakers at the NIH 2009 Women's History Month Observance held in Wilson Hall on the NIH Campus in Bethesda March 12. The event was sponsored by the NIH Office of Equal Opportunity and Diversity Management.

Hrynkow presented the keynote talk at the event, "Women Taking the Lead to Save the Planet." Birnbaum spoke briefly afterwards, underscoring the NIEHS commitment to "stepping up its activities in regard to climate change and global environmental health."

The audience was welcomed to the event by organizer Sally Lee, executive officer of the National Institute of General Medical Sciences, who noted that NIH employs more than 10,000 women, many of them in major roles — including seven who serve as directors of institutes and centers (ICs). Hrynkow and Birnbaum were introduced by Teresa Leland, coordinator of the NIH Environmental Management System. The talks were aired live via videocast and are now available in the NIH Videocast archive.

Hrynkow, who has worked in leadership and policy positions with the NIH Fogarty Center, U.S. State Department and United Nations Foundation, is the NIEHS lead in the area of global environmental health partnerships. Her talk explored the contributions of women's leadership in protecting the environment through research and activities designed to reverse ecological destruction.

Hrynkow has a special policy and research interest in the vulnerabilities of women to environmental threats, such as experiencing sexual abuse as a terror and genocidal tactic during war, handling hazardous waste in search of materials to sell and cooking indoors without proper ventilation. (Photo courtesy of Jennifer Haley and the NIH Office of the Director)

Opening her talk with a general overview of the benefits and challenges of the environment, Hrynkow emphasized that "we are very [intricately] tied to our environment." She described the importance of what the environment gives humans in terms of sustenance, medicines from plants and minerals, spiritual inspiration, and the psychological and physical healing power of natural beauty.

She balanced these positive aspects with the myriad health risks people face in their environments and the anticipated effects of climate change. Reflecting on the grim scenario envisioned by some observers, she referred to the sobering predictions of World Health Organization (WHO) Director-General Margaret Chan, M.D., who described climate change as the "fifth horseman" of a looming potential environmental apocalypse.

Hrynkow moved on to profiles of two of the women whose contributions to global environmental health may help to avert that apocalypse — former WHO Director-General Gro Harlem Brundtland, M.D., and Peruvian social entrepreneur and Ashoka Foundation Fellow Albina Ruiz. Brundtland, she explained, epitomizes the contributions of women at the highest policy levels, while Ruiz exemplifies the community-based bottom-up approach of activists making significant contributions to environmental health at the local level.

Both approaches, Hrynkow noted, are essential, and both are examples of how women everywhere can take the lead to save the planet. She closed by paraphrasing philanthropist Ted Turner, "Men have had a chance to run the planet for a long time, and we've seen the outcomes. Now it's time to give women a chance."

After thanking Hrynkow for "an inspiring talk," Birnbaum concluded the presentation by expressing her sense that "we have a window of opportunity now in our nation to address our environmental issues." She also talked of a collective responsibility for "nurturing the next generation of women in science" — something, she said, "I take very seriously as a part of what I do personally."

Like Hrynkow, Birnbaum strove to highlight new possibilities at the center of the global environmental challenge. As difficult as the future will be, she concluded, "I see lots of opportunities for us, … and I look forward to the journey [ahead]."

The women of the day show off their global awards from Office of Employment Opportunity and Diversity Management (OEODM) presented by Director Lawrence Self. Shown from left to right, are Leland, Lee, Self, Birnbaum, Hrynkow and OEODM Federal Women's Employment Program Manager Margarite Curtis-Farrell. (Photo courtesy of Jennifer Haley and the NIH Office of the Director)

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Superfund Student Honored at Annual Toxicology Meeting

By Rebecca Wilson

The NIEHS Superfund Basic Research Program (SBRP) was well represented at this year's Society of Toxicology Annual Meeting March 15–19 in Baltimore (see related Spotlight story), where Dartmouth College Ph.D. candidate and SBRP trainee Courtney Kozul was awarded an impressive four awards in recognition of her research.

Courtney Kozul's research has received the attention of the scientific community and mainstream media alike. (Photo courtesy of Dartmouth SBRP)

Kozul was honored with awards from the Women in Toxicology Scholarship Fund, the Northeast Society of Toxicology, and the Molecular Biology Specialty Section. She also received a graduate student travel award from the meeting organizers. The awards point to the quality of research and caliber of students trained under the SBRP.

"Courtney is an exceptionally bright and hard-working young scientist and very deserving of these awards," said Joshua Hamilton, Ph. D., Kozul's research advisor and professor in the Dartmouth Medical School Pharmacology and Toxicology Graduate Program. "The success of her project also highlights how the interdisciplinary environment of the Superfund Training Program fosters high-caliber, innovative and highly translational science that addresses real-world problems."

Kozul and the Dartmouth program are no strangers to mainstream media attention. Some of Kozul's early work on the purity of lab mouse feed was featured in a March 2009 article, "A Matter of Chow," in *The Scientist* magazine. "It was some great national attention for our SBRP work," Kozul said of the piece.

Kozul also enjoys a long list of other awards and honors for her research, including the Best Student Poster award at the SBRP Annual Meeting in 2007 and 2008 and an Outstanding Oral Presentation award and travel scholarship at the International Central and Eastern European Conference on Health and the Environment in 2008. Her research was also recognized with the 2008 Karen Wetterhahn Award from the New England Membrane Enzyme Group.

Work as an SBRP trainee has opened many doors in Kozul's research career. "The SBRP is a wonderful example of the success that can be achieved by working at the interface of different scientific disciplines," she explained. "While my research focuses on the human health effects of metal exposure, I have had the opportunity to integrate knowledge and techniques from many other fields including remediation, analytical measurement, epidemiology and outreach."

Kozul adds that these interactions have provided her with the skills she needs to become a successful and respected environmental health researcher — a career she intends to further through a postdoctoral fellowship following her graduation in May 2010.

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Basic Research Program and Worker Education and Training Program.)

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Dudek to Receive A. E. Bennett Research Award

By Eddy Ball

NIEHS Principal Investigator Serena Dudek, Ph.D., will be honored on May 16 by the president of the Society of Biological Psychiatry at the 64th Annual Scientific Convention and Meeting in Vancouver, British Columbia. The theme of the 2009 meeting is "Modern Neuroscience Methods to Understand Plasticity and Development of Psychiatric Disorders." Dudek, who joined NIEHS in 2001, is the head of the NIEHS Synaptic and Developmental Plasticity Group.

A.E. Bennett Award winner Serena Dudek (Photo courtesy of Steve McCaw)

Dudek will receive the A.E. Bennett Research Award for basic science research in biological psychiatry. The awards are intended to stimulate international research in the field by young investigators.

Dudek was nominated by NIEHS Principal Investigator David Armstrong, Ph.D., acting chief of the Laboratory of Neurobiology. Armstrong praised Dudek as "one of the youngest luminaries in one of the most dynamic and distinguished fields in neuroscience…, [an investigator who has made] many important contributions to characterizing and understanding the mechanisms of synaptic plasticity in the developing brain."

Founded in 1945, the Society of Biological Psychiatry is the leading professional organization in the integration, advancement, and promulgation of science relevant to psychiatric disorders. It published the journal *Biological Psychiatry*, one of the most selective and highly cited journals in the field of psychiatric neuroscience. The A.E. Bennett Neuropsychiatric Research Foundation funds the annual awards of $2,000 each in basic science and clinical science.

After citing several examples of Dudek's "groundbreaking research on the mechanism of synaptic plasticity" in his nominating letter, Armstrong pointed to what he considers "perhaps her most important work to date, which was published last year in the *Proceedings of the National Academy of Sciences, USA*. The study found that long-term weakening of synaptic contacts could lead to synapse loss in hippocampal slice cultures, reflecting the driving force of experience on brain development. "Because the finding has important links to diseases such as schizophrenia that have synapse loss as a major component of the pathology," Armstrong continued, "this paper was highlighted by the Faculty of 1000 and was chosen by NIEHS leaders to be part of a congressional briefing on NIEHS research into potential targets of environmental toxicants that impair human cognitive potential."

Armstrong's nomination was supported by letters from John H. Gilmore, M.D., the Thad and Alice Eure Distinguished Professor in the Department of Psychiatry at the University of North Carolina School of Medicine and Charles F. Zorumski, M.D., the Samuel B. Guze Professor, head of Psychiatry, and professor of Anatomy and Neurobiology at the Washington University School of Medicine in St. Louis.

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Birnbaum Taps Pritchard as Acting Scientific Director

By Eddy Ball

NIEHS Director Linda Birnbaum, Ph.D., announced the selection of retired NIEHS Principal Investigator John Pritchard, Ph.D., to serve as acting scientific director during a period of comprehensive national searches to fill key leadership positions at the Institute. Pritchard, who retired in 2008 from his post as chief of the NIEHS Laboratory of Pharmacology and Chemistry, assumed his new duties in March overseeing more than 600 scientists, staff and trainees in nearly sixty Division of Intramural Research (DIR) laboratories.

Acting Scientific Director John Prichard. "I think he's doing it because this is his home," Birnbaum said of Pritchard's decision to accept the appointment. "He cares about NIEHS, just as we all do." (Photo courtesy of Steve McCaw)

As well as heading the Laboratory of Pharmacology, during his tenure at NIEHS Pritchard had also served as acting chief of the Laboratory of Molecular Toxicology and director of the Environmental Toxicology Program. In 2004, Pritchard was voted Mentor of the Year as part of the annual DIR Science Day activities.

He has published approximately 100 peer-reviewed articles in leading biomedical journals, as well as more than 15 book chapters. He also served as associate editor of the *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology* from 2001 to 2007.

Before joining NIEHS in 1976, Pritchard was an associate professor of Physiology at the Medical University of South Carolina. He received his Ph.D. in physiology from Harvard University in 1970.

One of Birnbaum's first official acts involved launching national searches for several key positions that have been filled with acting personnel for as long as two and one-half years. These include the deputy director, the scientific director, the director of the Division of Extramural Research and Training, and the director of Clinical Research. She is also looking for an ethics officer and someone to fill a diversity and educational position similar to the one held by Director of Education and Biomedical Research Development Marian Johnson-Thompson, Ph.D., prior to her retirement in September 2008.

Birnbaum explained that her goal is a transparent, open and inclusive selection process. The end result, she said, should be a "senior leadership team that will work together — people who are looking at the Institute as a whole and not only at their specific part" to achieve a revitalized NIEHS, which she perceives as "poised at the point of a lot of opportunity."

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Zeldin Recognized at AAAAI Meeting

By Eddy Ball

Acting Clinical Director Darryl C. Zeldin, M.D., was recognized for his professional accomplishments at the 2009 Annual Meeting of the American Academy of Allergy, Asthma and Immunology (AAAAI), held March 13 – 17 in Washington, D.C. Zeldin presented a "State-of-the-Art" lecture to a standing room only crowd at the meeting on "Asthma and Indoor Allergens: The Environmental Perspective" — one of only seven such keynote talks given at the meeting. He also was elected to the Editorial Board of the organization's official publication, the *Journal of Allergy and Clinical Immunology (JACI)*.

Zeldin's talk took place March 14 as part of a series of lectures that offered attendees continuing medical education and education credits. The lecture dealt with the impact of indoor air quality including allergens on asthma and the evaluation and management of indoor air to optimize the care of asthma.

As a member of the *JACI* Editorial Board, Zeldin will be an advisor to a leading journal in the fields of allergy and immunology with an impact factor of 8.115 — placing it first of 17 in the allergy category and ninth of 119 in the immunology category on the 2008 Journal Citation Reports published by Thomson Reuters.

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

The AAAAI represents asthma specialists, clinical immunologists, allied health professionals and others with a special interest in the research and treatment of allergic disease. Established in 1943, the AAAAI has nearly 6,500 members in the United States, Canada and 60 other countries.

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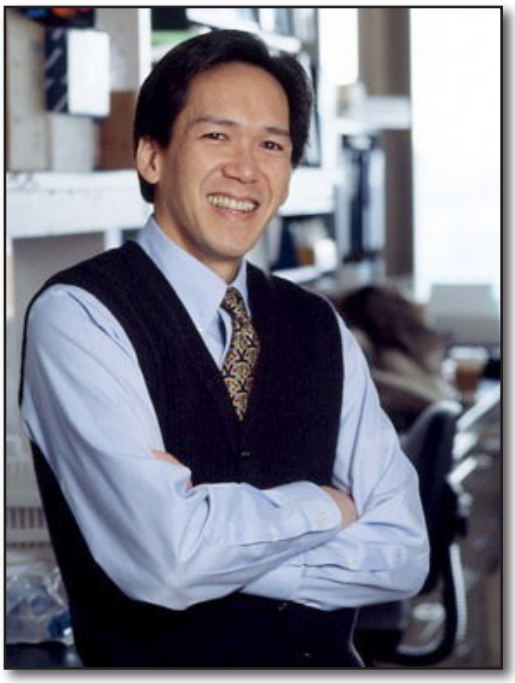
NIEHS-Funded Food Allergen Study Highlighted at AAAAI Meeting

By Eddy Ball

Findings of an NIEHS-funded food allergen study, presented by lead author Andrew Liu, M.D., were highlighted in a national press release issued by the American Academy of Allergy, Asthma and Immunology (AAAAI), following the group's 2009 Annual Meeting held March 13–17 in Washington — one of only seven such news alerts issued from the meeting.



Liu also collaborated with Zeldin on a study analyzing NHANES data on obesity and allergy symptoms in children and adolescents published online in the Journal of Allergy and Clinical Immunology in February. (Photo courtesy of Andrew Liu and National Jewish Health)

Liu, who is a professor in the Department of Pediatrics at National Jewish Health in Denver, was one of the presenters at a special session March 13 on "The Asthma and Allergy Component of NHANES [National Health and Nutrition Examination Survey]," moderated by NIEHS Acting Clinical Director Darryl Zeldin, M.D., and Peter Gergen, M.D., a pediatrician at National Institute of Allergy and Infectious Diseases. Liu spoke on the topic of "Food Allergen Sensitivity in the U.S. and Relationship to Allergic Disease." He was lead author on the study "In the United States, Black Male Children have an Increased Risk of Food Allergy: Results from NHANES 2005-2006" (abstract # 1037), whose results were reported in his talk.

The study by Liu et al. is the first representative U.S. survey in which quantitative sensitization to multiple foods — milk, egg, peanut and shrimp — was assessed in more than 8,000 subjects ranging in age from 1 to 85. Using measures of serum-specific IgE, the researchers reported a 2.6 percent prevalence for likely food allergy and a 16.8 percent prevalence for food sensitization, with peanut and shrimp being the most common foods in each category. Significantly, lower-income, non-Hispanic black male children were found to be at the greatest risk for these food allergies and sensitivities, pointing to the probability that discrete environmental and genetic factors are involved.

Along with Zeldin, who was principal investigator on the study, and Liu, other speakers with ties to NIEHS included former NIEHS Staff Scientist Sam Arbes, D.D.S., Ph.D., who is now with Rho, Inc., and NIEHS Postdoctoral Fellow Päivi Salo, Ph.D., a member of the NIEHS Environmental Cardiopulmonary Disease Group.

The AAAAI represents asthma specialists, clinical immunologists, allied health professionals and others with a special interest in the research and treatment of allergic disease. Established in 1943, the AAAAI has nearly 6,500 members in the United States, Canada and 60 other countries.

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Dearry Represents NIEHS at Ocean Science Public Policy Forum

By Eddy Ball

NIEHS Director of the Office of Environmental Public Health Allen Dearry, Ph.D., was at the speakers' table March 5 when the Consortium for Ocean Leadership held its Annual Policy Forum and reception at the new Capitol Visitor Center on Capitol Hill in Washington. Dearry, the sole NIH scientist on the agenda, was there to offer the NIEHS perspective with a presentation on "Oceans and Human Health" — one of the Consortium's emerging priorities.

Dearry represents NIEHS, NIH and DHHS on interagency coordinating bodies, including the U.S. Climate Change Science Program and National Science and Technology Council Joint Subcommittee on Ocean Science and Technology. (Photo courtesy of the Consortium for Ocean Leadership)

The daylong meeting featured panels and presentations by representatives from federal agencies, Congress, and the ocean science community, with keynote talks by Admiral James D. Watkins, U.S. Navy (Ret.), and Senator Sheldon Whitehouse (D-RI) and Congressman Brian Baird (D-WA).

Dearry's presentation opened with an outline of the range of research at NIEHS and a review of the oceans' impact on human health. Dearry reminded his audience of new and existing initiatives related to the oceans and the successes in both research and translation produced by the NIEHS Centers for Oceans and Human Health, which are funded jointly by the NIEHS and the National Science Foundation (NSF).

Pointing to the impact of global warming on oceans and their growing threat as a vector of disease, Dearry discussed research initiatives ongoing at NIEHS that can have an impact on ocean research. He explained that much of the Institute's work to improve detection and quantification methods, better understand genomics and proteomics to improve the understanding of pathogenicity and more accurately evaluate the risks of pathogens epidemiologically can be readily adapted to ocean research.

Dearry described collaborations among NIEHS, NSF and the National Oceanic and Atmospheric Administration (NOAA). Researchers at such institutions as the University of Hawaii, University of Washington, University of Miami and Woods Hole Oceanographic Institution receive funding and work with investigators from all three federal agencies. NIEHS, NSF and NOAA also work to coordinate oceans and human health research through various interagency committees and by participating in relevant conferences. Together, for example, they have developed an interagency oceans and human health research implementation plan.

Attendees included leaders from oceans research and educational institutions from around the country, interested non-governmental organizations and congressional staff. The forum was an important opportunity to discuss national issues of importance to the ocean community with this year's forum focusing on the oceans' effects on climate change, human health and energy security. For NIEHS, the forum was a time to build on existing relationships with partners and cultivate new ways to leverage resources in an effort to improve the health of the oceans and ameliorate their adverse health effects on humans.

A reception followed at the Dirksen Senate Office Building.

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Institute Enjoys a Banner Year at SOT

By Eddy Ball

It was a record-setting year at the Society of Toxicology (SOT) 48th Annual Meeting in Baltimore March 15–19 — both for SOT itself and for NIEHS and top-level sponsor the National Toxicology Program (NTP). NIEHS and NTP rolled out their largest exhibit ever and showcased new Director Linda Birnbaum, Ph.D., a major NTP initiative and a range of continuing and American Recovery and Reinvestment Act (ARRA) funding opportunities (see related "Extramural Update").

SOT reports that first day registrations hit a record of 6,671 participants for the five days that included an unprecedented 27 symposia, 19 workshops, 14 roundtables, and six keynote and named lectures — many of them featuring scientists and students with ties to NIEHS programs. The SOT Annual Meeting is the major professional development forum for the scientists of NIEHS and the NTP, as well as for Superfund Basic Research Program (SBRP) and other extramural program grantees worldwide. One of those NIEHS grantees, SOT President Ken Ramos, Ph.D., who served as chair of this year's meeting, is also a member of the NIEHS National Advisory Environmental Health Sciences Council.

Current and former NIEHS grantees received awards at the meeting. SBRP trainee Courtney Kozul (see related Spotlight story) and NTP Postdoctoral Fellow Scott Auerbach, Ph.D., were also honored (see textbox).

A "Meet the NIEHS Director" session drew a capacity audience to hear Birnbaum speak on March 18, as the new NIEHS and NTP leader — a toxicologist and former president of SOT — outlined her vision for the Institute in a time of great challenges and opportunities. Toxicologists were naturally eager to hear how one of their own will guide NIEHS research and funding priorities in the months and years ahead.

NTP scientists Paul Foster, Ph.D., and Dori Germolec, Ph.D., were featured speakers for the March 17 NTP Exhibitor Hosted Session "NTP Criteria for Hazard Identification in Non-Cancer Studies." They explained how NTP plans to predict developmental, reproductive and immune system challenges of chemicals with

The NIEHS and NTP booth was a four-spot, three-dimensional coordinated exhibit. Shown above is the NIEHS portion of the booth. (Photo by Christine Bruske Flowers)

The NTP portion, above, was centered around the theme "30 Years of Toxicology Excellence." (Photo by Christine Bruske Flowers)

SOT members were delighted to see one of their own taking the helm at NIEHS. (Photo courtesy of SOT)

more subtle, but significant functional and biological pathway effects — offering the public and regulatory agencies a clearer and more comprehensive estimate of the health risks they may pose.

Two events were of special interest to current and potential grantees — an NIH Brown Bag Lunch on March 17 and two full days of walk-in and appointment opportunities for one-on-one discussions with NIEHS grant administrators. Staff from the NIH Center for Scientific Review joined NIEHS grant administrators at the lunch on March 17 to field questions about the review process and grant opportunities, including those newly available through the ARRA.

NTP Deputy Program Director for Science Nigel Walker, Ph.D., entered the nanotechnology fray as the SOT scientific delegate at the annual debate on March 16 arguing the proposition "Nanotoxicology Is NOT Much Ado About Nothing" with European Societies of Toxicology (EUROTOX) delegate Kai Savolainen, Ph.D., of the Finnish Institute of Occupational Healthreceives. Walker and Savolainen will give an encore performance of their encounter at the 46th Congress of EUROTOX in Dresden, Germany September 13–16.

Risk Assessment SS Perry J. Gehring Best Postdoc Abstract Award winner Scott Auerbach (Photo courtesy of Steve McCaw)

NIEHS and NTP investigators and program officers led no fewer than 24 sessions, ranging from educational and career development to platform and symposium sessions. Nearly 60 poster displays featured the research of NIEHS and NTP senior scientists and trainees.

Along with her own luncheon session and posters, Birnbaum also had a chance to see the fruits of her labors as a mentor. On March 18, Birnbaum was recognized as the sponsor of trainee Michele La Merrill (see related story), who received the Award for Best Manuscript at the Meeting from the Occupational and Public Health Specialty Section (OPHSS).

NTP's Auerbach Wins Prestigious SOT Poster Award

NTP Toxicology Branch Fellow Scott Auerbach, one of NTP's three postdoctoral fellows, won the SOT Risk Assessment Specialty Section Perry J. Gehring Best Postdoc Abstract Award. Auerbach was selected for the award by a panel of judges chaired by Elaine Faustman, Ph.D. after submitting an extended description of the data presented in his poster, which detailed the research observations and their relevance to hazard characterization. The award is funded by an endowment to honor the legacy of Perry J. Gehring, D.V.M., Ph.D., who served as SOT president in 1980-1981. It consists of a $500 check to Auerbach and achievement plaques for him and his advisor, NTP Senior Toxicologist Richard D. Irwin, Ph.D.

Auerbach was lead author on the study "Independent validation of gene expression based hepatocarcinogenicity prediction models," which was part of the Bioinformatics and Prediction of Toxicity Poster Session on March 17. Co-authors included SRI statisticians Deepak Mav, Ph.D., and Ruchir Shah, Ph.D., Biologist Molly Vallant, NTP Deputy Program Director for Science Nigel Walker, Ph.D., retired NTP Pathologist Gary Boorman, D.V.M., Ph.D., and Irwin.

This award is Auerbach's second in less than a year. In October, he won a North Carolina Society of Toxicology (NCSOT) President's Award for Research Competition. Auerbach began his NIEHS career as a fellow in the NIEHS Laboratory of Respiratory Biology, where he worked until transferring to the NTP in 2007.

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Science Notebook

Transcriptional Control During Embryogenesis

By Robin Arnette

Studies with the common fruit fly (*Drosophila melanogaster*) and sea squirt (*Ciona intestinalis*) are helping to unravel the connection between transcriptional networks and cellular behavior. Michael Levine, Ph.D., a specialist in the genetic control of dorsal-ventral patterning and heart cell migration, gave a seminar at NIEHS that featured some of his latest findings. "Transcriptional Precision in the *Drosophila* Embryo" took place on March 10 and was hosted by Karen Adelman, Ph.D., a principal investigator in the Laboratory of Molecular Carcinogenesis.

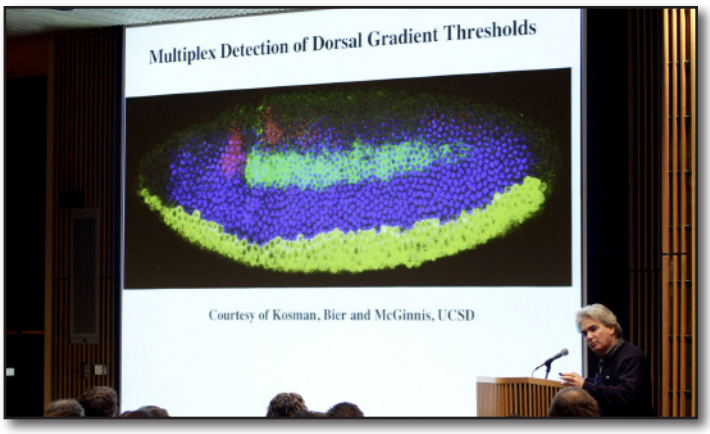
Levine said that the genetic control of dorsal-ventral patterning in *Drosophila* is controlled by a sequence-specific transcription factor called dorsal (Dl), which is related to mammalian NF-κB. In a two-hour fly embryo, Dl is distributed in a broad nuclear gradient with peak levels present in ventral regions — the future belly of the adult fly — and progressively lower levels in lateral and more dorsal regions. This Dl gradient controls dorsal-ventral patterning by regulating 60–70 target genes in a concentrated-dependent fashion.

"To understand how the Dl gradient generates these distinct threshold readouts of gene activity, we've isolated and analyzed about 35 Dl target enhancers," he said. "The Dl gradient generates six distinct patterns of gene expression across the dorsal-ventral axis of the embryo, and the protein works in a highly combinatorial fashion with other regulatory factors to produce these different threshold readouts."

Levine explained that the Dl gradient activates the target gene Twist (Twi) and the two work synergistically to regulate most of the Dl target genes. Because the binding sites for these two proteins are very close and oriented toward each other on the DNA template, they are inextricably linked.

Levine is an animated and engaging speaker, who is a professor and head of the Division of Genetics, Genomics and Development in the Department of Molecular and Cell Biology at the University of California-Berkeley. He was profiled in the March 2007 issue of ***The Scientist****. (Photo courtesy of Steve McCaw)*

When Adelman introduced Levine, she acknowledged her longtime friend's seminal work characterizing the homeobox, a DNA sequence found in many genes involved in controlling embryogenesis. (Photo courtesy of Steve McCaw)



Levine showed a side view of an early ***Drosphila*** *embryo stained with an antibody against the Dl protein. (Photo courtesy of Steve McCaw)*

Levine said, “If the Twi binding site points away from Dl, it disrupts cooperative interactions between the two and leads to a severe reduction in expression. This is an example of how [developmental] grammar — a fixed arrangement of binding sites — is absolutely essential for enhancer function.”

Levine’s group, along with a collaborator at Massachusetts Institute of Technology, used chromatin immunoprecipitation techniques, ChIP-chip or ChIP-seq assays, to look for Dl/Twi binding sites throughout the *Drosophila* genome. The surprising finding is that nearly half of the 60–70 Dl target sites that contain a 5’ primary enhancer also contain a duplicate enhancer for a single pattern of gene expression. Levine calls these secondary enhancers “shadow” enhancers and, in some cases, they are located within the intron of neighboring genes. Further ChIP-chip studies using the distantly-related *Anopheles* mosquito proved that the intronic enhancer was actually the primary one.

Additional ChIP-chip assays identified stalled RNA Polymerase II (Pol II) in the promoter regions of most Dl target genes prior to their activation in the early embryo. Quantitative confocal imaging suggests that genes containing stalled Pol II are activated in a synchronous manner throughout the field of cells where they are expressed.

Levine spent the last few minutes of his talk discussing the other organism that his lab studies — the sea squirt. The larval stage of this simple chordate looks like a tadpole and is composed of about 1000 cells, but the sea squirt heart arises from the 110 cell stage from a pair of blastomeres — undifferentiated cells formed by the cleavage of a fertilized egg. During this stage, several transcription factors such as Mesp, Xp2 and Fox4, along with the fibroblast growth factor (FGF) signaling pathway allow these procardio myocytes to migrate from the anterior tail region to the head region to form the heart. According to Levine, if FGF signaling is blocked, these tail cells don’t receive the signal and remain in the tail to become muscle.

Levine explained why his sea squirt studies are important. “Recent molecular phylogenetic studies suggest that this chordate is the closest living relative of the vertebrates, so whatever we can learn from this system will be directly applicable to far more complex vertebrates, which isn’t always the case in *Drosophila*.”

NIEHS Principal Investigators Ken Korach, Ph.D., left, and Mike Resnick, Ph.D., were drawn to the talk by Levine’s work in embryo development. (Photo courtesy of Steve McCaw)

NIEHS Postdoctoral Fellows Cynthia Holley, Ph.D., and Mark Jezyk, Ph.D., were on hand for Levine’s talk. Both work in the NIEHS Macromolecular Structure Group headed by Principal Investigator Traci Hall, Ph.D. (Photo courtesy of Steve McCaw)

NIEHS Bioinformatics Information Specialist David Fargo, Ph.D., seemed to ponder the implications of Levine’s findings about heart development in the sea squirt. (Photo courtesy of Steve McCaw)

TAC Seminar Explores Y-Family Polymerases

By Brian Chorley

On March 9, the NIEHS Trainee Action Committee (TAC) of the Laboratory of Molecular Genetics welcomed Roger Woodgate, Ph.D., chief of the Laboratory of Genomic Integrity at the National Institute of Child Health and Development. Woodgate spoke about a special group of DNA polymerases, known as the Y-family, and their role in DNA replication and mutagenesis. Amy Abdulovic, Ph.D., a postdoctoral fellow in the DNA Replication Fidelity Group, hosted Woodgate's morning seminar.

*Woodgate's research on Y-family polymerases has utilized a number of diverse model systems which have related back to the human condition. "We started studying **E. coli** mutagenesis in bacteria and ended up with homologues that are involved in mutagenesis and carcinogenesis in humans." (Photo courtesy of Steve McCaw)*

Woodgate's lecture, "Y-Family DNA Polymerases: Facilitators and Suppressors of Mutagenesis and Carcinogenesis," focused on the process of genome replication, a key aspect of an organism's survival. Not only is this process essential for cell replication and continual function, it is also critical for passing genetic information to offspring. There are more than six billion nucleotides in the human genome and the machinery responsible for genome replication needs to be not only accurate, but also consistent.

The enzymes central to genomic replication are DNA polymerases. These polymerases and other enzymes involved in proofreading and base mismatch repair all cooperate to make DNA replication a near error-free event. By some measurements, Woodgate explained, this process is marked by less than one mistake per billion nucleotide replication events. The result is what could otherwise be touted by audiophiles referring to quality sound production as "high fidelity."

Abdulovic introduced Woodgate as a "guru on the biochemical and enzymatic properties of Y-family polymerases," which became evident during his talk. (Photo courtesy of Steve McCaw)

In addition to an organism's need for high fidelity genome replication, there are multiple situations where "hi-fi" is not always a good thing. Woodgate offered an example, pointing to environmental stressors, such as UV radiation and oxidative stress, that can damage DNA. Because of the very biochemical properties possessed by the polymerases that allow for high fidelity replication, these lesions would go unrecognized by these enzymes and replication would fail. Luckily, Woodgate explained there are translesion synthesis (TLS) polymerases — the cassette tapes of DNA replication.

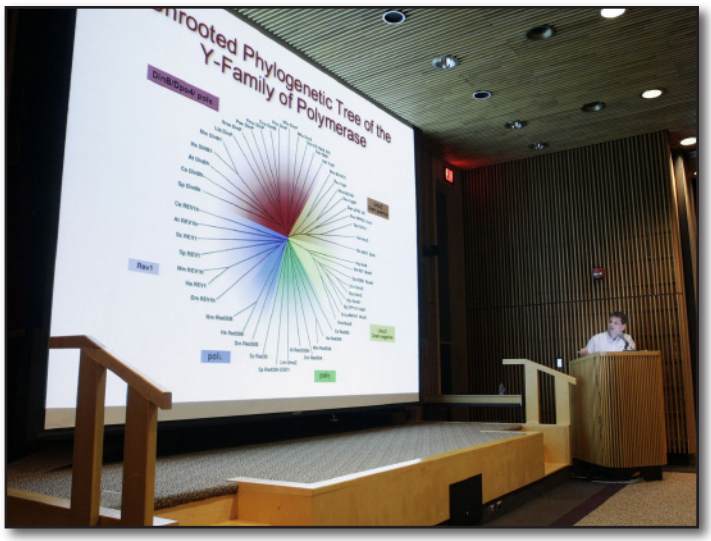
TLS polymerases are mostly grouped into a special class of polymerases known as the Y-family. During his seminar, Woodgate delved into the world of Y-family polymerases, which have been central to his laboratory's ground-breaking research for nearly 25 years. He demonstrated the consistent presence of the Y-family

polymerases in multiple organisms by presenting a slide that outlined approximately 300 orthologues known to exist in multiple species. As he explained, "The conservation of proteins from *E. coli*, through yeast and *Archaea*, and on to humans suggests that mechanisms of translesion synthesis…are conserved [as well]."

TLS polymerases can read through lesion-laden DNA without interrupting the replication event; however not without some cost to replication fidelity.

Woodgate stressed the importance of balance and interplay of these enzymatic members of the Y-family and their high fidelity brethren. He demonstrated in an *E. coli* model that by altering the activity of TLS polymerases and high fidelity polymerases, the rates of certain types of mutagenesis occurring at sites of DNA damage also change. Woodgate explained that while all polymerases affect mutagenesis to certain degrees, it is clear that members of the Y-family coordinate primarily "transversion mutations." Tranversions substitute purine residues for pyrimidine residues, or vise versa, and are the most dramatic mutation at the nucleotide level — hence the brand "low fidelity."

The processes of spontaneous mutagenesis coordinated by these enzymes are central to evolutionary adaptability and stress response. They also help us understand disease morphogenesis when these polymerases fail. Woodgate gave an example of a novel, "more efficient" Y-family polymerase called Rad30 his lab had discovered in yeast. He explained that soon after its discovery, it was found that homologues of this polymerase are defective in humans with the variant form of *xeroderma pigmentosum*, and that the defect predisposes affected individuals to sunlight-induced skin cancers.



During the seminar, Woodgate presented a slide generated in 2001 that outlined fifty-two known orthologues of the Y-family polymerases at that time. Today, he stated, there are nearly three hundred, illustrating the ubiquitous nature of these enzymes in many species. (Photo courtesy of Steve McCaw)

LMG Principal Investigator Bill Copeland, Ph.D., center pondered Woodgate's findings as he sat with LMG Chief Jan Drake, Ph.D., right, Principal Investigator Mike Resnick, Ph.D., far left, and Principal Investigator Sam Wilson, M.D. (Photo courtesy of Steve McCaw)

Woodgate cited ongoing studies in his lab focused on isolation and structural characterization of the Y-family polymerases. He expects his work will lead to a more complete understanding of how this essential family of polymerases function and operate.

(Brian Chorley, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

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First Sister Study Results Reinforce the Importance of Healthy Living

By Robin Mackar

Women who maintain a healthy weight and who have lower perceived stress may be less likely to have chromosome changes associated with aging than obese and stressed women, according to a pilot study that was part of the NIEHS-sponsored Sister Study. The long-term Sister Study is looking at the environmental and genetic characteristics of women whose sister had breast cancer to identify factors associated with developing breast cancer. This early pilot used baseline questionnaires and samples provided by participants when they joined the Sister Study.

Two recent papers published in *Cancer Epidemiology Biomarkers and Prevention* looked at the length of telomeres, or the repeating DNA sequences that cap the ends of a person's chromosomes. Telomere length is one of the many measures being looked at in the Sister Study. Telomeres protect the ends of chromosomes and buffer them against the loss of important genes during cell replication.

Over the course of an individual's lifetime, telomeres shorten, gradually becoming so short that they can trigger cell death. The papers show that factors such as obesity and perceived stress may shorten telomeres and accelerate the aging process. "Together these two studies reinforce the need to start a healthy lifestyle early and maintain it," said NIEHS Director Linda Birnbaum, Ph.D., "[to] maintain a healthy weight and cultivate healthy responses to stress."

The papers are the first findings coming out of the Sister Study. The Sister Study is just completing its enrollment of 50,000 women aged 35-74 to prospectively study risk factors for breast cancer. "We anticipate a wealth of information," said Dale Sandler, Ph.D., chief of the Epidemiology Branch at NIEHS and principal investigator of the Sister Study, "not only about the environmental and genetic factors that might lead to breast cancer, [but also] about how factors such as stress, diet and exercise might impact cancer and other disease risks."

The latest paper found that women who were obese for a long time had reduced telomere length. The researchers, NIEHS epidemiologists, looked at the relationship between various measures of current and past body size and telomere length in 647 women enrolled in the Sister Study. They found that women who had an overweight or obese body mass index (BMI) before or during their 30s — and maintained that status since those years — had shorter telomeres than those who became overweight or obese after their 30s, said NIEHS Visiting Fellow Sangmi Kim, Ph.D., lead author on the paper published in March.

As Kim, shown above at a lecture at NIEHS in 2008, explained, "Our results support the hypothesis that obesity accelerates the aging process… [and] that duration of obesity may be more important than weight change per se." (Photo courtesy of Steve McCaw)

"Among women with both higher perceived stress and elevated levels of the stress hormone epinephrine, the difference in telomere length was equivalent to or greater than the effects of being obese, smoking or 10 years of aging," said Parks, above.

An earlier paper published in February looked at the association between telomere length and the perceived stress levels of 647 women enrolled in the Sister Study, and found that similar to the obesity finding, stress can also impact telomere length. The researchers extracted DNA from blood drawn during initial enrollment to estimate telomere length, and measured levels of stress hormones in urine samples the women provided. Additionally, the researchers used a standardized scale to characterize levels of perceived stress based on answers to questions about how stressful participants perceived their life situations. In general, the researchers report that women in the Sister Study typically reported low levels of perceived stress.

Sandler, above, is also a principal investigator on the Two Sister Study, which is closely related to the Sister Study and will focus on young-onset breast cancer. (Photo courtesy of Steve McCaw)

"Even so, women who reported above-average stress had somewhat shorter telomeres, but the difference in telomere length was most striking when we looked at the relationship between perceived stress and telomere length among women with the highest levels of stress hormones," said Christine Parks, Ph.D., lead author on the paper.

The researchers also found that the effects of stress may be stronger in older women. They found that among women 55 years and older, those with higher perceived stress had 5 percent shorter telomeres than women with low stress levels. "More research is needed to determine if the shortening of telomeres in these women is related to aging or hormonal differences in the stress response, or simply represents the accumulated effects of stress across the lifespan," said Parks.

Citation: Kim S, Parks CG, DeRoo LA., Chen, H, Taylor JA, Cawthon RM, Sandler DP. 2009. Obesity and Weight Gain in Adulthood and Telomere Length. Cancer Epidemiology Biomarkers & Prevention 18(3):816-820.

Citation: Parks CG, Miller DB, McCanlies EC, Cawthon RM, Andrew ME, DeRoo LA, Sandler, DP. 2009. Telomere Length, Current Perceived Stress, and Urinary Stress Hormones in Women. Cancer Epidemiology Biomarkers & Prevention 18(2): 551-560.

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

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Study Links Maternal Exhaust Exposure to Childhood Asthma

By Eddy Ball

A recent proof-of-principle study, funded in part by NIEHS, reports preliminary evidence of an association between transplacental exposure to traffic-related polycyclic aromatic hydrocarbons (PAHs) and childhood asthma among a cohort in New York City — where more than 25 percent of children are affected by the disease. The seven-member team of researchers at Columbia University and the University of Cincinnati maintain that their study is the first to "examine the effects of prenatal exposure to ambient air pollutants on DNA methylation patterns in genes potentially associated with the asthma phenotype in the offspring."

Lead authors on the study, published online in *PLoS ONE*, were Frederica Perera, Dr.PH., professor of environmental health sciences and director of the Columbia Center for Children's Environmental Health (CCCEH) and NIEHS grantee Wan-yee Tang, Ph.D., of the University of Cincinnati (UC). The principal investigator and corresponding author was Shuk-mei Ho, Ph.D., chair of the Department of Environmental Health at UC.

The paper outlines a novel study design for identifying biomarkers and surrogate disease endpoints that could serve as what the authors call a "new blueprint" for use in population-based studies. The authors described their approach as "environmental epigenetics" — a research focus that incorporates analysis of epidemiologic data with unbiased investigation into epigenetic alterations associated with disease to identify the most promising candidate genes associated with the population data. The approach is based on the concept that environmental exposures can interact with genes during key developmental periods to trigger disease onset later in life.

Subjects in the study were nonsmoking Dominican and African-American women from the Washington Heights, Central Harlem and South Bronx areas of New York City. The women were members of a CCCEH cohort who were willing to complete prenatal air monitoring and collection of a maternal and/or umbilical cord blood sample at birth. Childhood asthma in the offspring was verified by parental report of a doctor's diagnosis.

Using this approach with unbiased profiling by methylation sensitive restriction fingerprinting, the researchers were able to identify 31 candidate genes that showed differential methylation patterns between those with maternal PAH above and those with levels below the median in the cohort of 20 children. From that group of genes, they were able to narrow the field to six candidates that are known genes with CpG islands in the 5' promoter flanking region using computer-based, or *in silico*, analysis.

"This research is aimed at detecting early signs of asthma risk, so that we can better prevent this chronic disease that affects as many as 25 percent of children in Northern Manhattan and elsewhere," Perera explained. (Photo courtesy of Columbia University's Mailman School of Public Health)

Second author Tang took the lead in performing experiments for the basic research component of the study and made major contributions to design, data analysis and write-up of the study. (Photo courtesy of Shuk-mei Ho)

The team found a positive and significant association between methylation of a 5'-CpG island in a gene known as *acyl-CoA synthetase long-chain family member 3 (ACSL3)* and the level of maternal PAH exposure and parental reports of asthma symptoms in offspring prior to age five. *ACSL3* is one of the candidate genes critical to T-helper cell differentiation that may induce polarization toward or away from an allergic phenotype. T cells are important in the production of cytokines and other asthma mediators. The researchers reported that additional testing showed methylation status was predicted with 75 percent sensitivity and 82 percent specificity — suggesting strongly that the methylation of *ACSL3* is a putative epigenetic marker associated with PAH exposure and asthma.

In their conclusion, the study's authors described their work as "an important first step" in much-needed research to help scientists understand a theoretically preventable disease by pinpointing environmental triggers and establishing the mechanisms that initiate this complex condition. Further research is needed, they wrote, "to identify an epigenetic profile related to PAH-associated childhood asthma and determine whether reprogramming events associated with transplacental exposure to PAHs increase risk of childhood asthma."

Citation: Perera F, Tang WY, Herbstman J, Tang D, Levin L, Miller R, Ho SM. 2009. Relation of DNA methylation of 5'-CpG island of ACSL3 to transplacental exposure to airborne polycyclic aromatic hydrocarbons and childhood asthma. PLoS ONE 4(2):e4488. doi:10.1371/journal.pone.0004488.

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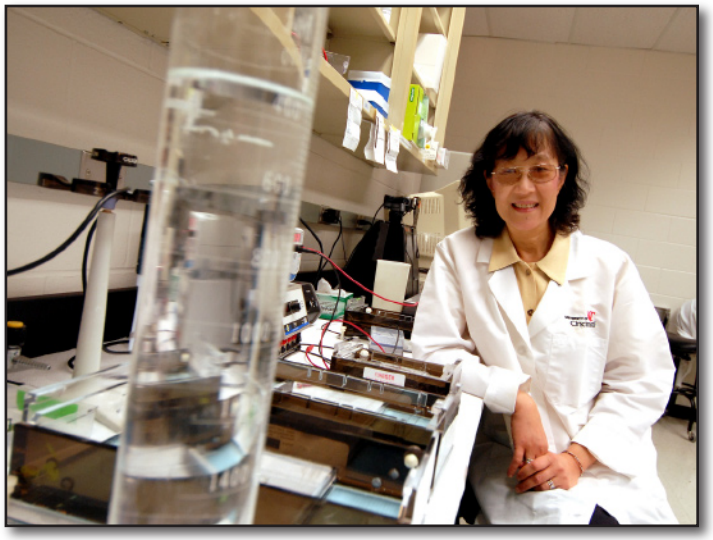
Addressing a Newly Recognized Gap in Asthma Research

This paper by Perera et al. addresses a major research priority area described in a recently published report by the National Heart, Lung and Blood Institute Working Group on its "Pediatric Pulmonary Diseases Strategic Planning Workshop," held July 9-10, 2008. The group outlined multiple opportunities for leading-edge research into epigenetic influences on lung programming and translation of early life epigenetic programming to specific disease states.

Two of the study's authors, Rachel Miller, M.D., and Ho had identified the same research need in an earlier review, "Environmental Epigenetics and Asthma: Current Concepts and Call for Studies," that appeared in the March 2008 issue of the *American Journal of Respiratory and Critical Care Medicine*. They reviewed research into the genetic and environmental components of asthma as they called for novel approaches to understand the role of epigenetic alterations by applying newly developed technologies to epidemiologic studies.



Chief author Shuk-mei Ho maintained, "Our data support the concept that environmental exposures can interact with genes during key developmental periods to trigger disease onset later in life and that tissues are being reprogrammed to become abnormal later." (Photo courtesy of the UC Academic Health Center)

Metabolic Syndrome and Breast Cancer Models

By Negin Martin

In a new study, funded in part by NIEHS, a collaborative research team reports data supporting the hypothesis that distinct mouse models of breast cancer respond differently to high fat diet and exposure to the endocrine disruptor dioxin and manifest different phenotypes of metabolic syndrome. Their findings were published in the *American Journal of Physiology – Endocrinology and Metabolism*. The authors conclude that their findings "may have utility in elucidating the mechanisms of those metabolic syndrome-associated phenotypes that are etiologically linked to breast cancer risk."

La Merrill is currently a postdoctoral fellow in community and preventive medicine at the Mount Sinai Medical Center. She received the Best Manuscript Award from the Occupational and Public Health Specialty Section at this year's Society of Toxicology Annual Meeting (see related story) — the latest of several she has won during her studies as a doctoral student and postdoctoral fellow. (Photo courtesy of Michele La Merrill)

The team included lead author Michele La Merrill, Ph.D., Principal Investigator David Threadgill, Ph.D., of the University of North Carolina Chapel Hill (UNC), NIEHS Director Linda Birnbaum, Ph.D., and colleagues from the Environmental Protection Agency (EPA), UNC and University of California, Davis (UCD).

The study investigated the effects of high fat diet and dioxin exposure in litters of three different mouse breast cancer models — HER2, PyMT, and DMBA. These mice have a uniform genetic background with the exception of specific oncogenes or exposures to carcinogen that make them more prone to developing breast cancer. The mouse models used in this cross-model comparison represent three different subtypes of human breast cancer. Women with these different types of breast cancer could react similarly to environmental factors such as dioxin and high-fat diets.

The team dosed pregnant mice with low levels of dioxin and placed the pups on a high- or low- fat diet after birth. Researchers measured weight, percent body fat and blood glucose levels of pups throughout the study. Triglyceride levels were measured at the end of the study.

Breast cancer model mice raised on HFD had earlier pubertal growth spurts. Body fat and adipose tissue accumulated faster in the HER2 model after puberty as compared to DMBA and PyMT mice. DMBA mice had higher glucose levels than the other two. Dioxin influenced the triglyceride levels only in the PyMT mice that were fed HFD. These data are the first to show that mouse breast cancer models manifest different phenotypes of metabolic syndrome even before developing cancer.

Despite shared risk factors, the association between developing metabolic syndrome and breast cancer has not been well studied. Breast cancer in humans can be categorized into several subtypes depending on such factors as genetic background, prognosis and response to different treatments. Prior to this study, the ways each breast cancer type could predispose an individual to developing metabolic syndrome when exposed to environmental toxins and high-fat diets remained unclear.

Metabolic syndrome is a combination of risk factors, such as obesity, high levels of blood glucose and overproduction of insulin, that make an individual susceptible to developing cardiovascular disease or diabetes. According to the study, statistical analysis of the third National Health and Nutrition Examination Survey (NHANES) indicates that more than 47 million US residents are affected by diseases stemming from metabolic

syndrome — with the number expected to increase in the future. In addition, the prognosis for people with metabolic syndrome worsens with advanced age, high-fat diet and a sedentary lifestyle.

Metabolic syndrome and breast cancer share several common risk factors. For example, obesity — a component of metabolic syndrome — can cause insulin insensitivity, type 2 diabetes and hormonal imbalance. Scientific evidence supports an association between type 2 diabetes, obesity, hormonal disruption and high risk of breast cancer among postmenopausal women. Another component of metabolic syndrome — accumulation of adipose tissue — results in storage of fatty acids and triglycerides and causes estrogen aromatization that also increases the chances of breast cancer.

Typically, individuals with metabolic syndrome or obesity consume more fatty food from animals, which raises their dioxin intake. Dioxin disrupts endocrine signaling, and chronic low-dose exposure promotes diseases such as type 2 diabetes and breast cancer. The resulting excess adipose tissue slows clearance of dioxin and increases susceptibility to the toxin.

(Negin Martin, Ph.D., is a research fellow in the NIEHS Membrane Signaling Group. She was recently chosen as a 2009 Science Communication Fellow with Environmental Health Sciences.)

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Dietary Broccoli Can Help Protect Against Airway Oxidative Stress

By Shweta Trivedi

Researchers at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA) and the Environmental Protection Agency (EPA) report that orally administered sulforaphane (SFN) — a compound that is found in cruciferous vegetables and is especially high in broccoli sprouts — can enhance Phase II antioxidant enzyme levels in human airways. According to the authors, their study provides the first data to clearly demonstrate this biological effect of SFN in the human airway and may have therapeutic implications in regard to asthma and other conditions associated with airway oxidative stress.

The study, funded by NIEHS, NIH and EPA and published in *Clinical Immunology*, explores an important endogenous protective mechanism whereby cellular damage can be prevented by dietary intake of a vegetable rich in a reactive oxygen species (ROS) scavenging compound. This placebo-controlled clinical study demonstrated the positive *in vivo* effects of oral SFN administration on up-regulation of a variety of antioxidant enzymes. Inflammation caused during oxidative stress has also been linked to allergic rhinitis and other respiratory diseases such as chronic obstructive pulmonary disease.

Lead author Marc Riedl, UCLA assistant professor of clinical immunology and allergy, is shown in the Hart and Louise Lyon Laboratory where the study was conducted (Photo courtesy of UCLA)

Lead author Marc Riedl, M.D., and Andrew Saxon, M.D., of the Hart and Louise Lyon Laboratory at David Geffen School of Medicine at UCLA co-authored the study with David Diaz-Sanchez, Ph.D., a principal investigator with the Human Studies Division at U.S. Environmental Protection Agency at UNC- Chapel Hill.

Endogenous Phase II enzymes are known to abrogate oxidative stress by scavenging ROS and free radicals. Previous *in vitro* and animal studies had shown that SFN is a potent inducer of Phase II enzymes. Findings of the new study support the hypothesis that oral SFN is capable of elevating Phase II enzymes in human airway cells.

"This study provides support for the concept that we can enhance the body's own natural antioxidant and cytoprotective mechanisms," Diaz-Sanchez commented. "Oxidative stress is a critical pathway in asthma, airway inflammation and air pollution health effects. Interventions using exogenous antioxidants [in supplement form] have been disappointing, perhaps due to bioavailability. This study takes a novel approach by encouraging the body to increase its own antioxidants by the use of dietary intervention."

Sixty-five healthy non-smoking volunteers were enrolled for the study at UCLA campus and from neighboring communities. Study design involved assessment of baseline Phase II enzyme expression in day 1 nasal lavage. Different groups of subjects were then given a measured amount — 25, 50, 75, 100, 125, 150, 175 and 200 grams — of broccoli sprout homogenate (BSH) once daily for three days. The control subjects received a placebo, alfalfa sprout homogenate, which is similar in taste and appearance to the BSH but does not have high levels of sulforaphane glucosinolates. There was no apparent toxicity in administering BSH orally, and it was well tolerated by the subjects.

Nasal lavage samples for Phase II enzyme expression analysis were collected on day three, and on day four blood was drawn for assessing serum SFN levels. RNA from cells in pellets of nasal lavage was analyzed with quantitative real-time PCR.

At doses of 100g daily, BSH induced expression of Phase II enzyme genes — glutathione s-transferase M1 (GSTM1), glutathione S-transferase P1 (GSTP1), heme-oxygenase-1 (HO-1) and NADPH quinone oxidoreductase 1 (NQO1) — in the cells. There was also a dose-dependent increase in the expression of the enzymes. The maximum BSH dosage of 200 grams generated a 101 percent increase in GSTP1 and a 199 percent increase in NQO1. Expression of GSTM1 and HO-1 also increased by more than 100 percent at the maximum dosage.

Citation: Riedl MA, Saxon A, Diaz-Sanchez D. 2009. Oral sulforaphane increases Phase II antioxidant enzymes in the human upper airway. Clin. Immunol. 130(3):244-251.

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

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Nobel Winner Oliver Smithies to Give Rodbell Lecture April 14

By Eddy Ball

Nobel Laureate Oliver Smithies, D.Phil., will deliver the eleventh annual Rodbell Lecture on April 14 at 2:00 p.m. in Rodbell Auditorium. Smithies' seminar, "Turning Pages: From Gels to Genes," is part of the NIEHS 2008–2009 Distinguished Lecture Series.

Rodbell Lecturer Oliver Smithies (Photo courtesy of the University of North Carolina at Chapel Hill)

Smithies is an Excellence Professor in the Department of Pathology and Laboratory Medicine at the University of North Carolina at Chapel Hill School of Medicine. He has collaborated with NIEHS principal investigators on several studies related to genetic medicine and gene therapy.

In 2007, Smithies shared the Nobel Prize in Physiology or Medicine with Mario R. Capecchi, Ph.D., of the University of Utah's Howard Hughes Medical Institute and Sir Martin J. Evans, D.Sc., of Cardiff University in Wales. In its announcement of the prize, the Nobel Foundation praised the trio "for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells." The scientists' work in the mid-1980s co-discovered a technique, gene targeting, to introduce DNA material in cells, replicating a natural process called homologous DNA recombination and establishing the basis for creating transgenic mice that replicate human disease.

Polypeptide Hormone Action Group Principal Investigator Perry Blackshear, M.D., D.Phil., will host the talk.

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This Month in EHP

By Eddy Ball

The April 2009 issue of *Environmental Health Perspectives* is now available on-line, with a feature story on the controversy surrounding health risks related to oil sands development. The issue also includes an examination of the national strategy regarding nanomaterials and investigations of the health effects of childhood asthma, climate change, lead exposure and bisphenol A (BPA).

- **Oil Sands Development: A Health Risk Worth Taking?** — Examining the potential human and environmental hazards involved in exploiting this untapped source of petroleum in oil sands

- **Nanotechnology-Related Environmental, Health and Safety Research** — Critiquing the strategic document issued in 2008 by the National Research Council on research needs and their priority

- **Childhood Asthma and Exposures at Swimming Pools** — Reporting on a 2007 workshop that identified important data gaps remaining in exposure assessment of new-onset asthma risk for children from swimming pool disinfection by-products

- **Climate Change, Agriculture and Human Health** — Investigating the anticipated health risks from increased exposures to pathogens and agricultural chemicals due to climate change and suggesting research and policy changes that may help to manage them

- **Lead Exposure and Cognition in Older Women** — Focusing on the association of blood and bone lead levels with cognition deficits specifically in older women, even at low levels experienced in community settings

- **BPA Exposure Among Premature Infants in a Hospital Setting** — Finding BPA levels one order of magnitude higher than estimates for the general population in infants in two neonatal intensive care units in the Boston area and calling for further studies to pinpoint the sources

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Extramural Update

NIEHS Extramural Research and the AARA

NIH announced in a March 10 press release that $1.5 billion is currently available to fund grants for scientific research, construction and improvement of research facilities, and the purchase of scientific equipment. This is the first installment of the $10.4 billion to be provided to NIH as part of the American Recovery and Reinvestment Act of 2009 (ARRA), which was signed into law on February 19. The funds will be available over two years – through September 2010. $8.2 billion is allocated in support of scientific research opportunities.

In keeping with the goals of the ARRA to preserve and create jobs and promote economic recovery in the United States, applications for the announcements described below must be from domestic institutions/organizations located in the 50 states, territories and possessions of the United States, Commonwealth of Puerto Rico, Trust Territory of the Pacific Islands or District of Columbia.

Potential applicants should note that all opportunities for funding with ARRA funds will handled through Funding Opportunity Announcements (FOAs) and Notices in the NIH Guide. There will be no opportunities for unsolicited or "investigator-initiated" applications. Researchers interested in applying for ARRA funds should carefully read announcements on the NIH ARRA Grant Funding Opportunities website and the NIEHS Information Related to the ARRA website. Information is being added to the websites daily, and potential applicants are encouraged to check these websites regularly. NIEHS program staff will be happy to address any questions that potential applicants may have.

NIH is working closely with the Department of Health and Human Services (HHS) Recovery Act Implementation team to ensure transparency and accountability for the Recovery Act funds. As NIH spending plans are approved through this process, NIH will post information about these critical projects and their impact on the economy at the DHHS Recovery website.

Although the FOAs listed below were announced through NIH and NCRR, they are available to grantees of all NIH Institutes. Eligible NIEHS grantees with construction, renovation, and/or instrumentation needs are encouraged to apply for these opportunities.

Current Opportunities

Challenge Grants in Health and Science Research (RC1) — RFA-OD-09-003 — Applications due April 27, 2009. Challenge Grants focus on specific knowledge gaps, scientific opportunities, new technologies, data generation, or research methods that would benefit from an influx of funds to quickly advance the area in significant ways. Within each broad Challenge Area, the NIH Institutes, Centers and Offices have specified topics that address their missions. Topics listed on the NIEHS Recovery Act website are areas of high interest for NIEHS.

Construction/Renovation

Core Facility Renovation, Repair, and Improvement (G20) — RFA-RR-09-007 — Applications due September 17, 2009

Extramural Research Facilities Improvement Program (C06) — RFA-RR-09-008 — Multiple receipt dates.

Instrumentation

High-End Instrumentation Grant Program (S10) — PAR-09-118 — Applications due May 6, 2009

Supplement Awards

Please see NIEHS ARRA Information Related to the ARRA website for NIEHS-specific information, including contacts and application instructions, related to these supplement funding opportunities.

Administrative Supplements — NOT-OD-09-056 — See IC websites for specific deadlines

Administrative Supplements to Research Grants Providing Summer Research Experiences for Students and Science Educators — NOT-OD-09-060 — See IC websites for specific deadlines

Competitive Revision Applications — NOT-OD-09-058 — Applications due April 21, 2009

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Extramural Papers of the Month

By Jerry Phelps

Read the current Superfund Basic Research Program Research Brief. New issues are published on the first Wednesday of each month.

Nanotechnology Delivers – First Report of Targeted Killing of Tumor Cells

Within the family of nanomaterials, carbon nanotubes have emerged as a new alternative and efficient tool for transporting drugs. In new research sponsored by NIEHS, researchers report the first targeted killing of cancer cells in animals using a single wall carbon nanotube drug-delivery system.

Single-walled carbon nanotubes are on the order of a few nanometers (about 1/50,000th of the width of a human hair) in diameter and can be several millimeters in length. They have many novel properties that make them potentially useful in a number of applications including electronics, optics, material sciences, architecture and as targeted drug-delivery devices.

In the current study, carbon nanotubes were conjugated with the anti-cancer agent cisplatin along with epidermal growth factor (EGF) to specifically target head and neck squamous carcinoma cells in mice. *In vitro* experiments showed that cancer cells treated with carbon nanotubes bound to cisplatin and epidermal growth factor killed selectively. Control treatments that did not include epidermal growth factor did not affect cell proliferation. *In vivo* experiments demonstrated rapid regression of tumor growth in mice treated with carbon nanotubes with both cisplatin and epidermal growth factor. Other studies showed that without epidermal growth factor, carbon nanotubes were cleared from the treated areas in less than 20 minutes. These results point to the potential of carbon nanotubes as targeted anti-cancer drug-delivery systems.

Citation: Bhirde AA, Patel V, Gavard J, Zhang G, Sousa AA, Masedunskas A, Leapman RD, Weigert R, Gutkind JS, Rusling JF. 2009. Targeted killing of cancer cells *in vivo* and *in vitro* with EGF-directed carbon nanotube-based drug delivery. ACS Nano 3(2):307-316.

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New Genetic Markers Identified for Increased Heart Attack Risk

An international team of scientists partially supported by NIEHS has found nine new gene variants, also known as single nucleotide polymorphisms, associated with an increased risk of myocardial infarction or heart attack. These polymorphisms provide new insight for understanding genetic patterns of heart attack and for developing new treatment options.

One key finding of the report is that people who carry more than one of the markers have more than twice the risk for heart attack. The scientists performed a genome-wide scan of thousands of patients with hundreds of thousands of genetic markers. Heart attack patients, previously enrolled in an existing study, and healthy control persons participated in the study.

In one study, suspect genes were mapped to chromosomes 3 and 12. One of these genes, known as MRAS, plays an important role in cardiovascular biology. Another gene, HNF1A, is closely associated with cholesterol metabolism. Another study identified three previously unknown genes on chromosome 2, 6 and 21. Results from this study show that the higher the number of disease genes a person has, the higher the risk for heart attack.

The scientists conclude that the knowledge gained from their work will aid in addressing the risk of heart attack in order to develop preventive and early intervention strategies.

Citation: Myocardial Infarction Genetics Consortium. 2009. Genome-wide association of early-onset myocardial infarction with single nucleotide polymorphisms and copy number variants. Nat Genet 41(3):334-341.

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Autism Increase Not Due to Better Diagnosis

A study conducted by NIEHS-funded researchers at the University of California Davis found that the seven- to eight-fold increase since 1990 in the number of children born in California and later diagnosed with autism cannot be explained by changes in how the condition is diagnosed or counted. The researchers also conclude that the trend is not slowing and suggest that the research focus should shift from genetics to the multitude of chemical and infectious agents in the environment that could be involved in the rapid rise in the incidence of autism.

The results of the investigation show that the incidence of autism by age six in California increased from fewer than 9 cases per 10,000 children born in 1990 to more than 44 per 10,000 children born in 2000. Migration patterns and changes in diagnosis were ruled out as possible reasons for the increase. The results show that less than one-tenth of the increase can be attributed to the inclusion of milder cases of autism.

These researchers are currently involved in two large studies aimed at discovering possible environmental factors and gene-environment interactions responsible for autism. They are focusing on the potential effects of metals, pesticides and infectious agents on neurodevelopment.

Citation: Hertz-Picciotto I, Delwiche L. 2009. The rise in autism and the role of age at diagnosis. Epidemiology 20(1):84-90.

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Extreme Temperature and Mortality Risk

A study on weather-related mortality conducted by Yale University researchers with funding from NIEHS found that extremes of hot and cold temperatures are risk factors for all cause mortality. The study was conducted in 107 communities in the U.S. It identified regional variation, susceptible populations, acclimatization strategies and air pollution as mediating factors.

Previous studies have identified links between mortality and temperature extremes, and extreme weather events such as the 2003 European heat wave, and concerns over global climate change have focused more attention on the issue. The researchers point out that a better understanding of how temperature affects mortality and susceptible populations is critical for the medical community, community leaders and policy makers responsible for intervention strategies.

Results show that heat-related mortality has a shorter lag time than cold-related mortality, suggesting differences in intervention strategies. The strongest heat-related mortality association occurred with previous or same day exposure while cold-related mortality lagged up to 25 days, suggesting that cold temperatures affect mortality more indirectly. Some of this lag is attributable to death from infectious diseases.

Heat effects were generally lower in communities with higher average temperatures, suggesting that communities and individuals can adapt even to extreme weather changes. However, adaptation to extreme cold even in communities with average lower temperatures was not as apparent.

Citation: Anderson BG, Bell ML. 2009. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 20(2):205-213.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training. Each month, he contributes summaries of extramural papers to the *Environmental Factor*.)

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Intramural Papers of the Month

By Robin Arnette

Infants Fed Soy Formula Have High Exposure to Isoflavones

Since 25 percent of all infant formula is based on soy protein, and soy has been linked to estrogenic effects in adults, a study was performed to examine isoflavone levels in infants and possible hormone effects. The study was a collaborative effort between scientists at the NIEHS, CDC, FDA and The Children's Hospital of Philadelphia.

A total of 166 infants between birth and one year of age were engaged in a partly cross-sectional/longitudinal pilot study to examine their exposure to three isoflavones — genistein, daidzein and equol — from soy formula, cow milk formula and breast milk. Samples were analyzed using high-performance liquid chromatography (HPLC) and mass spectrometry (MS). Saliva, blood and urine samples taken simultaneously demonstrated that genistein and daidzein were undetectable in blood and saliva from children fed breast milk or cow milk formula, while equol was only found in a few urine samples. Urinary concentrations of genistein and daidzein were approximately 500 times higher in soy formula-fed infants than those fed cow milk formula.

Although it was known that infants fed soy formula had a higher exposure to these compounds than did those fed cow milk formula or breast milk, this study was the largest to date and the only one to include measurements in blood, saliva and urine. Future longitudinal studies will examine the physical and developmental effects of estrogen exposure on infants, aged birth through two years, fed soy formula, cow milk formula and breast milk.

Citation: Cao Y, Calafat AM, Doerge DDR, Umbach DM, Bernbaum JC, Twaddle NC, Ye X, Rogan WJ. 2009. Isoflavones in urine, saliva, and blood of infants: data from a pilot study on the estrogenic activity of soy formula. J Expo Sci Environ Epidemiol 19(2):223-234.

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PXR and CAR are Responsible for Bone Loss in Patients Taking Antiepileptic and Antimicrobial Medications

According to researchers at NIEHS, the locking of xenobiotic receptors pregnane X receptor (PXR) and constitutive active/androstane receptor (CAR) to the corepressor silencing mediator for retinoid and thyroid hormone receptors (SMRT) is the key mechanism to the repression of vitamin D_3 activation of the CYP24A1 promoter. Since the activation of the CYP24A1 gene was thought to be responsible for bone mineral density loss that occurs in patients taking antiepileptic and antimicrobial drugs, the research team tested the hypothesis using *Pxr(+/+)* and *Pxr(-/-)* mice. This research may provide an opportunity to develop drugs for treating hormone- or vitamin-related diseases such as diabetes and osteoporosis by targeting nuclear xenobiotic receptors.

Vitamin D_3, essential for the development and maintenance of calcium in bones, dissociates the SMRT from the CYP24A1 promoter and binds to the vitamin D receptor (VDR) within the vitamin D-response element (VDRE) of the CYP24A1. In the absence of vitamin D_3, PXR binds to the VDRE of the CYP24A1 and activates the CYP24A1 gene. When *Pxr(+/+)* and *Pxr(-/-)* mice were treated with a PXR-activating drug, only the *Pxr(+/+)* mice exhibited bone mineral density loss. The data suggest that PXR and CAR can be responsible for the bone loss in patients taking PXR-activating drugs.

Citation: Konno Y, Kodama S, Moore R, Kamiya N, Negishi M. 2009. Nuclear xenobiotic receptor pregnane X receptor locks corepressor silencing mediator for retinoid and thyroid hormone receptors (SMRT) onto the CYP24A1 promoter to attenuate vitamin D_3 activation. Mol Pharmacol 75(2):265-271.

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The Importance of Pol32 in the Repair of Clustered Lesions

Single-strand break (SSB) and base excision repair (BER) enzymes usually fix damage or breaks in one DNA strand, but clustered damage formed by two or more closely spaced base damages or SSBs on opposing strands can cause double-strand breaks (DSBs). The resulting DSBs pose a unique threat to the genome. In a new study, a research team, comprised of investigators from NIEHS and the University of Pittsburgh Cancer Institute, determined this mechanism using single and double mutants of the budding yeast, *Saccharomyces cerevisiae*.

Since there were few studies that focused on the repair of clustered lesions in living cells, the researchers developed an *in vivo* assay that measured such lesions produced by methylmethanesulfonate (MMS) — a DNA damaging agent, — in G_1 stationary-phase haploid yeast. DNA Polymerase δ (Pol δ), its subunit Pol32, Rad27/Fen1 nuclease, Cdc9 ligase, and the sliding clamp protein PCNA all interact and must be coordinated to process lesions. *pol32Δ* and *rad27-p* single mutants had little effect on the repair of MMS clustered damage, but *pol32Δ rad27-p* double mutants were unable to repair closely spaced lesions, which resulted in DSBs. However, repair of single-strand damage was not altered.

The findings suggest that clustered lesions are effectively repaired only when repair components are tightly coordinated.

Citation: Ma W, Panduri V, Sterling JF, Van Houten B, Gordenin DA, Resnick MA. 2009. The transition of closely opposed lesions to double-strand breaks during long-patch base excision repair is prevented by the coordinated action of DNA polymerase delta and Rad27/Fen1. Mol Cell Biol 29(5):1212-1221.

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Protein Kinase Cζ Controls Organic Anion Transporters

The activation of protein kinase C zeta (PKCζ) up-regulates organic anion transporter 1 (OAT1) and OAT3, two proteins that play a crucial role in the removal of small anionic drugs, xenobiotics and their metabolites from the kidney, according to a study by a team of researchers from NIEHS and the Medical University of South Carolina. The investigators also found that protein-protein interactions control these two important renal drug transporters.

To examine the protein-protein interactions that are involved in the OAT-mediated secretion of drugs and toxins, the team employed a yeast two-hybrid assay to screen a human cDNA kidney library to identify proteins that associated with OAT3 in the kidney. PKCζ was one of the 23 putative binding partners identified in the assay. Using a fresh renal tissue preparation, the team was able to show that insulin — an upstream activator of PKCζ — increased PKCζ activity and OAT3-mediated uptake of estrone sulfate (ES). Both effects were abolished by using a PKCζ inhibitor.

Further studies demonstrated that PKCζ modified OAT1 activity as well. Inhibition of PKCζ was also shown to block the increase in drug transport seen in response to epidermal growth factor and the activation of protein kinase A. Future experiments with the other 22 putative binding partners of OAT3 may lead to better understanding of both transporter function and drug pharmacology in the kidney.

Citation: Barros SA, Srimaroeng C, Perry JL, Walden R, Dembla-Rajpal N, Sweet DH, Pritchard JB. 2009. Activation of protein kinase Czeta increases OAT1 (SLC22A6)- and OAT3 (SLC22A8)-mediated transport. J Biol Chem 284(5):2672-2679.

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Inside the Institute

Assembly Forms to Represent Technical Staff

By Eddy Ball

As far as its organizers know, the first meeting of the Assembly of Laboratory Staff (AoLS) at NIEHS on March 4 may also be the only meeting of an organization of its kind ever anywhere in the NIH network of institutes and centers (ICs). Even Director Linda Birnbaum, Ph.D., who spoke at the well-attended meeting, said she'd never heard of an NIH organization devoted exclusively to communicating the interests of laboratory staff in the hiring, promotion and working-condition processes that impact their lives on a daily basis.

Spokesperson Goulding, a biologist in the NIEHS Gamete Biology Group with more than 25 years experience in labs at NIEHS, said that the AoLS will provide a forum for training, career advancement and resource sharing through a database the assembly plans to develop for members — as well as develop Core Competency Models and explore displaced worker options for employees affected by labs that close when principal investigators leave the Institute for retirement or other positions and when jobs are outsourced to private contractors.

Empowering the Institute's estimated 176 laboratory staff with the means for being heard by lab chiefs and administrators is another reason for the AoLS, explained Goulding. "The group will take a careful look at promotion and evaluation guidelines," she added, "and work to get them updated." Goulding joined other members of the AoLS Steering Committee in encouraging lab staff to participate, to nominate officers and, most importantly, to vote for their Council members.

The keynote talk by Birnbaum took up most of the first half of the meeting, during which she emphasized her accessibility to employees throughout the Institute. She quickly established rapport with the group by telling them, "Please, I'm Linda. If you ask for 'Dr. Birnbaum,' I tend to look around for somebody else." She also assured the audience that "I'm really thrilled that this group has started" and said she foresees the AoLS as providing a lead for development of best practices across NIH by "working together to address common goals, common interests, to move things forward faster."

Early on in her talk, Birnbaum proved she was not afraid to confront some of the challenges that the technical staff face in their jobs. In response to a question about promotion potential for technical staff, for example, Birnbaum shared her opinion that "people shouldn't have to walk on water" to get promoted. She said of the promotion issue, "It's something that's already on my radar screen."

"One of things we discovered was that there was no [real] representation for us" — the Institute's technical staff, Goulding said of her experience on the NIEHS Organizational Climate Committee. (Photo courtesy of Steve McCaw)

Birnbaum noted that the AoLS would have a seat at important decision-making forums, including the national searches underway for people to fill open leadership positions. (Photo courtesy of Steve McCaw)

Following Birnbaum's remarks, Goulding outlined the history of the AoLS, which was created following a recommendation by the Organizational Climate Committee in the wake of last year's audit of NIEHS operations and morale. After addressing the purpose of the AoLS, she turned to the question of "where do we go from here?" and introduced her colleagues on the Steering Committee, who took turns presenting their reports on the group's constitution, organizational structure, and the nominating and voting procedure for choosing the group's officers.

AoLS Steering Committee member Stella Sieber, right, took minutes of the meeting, which are posted on the AoLS website. Member Biologist Mark Rubino, left, was seated beside her on the stage. (Photo courtesy of Steve McCaw)

Along with Birnbaum, Assembly of Scientists (AoS) Secretary and National Toxicology Program Biologist Dori Gormolec, Ph.D., was on hand to show support for the group and offer tips on how the AoLS can become an effective voice for its members. She encouraged members to petition for seats on the AoS, search committees and the NIEHS Division of Intramural Research Council, which is made up of principal investigators and the scientific director.

(Note: The AoLS has set up a website, which employees may access within the Institute's internal network or offsite via an NIH/NIEHS connection.)

Making a Difference for NIEHS Lab Staff — The Men and Women Behind AoLS

Spokesperson Gina Goulding was quick to note that it took the concerted efforts of an energetic group of volunteers, several of whom made presentations at the meeting, to make the AoLS a reality:

- Biologist Lisa Padilla-Banks, Reproductive Medicine Group, who outlined the nomination and election process for choosing the group's representatives
- Biologist Paula Brown, Gamete Biology Group, who introduced the AoLS website and explained the roles of the four Council members
- Biological Science Laboratory Technician Laura Miller DeGraff, Molecular and Cellular Biology Group, who co-presented ideas the Steering Committee had gathered for future directions and discussion
- Biologist Page Myers, Comparative Medicine Branch, who presented with DeGraff
- Biologist Mark Rubino, Metastasis Group, who joined fellow Steering Committee members on the stage
- Biological Science Laboratory Technician Stella Sieber, Laboratory of Molecular Toxicology, who is the group's secretary and scribe

Organizers were pleased with the turnout for the initial meeting of the AoLS. Shown above, left to right, are Biologist Michelle Sever, Biologist Jacquie Marzec and Biologist Jennifer Madenspacher. (Photo courtesy of Steve McCaw)

Germolec shared insights from her experience on the AoS, which was the model for the AoLS. "The idea is to have a widely distributed Council so you get some input from the different programs and branches," she told the audience. (Photo courtesy of Steve McCaw)

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NIEHS Welcomes Japanese Students

By Eddy Ball

On March 9, 16 high school students from the Mizusawa Super Science High School in Iwate, Japan visited NIEHS for an afternoon seminar as part of an ongoing exchange program with the North Carolina School of Science and Mathematics (NCSSM). The half-day program featured an overview of environmental health science research at the Institute and hands-on learning in three of the Institute's laboratories.

The program, one of several outreach efforts for secondary school students conducted each year by NIEHS, was organized by NIEHS Public Information Officer John Peterson and Steve Warshaw, Ph.D., vice chancellor for academic affairs at NCSSM. NIEHS Pharmacogenetics Group Principal Investigator Masahiko Negishi, Ph.D., and Staff Scientist Tatsuya Sueyoshi, Ph.D., provided classroom instruction in Japanese on "Environment-Gene Interactions" and "Fluorescent Protein GFP and Biology."

Negishi also translated Peterson's introductory comments and a presentation by Greg Scott on "Genetically Engineered Mice to Study Diseases." Visiting Fellows Kosuke Saito, Ph.D., and Hisako Miyakawa, Ph.D., accompanied students on lab tours and translated for them.

Negishi oriented the students to their institutional and geographic setting before launching into gene-environment interactions and his work in pharmacogenetics. One of his examples involved individual differences in the rate of drug detoxification. (Photo courtesy of Steve McCaw)

Lab presentations included “Electron Microscopy, Histology and Immunohistochemistry” by Electron Microscopy Biologist Deloris Sutton, “See GFP in a Cell with Your Own Eyes” by Sueyoshi, and “See the Atomic Structure of Protein Through X-Ray” by Structure and Function Research Group Leader Lars Pedersen, Ph.D.

As the students prepared to return to Durham, Negishi said of the program, “If just one of these kids gets interested in research and decides to pursue a career in biomedical research, it will be a success.”

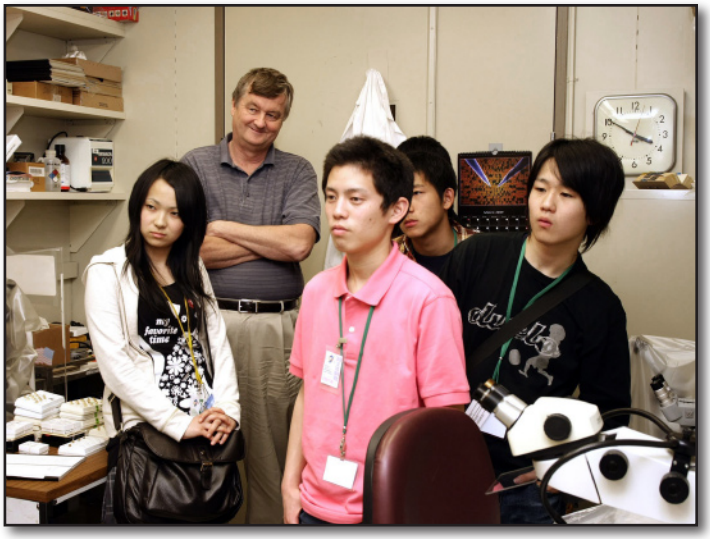
Although they didn’t ask many questions, most of the students, like this young man, stayed attentive during the ninety minutes of classroom instruction. Listening to the presentations in Japanese meant they could pay attention to the topic without having to simultaneously translate the speaker’s words. (Photo courtesy of Steve McCaw)

The exchange program between NCSSM and schools in the Iwate Prefecture, a district in northern Japan, was started six years ago. The program is part of an initiative by schools in Iwate to expose students in the largely rural district to science and technology. During their visit to the Triangle, the students also visited Duke University and the University of North Carolina at Chapel Hill and stayed on the NCSSM campus. Next year, according to Warshaw, NCSSM students will visit Japan as part of the exchange program.

In the relaxed environment of the NIEHS Executive Conference Room, Negishi provided a running translation of Scott’s talk on the creation of knock-out and knock-in strains of mice. (Photo courtesy of Steve McCaw)

Sueyoshi used slides to illustrate the way the fluorescent protein GFP allows researchers to observe previously invisible processes, such as the development of nerve cells in the brain or the way cancer cells spread. (Photo courtesy of Steve McCaw)

With Saito, right, translating, Sutton, left, and Biologist Mack Sobhany showed students the photo of a cell with its nucleus magnified 9,000 times. (Photo courtesy of Steve McCaw)



Peterson, in the background, seemed to enjoy the microscopy demonstration as much as his young colleagues did. (Photo courtesy of Steve McCaw)

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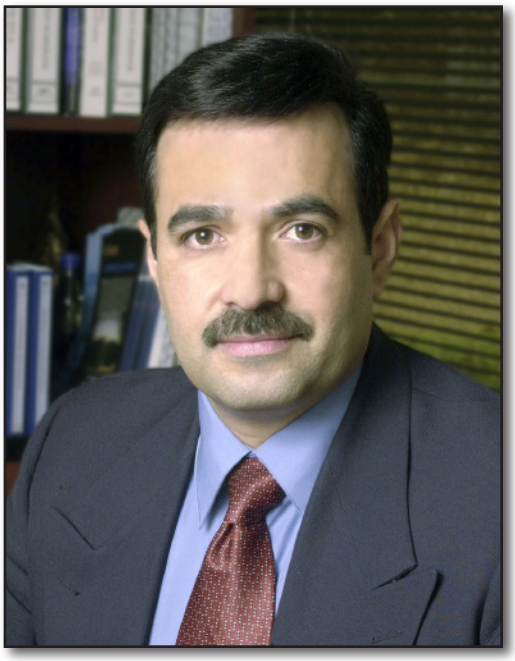
Roman Outlines New ADA Amendment

By Eddy Ball

A new amendment to the 1990 Americans with Disabilities Act (ADA) and 1973 Rehabilitation Act went into effect on January 1, 2009 extending coverage of employees with disabling conditions. Despite some initial challenges for supervisors, the legislation will offer a wider range of equal employment opportunities to everyone, said NIH Equal Employment Opportunity (EEO) Specialist Gerard Roman in his "ADA Rehab Act Update" presentation March 10.

The ADA Amendments Act of 2008, Roman explained, does not change the basic provisions of the act, which he described as "a major step in the long journey toward equal rights for all citizens." However, the legislation does change the meaning of some of some key terms used to determine just which individuals are covered by the law.

The new legislation, Roman said, expands the concept of "substantial limitation" due to disability, broadens the range of "major life activities" and limits the application of the "mitigating measures" provision. As a result, the act extends the protection of the law to many people who were not considered "disabled enough" under previous interpretations of the law.



In his presentation, Roman observed, "Sometimes the worst thing about a disability is that people meet it before they meet you." (Photo courtesy of Steve McCaw)

The 2008 Act includes people with "episodic or in remission" impairments as people with disabilities protected by the law if the impairments would "substantially limit a major life activity when active." The Act also clarifies what it means to be "regarded as" having a disability. People experiencing discrimination based on the perception that a person has a disability, whether the person has a disability or not, will now have extended grounds for protection by the law.

Sponsored by the NIEHS Disability Advocacy Committee, the presentation was a "heads-up" for supervisors and employees at NIEHS. Roman said that more details would be forthcoming as revised regulations are issued within the next few months. He gave attendees a Job Accommodation Network (JAN) Bulletin on the new law and a copy of the presentation given at the December 9 NIH Office of Equal Opportunity and Diversity Management NIH-only seminar on the subject by consultant Ernest Hadley, president of the Federal Employment Law Training Group.

According to Roman, the legislation was a response to Equal Employment Opportunity Commission (EEOC) interpretations, as well as high profile legal decisions that set too high a standard for coverage under the 1990 ADA and the 1973 Rehabilitation Act. Previous interpretations denied redress to many individuals who experienced employment discrimination related to their disabilities. Roman referred to court rulings that impairments could not be considered as disabilities under the narrow definitions then in force — even though the conditions later resulted in the deaths of the plaintiffs.

Roman began his talk by offering some perspective on "the dark history of discrimination on the basis of disability" and why the new legislation is so important in the struggle to provide fair treatment for all people. The amendments, he said, promise to help "restore the original intent of our disability laws."

Underscoring the need for the new legislation, Roman said, are the significant employment and income disparities experienced by persons with disabilities. The new provisions, he said, will help people with disabilities overcome the "myths and fears [that] are as limiting as the impairment itself," offering them a more equal opportunity for fulfilling their potential as productive individuals.

Members of the NIEHS Disability Advocacy Committee gathered for their most recent group photo. Shown seated are, left to right, J. J. Bell-Nichols, Cindy Innes, Carol Pearce and committee chair Alicia Moore, who introduced Roman. Standing are, left to right, Clyde Hasty, Molly Vallant, Tina Jones and Andy Ewens. (Photo courtesy of Steve McCaw)

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A Belated Retirement Get-Together for Janet Guthrie

By Robin Mackar

A group of about 30 NIEHS employees and retirees gathered February 26 to give longtime NIEHS employee Janet Guthrie a belated retirement party. The colleagues reminisced and shared a few hearty laughs and offered their best wishes at Janet's well-deserved sendoff.

Guthrie opened her gifts and smiled as she read cards from her longtime friends at NIEHS. (Photo courtesy of James Huff)

Janet retired in December after a successful stint of more than 30 years at NIEHS. At her party, her friends and colleagues enjoyed the usual fare of food, beverages, decorations, cake, gifts and fond memories of yesteryear.

Colleagues Jerry Phelps and John Schelp told stories about taking Janet to her first rock concert and drinking a beer with her. Whether Janet's sardonic remarks about not recalling the evening were true or not, the tales set the right tone for some light-hearted trips down memory lane, as colleagues recalled how much they enjoyed working with Janet over the years.

Long-time colleague Tom Hawkins shared an anecdote about carpooling with Janet in the 1980s, and she seemed to remember that one. Many even recalled studying or collaborating with her dad, Dr. Frank E. Guthrie, while he was a professor at nearby North Carolina State University. Retired NIEHS staffers, such as Betty Mills, Donna Shields and others, contributed their stories and wished Janet well.

Janet's face lit up as she relived the memories. "I miss all of you and will forever have fond memories of working with you," she said in a thank you note to the group afterwards, reflecting on her impressive career at NIEHS and the good times she shared with her friends at the Institute.

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

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