Birnbaum Speaks at Milwaukee Town Hall

As the crowning event of a visit to Milwaukee, NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., spoke October 1 at the latest NIEHS Town Hall Meeting. The event drew a capacity crowd to the Milwaukee Public Library’s Centennial Hall. ...read more

Trainees Turn Out in Record Number for National Postdoc Appreciation Day

As part of the NIEHS Trainee Assembly (NTA) fall General Meeting on September 24, NTA and the NIEHS Office of the Scientific Director celebrated the first annual National Postdoc Appreciation Day with snacks, fellowship and prizes. ...read more

Fellows and Investigators Showcased at Annual NIH Research Festival

When NIH held its week-long annual Research Festival October 6-9, seven postdoctoral fellows and two investigators from NIEHS were on hand in Bethesda to celebrate the accomplishments of NIH scientists. ...read more

First Annual Meeting of the NIEHS Centers for Neurodegeneration Science

The NIEHS Centers for Neurodegeneration Science (CNS) — formerly The Collaborative Centers for Parkinson’s Disease Environmental Disease Research (CCPDER) — held the program’s first annual meeting on October 8 and 9 at NIEHS. ...read more

GEMS Holds 27th Annual Fall Meeting

The Genetics and Environmental Mutagenesis Society (GEMS) celebrated the anniversary of its annual meeting series October 5 at the William and Ida Friday Center on “Dissecting Genome Structure, Genetic Traits and the Basis for Complex Diseases.” ...read more

Researchers Find Link Between Cholesterol and Asthma

High cholesterol levels have been linked to a variety of illnesses such as heart attack, stroke and diabetes, but recent research published in the Journal of Allergy and Clinical Immunology suggests that cholesterol may also play a role in asthma. ...read more

Experts Review Revisions to Local Lymph Node Assay Method

On October 20–22, scientists from NIEHS, the Environmental Protection Agency, the Food and Drug Administration (FDA), and the Consumer Product Safety Commission (CPSC) participated in an international expert consultation to evaluate modifications of the murine local lymph node assay (LLNA)... ...read more

Nobel Winner Speaks at RNA Society Meeting

Sponsored in part by NIEHS, the “Symposium on RNA Biology VIII: RNA Tool and Target” was held on October 16 and 17 at the North Carolina Biotechnology Center in the RTP. ...read more
Shaughnessy Represents NIEHS at Biotech Conference
NIEHS Health Science Administrator Dan Shaughnessy, Ph.D., served as the NIEHS/NIH representative at the Eighth Annual Charlotte Biotechnology Conference, held October 8 at the University of North Carolina at Charlotte (UNCC). ....read more

Harry Gives Special Guest Lecture at Stereology Workshop
NIEHS Neurotoxicology Group Principal Investigator Jean Harry, Ph.D., delivered the special guest lecture at the 15th Annual Fall Stereology Workshop, “Applications of Unbiased Stereology To Neural Systems” — held October 14-16 in Chicago as a pre-conference event of the 38th Annual Meeting of the Society for Neurosciences. ....read more

Sister Study Exceeds Recruitment Goal: Now the Real Work Begins
NIEHS has many reasons to celebrate this October as it recognizes Breast Cancer Awareness Month. The NIEHS Sister Study began recruiting women for this landmark study during Breast Cancer Awareness month in October 2004 and this October has reached a milestone. ....read more

WETP Grantees Look at Global Issues in Worker Safety
At their annual fall workshop last month, NIEHS Worker Education and Training Program (WETP) grantees were treated to a forum on emerging developments in global health and safety that promise to have a major impact on worker training. .....read more

Oceans Center Study Offers Caveat for Beachgoers
By combining solid research and relationship building, the National Science Foundation (NSF)-NIEHS Center for Oceans and Human Health (COHH) at the University of Miami and its collaborators are taking their science to the people on the beaches of America — and highlighting an under-appreciated human source of exposure to bacteria, including the potentially deadly methicillin-resistant *Staphylococcus aureus* (MRSA) ....read more

Superfund Study Links PCE and Birth Defects
Prenatal exposure to a chemical solvent can put babies at increased risk for birth defects, according to an NIEHS-funded study published in the September 2009 issue of *Environmental Health*. ....read more

SNPs and Dog Ownership Associated with Eczema Status
New findings by NIEHS-funded researchers at the University of Cincinnati (UC) report genetic and environmental risk and protective factors involved in the development of eczema in children — an atopic condition that is considered the result of complex interactions between genetic susceptibility and skin-barrier aberrations. ....read more

NC State Professor Discusses Nanoparticle Toxicity
NIEHS grantee James Bonner, Ph.D., an associate professor in the Department of Environmental and Molecular Toxicology at North Carolina State University, gave a seminar at NIEHS on October 15 outlining some of his latest findings on engineered nanoparticles. ....read more
NIEHS Spotlight

NIEHS Center Intern Recognized by EPA Head
Fifteen-year-old NIEHS-supported center intern Otana Jakpor enjoyed the latest boost in her burgeoning career in the environmental health sciences on September 30 when she received special recognition from Lisa Jackson, administrator of the U.S. Environmental Protection Agency (EPA), during Jackson’s visit to Los Angeles. ...read more

Superfund Announces Wetterhahn Award Winner
The NIEHS Superfund Research Program (SRP) announced that Kathleen Radloff, a doctoral student at Columbia University, is the twelfth recipient of the Karen Wetterhahn Memorial Award. Radloff will be presented with the award at the SRP Annual Meeting in New York where she will deliver a keynote address highlighting her research ....read more

NIEHS Center Director Honored by Oregon State
On September 23 in Corvalis, Ore., Oregon State University (OSU) recognized the achievements of NIEHS grantee David Williams, Ph.D., with its Alumni Association Distinguished Professor Award — the highest award the university presents to members of its faculty. ....read more

WETP Grantee To Be Nominated for FEMA Post
On October 9, President Barack Obama announced his intention to make several high-level nominations, releasing a list that includes NIEHS Worker Education and Training Program (WETP) grantee Elizabeth M. Harman. .....read more

Science Notebook

Cumulative Lead Exposure Linked to Death from CVD
A collaborative study that included three NIEHS grantees – Marc G. Weisskopf, Ph.D., Sc.D., Joel Schwartz, Ph.D., and Howard Hu, M.D., Sc.D. – underscores the cumulative effects of exposure to lead and is the first study to investigate the association between mortality and lead levels in bone. ...read more

Artificial Protein Can Direct Alternative Splicing of Genes
What started out as a very basic research project looking at a fly protein, has now morphed into a plausible method that may help researchers better study and manipulate disease-associated gene activity. ...read more

Prenatal Exposure Can Influence Gene Regulation and Later-Life Events
On October 14, Rebecca Fry, Ph.D., of the University of North Carolina at Chapel Hill (UNC-CH), presented the second in a series of talks sponsored by the NIEHS Division of Extramural Research and Training (DERT). ...read more

This Month in EHP
This month, Environmental Health Perspectives (EHP) considers so-called “beneficial uses” of the more than 131 million tons of coal combustion waste (CCW) produced each year in the U.S. The focus article, “Trash or Treasure? Putting Coal Combustion Waste to Work,” investigates whether using CCW in construction brings with it a potential for toxic leaching from building materials. ...read more
NIEHS Spotlight

Editorial Recognizes NIEHS-Funded Research
A University of Southern California (USC) study on prenatal tobacco smoke (PTS) exposure and DNA methylation partially funded by NIEHS has been commended for the quality of the research. ...read more

Kim Receives Congressionally Directed Medical Research Program Award
Sangmi Kim, Ph.D., a postdoctoral fellow in the Chronic Disease Epidemiology Group, received a Postdoctoral Fellowship Award from the Breast Cancer Research Program (BCRP) of the Department of Defense Congressionally Directed Medical Research Program for 2009 on October 7. ...read more

NIEHS-Funded Training for HazMat Emergency Response in American Samoa
In June 2009, University of California, Davis Extension (UCDE) instructors taught three health and safety courses for handling hazardous materials and emergency response in American Samoa on the main island of Tutuila. ...read more

Call for Nominations to the Interagency Breast Cancer and Environmental Research Coordinating Committee
In the October 16 Federal Register, NIEHS issued a request for the nomination of voting members to serve on the NIH/NIEHS Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC). ...read more

Science Notebook

Upcoming Distinguished Lecturer Gail Mandel
The 2009-2010 NIEHS Distinguished Lecture series continues this month with a November 12 talk by Gail Mandel, Ph.D., on “Repression Mechanisms and Neuronal Phenotype.” ...read more

Extramural Research

Extramural Update
NIH received $10 billion under the American Reinvestment and Recovery Act (ARRA). Of that NIEHS received $168 million for environmental health research grants and $19.4 million for the Superfund program, to be awarded over fiscal years 2009 and 2010. In fiscal year 2009, the NIEHS funded 322 grants, allocating approximately $133 million and $27 million respectively for awards and supplements. ...read more

• Carbon Nanotubes Can Affect the Lining of the Lungs
• Electronic “Nose” Smells Toxins
• Arsenic and Heart Arrhythmia
• Prostate Gene Polymorphism Linked to Bladder Cancer

Intramural Research

Intramural Papers of the Month
• DNA Scrunching Can Facilitate Repair by Filling the Gaps
• Hippocampal Synaptic Plasticity Can Be Modulated by Differential Calcium Handling
• UV Radiation Modulates the Expression of Certain Autoimmune Diseases in Women
• A Novel Chromosomal Candidate Region for Childhood Asthma
Presentation Addresses Obesity as a Disability

The NIEHS Disability Advocacy Committee (DAC) began its observance of National Disability Employment Awareness Month on September 30 with a presentation on “Obesity, Mortality and Quality of Care: Implications for Disability.” ...read more

Speaker Explores the Secret History of Columbus

During its latest Hispanic Heritage Celebration on October 6, the NIEHS Diversity Council offered employees and contractors a novel perspective on explorer Christopher Columbus with a lecture by historian Manuel Rosa. ...read more

Motivational Speaker Wows Disability Event Audience

As one of its featured presentations in observance of National Disability Employment Awareness Month, on October 14 the NIEHS Disability Advocacy Committee (DAC) featured the multi-talented motivational speaker and mentor Tawana Williams. .....read more

DERT Celebrates the Completion of ARRA Work

Employees in the NIEHS Division of Extramural Research and Training (DERT) do an exceptional job of funding and managing environmental health sciences research grants to investigators throughout the country. .....read more

CFC Nears Goal as Campaign Continues

By the end of the day on October 30, NIEHS employees had pledged nearly $60,000 or 85 percent of the campaign’s 2009 goal of $70,000, and Combined Federal Campaign (CFC) organizers were confident NIEHS would reach or exceed the goal as the campaign continues through November 20. .....read more

Calendar of Upcoming Events

- **November 2–4 (Offsite Event)** at the Hilton Research Triangle Park, 8:30–5:00 — National Toxicology Program Report on Carcinogens Expert Panel Meeting on Formaldehyde

- **November 3–4 (Offsite Event)**, at Columbia University, New York, 8:30–5:00 — Superfund Research Program Annual Meeting

- **November 3–6 (Offsite Event)**, at the Twin City Quarter in Winston-Salem, N.C. — “Faces of a Healthy Future: National Conference to End Health Disparities II”

- **November 5**, in Rodbell Auditorium, 8:00–5:00 — NIEHS 2009 Science Day

- **November 7–11 (Offsite Event)**, at the Pennsylvania Convention Center in Philadelphia — American Public Health Association 137th Annual Meeting & Exposition

- **November 10**, in Keystone 1003AB, 10:00–11:00 — DERT Keystone Seminar with Patty Opresko, Ph.D., topic TBA

- **November 12**, in Rodbell Auditorium, 11:00–12:00 — Distinguished Lecture featuring Gail Mandel, Ph.D., speaking on “Repression Mechanisms and Neuronal Phenotype”

- **November 16**, in Rodbell Auditorium, 10:00–11:00 — Seminar featuring Brian Strahl, Ph.D., speaking on “Regulation and Function of Histone-Modifying Enzymes in Transcription”

- **November 18–20 (Offsite Event)**, in San Francisco — Annual Breast Cancer and the Environment Research Centers Meeting with a November 18 Town Hall Meeting featuring Linda Birnbaum, Ph.D.

- **November 19–20 (Offsite Event)**, in Sausalito — Sixth Annual Early Environmental Exposures Meeting, with keynote address by Linda Birnbaum, Ph.D.


- **November 20–22 (Offsite Event)**, at the Hilton Research Triangle Park, 8:30–5:00 — National Toxicology Program Report on Carcinogens Expert Panel Meeting on Formaldehyde

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- View More Events: NIEHS Public Calendar
As the crowning event of a visit to Milwaukee, NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., spoke October 1 at the latest NIEHS Town Hall Meeting. The event drew a capacity crowd to the Milwaukee Public Library’s Centennial Hall.

Birnbaum’s talk was the culmination of a busy day of meetings with directors of NIEHS Environmental Health Sciences Core Centers gathered at the University of Wisconsin, Milwaukee (UWM) for a three-day annual conference. Birnbaum also participated in a trolley tour of Milwaukee neighborhoods and a reception prior to the 6:00 p.m. town hall meeting.

Introduced by moderator Sandra McLellan, Ph.D., of the UWM Great Lakes WATER Institute, as the “top cheese,” Birnbaum set the stage for a panel discussion by environmental public health specialists and city and regional officials. Birnbaum began her presentation with impressions from the afternoon trolley tour of the city — recounting the neighborhoods, gardens and river valley industrial brownfield sites she saw that day to emphasize the interconnectedness of the environment with public health and quality of life.

In her talk, Birnbaum highlighted “some of the outstanding work that NIEHS is supporting here at UW-Milwaukee,” including basic research into the biological mechanisms of toxicity, detection of freshwater viral, bacterial and chemical contaminants, and the innovative outreach initiative, Healthy Latino Families and Schools. She described work at UWM as an example of the productive mix of “small science’ conducted by individual labs” with the work of “‘big science’ teams, which may be needed to answer some of the most intractable questions.”

Moving to the national and international levels, Birnbaum surveyed the Institute’s “larger research investment” in environmental health science, especially in research on the long-term health effects of early environmental
exposures. She focused on new and renewed efforts to prevent disease through effective translation of research results into public health initiatives for improving children’s health and development by preventing and treating chronic diseases.

Among the many such initiatives, she singled out a “small sampling” of NIEHS programs in autism and asthma, along with such programs as the Partnerships for Environmental Public Health. As she has in several recent talks, Birnbaum underscored the need for partnerships and collaborations at every level of science and government in a unified effort to improve environmental health in the U.S. and worldwide.

Birnbaum’s closing comments brought her back to the streets and neighborhoods of Milwaukee. “We look forward to supporting and working with scientists, health care providers and community members here in a great city on a great lake,” she concluded, “to continue the success of this work, to better understand how the environment affects our health, and to develop effective prevention strategies to protect public health.”

In closing, Birnbaum emphasized the pressing need for environmental health research. “You can’t change your genes, but you can change your environment,” she said. “The question is not, ‘Can we afford to do this research?’” she said. “It’s, ‘Can we afford not to?’”

Trainees Turn Out in Record Number for National Postdoc Appreciation Day

By Laura Hall

As part of the NIEHS Trainee Assembly (NTA) fall General Meeting on September 24, NTA and the NIEHS Office of the Scientific Director celebrated the first annual National Postdoc Appreciation Day with snacks, fellowship and prizes. Nearly half of all the trainees at NIEHS turned out to enjoy their special day of recognition, which was organized by the NTA Steering Committee and Diane Klotz, Ph.D., director of the Office of Fellows’ Career Development (OFCD).

In his keynote address, Acting NIEHS Scientific Director John Pritchard, Ph.D., emphasized how critical trainees are to the work of the Institute. “We have two products [at NIEHS]. We have our research, and we have our trainees,” Pritchard observed.

“I’ve never seen such a turnout before at NTA meetings,” Gosavi noted. He explained the functions of the NIEHS Trainee Assembly and thanked organizers for their help in organizing the event. (Photo courtesy of Steve McCaw)
“Without our trainees, we wouldn’t have our research … We’re thankful that you’re here.”

NTA Co-chair Rajendrakumar Gosavi, Ph.D., a postdoctoral fellow in the Structure and Function Research Group, opened his part of the program by noting that National Postdoc Appreciation Day was organized by the National Postdoctoral Association (NPA) to recognize the contributions of postdoctoral scholars to U.S. scientific research. He then gave a quick overview of the history, purpose and organization of the NTA — as well as the many opportunities sponsored by the NTA for postdocs at the Institute (see text box).

In her discussion of the OFCD, Klotz said its purpose is to “provide lots of scientific career and professional development programs” for trainees. She provided the cookies and door prizes, while NIEHS principal investigators showed their appreciation for trainees by contributing money for the ice cream, a great crowd pleaser.

According to Klotz, all of the other intramural programs at NIH also held special events for their trainees. To encourage attendance throughout NIH, Director of the NIH Office of Intramural Training and Education (OITE) Sharon Milgram, Ph.D., and Lori Conlan, Ph.D., director of the NIH Office of Postdoctoral Services, made a commitment to personally donate money to a charity chosen by the postdocs.

Trainees responded positively to the meeting. They found the information useful and enjoyed the snacks, ice cream and prizes. “I definitely enjoyed the ice cream social afterwards! It’s always nice to have an opportunity to get to know other trainees,” said Jenna Waggoner, a special volunteer in the Chronic Disease Epidemiology Group. “I enjoyed the activity because I was able to learn more about the NTA,” added Ion Channel Physiology Group member José Colón Sáez, Ph.D. “It gave us a sense of community and brought together postdocs from different groups that otherwise rarely interact with each other.”

“We greatly appreciate the organizers who took some time out and made this event happen,” noted Deepti Dwivedi, Ph.D., a visiting fellow in the Laboratory of Molecular Genetics. “Also, door prizes, free cookies and ice cream are always welcome.”

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)
NIEHS Trainee Assembly Activities

The NTA membership includes all non-tenured non-permanent scientists training at NIEHS. Through the NTA, trainees have the opportunity to receive career training, network with their peers, develop more mentoring relationships and voice their concerns to NIEHS management. Volunteers on the NTA Steering Committee represent the trainees from all the laboratory branches and vote on matters that come before the committee, as well as take leadership roles by representing NTA inside and outside of NIEHS.

Gosavi told the trainees that the committee currently needs an international fellows liaison and representatives from the Laboratory of Neurobiology and the Laboratory of Pharmacology. He also said that standing subcommittees would welcome volunteers.

The NTA hosts monthly and special events throughout the year:

**Monthly Events**

NTP Steering Committee Meetings — every third Wednesday of the month at 3:30 pm in the Executive Conference room by the cafeteria.

Fellows’ Coffee Hours — last weekday of the month at 9:30-10:30 am in the F-module second floor break room F297.

Science Career Workshops — NTA hosts a monthly series of workshops that provide career advice. They are sponsored by Felcom, the NIH Fellows Committee and OITE. The workshops are webcast from NIH, and past webcasts are posted online.

Distinguished Lecture Luncheons — NTA hosts a lunch with each NIEHS Distinguished Lecture speaker to discuss science and career development. The lecture series is a monthly series of seminars given by renowned scientists.

**Special Events**

NIEHS/NTA Biomedical Career Fair — NTA helps to organize the annual career fair for young area scientists bringing them together with biomedical organizations and providing career panel discussions, workshops, and networking opportunities. The next Biomedical Career Fair will be on April 30, 2010.

Mentor of the Year Award — The NTA award committee selects and gives this award at the annual NIEHS Science Awards Day in November.
Fellows and Investigators Showcased at Annual NIH Research Festival

By Eddy Ball

When NIH held its week-long annual Research Festival October 6-9, seven postdoctoral fellows and two investigators from NIEHS were on hand in Bethesda to celebrate the accomplishments of NIH scientists. A total of 20 NIEHS fellows were recognized as recipients of the 2010 Fellows Award for Research Excellence (FARE), and seven of the fellows made poster or oral presentations.

In a message afterwards, NIEHS Deputy Scientific Director Bill Schrader, Ph.D., congratulated the NIEHS participants and “the very high number [of FARE winners] for an institute of our size.” The FARE is an annual competition that selects the top twenty-five percent of abstracts from fifty different study sections to receive a $1,000 travel award.

In a symposium on “From Synapse to Stroke: The Plastic Nervous System” on October 7, Laboratory of Neurobiology Investigator Serena Dudek, Ph.D., spoke on “From Stroke to Synapse: What’s New in Hippocampal CA2?” NIEHS Bioinformatics Branch Investigator Raja Jothi, Ph.D., chaired a symposium on “Epigenetics, Chromatin, and Gene Regulation” held the same day.

NIEHS FARE winners David Draper, Ph.D., and Erica Lannan, Ph.D., also made oral presentations at symposia. Draper spoke on “ABCG1 is a Negative Regulator of Pulmonary Host Defense” as part of the symposium on “Cross-regulation of Innate Resistance and Adaptive Immunity,” and Lannan addressed “Identification and Classification of Inflammatory Genes Co-regulated by Dexamethasone and TNF-Alpha” during the symposium on “Understanding Human Immunology.”

Also on hand was Director of the Office of Fellows’ Career Development (OFCD) Diane Klotz, Ph.D., who attended both talks. “This is the first year that postdocs have been included in the oral presentations at the Research Festival,” she said. “David and Erica both did an excellent job of representing the high caliber of postdoctoral research being performed at the NIEHS.”

Another five NIEHS fellows made poster presentations at the Research Festival:

- Omari Bandele, Ph.D., “Single nucleotide polymorphisms alter sequence-specific p53-DNA binding to gene regulatory elements”

- Rongqin Ren, Ph.D., “Mechanisms of glucocorticoid dependent cardiac hypertrophy”

- Ramendra Saha, Ph.D., “Rapid induction of neuronal arc is mediated by a promoter proximal RNA polymerase-II stalling mechanism”

- Jeremy Smyth, Ph.D., “Phosphorylation of the endoplasmic reticulum calcium sensor STIM1 underlies suppression of store-operated calcium entry during mitosis”

The NIEHS FARE winners posed with NIH Deputy Director of Intramural Research Michael Gottesman, M.D. Shown, left to right, are Saha, Ren, Lannan, Gottesman, Sunman and Smyth. (Photo courtesy of NIH and Diane Klotz)
Jeffrey Sunman, Ph.D., “The hemopexin domain of matrix metalloproteinase-9 (MMP-9) induces a pro-migratory phenotype in human melanoma cells independent of MMP-9 catalytic activity”

In addition to fellows attending the festival, thirteen others from NIEHS were also winners (see text box). Abstracts for FARE winners can be downloaded from the NIH Felcom Web page. NIEHS winners begin on page 153 of the “Winners by IC” list.

The NIEHS Fellows Honor Roll (Continued)

An additional 13 FARE winners were unable to attend the festival, but still received formal recognition for their scientific achievements:

• Jim Aloor, Ph.D., “HIV-1 envelope protein gp41 triggers pro-inflammatory responses in the macrophage through toll like receptors-2 and -4 and their adaptors”

• Abee Boyles, Ph.D., “Maternal alcohol consumption and infant clefts: the role of alcohol metabolism gene variants”

• Ryan Dackor, Ph.D., “Prostaglandin E2 (PGE2) protects murine lungs from bleomycin-induced pulmonary fibrosis and lung dysfunction”

• Dana Hancock, Ph.D., “Chromosome 9q21.31 as a novel susceptibility locus for childhood asthma: evidence from a genome-wide association study in Mexicans”

• Andrew Kraft, Ph.D., “The neurites of striatal neurons expressing mutant huntingtin protein are sites of microglial association and proliferation, which facilitates the progression of degenerative phenotypes”

• Andreas Larrea, Ph.D., “Scrunching during DNA replication”

• Hideki Nakano, Ph.D. “The impact of surface ALDH1a2 on pulmonary dendritic cells for generation of regulatory T cells leading to immunotolerance to inhaled antigens”

• Aparna Purushotham, Ph.D. “Hepatocyte-specific deletion of SIRT1 alters fatty acid metabolism and results in hepatic steatosis and inflammation”

• Li Qian, Ph.D., “Potent neuroprotective effects of long-acting beta2-adrenergic receptor agonists: a potential new therapeutic indication through a novel mechanism”

• Ritu Rana, Ph.D., “Mediator 25 (Med25) functions as an essential coactivator for HNF4alpha and recruits RNA Pol II to initiate the human CYP2C9 gene expression”

• Thaddeus Schug, Ph.D., “SIRT1 regulates NF-kB-dependent transcription and attenuates macrophage-mediated inflammation”

• Jeffrey Stumpf, Ph.D., “Yeast homologues of eighteen disease mutations in DNA Polymerase Gamma cause mtDNA depletion and mutagenesis”

• Xueqian Wang, Ph.D., “The aryl hydrocarbon receptor (AhR) regulates P-glycoprotein at the blood-brain barrier (BBB)”
First Annual Meeting of the NIEHS Centers for Neurodegeneration Science

By Dixie Ann Sawin

The NIEHS Centers for Neurodegeneration Science (CNS) — formerly The Collaborative Centers for Parkinson’s Disease Environmental Disease Research (CCPDER) — held the program’s first annual meeting on October 8 and 9 at NIEHS. Speakers included scientists from the centers at Emory University, The Burnham Institute and the University of California, Los Angeles (UCLA), as well as investigators with the NIEHS Intramural program and the National Toxicology Program (NTP). NIEHS Health Science Administrator Cindy Lawler, Ph.D., is the extramural officer who oversees the NIEHS-funded centers.

The goals of the meeting included fostering interaction among the centers that could lead to collaborative research, highlighting the findings of all the Centers, enabling trainees to become more integrated within the program, and introducing center investigators to NIEHS investigators involved in related research (see text box). As Lawler observed, interaction of trainees across centers is “a key part of the program.”

The CNS program addresses the need for integrated research efforts involving basic and clinical scientists in a quest to discover the causes of and possible treatments for neurodegenerative diseases. In 2008, NIEHS awarded five-year CNS grants totaling $4.2 million per year to Emory, UCLA and Burnham. Each Center supports an administrative core, service/facility cores and a research development core for pilot projects by investigators studying Parkinson’s Disease (PD).

According to NIEHS Acting Deputy Director Steve Kleeberger, Ph.D., NIEHS has a significant commitment to this type of research on neurodegenerative disease and supports more than 20 individual RO1 and R25 grants on PD, ranging from the epidemiology of PD to the development of new animal models of PD and studies of brain transport and regenerative mechanisms. “These Centers are especially important for helping move this research forward,” Kleeberger stressed, “and the interaction between multiple disciplines within the centers… is a really important mechanism to enable the kind of research necessary to understand the pathogenesis of disease.”

The Emory group started off the presentations on the first day with an overview by Center Director Gary Miller, Ph.D. The overall goals of this Center are to determine how environmental and genetic disruption of dopamine (DA) storage leads to oxidative damage; to identify novel mechanisms by which DA neurons respond to oxidative stress; to determine how environmental toxicants disrupt redox balance; and to identify novel biomarkers of environmental toxicant exposure associated with PD.

Moderator Cindy Lawler kept the meeting on schedule — and on track — as the grantees addressed a capacity audience in Rodbell Auditorium. (Photo courtesy of Steve McCaw)

Miller described his group’s efforts to discover markers that can help clinicians identify early symptoms of PD in their patients in order to slow disease progression. (Photo courtesy of Steve McCaw)
The overall goals of the Burnham investigators were outlined by Center Director Stuart Lipton, M.D., Ph.D. His group focuses on the ability of S-nitrosylation and oxidation of proteins to mimic genetic mutations seen in PD. These mutations cause protein mis-folding, abnormal signaling and eventual cell injury and death. Lipton’s group proposes to generate “novel hits” from chemical library screens that could possibly be used as targets for therapeutic intervention.

The UCLA researchers, headed by Marie-Françoise Chesselet, M.D., Ph.D., seek to identify novel mechanisms that contribute to the pathogenesis of sporadic PD by investigating primary cellular pathways affected by agricultural pesticide use, particularly in the well-characterized patient cohort in the agricultural region of the California Central Valley. Initial evidence suggests that pesticides lead to aberrant folding of proteins and the involvement of the ubiquitin-proteasome system (UPS), adverse effects on microtubule assembly and inhibition of aldehyde dehydrogenase — an important detoxification enzyme. The overall objective is to determine whether disruption of these processes can increase the risk of developing PD.

A poster session featuring the work from the different laboratories within each center was held after the first day of talks. A trainee meeting, organized by NIEHS Health Science Administrator Mike Humble, Ph.D., provided useful information on training and career development.

(Dixie-Ann Sawin, Ph.D., is a post-doctoral research fellow in the NIEHS Laboratory of Neurobiology Neurotoxicology Group on detail as a writer for the Environmental Factor.)
Several Intramural scientists attended the CNS meeting and interacted with the CNS grantees. They were also interested in the poster presentations by investigators and trainees.

On the second day of the CNS meeting, NIEHS and NTP investigators presented their work. Jau-Shyong Hong, Ph.D., head of the Pharmacology Group, and G. Jean Harry, Ph.D., head of the Neurotoxicology Group, shed light on the neurotoxic and neuroprotective effects of microglia, the brain macrophage cells, and their putative role in PD.

Raymond Tice, Ph.D, chief of the NTP Biomolecular Screening group highlighted the goals of the Tox21 Community and the pursuit of molecular biomarkers of exposure to drugs or toxicants.

Epidemiology Branch Staff Scientist Freya Kamel, Ph.D, and Tenure Track Investigator Honglei Chen, M.D., Ph.D, highlighted their studies of the associations of pesticides and smoking with PD development.

Kamel discussed insights from her studies of pesticide exposure and PD in the Agricultural Health Study cohort of licensed pesticide applicators and their families. (Photo courtesy of Steve McCaw)
Shaughnessy Represents NIEHS at Biotech Conference

By Eddy Ball

NIEHS Health Science Administrator Dan Shaughnessy, Ph.D., served as the NIEHS/NIH representative at the Eighth Annual Charlotte Biotechnology Conference, held October 8 at the University of North Carolina at Charlotte (UNCC). Shaughnessy spoke as part of the federal panel on “Future Trends in Biotechnology Funding” at the conference’s “University Opportunities Workshop,” and along with several other participants, toured the new North Carolina Research Campus the following day.

Shaughnessy’s talk was an opportunity to inform students and investigators about funding and employment opportunities at NIEHS and other NIH centers and institutes, as well as to lay the groundwork for possible future collaborations between scientists at the North Carolina Research Campus (NCRC) and investigators at NIEHS in the areas of genomics, proteomics and metabolomics. According to organizers, the conference brought together some of the most recognized biotechnology, business and research professionals from around the globe and highlighted regional opportunities and investment trends within the local biotechnology sector.

As Shaughnessy explained afterwards, nurturing a relationship between NIEHS and the NCRC could also be an investment in the future for people at NIEHS. “As more and more research comes online at the facility,” he noted, “the campus may become a job placement option for fellows in training at NIEHS looking for opportunities to work in the area.”

The NCRC was started with a $1.5 billion investment by David Murdock, owner of Dole Foods Company, Inc., and it now occupies its first three buildings in Kannapolis, NC., When completed, the facility will offer more than a million square feet of state-of-the-art lab and office space, including the David H. Murdock Research Institute, which houses one of the largest and most advanced scientific equipment collections of its kind anywhere in the world, including state-of-the-art technology in genomics, proteomics and metabolomics.

Universities participating at the NCRC include Duke University, UNC Chapel Hill, UNC Charlotte, North Carolina State University, North Carolina Central University, North Carolina A&T State University and UNC Greensboro.
Harry Gives Special Guest Lecture at Stereology Workshop

By Eddy Ball

NIEHS Neurotoxicology Group Principal Investigator Jean Harry, Ph.D., delivered the special guest lecture at the 15th Annual Fall Stereology Workshop, “Applications of Unbiased Stereology To Neural Systems” — held October 14-16 in Chicago as a pre-conference event of the 38th Annual Meeting of the Society for Neurosciences. Harry addressed an audience of specialists in the neurosciences, psychology, toxicology and pathology participating in the workshop with her talk on “Heterogeneity of microglia and brain macrophages: Impact on evaluating response to brain injury.”

Stereology is a method for quantifying two-dimensional structures from random, systematic sampling to provide unbiased and quantitative data. It is largely concerned with the three-dimensional interpretation of planar, or cross, sections of materials or tissues and offers researchers important insights into biological mechanisms of the brain and nervous system. With their course completed, the trainees join more than 1,600 scientists from academia, government agencies and private industry who have completed the course on using state-of-the-art, design-based stereology for morphometric analysis of biological tissue.

Harry’s talk highlighted the roles of microglia in the brain. Also known as the brain macrophage, microglia exhibit variable phenotypes with different roles that may be either beneficial or neurotoxic. Using examples from her work at NIEHS, Harry demonstrated the complicated nature of interpreting changes in morphological evidence of a microglial response, as well as associated neuroinflammatory factors. Along with the negative role often attributed to them during injury in the brain, microglia are also of interest to neuroscientists because of their critical role in the removal of excess or aberrant proteins from the brain, such as amyloid beta, implicated in Alzheimer’s disease, and alpha synuclein, mutations in which are present in Parkinson’s Disease.

According to Harry, stereology is a valuable tool for helping researchers gain a more complete understanding of the heterogeneity of these cells and for uncovering significant information for evaluating responses to brain injury. A better understanding of these responses can ultimately lead to improved therapeutic interventions for minimizing both short-term and long-lasting brain damage.

Afterwards, Harry said of her experience at the workshop, “I was honored to be given the opportunity to present information regarding the need to understand the cell changes being measured in order to pose the right questions and interpret the data correctly.”

In the early 1990s, workshop leader Peter R. Mouton, Ph.D. — a faculty member of the Department of Pathology at the Johns Hopkins University School of Medicine and currently director of the Stereology Resource Center — organized the first comprehensive three-day Stereology Workshop in the United States. Shortly thereafter, journal editors and grant reviewers began to favor state-of-the-art stereological methods, and today, stereology is the method of choice for morphometric analysis of biological tissue.
Along with Harry, expert stereologists speaking at the workshop included Arun Gokhale, Ph.D., professor of Materials Sciences and Engineering at the Georgia Institute of Technology; Jeffrey Long, Ph.D., principal investigator in the Laboratory of Experimental Gerontology at the National Institute on Aging; and Kebreten Manaye, M.D., associate professor of Physiology and Biophysics at the Howard University College of Medicine.

Sister Study Exceeds Recruitment Goal: Now the Real Work Begins

By Robin Mackar

NIEHS has many reasons to celebrate this October as it recognizes Breast Cancer Awareness Month. The NIEHS Sister Study began recruiting women for this landmark study during Breast Cancer Awareness month in October 2004 and this October has reached a milestone. It has recruited nearly 51,000 women from all walks of life, whose sisters had breast cancer, to participate in this long-term study focusing on uncovering environmental and genetic factors to help prevent breast cancer.

“What an amazing group of women we have enrolled in this study. Every single one of them should be congratulated for their commitment to participating in research to help identify factors that lead to breast cancer,” said Dale Sandler, Ph.D., chief of the Epidemiology Branch at NIEHS and principal investigator of the Sister Study. “We have exceeded our recruitment goal and I’m thrilled with the diversity of age, race, ethnicity and education represented in the cohort.”

The women come from all 50 states as well as Puerto Rico, and include women with different ethnic, educational and employment backgrounds. Since the study began in 2004, 50,884 women have enrolled including 4,438 African-American women, 2,631 Hispanic women, and 1,160 women from other racial/ethnic groups. The study also includes 8,230 women aged 65 and over, and 7,212 with a high school degree or less. All of the women in the study have a sister who has been diagnosed with breast cancer. Researchers hope to uncover clues about causes of breast cancer and other diseases by comparing women who develop breast cancer or other conditions while in the study with those who remain disease-free.

“Recruiting more than 50,000 Sister Study participants in five years was a huge accomplishment for the NIEHS,” said NIEHS Director Linda Birnbaum, Ph.D. “Over the years, we’ve received substantial support from a sister NIH agency, the National Center on Minority Health and Health Disparities, whose support enabled our researchers to develop unique strategies to recruit a diverse cohort. We appreciate the value that they and our many community partners and participants place on the promise of this research, and look forward to providing more insight into how to prevent breast cancer and other diseases that are influenced by the environment.”

Sandler, right, and Weinburg are shown last year when they launched the Two Sisters Study of early onset breast cancer.
(Photo courtesy of Steve McCaw)
“We owe a debt of gratitude to our participant volunteers who worked so hard to recruit women into the study and to our partner organizations that lent us their support,” added Lisa DeRoo, Ph.D., lead investigator of the study. These organizations included the American Cancer Society, the Susan G. Komen for the Cure, the Sisters Network, the Intercultural Cancer Council, the Love/Avon Army of Women, the Breast Cancer Network of Strength, and many more local and national groups interested in breast cancer and women’s health.

Sandler points out that sustaining the same level of enthusiasm as the project moves forward is going to be the next challenge. “What we need now is for everyone to realize this is a 10-year study and that the work is really just beginning,” Sandler said. The participants are asked to complete a yearly one-page update by mail, e-mail or phone. They are also asked to share more detailed information about changes in their health, jobs and lifestyle every two or three years.

The study has already reported some preliminary findings about how factors such as weight and perceived stress may influence health, and investigators are beginning to use the biological samples participants contributed to learn how some genetic factors may affect breast cancer risk. The researchers point out key results on gene-environment interactions may be just a few years away.

Under the direction of Clarice Weinberg, Ph.D., chief of the Biostatistics Branch at the NIEHS, the researchers are also using the Sister Study as a way to better understand early-onset breast cancer among a targeted subgroup of participants participating in what is called the Two Sisters Study.

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

**WETP Grantees Look at Global Issues in Worker Safety**

*By Eddy Ball*

At their annual fall workshop last month, NIEHS Worker Education and Training Program (WETP) grantees were treated to a forum on emerging developments in global health and safety that promise to have a major impact on worker training. As attendees learned during the meeting in Chapel Hill October 21–22, new developments in nanomaterials manufacturing, hazard communication and regulation of chemicals in the European Union could fundamentally influence workplace safety at home and abroad.

WETP Director Chip Hughes described the agenda as an engagement of “back-burner issues that are now becoming front-burner issues” in worker safety and health. He also said he looked forward to a meeting that would address the “two-way street” of interaction between American workers and workers worldwide, as he introduced the first speaker at the workshop, Division of Extramural Research and Training Acting Director Gwen Collman, Ph.D. In her survey of NIEHS global environmental health initiatives, Collman said she hoped to help the grantees better understand “how your work does dovetail with other programs” funded by NIEHS in an increasingly interconnected world.
Following Collman were two representatives from one of WETP’s partner agencies, the National Institute for Occupational Safety and Health (NIOSH) — Deputy Director for the program Margaret Kitt, M.D., and Director for the Education and Information Division Paul Schulte, Ph.D. They described what Schulte called “NIOSH’s global view” as the Institute explores the future of worker safety. Schulte also introduced the topics of the first day’s three panel discussions.

The first of the meeting’s panel presentations expanded on the implications of the United Nations Globally Harmonized System (GHS) of Classification and Labeling of Chemicals and progress by the Occupational Safety and Health Administration (OSHA) in bringing its current Hazard Communication Standard into alignment with the provisions of GHS. The new program requires manufacturers and importers to adopt a labeling protocol with a globally harmonized signal word, pictogram and a more extensive hazard statement for each hazard class and category. As GHS is implemented, the panelists concurred, it will influence the design of worker training programs.

The next panel addressed the increase of engineered nanomaterials in the workplace and potential hazards both in manufacturing and waste disposal, exploring the use of a method known as “control banding” as a transitional preventive protocol in manufacturing and materials handling. Industrial hygienists Rick Niemeir, Ph.D., of NIOSH and Sam Paik, of the Lawrence Livermore National Laboratory, described procedures for implementing control measures, such as ventilation, for handling nanomaterials based on experiences with other materials with functional similarities along a range or “band” of hazards.

Rice University Professor Kristen Kulinowski, Ph.D., discussed the program she oversees developing the curated-wiki GoodNanoGuide, a repository of up-to-date information about research on nanomaterials and good practices for handling these materials in the workplace.

In 2010, progressive implementation of what panelist Sean Mahar, of Euro Safety and Health, called “the largest bit of EHS legislation ever devised” begins in earnest with potential benefits for American workers. By the time the European Union mandate on the Registration, Evaluation, Authorisation and Restriction of Chemical substances (REACH) is fully implemented in 2018, business with America’s largest trading partner could change dramatically, with implications for the use of chemicals in the U.S. as well. Rather than regulators having to prove a hazard exists after a chemical is introduced, as is the practice in the U.S., REACH will mandate that manufacturers prove a chemical is safe before it can be sold or used in Europe, giving rise to the mantra “no data—no market.”

The first day of the workshop concluded with roundtable discussions involving the panelists. When the workshop convened the next day for a different kind of panel presentation (see text box), the grantees were still far from mastering their challenges, but at least Hughes, the WETP staff and the workshop’s expert panelists had helped them begin to ask some of the right questions.
Training consultant and retired Toronto firefighter Rem Gaade gave an overview of the provisions of GHS, which will employ universal pictograms that people worldwide will be able to understand even if they don’t speak the language of the warnings. (Photo courtesy of Steve McCaw)

Hughes, left, helped Schulte load his presentation. Speaking of nanomaterials exposures, Schulte observed, “How do you inform workers about hazards when you don’t know what the hazards are?” (Photo courtesy of Steve McCaw)

Looking South — Awardee Experiences in Latin America

The final half day of the workshop on October 22 offered some elaboration on the “two-way street” theme from Hughes’ opening remarks, as the concluding panel session highlighted health and safety activities outside the U.S. in conjunction with foreign partners.

WETP Education Specialist Ted Outwater moderated the session, offering grantees some context about the “grim situation” for worker health and safety in Latin America. There are some 60,000 workplace deaths each year in the region, he said, and as many as 80 percent of the workforce is exposed to hazardous conditions.

The session opened with a report by Ingrid Zubieta, Ph.D., of the University of California, Los Angeles, and Mike Wright, of the United Steel Workers, on a collaborative occupational health research study at the Cananea Copper Mine in the Mexican state of Sonora. Zubieta presented a catalogue of health and safety violations that she illustrated with photographs from the mine and supported with data from physical examinations of miners and statistics on injuries and fatalities there. Wright, who has worked in a number of overseas sites, called for increased funding, saying that “the more NIEHS can facilitate it [these kinds of studies], the better.”

Don Ellenberger, of CPWR–The Center for Construction Research and Training, reported on the growing number of Hispanics working in U.S. construction. Noting that “overseas is coming to our industry,” he described an unusual take on worker training — a cooperative program with partners in Tijuana and Matamoros to build empathy and understanding among U.S. worker-safety trainers by letting them see firsthand why so many residents come north for work.

Closing out the session was Javier Saracho of the Universidad Metropolitana (UMET) in Puerto Rico. Saracho described the worker-training curriculum at UMET and the growing demand for Spanish-language training programs elsewhere in South and Central America. UMET has conducted OSHA and hazardous material training thus far in Mexico, the Dominican Republic, El Salvador, Columbia, Ecuador and Peru.
Panelists listened as moderator Bruce Lippy, of the Lippy Group, opened the panel on control banding with nanomaterials. Seated, left to right, are Neimeier and Kulinowski. (Photo courtesy of Steve McCaw)

Panel moderator Don Elisburg, of the National Clearinghouse, said GHS could produce “sea change” in worker training, but he noted that time and money are issues in effective implementation of new programs. (Photo courtesy of Steve McCaw)

University of Massachusetts, Lowell grantee Craig Slatin, Ph.D., left, expressed concern about waste haulers and their exposures to nanomaterials outside the manufacturing environment. (Photo courtesy of Steve McCaw)

REACH panel moderator Paul Renner, left, shown afterwards with USW Tony Massocchi Center colleague Joe Anderson, said the European registration program is “better than what we have now” and promises to expand workers’ right to know. (Photo courtesy of Steve McCaw)

As he talked about his experiences with unions outside the U.S., Wright said there was “too little globabiliation” in terms of worker rights, environmental protection and public health. (Photo courtesy of Steve McCaw)

Zubieta pointed the irony of the message, as she showed a photo of a welcome sign at the Cananea Copper Mine describing it as “the largest and safest mine in Mexico.” (Photo courtesy of Steve McCaw)
NIEHS Center Intern Recognized by EPA Head

By Eddy Ball

Fifteen-year-old NIEHS-supported center intern Otana Jakpor enjoyed the latest boost in her burgeoning career in the environmental health sciences on September 30 when she received special recognition from Lisa Jackson, administrator of the U.S. Environmental Protection Agency (EPA), during Jackson’s visit to Los Angeles. Jakpor is affiliated with the Southern California Environmental Health Sciences Center (SCEHSC) at the University of Southern California (USC) Keck School of Medicine.

Jakpor was part of an audience of more than 2,000 international attendees and dignitaries at the three-day Governors’ Global Climate Summit 2: On the Road to Copenhagen, as Jackson delivered a videocast keynote address. Jackson pointed to new rules issued by EPA under her leadership to “put climate solutions into action” as this administration takes creative, responsible and aggressive action to reduce greenhouse gas emissions.

Toward the end of her talk, Jackson made an appeal on behalf of “generations yet to come” and singled out Jakpor for “her extraordinary work [that] helped to move California to pass [stronger] legislation on clean air.”

At Jackson’s request, Jakpor stood, and the audience gave her a vigorous round of applause. Moving to the end of her address, Jackson used the intern’s advocacy of clean air to challenge her audience. “She is an extraordinary young woman [who] has done her part,” Jackson said. “Now it’s time to do our part.”

On the opening day of the summit, Jackson shared the stage with keynote speakers California Governor Arnold Schwarzenegger and actor Harrison Ford. Among the other distinguished scientists and political figures at the historical event were Former Prime Minister Tony Blair of the United Kingdom, and Rajendra Pachauri, Ph.D., Chairman of the Intergovernmental Panel on Climate Change and former North Carolina State University professor. Blair and Pachauri joined Schwarzenegger for a “Very Special Conversation” about the challenge and promise of the upcoming the UN Climate Change Conference in Copenhagen in December.

With her remarks about Jakpor, Jackson joined an impressive list of officials at EPA, scientific groups and elsewhere — including former President George W. Bush — who have acknowledged the young woman’s contributions to environmental health. She first came to public attention at age 13, and since then, has continued to win recognition and awards for her work (see text box).
In the years to come, state and federal regulatory agencies will no doubt hear much more from the young scientist, who was first inspired by the difficulties her mother, obstetrician Karen Jakpor, faced with severe chronic asthma. As Jakpor digs deeper into the health effects of air pollution, she is sure to bring additional evidence to support her scientific and humanitarian crusade for stronger efforts to ensure people have cleaner air to breathe everywhere — in their homes, schools and offices as well as outdoors.

Jackson and Schwarzenegger shared the stage once again on October 1 at nearby Long Beach as she announced $26.5 million in funding for diesel emission reduction projects in Southern California under the American Recovery and Reinvestment Act of 2009. Jackson praised California and its governor for leadership in the area of environmental health. (Photo courtesy of EPA)

One Teenager’s Personal “Road to Copenhagen”

When SCEHSC epidemiologists first encountered Jakpor, the Riverside, Calif. high-school junior was presenting her research findings at the May 2009 meeting of the American Thoracic Society (ATS) in San Diego. They immediately recognized a talented young scientist they wanted to help nurture.

At the same ATS meeting, Jakpor also caught the attention of representatives of the American Lung Association. She is currently a volunteer spokeswoman for the American Lung Association in California - Inland Counties chapter as well as a USC intern.

Jakpor first came to the public’s attention in 2007 during a California Air Resources Board meeting, where she spoke as an advocate for people with asthma exacerbated by poor air quality. Since then she has articulated her concerns at conferences and federal hearings — consistently winning over audiences with her insightful statements, professionalism and persistence.

In the past few years, Jakpor has won science fairs, received awards from the Discovery Channel and the National Association for the Advancement of Colored People, been honored by the Environmental Protection Agency with a 2007 President’s Environmental Youth Award, and earned recognition from members of Congress and President George W. Bush in 2008 for her research into the effects of ozone-producing air purifiers on lung function. Earlier this year, Jakpor received a first-place Action For Nature 2009 International Young Eco-Hero Award.

During her internship at the USC NIEHS Center, the aspiring environmental health scientist has worked on projects mapping demographic issues around rail yards and exploring environmental justice issues that arise when schools are planned near sources of air pollution generated by highway, ship and rail traffic. She has also developed an interest in the health effects of water pollution.

The future looks bright for Jakpor. She skipped a grade at Riverside’s Woodcrest Christian High School and is now starting to apply to colleges. She already has the ATS conference presentations to her credit and a paper accepted for publication.

Jakpor may not be able to attend this year’s conference in Copenhagen, but her friends and colleagues probably won’t be too surprised if her research takes her deeper into the issues surrounding global climate change — and the important co-benefits for respiratory health that could come from decreasing the accumulation of greenhouse gases worldwide.
Superfund Announces Wetterhahn Award Winner

By Rebecca Wilson

The NIEHS Superfund Research Program (SRP) announced that Kathleen Radloff, a doctoral student at Columbia University, is the twelfth recipient of the Karen Wetterhahn Memorial Award. Radloff will be presented with the award at the SRP Annual Meeting in New York where she will deliver a keynote address highlighting her research.

Radloff was chosen for this award based on the excellence of her scientific research. She is conducting research to increase understanding of the mechanisms of arsenic mobility and transport in groundwater using samples from a field site in Bangladesh. Her results have been published in Environmental Science and Technology and Applied Geochemistry. Radloff also serves as a mentor to female undergraduate students interested in careers in science. According to Columbia SRP Program Director Joseph Graziano, Ph.D., Radloff is “exceptionally smart, mature, curious, [and] driven …. She also has the gift of motivating younger students.”

The award is presented annually in honor of Karen Wetterhahn, Ph.D., who was the program director of the Dartmouth College SRP from 1995 to 1997. Wetterhahn died in 1997 as a result of dimethylmercury poisoning caused by the accidental spill of a few drops of the compound on her hand. As a way of honoring Wetterhahn’s life and scientific accomplishments, the SRP established an annual award to recognize an outstanding graduate student or post-doctoral researcher who best demonstrates the qualities of scientific excellence exhibited by Wetterhahn.

As part of the award, Radloff will receive support to attend one major scientific conference, in addition to travel funds to attend the SRP Annual Meeting.

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

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NIEHS Center Director Honored by Oregon State

By Eddy Ball

On September 23 in Corvalis, Ore., Oregon State University (OSU) recognized the achievements of NIEHS grantee David Williams, Ph.D., with its Alumni Association Distinguished Professor Award — the highest award the university presents to members of its faculty. Williams joined more than two dozen leading faculty and staff members honored in 21 award categories as part of University Day, the annual kick-off of the new school year.

Williams is a professor in the Department of Environmental and Molecular Toxocology at the OSU College of Agricultural Sciences and director of the Superfund Research Program (SRP) at OSU and an investigator in the OSU Linus Pauling Institute. Williams is a principal investigator on two NIEHS grants — PAHs: New Technologies and Emerging Health Risks and Ultra-Low Dose Carcinogen Testing with the Trout Model. He co-authored an NIEHS-funded study on colon cancer and chlorophyllin that was selected in September as an Extramural Paper of Month.
“I was very surprised and honored by this award,” Williams said of the announcement. “It recognizes a team effort over my 22 years at OSU conducting research funded in large part by NIEHS through the Centers program, an associated program project, and now our newly awarded SRP grant.”

Commenting on Williams’ award, NIEHS SRP Director Bill Suk, Ph.D., described Williams as “a leader in the field of environmental carcinogenesis, who has brought together a multi-disciplinary team of outstanding scientists to explore new mechanisms of Polycyclic Aromatic Hydrocarbons (PAHs) and their impact on human health. Suk characterized Williams’ group as “an innovative and exciting program” engaged in cutting-edge environmental research. “David is certainly worthy of this award, and we are proud of his accomplishments.”

The OSU Alumni Association Distinguished Professor Award is given to the person who demonstrates outstanding professional achievement through teaching and scholarship, service to the university and the community, and professional leadership, nationally and internationally. The recipient receives a plaque and $3,000 from the OSU Alumni Association. Nominees for this award may also be considered for nomination for the CASE U.S. Professor of the Year Award, which is presented by the Carnegie Foundation.

The awards were formally presented at an evening banquet, and the recipients were also honored during a presentation to the campus at LaSells Stewart Center as part of University Day events.

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WETP Grantee To Be Nominated for FEMA Post

By Eddy Ball

On October 9, President Barack Obama announced his intention to make several high-level nominations, releasing a list that includes NIEHS Worker Education and Training Program (WETP) grantees Elizabeth M. Harman. The President nominated Harman to fill the post of Federal Emergency Management Agency (FEMA) Assistant Administrator for the Grant Programs Directorate (GPD) in the U.S. Department of Homeland Security (DHS).

A former firefighter and paramedic in Fairfax City, Va., and a member of the International Association of Fire Fighters (IAFF) Local 2702, Harman has served as the director of the NIEHS-supported Hazardous Materials Training Program at the IAFF since 2005. She has also worked extensively with the emergency management community in the areas of administration, exercise and evaluation, and she has taught at various institutions of higher education.

In her FEMA position, Harman will oversee the management of more than 50 grant and financial assistance programs representing approximately $4 billion in non-disaster grant funding annually. She will work to ensure
that the grants process is transparent, collaborative and consistent with the Department’s major responsibilities and priorities.

In his announcement about Harman and four other nominees, President Obama said, “As we take on the 21st century challenges facing our nation, I am confident that these individuals will work to keep our nation safe at home, and strengthen our partnerships abroad. I look forward to working with them in the months and years ahead.”

The nomination quickly drew praise from the office of DHS Secretary Janet Napolitano. “Elizabeth’s years of experience in emergency management and program administration will help the Department maximize every security dollar to protect our nation,” Napolitano said in a press release about the nomination.

Harman’s long-time friend and colleague, WETP Director Chip Hughes, pointed to Harman’s “frontline experience as a firefighter and paramedic, as well as her involvement in administering state and federal emergency response programs” as reasons to applaud her nomination.

“With her clear focus on responders at the local level,” Hughes said, “Elizabeth will bring a wealth of talent and dedication to DHS and FEMA and be a great asset for integrating training and response programs at all levels.”

**Editorial Recognizes NIEHS-Funded Research**

*By Laura Hall*

A University of Southern California (USC) study on prenatal tobacco smoke (PTS) exposure and DNA methylation partially funded by NIEHS has been commended for the quality of the research. First author, Carrie Breton, ScD., is a USC assistant professor in the NIEHS-supported Southern California Environmental Health Science Center (SCEHS). Second author, Hyang-Min Byun of the USC Department of Hematology, was an equal contributor.

“The results from Breton and colleagues provide a framework for further studies,” wrote Seif Shaheen, Ph.D., and Ian Adcock, Ph.D., internationally recognized scientists of the National Heart and Lung Institute at the Imperial College London, in an *American Journal of Respiratory and Critical Care Medicine* editorial. They affirmed the need for epidemiological studies examining the effects of environmental exposures during prenatal and postnatal development to incorporate epigenetic analyses as Breton’s study did.

Breton has received NIEHS support for much of her career. Her mentors see Breton as a rising star in epidemiology research. Director of Community Outreach and Education in the SCEHS Andrea Hricko declared, “I take some pride in Carrie’s trajectory with our Center, since she was the first person we hired to work in the NIEHS Outreach Program a year after she finished her undergraduate education at Amherst.”
While pursuing her master of public health degree, Breton worked under another NIEHS grantee, Beate Ritz, M.D., Ph.D., professor and vice chair of the Epidemiology Department at the University of California, Los Angeles (UCLA). Ritz is a member of the SCEHSC, the Center for Occupational Health, and co-directs the NIEHS-funded UCLA Center for Gene-Environment Studies of Parkinson’s Disease.

Senior scientist, Frank Gilliland, M.D., Ph.D., director of the SCEHS said, “As Dr. Breton’s primary mentor at USC, I have seen how NIEHS support and careful nurturing has led to her independence as a researcher and member of our faculty.” He added that Breton has “demonstrated the ability to successfully direct research projects, all of which have resulted in original, quality scientific proposals.”

Mentor John Peters, M.D., ScD., deputy director of the SCEHS who has known Breton for over 10 years said he has “witnessed her transition from budding young investigator to the independent faculty researcher she is today.” He added, “Her strong foundation in epidemiologic principles, coupled with her dedication to environmental epidemiology and public health, promises a bright future for her forthcoming contributions to environmental health sciences.”

In the PTS study, DNA from buccal scrapings of a subset of kindergarten and first grade children enrolled in the Children’s Health Study was screened for global and gene-specific DNA methylation patterns. DNA methylation is an epigenetic factor that can prevent DNA and RNA replication machinery from accessing the DNA template. The result is that proteins that are coded for in the methylated genes are prevented from being made. These methylation patterns can persist for the life of the individual and be inherited by the next generation with no alteration of the DNA sequence.

PTS exposure has been shown to increase the risk of diseases such as asthma later in the child’s life. How this association occurs is not well understood. Breton’s study rationale was that the mechanism for this association could be alterations in DNA methylation. The study showed that children exposed to PTS have differences in global and gene-specific DNA methylation.


(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)
Kim Receives Congressionally Directed Medical Research Program Award

By Laura Hall

Sangmi Kim, Ph.D., a postdoctoral fellow in the Chronic Disease Epidemiology Group, received a Postdoctoral Fellowship Award from the Breast Cancer Research Program (BCRP) of the Department of Defense Congressionally Directed Medical Research Program for 2009 on October 7. “This prestigious fellowship will serve as a tremendous asset in helping me attain my goal of a career in academic research,” said Kim. “With this fellowship, I will gain invaluable experience in the detailed process of designing and conducting molecular epidemiologic studies.”

The two-year award was given to Kim to pursue a project that involves determining the influence of endogenous levels of prostaglandin E2 on estrogen bioavailability and subsequent breast cancer risk. In addition, Kim will study how the inflammation pathway is involved in the effects of environmental factors on estrogen bioavailability.

The BCRP funds innovative research that could significantly impact breast cancer research or addresses neglected issues. The program seeks to instigate multidisciplinary and multi-institutional collaborations and seeks to involve early career investigators with a “strong desire to pursue a career in breast cancer research.” The BCRP has a two-tiered review process that engages breast cancer survivors as well as scientists in evaluating research projects.

The BCRP reviewers mentioned the strong training environment at NIEHS as one of the elements in Kim’s favor. Training and mentoring that facilitates the development of the awardee as a breast cancer researcher is an important BCRP goal.

Kim’s mentor, Dale Sandler, Ph.D., said she is “thrilled that Dr. Kim received this award.” Sandler noted that “the research plan represents Dr. Kim’s independent work. The award will provide an opportunity for Dr. Kim to further demonstrate she has what it takes to become an independent investigator.” Jack Taylor, M.D., Ph.D., principal investigator in the Molecular and Genetic Epidemiology Group will act as co-mentor.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)

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NIEHS-Funded Training for HazMat Emergency Response in American Samoa

By Laura Hall

In June 2009, University of California, Davis Extension (UCDE) instructors taught three health and safety courses for handling hazardous materials and emergency response in American Samoa on the main island of Tutuila. The classes were funded by an NIEHS Workers Education and Training Program (WETP) grant to the Western Region Universities Consortium (WRUC) which includes UCDE. The attendees were American Samoan residents who could be involved in the first hours of a hazardous materials incident, including public safety, public works and community health personnel, and village mayors.

The need for training Pacific islanders in hazardous materials management became evident three months later. On September 29, a strong underwater earthquake followed by a tsunami caused widespread damage in American Samoa with 22 deaths and some villages along the coasts destroyed. In response, President Obama declared American Samoa a disaster area.

The WRUC grant targets underrepresented minorities including Pacific islanders. The grantees collaborate with community and tribal organizations to tailor training to specific needs. One of the American Samoan classes, Pulenu’u Health and Safety Training, was a one-day First Responder Awareness program designed for the village mayors, or pulenu’us. The course was suggested by Judith McCoy, training coordinator of American Samoa Department of Homeland Defense. It incorporated specific safety needs of the islanders such as handling hazardous materials safely, dealing with drums containing unknown materials and the dangers of compressed gas cylinders, with a role-playing “Tsunami Emergency Group Exercise.”

Sixteen village mayors and six interns attended the course. Janis Heple, academic coordinator at UCDE said, “The mayors noted that they could see the need for this information to be communicated directly to their villages.” Instructor Les Omans said that “from the verbal feedback and questions, I am confident that the mayors found the course interesting, informative and entertaining.”
In the other two courses, 46 participants were trained in best practices for handling hazardous materials and managing incidents. Participants utilized the factual knowledge gained from the first course in the role playing exercises of the second. They practiced the roles they would have to play in an actual emergency, such as blocking off roads, in a mock incident. The exercises were customized for locales on the island.

WETP is a part of the NIEHS Division of Extramural Research and Training (DERT) which plans and directs the institute’s grants programs. The WETP funds non-profit organizations to provide occupational safety and health education to train workers to identify and prevent hazardous exposures, to handle hazardous materials, and to respond to emergency releases of materials.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)

The program issued certificates to recognize the dedication of the trainees. Shown above, left to right, are Instructor Les Omans, Trainee Pago Pago Taumua and Training Coordinator Judith McCoy. (Photo courtesy of Les Omans and Forrest Adams)

Students in the Hazardous Materials Incident: Health & Safety for Responders class took a break from training to pose for a group photo. (Photo courtesy of Les Omans and Forrest Adams)

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Call for Nominations to the Interagency Breast Cancer and Environmental Research Coordinating Committee

By Eddy Ball

In the October 16 Federal Register, NIEHS issued a request for the nomination of voting members to serve on the NIH/NIEHS Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC). Nominations received on or before December 1, 2009 will be considered in a pool of candidates gathered from numerous sources for membership on the committee.

The IBCERCC is an interagency committee composed of federal officials, scientists, health professionals and individuals who represent those with breast cancer. This Committee will coordinate information on existing activities related to breast cancer and environmental research and make recommendations to the NIH and other Federal agencies on how to improve existing research programs.

The Federal Register notice is available as a downloadable pdf. For more information and to submit nominations, contact:

Jennifer Collins, Division of Extramural Research and Training, National Institute of Environmental Health Sciences, P.O. Box 12233, MD K3–12, RTP, NC 27709, Phone: 919–541–0117, FAX: 919–316–4606, E-mail: collins6@niehs.nih.gov

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The Genetics and Environmental Mutagenesis Society (GEMS) celebrated the anniversary of its annual meeting series October 5 at the William and Ida Friday Center on “Dissecting Genome Structure, Genetic Traits and the Basis for Complex Diseases.” Along with invited speakers, the daylong meeting featured oral and poster presentations by students and trainees (see text box). As it has since 1982, GEMS received what organizers described as “generous support” for the meeting from NIEHS and several corporate sponsors.

Organized by NIEHS toxicologist and GEMS President-elect Jef French, Ph.D., as a sequential series of lectures on the role of genome restructuring in complex disease, the 2009 series at the Spring meeting began in April with a talk by NIEHS Principal Investigator Michael Resnick, Ph.D., on the effects of DNA double-strand breaks in reshaping the yeast genome. It concluded with the final lecture of the Fall meeting on the applications of genomic analysis in the clinical setting and the growth of low-cost commercial genomic sequencing.

The meeting opened with a talk on “DNA Copy Number Variants (CNVs): Important Contributions to Phenotypic Variation” by oncologist Timothy Graubert, M.D., of the Washington University School of Medicine in St. Louis. Graubert’s interest in the molecular pathogenesis of myeloid leukemia led him to explore the influence of changes made during DNA replication on genetic susceptibility to disease, progression of disease and drug response.

According to Graubert, recent research has clearly established that “widespread copy number variation occurs [even] in apparently healthy individuals … [and that] copy number variation exceeds that of single nucleotide polymorphisms (SNPs) in the human genome” — with CNVs making up an estimated 12 percent of the human genome as compared to the approximately one-tenth of one percent contribution by SNPs. As he looked ahead, Graubert noted how much is not yet understood about the link between CNV and disease.
University of Lausanne geneticist Alexandre Reymond, Ph.D., next explored the topic of “The Influence of Genome Structure on Gene Expression.” Reymond began by observing that scientists have been aware of CNVs and “genomic disorder” since at least 1975, but until the development of advanced bioinformatics and hybridization-based methods for mapping CNVs, they weren’t able to establish how widespread structural variation is in the mammalian genome.

Reymond’s studies of CNV influence on gene expression have helped to identify variation by tissue and levels of expression, as well as establish that the effects on gene expression change during development. He has explored the effects of the interphase nuclear position of chromosomes and genes on changes in CNV and established that there is more variation in some organs than in others. He speculates that high levels of CNV, while important in disease, may also benefit an organism by contributing to survival and adaptation.

In the final talk of the day, University of North Carolina at Chapel Hill (UNC-CH) physician-scientist James Evans, MD., Ph.D., spoke on “Personal Medicine and Genomics: Too Much Information/Too Little Information — A Clinical Perspective.” Throughout his talk, Evans explored the irony inherent in his title. As a geneticist, Evans is excited by the promise of genome-wide screening, but as a clinician he has yet to see its “added value” for the treatment of disease.

When he turned to commercial genomic screening, Evans questioned the utility of information currently available and the ways it is being marketed to consumers. He pointed to medical and ethical concerns about the “$1,000 genome” and the interpretational Pandora’s box that such screening will inevitably open.

The Fall meeting marked a transition for French and outgoing President Jeff Ross, Ph.D., a U.S. Environmental Protection Agency (EPA) molecular biologist. In 2010, French will serve as GEMS president, as incoming President-elect Stephen Little, an EPA research chemist and 2007-2009 GEMS Councilor, assumes responsibility for organizing next year’s meetings.
Although genome-wide screening has become increasingly sophisticated and more affordable, Evans, above, argued that most of the “information is [still] so lacking in robustness that it is of questionable utility” in personal medicine. (Photo courtesy of Steve McCaw)

One of several oral presenters with ties to NIEHS, Senyene Hunter, Ph.D., left, took questions as French watched from the floor. Now at Duke, Hunter was a postdoctoral fellow in the lab headed by former NIEHS Principal Investigator Ben Van Houten, Ph.D. (Photo courtesy of Steve McCaw)

Although genome-wide screening has become increasingly sophisticated and more affordable, Evans, above, argued that most of the “information is [still] so lacking in robustness that it is of questionable utility” in personal medicine. (Photo courtesy of Steve McCaw)

On stage for awards at the end of the day, poster winners Amanda Smith, left, and Raju Prasad, Ph.D., applauded the winners of the oral presentation competition. (Photo courtesy of Steve McCaw)

Spotlight on Students and Trainees

During oral and poster competition sessions at its Fall meeting, GEMS gave students and trainees an opportunity to share their own research findings. Not surprisingly, NIEHS trainees and senior scientists were well represented, and many of the presentations meshed with the meeting’s theme, “Dissecting Genome Structure, Genetic Traits, and the Basis for Complex Diseases.”

The winners received cash awards that are typically used for professional development. In its 27 years of nurturing young scientists, GEMS has used support from NIEHS and other sponsors to make a total of more than $50,000 in awards to students and trainees who have gone on to make names for themselves in their fields.

Best Poster Presentation Awards ($250 each):

- NIEHS-supported Ph.D. student Amanda Smith for her poster on “Mitochondrial Fusion and Autophagy Aid in Removal of Persistent Mitochondrial DNA Damage,” conducted with colleagues at Duke University’s Integrated Toxicology and Environmental Health Program and advisor Joel Meyer, Ph.D.

- EPA Postdoctoral Fellow Raju Prasad, Ph.D., for his poster on “The Genotoxicity of Titanium Dioxide and Cerium Oxide Nanoparticles In Vitro,” conducted with colleagues in the EPA Integrated Systems Toxicology Division.

Best Oral Presentation Award ($1,500) — Shared by Two Speakers:

- NIEHS-supported Postdoctoral Fellow Stephanie Smith-Roe, Ph.D., for her talk on Replication Fork Stabilization Proteins Timeless and Timeless-Interacting Protein (Tipin) Maintain Genomic Stability.” Smith-Roe worked in the UNC-CH Lineberger Comprehensive Cancer Center with Principal Investigators William Kaufmann, Ph.D., and Marila Cordeiro-Stone, Ph.D.

- NIH-supported fourth-year Ph.D. student Stacey Winham for her presentation on “The effect of Retrospective Sampling on Estimates of Prediction Error for Data Mining Methods to Detect Epistasis.” Winham collaborated with her advisor, statistician Alison Motsinger-Reif, Ph.D., of the North Carolina State University Department of Statistics and Bioinformatics Research Center.
Researchers Find Link Between Cholesterol and Asthma

By Robin Arnette

High cholesterol levels have been linked to a variety of illnesses such as heart attack, stroke and diabetes, but recent research published in the *Journal of Allergy and Clinical Immunology* suggests that cholesterol may also play a role in asthma.

Researchers from NIEHS, SRA International and Rho Federal Systems, led by NIEHS Principal Investigator Michael B. Fessler, M.D., have concluded that serum total cholesterol (TC) and non high-density lipoprotein cholesterol (non-HDL-C) are inversely related to asthma and wheeze in a representative sample of the U.S. population. The authors noted that this finding in the overall population was chiefly driven by a marked relationship among Mexican Americans (MAs). This study signifies the first documented association between cholesterol and asthma in a national survey and the first to identify a determinant that may contribute to or serve as a biological marker for the reduced prevalence and morbidity of asthma in MAs.

Stavros Garantziotis, M.D., the medical director of the NIEHS Clinical Research Unit (CRU) said, “The results highlight the fact that patients need to be evaluated within the context of their individual genetic background when looking for clues and treatment options.”
Before they initiated the investigation, Fessler and his colleagues were aware of the work that had been done in other labs regarding the relationship between cholesterol and inflammation. A few groups had determined that dyslipidemia — a condition marked by abnormal concentrations of lipids or lipoproteins in the blood — caused vascular inflammation through the activation of innate immunity. Other laboratories had discovered evidence that cholesterol metabolism and inflammation were linked in the lung.

The team’s main goal was to test for an independent relationship between serum cholesterol concentrations and asthma prevalence, but it also wanted to test for a relationship between serum cholesterol and wheeze requiring medical attention, a strong indicator of poorly controlled asthma and other obstructive lung disease.

To this end, the Fessler group conducted a cross-sectional study of 7005 subjects, aged six years and older, who participated in the National Health and Nutrition Examination Survey (NHANES) 2005–2006, a program designed to assess the health and nutritional status of the U.S. population. Participants were classified into five racial/ethnic groups: non-Hispanic white (NHW), non-Hispanic black (NHB), MA, other Hispanic and other/multi-race. The NHANES measured serum TC and HDL-C, and administered questionnaires to assess physician-diagnosed asthma and wheeze.

At the start of the project, the group was unsure of what it would find. “We didn’t know whether cholesterol was going to have any relationship with asthma,” Fessler explained. “There wasn’t a lot of precedent for how to approach it.”

The results demonstrated that serum TC and non-HDL-C were lower in patients with asthma and wheeze compared to those without these illnesses. When the racial/ethnic results were examined, team members found that this inverse relationship was specific to MAs. They found no difference in HDL-C levels between asthmatics and non-asthmatics. In addition, the relationship was independent of body mass index (BMI), an established asthma risk factor, and serum C-reactive protein (CRP), an inflammatory biomarker.

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**Rising Star in Clinical Research**

Fessler, who holds dual appointments in the Laboratory of Respiratory Biology and the Clinical Research Program at NIEHS, recently received the Early Career Award for “novel and innovative research contributions in the field of Environmental Health Science.” The award is open to tenure-track investigators who have received their terminal degrees within the last 15 years and who have been at NIEHS for five years or less. “I’m pleased that people think that I’m on the right path,” Fessler said. “It helps to validate some hard work.”

When Fessler refers to the hard work he’s been doing, one can see why he was a good candidate for the Early Career Award. In addition to the cholesterol and asthma work, he is actively involved in another research project at the CRU. He collects blood from volunteers and isolates different leukocyte subtypes for ex vivo signaling studies. Fessler said that he became interested in this kind of analysis during his pulmonary critical care fellowship at National Jewish Health, formerly the National Jewish Medical and Research Center, in Denver, Colo. He said that depending on how one looks at his signaling work, it could be called clinical, translational or basic research. Fessler is currently collaborating with another group to determine if its immortalized human cell line results pertain to his primary human cell preparations. Fessler also plans to test hypotheses derived from cell lines and rodent models by the use of the NIEHS Environmental Polymorphism Registry (EPR).

One would think that Fessler spends all of his waking hours in the laboratory, but he also finds time to produce outstanding postdoctoral fellows. One of Fessler’s trainees, David Draper, Ph.D., recently won a Fellows Award for Research Excellence (FARE) and travelled to the NIH Research Festival to give a ten minute symposium talk. Being chosen to speak at the Festival is an honor since only a few FARE winners are chosen.

“This job is a fun and exciting opportunity for me,” Fessler concluded. “It has been a transformative experience and continues to be a work in progress.”
The data confirmed and built upon findings from other groups that had reported that MAs have the lowest prevalence of asthma in the country, despite increased asthma risk factors such as low socioeconomic status and obesity. Fessler said the reasons why this demographic group exhibits these features of asthma are unknown, but noted that further investigation into the topic may provide valuable information on asthma pathogenesis and treatment.

Darryl Zeldin, M.D., acting director of the NIEHS Clinical Research Program and a co-author on the paper, said that even though the results should be independently confirmed in another cohort, the study raised some interesting clinical questions. He added, “Is serum cholesterol a predictive biomarker of asthma diagnosis or treatment responsiveness? Do statins or other cholesterol lowering agents modify asthma risk? Further research will be necessary to address these issues in a more conclusive way.”


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Experts Review Revisions to Local Lymph Node Assay Method

By Debbie McCarley

On October 20–22, scientists from NIEHS, the Environmental Protection Agency, the Food and Drug Administration (FDA), and the Consumer Product Safety Commission (CPSC) participated in an international expert consultation to evaluate modifications of the murine local lymph node assay (LLNA) — a test method for detecting potential skin-sensitizing substances.

This expert consultation meeting, which also included experts from industry and other stakeholder organizations, was convened by the Organisation for Economic Co-operation and Development (OECD) and co-hosted by CPSC at its headquarters in Bethesda, Md. Also hosting the meeting were the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

The group of 20 scientists from five countries reviewed proposed revisions to OECD Test Guideline (TG) for the LLNA, TG 429. The proposed revisions provide multiple mechanisms for reducing the number of animals in each test by up to 40 percent. They also provide a standardized approach and improved guidance for establishing the highest test dose, as well as performance standards that can be used to expedite the validation of modified versions of the LLNA. All of the proposed revisions are based on the recommendations recently forwarded to U.S. federal agencies by ICCVAM, an interagency committee administered by NICEATM.
The expert group also reviewed drafts of two new proposed test guidelines for nonradioisotopic versions of the LLNA. These test methods — the LLNA: DA, which measures adenosine triphosphate (ATP) content, and LLNA: BrdU-ELISA, which measures bromodeoxyuridine (BrdU) incorporation — do not require radioisotopes to measure lymphocyte proliferation, which is a requirement in the traditional LLNA. The availability of OECD test guidelines for these test methods will allow more widespread use of the LLNA by enabling it to be used where use of radioisotopes is not permitted. The draft test guidelines are also based on an ICCVAM evaluation of LLNA: DA and LLNA: BrdU-ELISA. Final ICCVAM recommendations on the usefulness and limitations of these test methods in the U.S. are currently being finalized and will likely be forwarded to U.S. federal agencies by the end of the year.

The expert group will meet again later this year to consider revised versions of the test guidelines based on discussions and recommendations at the October meeting. The revised draft TGs will then be sent out for review and comment by OECD member countries.

U.S. federal agencies originally accepted the LLNA in 1999 for safety testing, based on ICCVAM recommendations that the LLNA was a valid substitute for the traditional guinea pig test methods used to identify potential sensitizers. The LLNA has many advantages, including using fewer animals, eliminating the potential discomfort that can occur with positive results in the guinea pig methods, and providing dose-response information. The LLNA also reduces the amount of time needed for testing of potential sensitizers, as it can be completed in one week, as compared to four weeks for the guinea pig test.

(Debbie McCarley is the Special Assistant to Rear Admiral William Stokes, D.V.M., D.A.C.L.A.M., director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods.)
Nobel Winner Speaks at RNA Society Meeting

By Dixie Ann Sawin

Sponsored in part by NIEHS, the “Symposium on RNA Biology VIII: RNA Tool and Target” was held on October 16 and 17 at the North Carolina Biotechnology Center in the RTP. One of the highlights of the program was the talk given by the recent winner of the Nobel Prize in Chemistry, Ada Yonath, Ph.D., of the Weizmann Institute of Science, Israel. Her seminar offered insights into “The identification of the prebiotic translation apparatus within the contemporary ribosome.”

The symposium was organized by the RNA Society of North Carolina. NIEHS Principal Investigator Traci Hall, Ph.D., was co-chair of the event’s organizing committee.

Ribosomes, which exist in eukaryotic and prokaryotic organisms, are the “cellular machines” that translate RNA into protein. However, eukaryotic and prokaryotic ribosomes exhibit several differences. In eukaryotic organisms, ribosomes exist either as free structures in the cytosol or bound to the endoplasmic reticulum (ER), a membrane-bound compartment within the cytoplasm.

Generally, proteins that are produced by the free ribosomes will function within the cell, while the proteins formed by ER-bound ribosomes will be exported from the cell. Eukaryotic ribosomes usually number in the millions and are larger compared to their prokaryotic counterparts. In contrast, ribosomes from prokaryotic sources, such as bacteria and viruses, occur only as free-standing organelles and may number in the thousands.

Yonath began her talk by showing a movie depicting the motions of the ribosome that guide the entrance and exit of tRNAs from a specific tunnel within the active site of the ribosome, the peptidyl transferase center (PTC). The PTC resides in an internal architectural unit within a highly conserved symmetrical region that facilitates the ribosome’s primary catalytic function of peptide bond formation and amino acid polymerization. Ribosomes can make 15–20 peptide bonds per second, with an accuracy rate of 99.99 percent.

Although differences exist between prokaryotes and eukaryotes, the universality of the symmetrical design and high conservation implies that this structure can transcend different environmental conditions and is most likely the remnant of the ancient protein biosynthetic machine, the proto-ribosome, akin to a “molecular fossil.”
As Yonath explained, “The chemical prebiotic process originated from an oligonucleotide …that proceeded into self-assembled dimers.” Thus, small pieces of RNA could spontaneously dimerize and form the building block for the protoribosome, the pre-protoribosome.

This internal symmetry supports the hypothesis that the protoribosome further evolved by gene duplication or fusion, with later genetic optimization into two similar but not identical substrates that contribute to the catalytic and decoding properties. Yonath’s work provided supporting evidence for the existence of an RNA world where the ribosome co-evolved with its substrate, prior to the contemporary one in which we live.

Ribosomes are common targets of antibiotics. If this site is highly conserved, antibiotics can bind to ribosomes in both bacteria and patients, which can cause death or side effects. Therefore, if an antibiotic targets the conserved PTC region, it is usually harmful, shows resistance and is useful only in treating cancer, and a patient’s remaining quality of life is often an issue. Yonath elucidated the modes of action of over twenty different antibiotics that target the ribosome. She illuminated mechanisms of drug resistance and synergism, deciphered the structural basis for antibiotic selectivity and showed that it plays a key role in clinical usefulness and therapeutic effectiveness, thus paving the way for structure-based drug design.

Yonath shares this year’s Nobel in Chemistry with two other scientists, Thomas Steitz, Ph.D., and Venkatraman Ramakrishnan, Ph.D.

(Dixie-Ann Sawin, Ph.D., is a post-doctoral research fellow in the NIEHS Laboratory of Neurobiology Neurotoxicology Group on detail as a writer for the Environmental Factor.)

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Oceans Center Study Offers Caveat for Beachgoers

By Eddy Ball

By combining solid research and relationship building, the National Science Foundation (NSF)-NIEHS Center for Oceans and Human Health (COHH) at the University of Miami and its collaborators are taking their science to the people on the beaches of America — and highlighting an under-appreciated human source of exposure to bacteria, including the potentially deadly methicillin-resistant Staphylococcus aureus (MRSA).
New research findings from investigators at the Miami COHH program and their network of collaborators are informing a cautionary message to beachgoers and beach managers about pathways for spreading of bacterial contamination by humans.

A new study authored by Samir M. Elmir, PE, Ph.D., Florida Department of Health, Miami COHH Principal Investigator Lora Fleming, M.D., Ph.D., and colleagues from the Florida Department of Health, University of Miami, National Oceanic and Atmospheric Administration (NOAA) and the Centers for Disease Control and Prevention (CDC) has been published in the October issue of Water Research. The group’s research quantified the extent of shedding of fecal bacteria by adults and toddlers.

The group’s study was the first ever evaluation of bacterial shedding from toddlers. It was also the first study of bacterial shedding to introduce additional advanced methods of fecal indicator bacterial analysis — chromogenic substrate (CS) and quantitative polymerase chain reaction (qPCR) — for purposes of supplementing the standard culture-based membrane filtration (MF) method and validating the far more rapid advanced methods within the study. The field experimental design was based upon a prior study, which also allowed for between-study validation.

Researchers gathered their human data from 20 adults and 14 diapered toddlers who dipped into large and small pools, respectively, set up on a beach in Miami for measurement of direct shedding of bacteria during bathing cycles. The adults were evaluated during 4 cycles of bathing, 2 cycles with no sand contact followed by 2 cycles with sand exposure. The children in their diapers played in the sand on the beach for 15 to 30 minutes before entering an individual small pool for 1 cycle of water exposure.

Surprisingly, the researchers found that adults and toddlers shed approximately the same amounts of bacteria into the water. In the adults, the effect of sand exposure had a relatively small contribution to this bacterial shedding until their bodies were washed several times. Furthermore, the sand contribution was proportional to the body surface area, with adults carrying more sand than children back into the water.

“This study demonstrates that humans of all ages are one of many sources of bacteria in recreational marine waters. Furthermore, these data support the universal recommendation of bathing before entering bodies of water to decrease the individual’s bacterial shedding contribution,” Fleming said of the study. “It’s gratifying to see our findings translated through our University of Miami OHU collaborations with the Florida Department of Health, NOAA, CDC and other partners to help get the word out to beachgoers.”

Along with the Miami COHH at the Rosenstiel School of Marine and Atmospheric Sciences of the University of Miami, collaborators on the study included scientists and public health specialists affiliated with the Florida Department of Health (FDOH), the NOAA Atlantic Oceanographic and Meteorological Laboratory, the Centers for Disease Control and Prevention (CDC), the University of Illinois, University of Miami Department of Civil, Architectural and Environmental Engineering, and the University of Miami Miller School of Medicine.

Children followed a special protocol during the study to mimic toddlers’ sand play patterns. (Photos courtesy of NSF-NIEHS COHH)

**Toddler Bather Shedding**

1. Nasal Swabbing
2. Playing in sand for 10 minutes
3. Microbial testing of water BEFORE
4. Nine liters of off-shore marine water poured over their body
5. Microbial testing of water AFTER
6. *S. aureus* testing

**Adult Bather Shedding**

1. Nasal Swabbing
2. Microbial water testing BEFORE bathers
3. Ten adults in pool for 15 minutes x 4 times. Submerge every 5 minutes.
4. Microbial water AFTER
5. No sand exposure before Cycles 1 and 2
6. Sand exposure before Cycles 3 and 4

Adults followed protocols between the bathing cycles that allowed investigators to measure the difference between sedentary rest between bathing and “adult” patterns of sand exposures. (Photos courtesy of NSF-NIEHS COHH)
Superfund Study Links PCE and Birth Defects

By Rebecca Wilson

Prenatal exposure to a chemical solvent can put babies at increased risk for birth defects, according to an NIEHS-funded study published in the September 2009 issue of Environmental Health. The study, led by Ann Aschengrau, Sc.D., of the Boston University Superfund Research Program, explored the relationship between a mother’s exposure to perchloroethylene (PCE) and the incidence of birth defects in children born around Cape Cod, Mass. between 1969 and 1983.

PCE, a chlorinated ethylene, is classified as a potential human carcinogen by the U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry. It is a commonly used solvent in the dry-cleaning industry and a metal degreaser. The mothers in this study were exposed to PCE through the municipal drinking water supply, which was carried through some 660 miles of asbestos cement pipes installed in the area from the late 1960s through 1980. Prior to their installation, the inner surface of the pipes was coated with vinyl toluene resin dissolved in PCE to improve the taste of the water.

The manufacturers who installed the lining thought the highly volatile PCE would evaporate prior to installation, but their assumption was wrong. When the water was tested, municipal authorities learned that PCE had been leaching into the water supply for years, and concentrations in some localities were nearly 200 times the U.S. Environmental Protection Agency’s 1980 maximum contaminant level of 40 ug/L. Once the contamination was detected, the pipes were cleared with a flushing process and are now in compliance with U.S. Environmental Protection Agency standards.

Aschengrau and her team of researchers painstakingly compiled municipal water records and matched them with birth certificates to find women exposed to the solvent during their pregnancies. Of the women contacted who lived in the area during the time of contamination, 70 percent — over 2,000 people — responded. Cleft lip and palate and neural tube defects were three times more common among babies who had been exposed in the womb to PCE than among babies who were not exposed.

This work stands out because Aschengrau was able to single out the ingestion of PCE as a single exposure route. Through leaching and transport models, she was able to estimate historical PCE exposures in the Cape Cod area. However, due to the small size of the study, Aschengrau recommends follow-up studies. She would like to conduct studies across Massachusetts in order to obtain a larger sample size. “Because PCE remains a commonly used solvent and frequent contaminant of ground and drinking water supplies,” she said, “it is important to understand its impact on the occurrence of congenital anomalies.”


(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)
SNPs and Dog Ownership Associated with Eczema Status

By Dixie Ann Sawin

New findings by NIEHS-funded researchers at the University of Cincinnati (UC) report genetic and environmental risk and protective factors involved in the development of eczema in children — an atopic condition that is considered the result of complex interactions between genetic susceptibility and skin-barrier aberrations. The study, by first author Jocelyn Biagini Myers, Ph.D, and an interdisciplinary team of investigators, was published online in the Journal of Investigative Dermatology (JID).

This study provides novel insights into the pathogenesis of eczema, from both genetic and environmental perspectives, that could ultimately impact outcomes and associated health care costs estimated to be as high as $3.8 billion. This is the first study to analyze the effects of genes and the environment on longitudinal eczema and allergen sensitization status in a birth cohort.

According to the researchers, the frequency of eczema in children is increasing, especially in industrialized nations, affecting an estimated 15 to 30 percent of children and often marking the first step in the “atopic march” toward allergic rhinitis and asthma. “Thus, early identification of risk factors and possible intervention strategies,” the authors wrote, “may lead to the discovery of measures that attenuate later expression of allergic disease.”

Using the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) cohort for single nucleotide polymorphism (SNP) analysis in the study, the scientists determined that carriers of the CD4-9C/T and IL4Ra 175V SNPs showed a significantly increased susceptibility to the development of eczema at both ages 2 and 3. Additionally, they found that children who were exposed to dogs were 40 percent less likely to develop eczema by the age of 1.

The combination of dog ownership and the CD4 CT or TT genotype was significantly protective against the development of eczema. The main symptoms of eczema include chronic, recurrent skin inflammation, disruptions in the ability of the epidermis to act as a barrier and IgE responses to food and environmental allergens.

The CCAAPS included 762 infants sampled from October 2001 to September 2003. The principal investigator for the Diesel, Allergens and Gene Interaction and Child Atopy and the Molecular Epidemiology in Children’s Environmental Health Training Program grants that funded the study.
investigator of the NIEHS-funded CCAAPS study was Grace LeMasters, Ph.D., an epidemiologist at UC. The co-investigator and senior author of the paper was UC Professor of Pediatrics Gurjit Khurana Hershey, M.D., Ph.D.

The participants lived within a 400-meter or 1.5-kilometer distance from the high traffic corridor in the Ohio and Kentucky River Valley (OKRV) region. This region has converging traffic from three federal highways and was chosen because it has one of the largest volumes of traffic within a 24-hour period, with up to 150,000 vehicles of which as many as 16,000 are trucks. Known as “allergy alley,” this region “represents an ideal location for understanding the impact that exposure to diesel exhaust particles (DEP) and aeroallergens have on development of childhood allergy and atopic respiratory disorders,” LeMasters explained in the Executive Summary of the CCAAPSS.

Biagini Myers and colleagues assessed participants’ characteristics and their association with environmental exposures such as dogs, cats, mold, cigarettes and DEP as well as aeroallergen and food specific skin prick tests (SPT). They identified that eczema was present in 9.7 percent of the children at age 1, increasing to 29.1 and 26.7 percent at ages 2 and 3, respectively. The percentages that showed SPT positivity for aeroallergens also increased between the ages of 1 and 3. Sensitivity to food was shown to be the most significant predictor of eczema at age 1.

Interestingly, children who were SPT-positive to at least one aeroallergen early in their lives were over two times more likely to develop eczema by age 3 and almost nine times more likely to have eczema at both ages 2 and 3.

The authors acknowledge that their study had limitations that come from an underpowered sample size, and that their findings are not applicable to the general public since all the children had at least one atopic parent. The implications for high-risk populations, however, cannot be ignored.

Maintaining a Cohort the CCAAPS Way

University of Cincinnati researchers have a remarkable record of keeping together research cohorts for longitudinal studies in the years ahead. One of Grace LeMasters’ favorite approaches to building a sense of community in the cohort is an annual afternoon picnic at the Cincinnati Zoo for families in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS). Funded by NIEHS, the study has followed a cohort of children since 2001 when they were 1 year old. Now nearing 7 years old, CCAAPS children have helped investigators make major strides in answering questions regarding allergies and asthma in young children and the role of traffic exhaust and indoor allergens in the development of disease.

As they ate lunch at the zoo on October 10, CCAAPS families mingled with investigators and staff who answered questions as their children interacted with zoo keepers and their animals. Staff members from the Bernstein Allergy and Abraham Research groups were also on hand to answer questions parents might have regarding their child’s allergies and asthma. Families were given educational information pertaining to fall and winter allergies as well as an update on recently published findings from CCAAPS investigators. The event coincided with the Cincinnati Zoo sponsored “HallZOOween,” and CCAAPS kids were given animal masks so they could participate in the festivities, which included pumpkin carving and trick-or-treating.
NC State Professor Discusses Nanoparticle Toxicity

By Thaddeus Schug

NIEHS grantee James Bonner, Ph.D., an associate professor in the Department of Environmental and Molecular Toxicology at North Carolina State University, gave a seminar at NIEHS on October 15 outlining some of his latest findings on engineered nanoparticles. Hosted by Robert Langenbach, Ph.D., a principal investigator in the NIEHS Laboratory of Molecular Carcinogenesis, Bonner’s talk addressed “Environmental Exposure to Engineered Nanomaterials as a Potential Cause of Lung Inflammation, Fibrosis, and Cancer.”

As Bonner told his audience, despite the growing use of nanoparticles in manufacturing, “we have no idea how some of these structures interact in biological systems — nor do we understand the potential toxicological risks they impose on our environment.” A former postdoc and group leader at NIEHS, Bonner is currently heading an effort to determine whether nanoparticle exposure presents risks similar to those associated with asbestos inhalation. “Although epidemiological data are lacking in nanotechnology toxicology and people are not sick yet,” he said, “we are in a position to fix a problem before it exists.” His group’s latest study appeared online October 25 in the journal *Nature Nanotechnology*.

Bonner explained that nanoparticles are engineered materials whose sizes fall into the 1-100 nanometer range — the smallest of which are similar in diameter to a DNA molecule. His group focuses on carbon nanotubes, which consist of a thin cylindrical string of carbon atoms engineered either as a single-walled tube or as multiple concentric tubes. He pointed to the tremendous potential for commercial applications of nanoparticles, ranging from the design of lightweight spacecraft to medical uses as filters for kidney dialysis, scaffolding for skin graphs and as shuttles for drug-delivery systems.

In an effort to better understand the health and safety risks associated with emerging nanoparticle technology, Bonner has teamed with a group of nanoscience experts to form an NIEHS-funded Grand Opportunity (GO) program, directed by Health Science Administrator Srikanth Nadadur, Ph.D. The aim of this consortium is to standardize the practices used in measuring and evaluating potential nanoparticle toxicity. Bonner cautioned...
that public perception of nanoparticle toxicity may not be consistent with published reports, and it is important for investigators to unify research procedures in nanotechnology in order to prevent misconceptions and avoid misinformed policy decisions.

In his lecture, Bonner reviewed some of his groundbreaking work in fiber toxicity, in which he discovered similarities between the reactions of lung cells to nanotubes and asbestos fibers. Bonner noted that when mice were exposed to a spray of single-walled carbon nanotubes, the nanotubes formed unique structures that bridged macrophages, the phagocytic cells in the lung. He compared these nanostructures to tangled fishing lines within the cell’s cytoskeleton and emphasized that it could be difficult to predict how different engineered nanomaterials might interact with biological systems at the molecular level.

Bonner concluded the seminar by describing his most recent published work, a collaboration involving investigators with NC State University, The Hamner Institutes for Health Sciences and NIEHS. This research shows that multiwalled carbon nanotubes inhaled by mice reach the outer lining of the lungs and cause unique pathological changes. The results suggest that minimizing the inhalation of nanotubes during handling of the material in occupational settings is advised until further long-term studies can assess whether carbon nanotubes cause pathological effects similar to those seen with asbestos fibers.

(Thaddeus Schug, Ph.D., is a postdoctoral fellow in the Laboratory of Signal Transduction at NIEHS, where he studies age-associated diseases in mammals.)

Cumulative Lead Exposure Linked to Death from CVD

By Negin Martin

A collaborative study that included three NIEHS grantees – Marc G. Weisskopf, Ph.D., Sc.D., Joel Schwartz, Ph.D., and Howard Hu, M.D., Sc.D. – underscores the cumulative effects of exposure to lead and is the first study to investigate the association between mortality and lead levels in bone. According to the findings, which were published in the journal Circulation, lead levels in bone are significantly associated with increased risk of mortality from cardiovascular disease (CVD) and lower life expectancy.

Measuring lead levels in bone allowed this group of scientists to take into account the cumulative lead exposure of each subject from predominantly non-occupational sources years earlier. Circulating lead has a half-life of 30 days in blood, but once deposited in bone tissue, it can persist for decades. “The findings with bone lead are dramatic,” observed Weisskopf, first author of the study. “This is the first time we have had a biomarker of cumulative exposure to lead and the strong findings suggest that it is a more critical biomarker than blood lead.”

Weisskopf is an assistant professor of Environmental Health and Epidemiology at the Harvard School of Public Health. Both Weisskopf and his co-author Schwartz are core members of the Harvard NIEHS Center for Environmental Health. The senior

“'The findings with bone lead are dramatic,'” said Weisskopf. “'It is the first time we have had a biomarker of cumulative exposure to lead and the strong findings suggest that it is a more critical biomarker than blood lead.'”

(Photo courtesy of Marc Weisskopf)
The author of the study, Hu, is a clinical investigator and a professor of Environmental Health Sciences, Epidemiology and Internal Medicine at the University of Michigan (UM).

The 868 men enrolled in the study were selected from the Normative Aging Study, a longitudinal cohort of men initiated in 1963 in the Greater Boston area by the Department of Veterans Affairs. At enrollment, the men were between 21 and 80 years old with no prior history of heart condition, diabetes or cancer. Volunteers reported every 3 to 5 years for an extensive health evaluation. In the 1990s, 1235 subjects provided blood samples, and 868 men submitted to K-shell x-ray fluorescence of the patella, or kneecap, and the tibia, a large bone in the shin, for lead measurements. By March 2007, 241 of the volunteers had passed away. A board-certified cardiologist reviewed the death certificates and categorized all cardiac-related deaths and cancers.

Higher levels of lead in patella were associated with increased rate of mortality for all causes and particularly ischemic heart disease. Patella lead levels were sorted into high, middle and low tertiles of exposure. After comparing the mortality in the high and low lead level groups, the researchers discovered that the high group had a 2.5-fold greater risk of death due to all causes, a 6-fold greater risk of death due to cardiovascular disease and an 8-fold increase in risk of death from ischemic heart disease. The researchers found no association between levels of lead in bone and cancer mortality.

Blood lead levels of volunteers were only slightly higher than the U.S. average and were not associated with risk of death in any category. These findings highlight the importance of using bone lead levels, and not just blood lead levels, as a biomarker for lead exposure in future studies.

Researchers acknowledged that since most volunteers in the study were white men, more research is needed before generalizing the results for women and minorities.

Based on these findings, the effects of exposure to lead are cumulative and increase the risk of death even years after exposure. Almost no organ is immune to lead toxicity. The authors believe that adverse effects of lead on cardiac rhythm, vascular structure and neuronal signaling, as well as enhanced oxidative stress, may contribute to the increased mortality due to cardiac disorders.

Heart disease is still the number one cause of death and disability in the U.S. despite a steady decline in cardiovascular mortality over the last few decades. Traditional risk factors do not entirely explain this decline; however, it does coincide with tougher measures on environmental exposures and the mid-1990s ban on lead in gasoline.


(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences. She recently completed a postdoctoral fellowship with the NIEHS Membrane Signaling Group.)

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Artificial Protein Can Direct Alternative Splicing of Genes

By Robin Mackar

What started out as a very basic research project looking at a fly protein, has now morphed into a plausible method that may help researchers better study and manipulate disease-associated gene activity.

Researchers at NIEHS have teamed with the Department of Pharmacology at University of North Carolina at Chapel Hill (UNC-CH) to develop artificial protein factors that can direct the alternative splicing of genes. Published online by *Nature Methods*, their paper provides scientists with a new strategy for studying factors that regulate splicing or other RNA processing pathways. It also demonstrates the ability of one such factor to make cancer cells more susceptible to chemotherapy through manipulating alternative splicing of cancer-related genes.

Alternative splicing is an important and common occurrence that enables genes in humans and other organisms to make the variety of proteins needed to carry out the functions of cells throughout the body. More than 90 percent of human genes undergo alternative splicing, and the disruptions of splicing have been shown to cause human disease.

To generate the RNA-binding module, the researchers used a human version of a *Drosophila* fruit fly protein, part of a family of proteins called PUF proteins. The PUF proteins constitute an evolutionarily highly conserved family of proteins present from yeast to humans and plants. “We really didn’t know much about the human protein at the time when we first began to study this family of proteins,” said Traci M. T. Hall, Ph.D., principal investigator in the Macromolecular Structure Group at NIEHS and co-author on the paper with lead author Zefeng Wang, Ph.D., assistant professor at UNC. “I used to joke that we were using the human protein as a model system for the fly.”

The NIEHS and UNC groups have used the technology to create unique splicing factors by combining different PUF domains with effector modules that activate or suppress splicing. To prove the design concept, the researchers created six engineered splicing factors (ESFs) with distinct RNA target specificity. To determine if the ESFs could modulate alternative splicing of endogenous genes, they designed a specific RNA-binding module to target a gene that can either protect or kill cancer cells. They found that these ESFs could increase the amount of the splicing that promotes cell death and increases chemo-sensitivity of cancer cells.

“The potential to use this approach therapeutically is certainly intriguing,” said William Schrader, Ph.D., deputy scientific director of NIEHS. “For starters, the method will have mostly investigational applications. But any cell-based method such as this provides in turn for assays that allow discovery of novel therapeutic drugs. The trick has been to find out how to target splicing events in specific ways, and this method is an advance along that path.”

One of the next steps is to see whether this method can be used in mice to modulate alternative splicing. The researchers at UNC are currently using lentiviruses, or retroviruses, to express the protein in cells. Then, the researchers can use such factors in animal models of human cancers to test if they can promote tumor death in animals. The development of such gene-therapy tools will provide the means to test the technology in other organisms.
A patent on this technology has been filed. The NIH Office of Technology Transfer has also worked with the researchers to issue a licensing abstract on the technology. Those interested in collaborative research to further develop, evaluate or commercialize Modular and Artificial Splicing Factors should contact Suryanarayana Vepa, Ph.D., in the NIH Office of Technology Transfer.


(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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Prenatal Exposure Can Influence Gene Regulation and Later-Life Events

By Dixie Ann Sawin

On October 14, Rebecca Fry, Ph.D., of the University of North Carolina at Chapel Hill (UNC-CH), presented the second in a series of talks sponsored by the NIEHS Division of Extramural Research and Training (DERT). Hosted by DERT Program Analyst Astrid Haugen, Fry’s talk addressed the “Identification of Genetic and Epigenetic Biomarkers of Metal Exposure and Metal-Induced Disease Using Environmental Toxicogenomics and Systems Biology.”

In her research, Fry seeks to characterize genome-wide effects of exposures to arsenic (As), identify specific proteins that could serve as biomarkers of exposure and determine whether prenatal exposure can trigger epigenetic reprogramming in humans. Her current research and earlier work in the same area are supported by NIEHS grants.

Fry began her talk by stressing, “We are continuously exposed to potentially harmful agents in the environment through the food we eat, the water we drink, the air we breathe, but even if we had identical exposures, the responses across individuals would be different.” These responses, she continued, are due to “complex gene-environment interactions from the various exposures, our genetic susceptibility, and the age and time at which we are exposed.”

Arsenic is a ubiquitous environmental pollutant and known carcinogen, and chronic exposure can lead to cancers, skin bladders and lesions, and death. Worldwide, some 40 million people are exposed to levels of As at least five-fold greater than the allowable limit of 10 parts per billion (ppb) set by the World Health Organization in 1994. Health problems associated with As are most prevalent in developing countries, but there are also many places in the U.S. where the As levels exceed 10 ppb.

Fry highlighted two study populations with high rates of arsenic poisoning or arsenocosis — Ron Pibul, Thailand (see related story) and Zimapan, Mexico. Due to intensive tin mining in Ron Pibul, the levels of As were as much as 100 times greater than the WHO limit. Analyzing samples from mothers and infants, Fry and her colleagues at MIT and in Thailand identified 170 genes that were associated with As exposure in newborns.
Using computational algorithms designed for identifying candidate gene signatures in response to As exposure, the researchers minimized the number of genes required for the analysis to 11 genes that showed 83 percent accuracy in predicting prenatal arsenic exposure.

As part of her research in both populations, Fry is striving to determine how exposure to As impacts the genome and to establish which biological pathways are affected in individuals with arsenocosis. She found that prenatal As exposure is significantly associated with an inflammatory response involving tumor necrosis factor alpha (TNFα) and the inflammation-associated nuclear factor kappa beta (NFκB) pathway. Stress response, cell adhesion, apoptotic, lipid metabolism, signal transduction and transcription pathways were also modulated in response to As exposure.

To answer whether epigenetic changes underlie disease, Fry looked at DNA methylation status in adults with arsenocosis. DNA methylation occurs at cytosine/guanine sites (CpG) across the genome and represents possible heritable changes in methylation. Alterations in methylation are associated with cancer development and exposures to environmental toxicants such as As.

Using a state-of-the-art deep sequencing approach, Fry identified genes that show deregulated DNA methylation. Genes in individuals from the Zimapán population with high-level exposure to As from mining — 21 to 1,000 ppb — showed increased hypomethylation, which may lead to increased gene transcription, and were also associated with the NFκB pathway.

As Fry noted, much more data on the effects of exposure over longer periods will be required to adequately prove the epigenetic effects of prenatal exposures. Her long-term objective is to be able to establish the role of epigenetic alterations that may link prenatal exposure to environmental contaminants with detrimental human health effects.

(Dixie-Ann Sawin, Ph.D., is a post-doctoral research fellow in the NIEHS Laboratory of Neurobiology Neurotoxicology Group on detail as a writer for the Environmental Factor.)

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This Month in EHP

By Eddy Ball

This month, *Environmental Health Perspectives (EHP)* considers so-called “beneficial uses” of the more than 131 million tons of coal combustion waste (CCW) produced each year in the U.S. The focus article, “Trash or Treasure? Putting Coal Combustion Waste to Work,” investigates whether using CCW in construction brings with it a potential for toxic leaching from building materials. November’s Spheres of Influence feature, “Balancing Act: Creating the Right Regulation for Coal Combustion Waste,” looks at how tighter regulation by state and federal agencies could impact the recycling of CCW.

Other highlights in the issue include the following studies:

- **Environmental Health Indicators of Climate Change** — Exploring the need for accurate surveillance data and indicators of vulnerability and preparedness to predict human health impacts and develop successful mitigation and adaptation strategies

- **Diesel Exhaust Particles (DEP) and Airway MicroRNA Expression** — Investigating effects of DEP and other environmental pollutants on micro RNA expression that may contribute to adverse health effects

- **Neighborhood Walkability and Air Pollution** — Analyzing neighborhoods in Vancouver, British Columbia in an effort to better understand how factors of the built environment influence levels of physical activity

- **Traffic Pollution: Preeclampsia and Preterm Birth** — Adding further evidence of the adverse effects of air pollution on reproductive outcomes

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Upcoming Distinguished Lecturer Gail Mandel

By Eddy Ball

The 2009-2010 NIEHS Distinguished Lecture series continues this month with a November 12 talk by Gail Mandel, Ph.D., on “Repression Mechanisms and Neuronal Phenotype.” Hosted by NIEHS Principal Investigators Serena Dudek, Ph.D., and Paul Wade, Ph.D., Mandel’s talk is scheduled to begin at 11:00 a.m. in Rodbell Auditorium.

Mandel is a senior scientist at the Oregon Health and Science University (OHSU) Vollum Institute in Portland and an investigator with the Howard Hughes Medical Institute. In 2008, she was elected a member of the National Academy of Sciences.

By exploring how neuronal cell identity is established and maintained, Mandel’s studies of gene regulation in neural differentiation have helped define the critical differences between specification of neural and non-neural cells. Her lab made the important discovery that neuronal cell identity is achieved primarily through a repressor mechanism. At the heart of this mechanism lies the DNA-binding protein, REST, which together with its interaction partners, controls the epigenetic status of neuronal gene chromatin.

Knowledge of this mechanism provides a window into the molecular events governing nervous system formation. Her work is highly relevant to understanding the causes of neurodevelopmental disorders, as well as developing novel therapies for neurological diseases.

Extramural Update

NIEHS American Reinvestment and Recovery Act (ARRA) Funding Overview

NIH received $10 billion under the American Reinvestment and Recovery Act (ARRA). Of that NIEHS received $168 million for environmental health research grants and $19.4 million for the Superfund program, to be awarded over fiscal years 2009 and 2010. In fiscal year 2009, the NIEHS funded 322 grants, allocating approximately $133 million and $27 million respectively for awards and supplements. NIEHS received an additional $11.5 million from the NIH Office of the Director, which allowed NIEHS to award additional 24 grants - 8 Challenge Grants, 5 Grand Opportunity Grants and 11 summer student supplements.

To achieve the ARRA spending goals NIEHS extended the pay line for applications already reviewed, including the percentiled R01 and P01 mechanisms and the unpercentiled R03, R21 and R15 mechanisms. In addition, NIEHS made awards under the following ARRA initiatives:
• Administrative supplements (within scope of parent grant, up to 24 month awards)

• Research Project Grants, Centers, Careers, Diversity Supplements, summer Supplements, Worker Education and Superfund

• Competitive revisions (expands the scope of the parent grant)

• Challenge Grants (RC1)

• Grant Opportunities program (RC2)

• Research to Address the Heterogeneity in Autism (ARRA 09 RFA)

• Research and Development contracts

The distribution of the awards is shown in the two figures for ARRA Grants Awarded and ARRA Dollars Awarded. The top figure shows the ARRA grants approved for funding, including the number and type. The bottom figure shows the dollars allocated to the various categories.

The graphic below shows the distribution of grants supported through the NIEHS ARRA expenditures.
NIEHS has approximately $8 million in ARRA funds for FY 2010. Potential funding announcements are shown below.

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<td>OD-09-010</td>
<td>Recovery Act Limited competition: Building sustainable Community-Linked Infrastructure to Enable Health Science Research (RC4)</td>
<td>09/18/2009</td>
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Over the coming months NIEHS will provide more detailed information on the FY2009 ARRA Awards. For information on how Recovery Act funds are being spent, see http://www.recovery.gov/Pages/home.aspx.

Extramural Papers of the Month

By Jerry Phelps

- Carbon Nanotubes Can Affect the Lining of the Lungs
- Electronic “Nose” Smells Toxins
- Arsenic and Heart Arrhythmia
- Prostate Gene Polymorphism Linked to Bladder Cancer

Carbon Nanotubes Can Affect the Lining of the Lungs

Carbon nanotubes are being used in many products including sports equipment, clothing and cosmetics and are being considered for additional uses such as targeted drug delivery devices. The toxicity of these materials is to a great extent unknown. However, a new collaborative study shows that inhalation of these particles can affect the outer lining of the lung. Long-term effects of the exposure are yet to be determined.

Laboratory mice were exposed, through inhalation, to nanotubules for a single six-hour window. Within one day, the research team noticed immune cells clustering on the surface of the pleura, the tissue that covers the outside of the lungs. Scarring or fibrosis began on the pleura about two weeks after exposure. These same effects at the same location are seen after exposure to asbestos, a known carcinogen.
The study showed that the scarring and immune responses disappeared about three months after the exposure. It is unknown if the effects would continue with chronic exposure to the nanotubes as is generally the case in asbestosis. Additional research with longer exposures is needed to determine the long-term effects of nanotube exposure.


Electronic “Nose” Smells Toxins

A modern-day sophisticated version of the canary in the coal mine has been developed by NIEHS grantees at the University of Illinois. As part of the NIH Genes, Environment and Health Initiative, the university researchers teamed up with a small biotechnology firm and developed a postage-sized sensor that detects poisonous gases and changes color to demonstrate the detection.

When the sensor is fully developed, it will be useful for detecting exposures to toxic materials in industrial and laboratory settings. While nuclear power workers, medical personnel and other people working with radiation wear badges to monitor their exposure, such technology does not exist as yet for chemicals. The investigators hope to be able to market the device within two years. And since the device monitors a variety of toxins, it can be customized for specific industrial settings. The sensor is engineered in such a way that the level of exposure can also be determined.

The developmental sensor detects 19 representative toxic industrial chemicals, including ammonia, chlorine, nitric acid and sulfur dioxide. In testing, the sensors were exposed to the chemicals for two minutes. Most of the chemicals were identified by the array color change in a matter of seconds and almost all were detected within two minutes.


Arsenic and Heart Arrhythmia

The consumption of arsenic-contaminated drinking water is a known risk factor for skin and bladder cancer and is associated with other diseases including diabetes and cardiovascular diseases. Now, NIEHS-funded researchers report that low-level exposure to arsenic is associated with a prolongation of the Q-T portion of the heart rhythm.
Long Q-T syndrome (LQTS) is a disorder of the heart’s conduction system that can be congenital or occur as a side effect of some medicines. The disorder affects the recharging of the heart after each heartbeat. LQTS can lead to an abnormal heart rhythm, fainting or even sudden death.

The researchers performed a cross-sectional analysis of elderly men from the Normative Aging Study. The study included 226 participants and analyzed toe nail clippings for arsenic content, which is a recognized biomarker for arsenic ingestion. Electrocardiograms were conducted on all study participants. Most of the participants lived in the Boston region and obtained their water from the Massachusetts Water Resources Authority. The arsenic concentration of this water resource is generally less than 1 microgram per liter, far below the current EPA standard of 10 micrograms per liter.

In the current study, there was no evidence of an effect of medication use on Q-T interval. The results of this study provide new information to guide efforts to reduce the arrhythmic effects of arsenic exposure.


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**Prostate Gene Polymorphism Linked to Bladder Cancer**

A fifty-member international and interdisciplinary team of researchers report the discovery of a single nucleotide polymorphism in the prostate stem cell antigen gene (PSCA) as a urinary bladder cancer gene. The research team includes NIEHS grantees from the M.D. Anderson Cancer Center and Dartmouth University.

The group conducted a genome-wide association study on 969 bladder cancer cases from Texas. This study was combined with ongoing efforts in three other US populations and nine European groups. A consistent association of a missense variant in the PSCA gene dubbed rs2294008 was found with bladder cancer in all populations. In combining all study subjects, the number of participants included 6,667 cases of bladder cancer and 35,590 controls and produced a highly statistically significant result.

The missense variant alters the start codon, is thought to shorten the protein by nine amino acids, and reduces promoter activity. Resequencing the PSCA genomic region identified rs2294008 as the only common missense polymorphism in the gene. Recent studies demonstrated that the same alteration is associated with gastric cancer in an Asian population. Whether this is true for people of European descent remains to be seen. Additional studies are planned to determine the physiological significance and functional consequences of the variant gene.


(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.)
Intramural Papers of the Month

By Dixie-Ann Sawin and Robin Arnette

- DNA Scrunching Can Facilitate Repair by Filling the Gaps
- Hippocampal Synaptic Plasticity Can Be Modulated by Differential Calcium Handling
- UV Radiation Modulates the Expression of Certain Autoimmune Diseases in Women
- A Novel Chromosomal Candidate Region for Childhood Asthma

DNA Scrunching Can Facilitate Repair by Filling the Gaps

Researchers from NIEHS, the University of North Carolina’s Lineberger Comprehensive Cancer Center and The Stony Brook University, N.Y., recently provided structural and biochemical evidence that DNA polymerase λ (Pol λ) has been implicated in repair of DNA double-strand breaks by nonhomologous end joining (NHEJ) and base excision repair (BER).

While binding and gap filling by pols β and λ were well characterized for 1-nucleotide gaps, the location of the yet uncopied nucleotides in longer gaps was not known until the recent work by Kunkel and colleagues. In their study, published in the September 2009 issue of *Nature Structural and Molecular Biology*, they structurally and biochemically elucidated this mechanism, demonstrating that Pol λ fills gaps longer than five or six nucleotides by DNA scrunching.

Like other family X members, pols β, µ, and TdT, it is well suited to fill short gaps in DNA because it can simultaneously bind both ends of the gap: the 3’ end by the polymerase domain and the 5’ end by the family X polymerase-specific 8 kDa domain. The study demonstrated structurally and biochemically that when filling a 2-nucleotide gap, Pol λ scrunches the template strand and binds the additional uncopied template base in an extrahelical position. This action takes place within a pocket comprising three conserved amino acids. The researchers concluded that, similar to DNA-scrunching by RNA polymerase during transcription initiation, scrunching occurs during DNA repair-associated gap filling synthesis.


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Hippocampal Synaptic Plasticity Can Be Modulated by Differential Calcium Handling

Synaptic plasticity, such as long-term potentiation (LTP), occurs in only some areas of the brain and only during some stages of development. Although the mechanisms involved in the induction of LTP are well known, those involved in its down regulation have not been characterized. Work published in the August 18, 2009 issue of the Proceedings of the National Academy of Sciences, USA (PNAS) by researchers from NIEHS shows that modulation of postsynaptic calcium (Ca$^{2+}$) concentrations can regulate plasticity in brain regions.

Dudek and colleagues investigated mechanisms that are involved in limiting brain plasticity, using the lack of significant LTP in pyramidal neurons in the CA2 region of the hippocampus as their paradigm. They tested whether Ca$^{2+}$ handling in these neurons differed significantly from that in CA1 or CA3 pyramidal neurons, which do exhibit robust LTP. Using 2-photon laser scanning microscopy, they demonstrated smaller increases in free intracellular Ca$^{2+}$ in CA2, compared to CA1 and CA3 neurons. Furthermore, CA2 neurons showed higher Ca$^{2+}$-buffering capacities and extrusion rates than CA1 or CA3 neurons, resulting in attenuated calcium levels. Blockade of Ca$^{2+}$ extrusion mechanisms could restore LTP to CA2 neurons.

As further mechanistic characterization, the researchers provide evidence that Pep-19, which is expressed in CA2 neurons, could be involved in regulating Ca$^{2+}$ extrusion. Additional studies, however, are required to determine the exact role of this protein.

Citation: Simons SB, Escobedo Y, Yasuda R, Dudek SM. 2009. Regional differences in hippocampal handling provide a cellular mechanism for limiting plasticity. Proc Natl Acad Sci U.S.A. 106(33): 14080-14084.

UV Radiation Modulates the Expression of Certain Autoimmune Diseases in Women

A recent study concluded that ultraviolet (UV) radiation influenced the relative frequencies of dermatomyositis (DM) and polymyositis (PM), two autoimmune conditions characterized by muscle weakness due to chronic muscle inflammation. Because previous research determined that UV radiation increased expression of the DM-specific Mi-2 autoantigen, the researchers examined whether a relationship existed between UV exposure and the relative frequencies of DM and anti-Mi-2 autoantibodies.

A collaborative team of scientists used information from referral centers that evaluated myositis patients in various regions of the U.S. The data generated from 380 patients suggested that geographic gradients of DM and anti-Mi-2 autoantibodies were related to the intensity of UV radiation at the location of disease onset. These findings were only found in women, suggesting that inherent differences in how men and women respond to UV radiation may play a role in the development of autoimmune disorders.

This work is the first to show that UV radiation may modulate the clinical and immunologic expression of autoimmune disease in women.

Citation: Love LA, Weinberg CR, McConnaughey DR, Oddis CV, Medsger TA, Reveille JD, Arnett FC, Targoff IN, Miller FW. 2009. Ultraviolet radiation intensity predicts the relative distribution of dermatomyositis and anti-Mi-2 autoantibodies in women. Arthritis Rheum 60(8):2499-2504.
A Novel Chromosomal Candidate Region for Childhood Asthma

An international team of scientists led by investigators from NIEHS have found evidence that single nucleotide polymorphisms (SNPs) in or near the transducin-like enhancer of split 4 (TLE4) gene on chromosome 9q21.31 are related to prevalence of childhood asthma in the Mexican population. The study represents the first asthma genome-wide association study (GWAS) in Mexicans and the most extensive coverage of genetic variation for an asthma GWAS in any Hispanic population.

The researchers conducted a GWAS in 492 Mexican children with asthma, along with their parents. Eleven of the most associated GWAS SNPs were tested for replication in an independent Mexican case-parent trios study and two SNPs in the 9q21.31 region gave evidence for replication.

Mexicans have a mixture primarily of European and Native American ancestries and ancestry analysis of the 9q chromosomal region suggests that the variants in this region could be related to ethnic differences in asthma risk.


_Story_

(Dixie-Ann Sawin, Ph.D., is a post-doctoral research fellow in the NIEHS Laboratory of Neurobiology Neurotoxicology Group on detail as a writer for the *Environmental Factor*.)

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The NIEHS Disability Advocacy Committee (DAC) began its observance of National Disability Employment Awareness Month on September 30 with a presentation on “Obesity, Mortality and Quality of Care: Implications for Disability.”

The lecture, hosted by DAC Chair Alicia Moore, featured physician and sociologist Virginia Chang, M.D., Ph.D. Chang offered encouraging news about trends in mortality and treatment trends among obese people. However, she also cautioned that the impact of obesity on quality of life and medical costs could increase as more obese people live longer with functional and activities-of-daily-living (ADL) disabilities.

With research interests in obesity and weight-related behaviors, social epidemiology and health disparities, Chang is an assistant professor of medicine and sociology in the Division of General Internal Medicine at the University of Pennsylvania (Penn) School of Medicine. She is also a member of the Asian American Studies Program at Penn as well as an attending physician at the Philadelphia Veteran Affairs (VA) Medical Center.

Chang opened her talk with a review of the conventional wisdom about obesity and health that her research findings have led her to question. Although the medical community has long considered obesity a major cause of “avoidable mortality” — and compared it to smoking as a risk factor for premature death — “There is another strain of literature out there,” she said, “showing that the obese population may actually have gotten healthier, especially when we consider cardiovascular [CV] aspects.”

Analyzing data from several cohorts spanning populations born from 1931 to the 1960s, Chang compared changes in mortality among different age groups of obese and normal-weight people over time, as well as trends in treatment for obese people reflected in VA and Medicare claims data. According to Chang, the evidence suggests that the added risk of death from obesity has fallen to the 3- to 5-percent range and is currently only “a modest contributor to mortality.” She said it also appears that “physicians are actually being
more attentive to obese patients and treating them more aggressively” than in the past, and for some conditions, obese patients are more likely to get preventive care.

For the final portion of her talk, Chang turned to trends in the relationship of obesity and disabilities. She compared the odds of having functional and ADL impairments among obese and normal-weight people aged 60 and over during two time periods, the 1980s and the late 1990s to 2004. Chang found that while obese people in the 1980s had 78 percent increased odds for functional disabilities and only insignificantly increased odds for ADL disabilities, in the 1990s, obese people in the age group showed nearly three times the odds of being functionally impaired and twice the likelihood of having ADL disabilities — at a time when normal-weight people experienced no increase in ADL impairment and a slight decrease in functional disability.

“The same amount of weight now confers a greater risk of disability than it did in the past,” Chang concluded, especially for people falling into obesity BMI classes I and II, and “people are getting obese at younger ages.” She ended her talk with a quote from a recent editorial — “Disability may be one of obesity’s most important and persistent effects.”

Speaker Explores the Secret History of Columbus

By Eddy Ball

During its latest Hispanic Heritage Celebration on October 6, the NIEHS Diversity Council offered employees and contractors a novel perspective on explorer Christopher Columbus with a lecture by historian Manuel Rosa. Hosted by council member and NIEHS biologist Eli Ney, Rosa’s talk, “Unmasking Columbus,” explored the topic of “Columbus, the who, what and where — his identity, his knowledge and his mission.”

A native of the Portuguese Azores who once worked on an information technology contract at NIEHS, Rosa has spent the past 18 years investigating historic events related to Columbus’ 1492 voyage to America. His research
findings are the basis of his two controversial books in Portuguese — the carefully documented account, *O Mistério Colombo Revelado* (*The Mystery of Columbus Revealed*), published in 2006, and a popular version of the study released this year, *Colombo Português* (*Portuguese Columbus*).

As the titles of his books suggest, Rosa rejects the depiction of Columbus as “an inexperienced, lost and confused” explorer — a self-made man and shipwrecked sailor from Genoa, Italy, who stumbled across the Americas in 1492 during his misguided search for a western route to India.

Basing his argument on DNA and documentary evidence, Rosa presented a revisionist account of the explorer, whose real name, he argued, was Cristóbal Colón. According to Rosa, Colón was in fact “a highly trained [and very well-educated] nobleman, a Portuguese spy who infiltrated the Spanish royal court on a mission to take Spanish ships as far from India as possible in order to protect India’s trade routes for the Portuguese king [Henry II].”

As Rosa explained, during this time of cataclysmic shifts in the global balance of power, Portugal used its most powerful weapons — artifice, secrecy and intrigue — to divert Spain to the Americas and preserve its own standing as a colonial power in Africa and the East Indies. Columbus, Rosa contends, was an expert navigator, a master prevaricator and accomplished cryptographer who plotted against Spain throughout the voyage, even stopping at Portuguese island ports on his way to America and on his return voyage before returning to Spain — presumably to give progress reports to his Portuguese handlers and co-conspirators.

Rosa contends that the new information he has discovered about Columbus offers a fresh context for understanding apparent contradictions in the established historical record. The new evidence also helps explain Spain’s readiness to sign the Treaty of Tordesillas in 1494, dividing newly discovered lands outside Europe between the two naval superpowers — and reserving Africa and India for Portugal.

Following the presentation, attendees and others from NIEHS gathered for a cultural food tasting, country information exhibits and entertainment by the group Mariachi Los Galleros de Mexico in the NIEHS cafeteria.
Displays highlighted the arts and culture of various Latin American countries represented by employees at NIEHS. (Photo courtesy of Steve McCaw)

NIEHS Diversity Council members Lysandra Castro, left, and Veronica Godfrey, enjoyed Latin American foods at the reception. (Photo courtesy of Steve McCaw)

The Mariachi Los Galleros featured three guitarists, shown above, two trumpeters and a violinist. They played several traditional favorites, including a rousing version of “La Bamba.” (Photo courtesy of Steve McCaw)

Musicians posed with members of the NIEHS Diversity Council. (Photo courtesy of Steve McCaw)

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Motivational Speaker Wows Disability Event Audience

By Eddy Ball

As one of its featured presentations in observance of National Disability Employment Awareness Month (see text box), on October 4 the NIEHS Disability Advocacy Committee (DAC) featured the multi-talented motivational speaker and mentor Tawana Williams. Hosted by DAC Chair Alicia Moore, Williams’ delivered an engaging hour-long monologue, “Unarmed but Dangerous,” that drew several rounds of applause from her enthusiastic audience.

Born without arms, but blessed with a dynamic personality, an irrepressible spirit and a powerful voice, Williams described herself as a “messenger of hope and inspiration” who is “blessed to be born without arms.” Williams wove the story of her determination to overcome her physical limitations, drug addiction and sexual exploitation into a six-part recipe for successful living.

Williams is a diminutive woman with an infectious sense of humor and a rhythmic pace of delivery, clearly rooted in the call-and-response tradition of revival-meeting evangelism. As she talked about the lessons of her journey from what she called (self) “pity parties” to her success as a wife, mother, business owner, author, artist, mentor and talk-show guest, Williams described for her listeners how “I’ve given myself permission to move into my greatness.”

As she encouraged the audience to take on challenges, she used rhyme to underscore her message — “You can’t grow where you don’t go” — and extended metaphor to make her point — “Life has a way of showing up at your door even though you never gave life your address.” At one point, she referred to the inherent pun in the title of her talk and her book by promising attendees, “You, too, can become unarmed and dangerous.

With a charming unselfconsciousness, Williams challenged her listeners, “If I can stand before you without arms, what’s your excuse?” She also used her very visible disability to draw the audience to the front of the room to watch as she changed a doll’s diaper, put on socks and even tied an attendee’s shoelace with her feet.

Taking advantage of street slang, Williams ended her presentation by assuring listeners, “Once you step into your greatness, it’s on and poppin’.” Visibly moved by the presentation, several members of the audience came to the front of the room afterwards to hug and thank Williams for her courage and her inspiration.
As the pensive expression of Bill Willis, foreground right, suggests, Williams’ “in-your-face” narrative at times inspired introspection among her listeners. (Photo courtesy of Steve McCaw)

The audience came from throughout the Institute, and attendees clearly showed their engagement. Seated above, left to right, are Lutz Birnbaumer, Mitzie Walker and Donald Cozart. (Photo courtesy of Steve McCaw)

The events sponsored by the NIEHS Disability Advocacy Committee in observance of National Disability Employment Awareness Month ranged from the heady to the visceral. They included the data-rich lecture by physician-scientist Virginia Chang on the associations between obesity and disability at one end of the spectrum, to the rousing motivational experience provided by a talented Tawana Williams at the other. Also featured were two other events in celebration of a special month:

- **October 20** — A presentation on “Shattering Attitudinal Barriers and Exemplifying Disability Etiquette” by Richard Espinosa, branch chief of the Disability Employment Program at the U.S. Department of Agriculture/Forest Service Civil Rights Division.

- **October 21** — An LRP Publications Audio Conference by federal employment law experts Gary Gilbert and Ernest Hadley on “Federal Employee Medical Documentation: Meeting Your New Requirements Under the Genetic Information Nondiscrimination Act of 2008 (GINA) and the Americans with Disabilities Act Amendments Act of 2008 (ADAAA)”

That Williams could cajole and endear — as well as confront and inspire — was reflected in the smiles of these women. Shown, left to right, are Bettie Harris, Tina Jones and Tiwande Masinde. (Photo courtesy of Steve McCaw)

As the pensive expression of Bill Willis, foreground right, suggests, Williams’ “in-your-face” narrative at times inspired introspection among her listeners. (Photo courtesy of Steve McCaw)

Toward the end of her presentation, Williams drew the audience to the front of the room as she demonstrated how she learned to change her daughter’s diaper with her toes. (Photo courtesy of Steve McCaw)
DERT Celebrates the Completion of ARRA Work

By Robin Arnette

Employees in the NIEHS Division of Extramural Research and Training (DERT) do an exceptional job of funding and managing environmental health sciences research grants to investigators throughout the country. These grantees, representing a variety of organizations, agencies and universities, examine everything from basic research to clinical studies involving human subjects. Recently, DERT staff took on an added responsibility — funding additional grants paid for through the American Recovery and Reinvestment Act (ARRA) of 2009.

Although everyone was happy to help the nation create thousands of new jobs, doing so required many long hours of hard work. Because DERT was successful in awarding all of the grants by the end of the fiscal year, staff members met in the Keystone building on October 7 to celebrate the accomplishment. NIEHS Director Linda Birnbaum, Ph.D., commended the men and women of DERT for their dedication to furthering environmental health sciences research. “I wanted to make sure that you understood what a fabulous job you’ve done,” Birnbaum said. “It’s absolutely incredible that we’ve processed as many awards as we normally do in a whole year or more in a few months. I wanted to say thank you and to keep on doing the great job that you do.”

Birnbaum, along with DERT Interim Director Gwen Collman, Ph.D., and Office of Management Administrative Officer Margarita Roque, passed out gift bags containing BPA-free water bottles and coffee mugs to each DERT employee. Staff members also enjoyed light refreshments that included soft drinks, sandwich platters, meatballs, chips, and several desserts.

Michael Humble, Ph.D., a health science administrator for the Cellular, Organ & Systems Pathobiology Branch said, “It [ARRA] was a lot of work, but I think we did a good job and hopefully we will have advanced some good science and created some jobs.”

William Suk, Ph.D., director of the Center for Risk and Integrated Sciences (CRIS) and a fellow DERT colleague, echoed Humble’s sentiments. “People worked late, worked weekends and didn’t take vacations,” he said, “but it was worth it because ARRA will benefit the nation.”

Birnbaum couldn’t stay for the entire ceremony because she had to catch a plane to Bethesda to attend meetings at NIH, but before she left, she acknowledged Collman’s outstanding leadership in helping steer DERT through a challenging, but rewarding period. Collman declared, “For the last six months, the DERT staff went above and
beyond in every conceivable way to complete ARRA award funding to many grantees who are doing exciting science. The money will create or expand well over 600 jobs across the country, and that is certainly something to celebrate.”
CFC Nears Goal as Campaign Continues

By Eddy Ball

By the end of the day on October 30, NIEHS employees had pledged nearly $60,000 or 85 percent of the campaign’s 2009 goal of $70,000, and Combined Federal Campaign (CFC) organizers were confident NIEHS would reach or exceed the goal as the campaign continues through November 20.

The smooth execution of the campaign is a testament to the concerted efforts of the co-chairs for the 2009 CFC campaign — Veronica Godfrey Robinson and Rachel Frawley — and division leaders Dona McNeill (OM), Robin Mackar (OD), Eli Ney (DIR), Claudia Thompson (DERT), and Rachel Frawley (NTP) — as well as a dedicated group of volunteer keyworkers.

The speakers at the kickoff events, Acting Scientific Director John Pritchard, Ph.D., and Acting Deputy Director Steve Kleeberger, Ph.D., also did their part with moving testimony on the importance of helping others.
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