NTP Outlines Challenges and Directions at Meeting of Scientific Counselors

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Wilcox Honored with Maternal and Child Health Epidemiology Award

NIEHS Senior Investigator Allen Wilcox, M.D., Ph.D., is the recipient of the 2009 Greg Alexander Award for Advancing Knowledge — one of the highest honors bestowed each year by the Coalition for Excellence in Maternal and Child Health (MCH) Epidemiology. ...read more

Agency Leaders Testify on TSCA Reform

The U.S. Senate Committee on Environment and Public Works convened a hearing on Dec. 2 to consider reform of the federal Toxic Substances Control Act (TSCA). ...read more

Deary Represents NIEHS and NIH in Copenhagen

As high-profile speakers and demonstrators took center stage at the Climate Change Conference in Copenhagen Dec. 7–18, hundreds of scientists, including Allen Deary, Ph.D., of the NIEHS Office of the Director, shared their data and projections in meetings and seminars held outside the range of the spotlights and cameras. ...read more

Kahn Gives Hans L. Falk Memorial Lecture

Each year scientists from the NIEHS Division of Intramural Research (DIR) set aside one of the distinguished guest lectureships to honor their first Scientific Director Hans L. Falk, Ph.D. ...read more

Grantee Explores Right-to-Know in Community-Based Participatory Research

On Dec. 1, NIEHS welcomed grantee Julia Brody, Ph.D. as the latest speaker in the Keystone Science Lecture Series sponsored by the NIEHS Division of Extramural Research and Training (DERT). ...read more

Slight Nerve Effect with Elemental Mercury Exposure from Fillings

On Dec. 4, Alfred Franzblau, M.D., discussed the effect of chronic low-level elemental mercury (Hg) exposure on dental professionals. In his study, researchers measured urine mercury concentrations and nerve function in 2,974 volunteers and found a very slight, but significant deleterious effect on sensory nerves. .....read more

Study Unveils Potential Genetic Links to Lung Disease Risk

A new NIH-funded study involving data from more than 20,000 individuals has uncovered several DNA sequences linked to impaired pulmonary function. .....read more
NIEHS Spotlight

Collegium Ramazzini Elects Birnbaum as Fellow
NIEHS/NTP Director Linda Birnbaum, Ph.D., received notification in December of her election as a fellow of the Collegium Ramazzini headquartered in Carpi, Italy. ...read more

Superfund Research Program Continues Strategic Planning Process
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Stokes Helps Build Pacific Rim Partnerships for Advancing Alternative Testing
With talks and meetings scheduled in Korea and Japan, NICEATM Director Rear Admiral William Stokes, D.V.M., faced a busy schedule when he traveled in Asia during November. ...read more

NIEHS Welcomes John Balbus as New Advisor for Public Health
NIEHS recently announced the appointment of John Balbus, M.D., as the Institute’s senior advisor for public health. ...read more

Androphy and Burr Appointed to Senior Posts at NIEHS
During the final weeks of 2009, NIEHS announced the appointments of Deputy Ethics Counselor Bruce Androphy, J.D., and Administrative Management Branch Chief Matt Burr to senior posts at the Institute. ...read more

Science Notebook

Increased Risk of Parkinson’s Disease with PON1 Gene Variant and Pesticide Exposure
University of California, Los Angeles (UCLA) researchers report that study participants with two copies of a common gene variant showed an increased risk of Parkinson’s disease (PD) when exposed to pesticides used in agriculture. ...read more

Group Gathers for Asbestos and Related Fibers Meeting
NIEHS scientists, federal partners, representatives from industry, and members of the academic community gathered in Chapel Hill, NC, Dec. 16–17 to discuss the state of the science on asbestos and develop recommendations for future work. ...read more

This Month in EHP
The January issue of Environmental Health Perspectives (EHP) is sure to catch the attention of sleep-challenged readers with its cover stories on light exposure, circadian rhythm, and sleep — “What’s in a Color? The Unique Human Health Effects of Blue Light” and “Lose Sleep, Gain Weight: Another Piece of the Obesity Puzzle.” ...read more

Dan Littman Will Give Next Distinguished Lecture
The NIEHS 2009–2010 Distinguished Lecture Series will feature a talk January 19 by Dan Littman, M.D., Ph.D., on the “Role of Environmental and Intrinsic Factors in the Differentiation of Inflammatory T Cells.” ...read more
**NIEHS Spotlight**

**Seminar Reviews**

**Public Health Role of Congressional Oversight**

During an invited lecture on Dec. 15 at NIEHS, Paul Jung, M.D., discussed his experience as a public health investigator for the U.S. House Committee on Energy and Commerce and outlined public health aspects of the congressional oversight process. ...read more

**Fellow Receives Lab Animal Medicine Award**

NIEHS Postdoctoral Fellow Coralie Zegre-Cannon, D.V.M., recently received first-place honors at the 60th annual American Association of Laboratory Animal Science (AALAS) National Meeting held Nov. 8-12 in Denver. ...read more

**Friends and Colleagues Remember Pioneering Woman Scientist**

Former NIEHS investigator and environmental attorney Carol Ann Masters Schiller, Ph.D., J.D., D.A.B.T., died Dec. 5 in Raleigh at age 68, following a seven-year battle with the rare neurological disease progressive supranuclear palsy (PSP). ...read more

**Library Hosts Visitors from Russian**

As part of their Sister Cities sponsored visit to Durham, a delegation of librarians from Kostroma, Russia spent several hours on Nov. 20 at the NIEHS Library with Library and Information Services Branch Chief Dav Robertson and his colleagues. ...read more

**NIEHS Is Accepting Applications for Extramural Director**

NIEHS began accepting applications for the director of its Division of Extramural Research and Training (DERT) on Dec. 7, with a deadline of Feb. 27, 2010. ...read more

**Extramural Research**

**Extramural Papers of the Month**

- Researchers Map the First Human Epigenome
- Metal and Diesel Exhaust Linked to Respiratory Symptoms in Children
- Spatial Epidemiology of Abused Drugs
- Traffic and Childhood Asthma

**Intramural Research**

**Intramural Papers of the Month**

- Initiation of Repair of Random DNA Double Strand Breaks Requires RAD50
- New Pathway for Viral Regulation of the Cell Cycle Through TGF-β
- Methoxyacetic Acid Disrupts Endogenous Estrogen Receptor Signaling
- Structural Studies Reveal Specificity of mRNA Regulatory Proteins
CFC Has Banner Year at NIEHS
By the time organizers completed the accounting in early December, the 2009 Combined Federal Campaign (CFC) at NIEHS exceeded its goal by more than $20,000, with a total of $91,392 in pledges. Following its kickoff on Sept. 28, the campaign continued through Nov. 20. ...read more

Director’s Awards Ceremony Recognizes Employee Achievements
NIEHS employees, friends, and family turned out in force on Dec. 17 in Rodbell Auditorium to watch as NIEHS/NTP Director Linda Birnbaum, Ph.D., presented Director’s Awards to employees who made meritorious contributions to the NIEHS mission in 2009. ...read more

Staffers Complete Clear Writing Workshop
NIEHS employees enjoyed an opportunity during the first week of December to look at their writing from the distinctive perspective of veteran communications consultant Ginny Redish, Ph.D. ....read more

Trainees Celebrate the Holiday Seasons
A group of the Institute’s youngest scientists accepted an invitation to leave their pipettes behind on December 11 and enjoy a holiday party sponsored by the NIEHS Trainee Assembly (NTA) and the Office of Fellows Career Development (OFCD). ....read more

Calendar of Upcoming Events

- **Jan. 5**, in Rall D350, 11:00–12:00 — Biostatistics Branch Seminar on “A Computational Study of Chromosome Structure and Genome Instability,” by Ankit Malhotra, Ph.D.
- **Jan. 5**, in Keystone 1003AB, 2:00–3:30 — Superfund Research Program Strategic Planning Meeting
- **Jan. 7**, in Rall D450, 10:00–11:00 — Laboratory of Molecular Carcinogenesis Seminar Series featuring Xiaoling Li, Ph.D., addressing “SIRT1 and Metabolic Diseases”
- **Jan. 11**, in Rodbell Auditorium, 11:00–12:00 — Laboratory of Molecular Genetics Fellows Invited Guest Lecture by James Lupski, M.D., Ph.D., speaking on “Genomic Disorders: Mechanisms and Assays for Copy Number Variations that Cause Human Disease”
- **Jan. 19**, in Rodbell Auditorium, 11:00–12:00 — Distinguished Lecture by Dan Littman, M.D., Ph.D., on “Role of Environmental and Intrinsic Factors in the Differentiation of Inflammatory T Cells”
- **Jan. 21**, in Rall D450, 10:00–11:00 — Laboratory of Molecular Carcinogenesis Seminar Series with Susan Fischer, Ph.D., presenting “Cox-2 Driven Pancreatitis and Pancreatic Ductal Adenocarcinoma”
- **Jan. 25–27** (Offsite Event) at the New Orleans Marriott Hotel, 8:00–5:00 — 2010 Conference on Environmental Justice, Air Quality, Goods Movement, and Green Jobs: Evolution and Innovation; and the Worker Education and Training Program Awardee Meeting
- **Jan. 27**, in Rall F193, 11:00–12:00 — Laboratory of Neurobiology Seminar Series presentation on “Illuminating the Epigenome Landscape by Deep Sequencing,” by Yuan Gao, Ph.D.
- **Jan. 31** (Deadline) — 11:59 p.m. (Spain’s local time) — Submission of abstracts for the 12th International Congress of Toxicology in Barcelona, Spain, July 19–23, sponsored by the Spanish Association of Toxicology (AETOX) and EUROTOX in the name of the International Union of Toxicology (IUTOX)

- View More Events: NIEHS Public Calendar
NIEHS Spotlight

NTP Outlines Challenges and Directions at Meeting of Scientific Counselors

By Thaddeus Schug

The National Toxicology Program (NTP) is “working to do more in terms of developing toxicology testing across the Federal government,” declared NIEHS/NTP Director Linda Birnbaum, Ph.D., as she opened a two-day meeting before the NTP Board of Scientific Counselors (BSC) at NIEHS December 9-10. Birnbaum’s themes of NTP leadership and innovation in toxicity testing in the 21st century through expanded partnerships with other agencies emerged repeatedly in the packed agenda.

In the course of the day and a half meeting, the Board heard presentations on activities by the NTP Center for the Evaluation of Risks to Human Reproduction (CERHR), concepts for contracts, a review of the Host Susceptibility Program, research concepts for NTP testing nominations, and an overview of NTP studies on herbals and supplements.

Bucher points to interagency collaborations on toxicity testing

NTP Associate Director John Bucher, Ph.D., followed Birnbaum with an update on recent programmatic activity and staff changes within the NTP. He also announced the opening of a shared NTP laboratory to be used by scientists to “better address the toxicological effects occurring in developmental periods that may result in long-term chronic disease later in life.”

Nomination proposes state-of-science literature review on obesity/diabetes

Early in the meeting Kristina Thayer, Ph.D., acting director of CERHR, presented a concept nomination to explore the “state-of-the-science evaluation of environmental exposures and diabetes and obesity.” Thayer said that the association between environmental contaminants and diabetes and obesity is an emerging topic of health concern in need of a focused review.

Thayer proposed that CERHR convene a panel of external scientists and hold a workshop to evaluate emerging literature for consistency and relevance and to provide direction for future research. Thayer’s presentation sparked a lively debate among Board members on the difficulties of identifying impact issues in an area of health science undergoing such rapid development.
Branch plans new mouse strains to evaluate variability in response

John (Jef) French, Ph.D., acting chief of the NTP Host Susceptibility Branch (HSB), spent a large part of the afternoon session updating the Board on the state of 12 projects in various stages of development within the HSB. French highlighted examples of several genetic variability testing projects with mice strains that the HSB considers “critical to understanding the role of population genetics in the origin and progression of environmental exposure related to toxicity and disease.”

Nominations highlight tiered testing protocol

Scott Masten, Ph.D., director of the NTP Office of Nomination and Selection, kicked off day two of the meeting with the nomination of five chemicals for Board consideration for extensive NTP testing. NTP Project leaders and Board members reinforced another position expressed earlier by Bucher and Birnbaum — that the NTP should “work to establish a better understanding of risk assessments associated with dosimetry, particularly during critical developmental periods.”

The Board and members of the public, including People for the Ethical Treatment of Animals representative Joseph Manuppello, commented on the importance of conducting in vitro studies prior to animal testing. NTP scientists addressed these concerns by outlining a tiered testing strategy in which NTP first tests chemical toxicity in cell-based assays before moving to animal models.

Dietary supplements become a higher priority for toxicity testing

As part of the program’s emphasis on determining toxicity of dietary supplements, three of the five chemicals nominated for future NTP testing were the herbal medicines butterbur, evening primrose, and valerian. NTP Deputy Program Director for Science Nigel Walker, Ph.D., wrapped up the meeting with a presentation on the NTP Dietary Supplements and Herbal Medicines Initiative, placing new and existing nominations into a context of interagency public health collaboration.

Walker noted that dietary supplements are a multi-billion dollar industry of products that often lack uniform strength, purity, and composition – presenting special challenges for toxicity testing. Walker stated that dietary supplement testing will remain a major priority for NTP, which is leading efforts to “increase coordination across federal agencies to ensure NTP obtains the most needed information to inform public health decision making.”

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction.)
Seated at the Board table following his presentation, French fielded questions about his branch’s efforts using multiple strains of mice to help define variable ranges of response and better extrapolate across species by identifying the parameters of a chemical’s modes of action. (Photo courtesy of Steve McCaw)

Board member Ruthann Rudel expressed her enthusiastic support for Thayer’s proposal, describing it as “proactive,” “synthesizing,” and “high-impact.” (Photo courtesy of Steve McCaw)

Walker explained that NTP is working closely with other NIH components, the Centers for Disease Control and Prevention, and the U.S. Food and Drug Administration to characterize the safety of herbals and supplements used by as many as 40 percent of adults and 11 percent of children in the United States. (Photo courtesy of Steve McCaw)

NTP study scientist Mike Devito, Ph.D., said one of the rationales for testing the dietary supplement valerian is its widespread use among women of childbearing age. (Photo courtesy of Steve McCaw)
Wilcox Honored with Maternal and Child Health Epidemiology Award

By Eddy Ball

NIEHS Senior Investigator Allen Wilcox, M.D., Ph.D., is the recipient of the 2009 Greg Alexander Award for Advancing Knowledge — one of the highest honors bestowed each year by the Coalition for Excellence in Maternal and Child Health (MCH) Epidemiology. Recognized for his outstanding contributions to public health knowledge through epidemiology and applied research, Wilcox received the award at the Coalition’s Fifteenth Annual Maternal and Child Health Epidemiology Conference Dec. 9-11 in Tampa, Fla.

In choosing recipients for the Greg Alexander Award, the selection committee gives preference to those whose focus is applied, recognizing originality of scientific work, contribution to the field, and impact on the health of mothers and children. “One of the hallmarks of this coalition,” Wilcox said, “is that it draws from a broad spectrum of public health people — from the very applied folks in the county health departments to university researchers.”

Wilcox is the tenth winner of the Greg Alexander Award. He joins former University of North Carolina at Chapel Hill (UNC-CH) colleagues Milton Kotelchuck, Ph.D., the first recipient of the award in 2000, and David Savitz, Ph.D., who won in 2004.

Wilcox enjoys an international reputation for high-impact research

A reproductive epidemiologist who recently celebrated his 30th year as an investigator at NIEHS, Wilcox is also the editor-in-chief of the journal, Epidemiology. He is a past president of both the American Epidemiological Society and the Society for Epidemiologic Research.

Wilcox serves as an adjunct professor of Epidemiology at the UNC-CH, where he earned M.P.H. and Ph.D. degrees after completing his M.D. at the University of Michigan. He is the author of a soon-to-be-published textbook, Fertility and Pregnancy: An Epidemiologic Perspective, described by Oxford University Press as “the first truly comprehensive textbook on the topic.”

In 2008, Wilcox received an honorary doctorate from the University of Bergen where he has long-standing collaborations. His recent studies on facial clefts among Norwegian children investigated the associations of genetic and environmental factors — such as smoking, caffeine consumption, and binge drinking — with the incidence of facial clefts.

Sixteen professional groups make up the transdisciplinary Coalition for Excellence

According to the Coalition, no single organization represents MCH Epidemiology as a profession from both an academic and practice perspective. MCH Epidemiology, however, is a major contributor and participant in many health organizations and professional groups.
The 16 national health organizations that formed the Coalition for Excellence in MCH Epidemiology to sponsor the National MCH Epidemiology Awards represent a broad range of scientific and public health interests, including several high-profile groups:

- Centers for Disease Control and Prevention
- American Academy of Pediatrics
- American Public Health Association
- Eunice Kennedy Shriver National Institute of Child Health and Human Development
- Society for Pediatric and Perinatal Epidemiological Research

Agency Leaders Testify on TSCA Reform

By Ed Kang

The U.S. Senate Committee on Environment and Public Works convened a hearing on Dec. 2 to consider reform of the federal Toxic Substances Control Act (TSCA). U.S. Environmental Protection Agency (EPA) Administrator Lisa Jackson, U.S. Government Accounting Office (GAO) Natural Resources and Environment Director, John Stephenson, and NIEHS/NTP Director Linda Birnbaum, Ph.D., provided remarks and testified to the committee chaired by Senator Barbara Boxer of California.

TSCA was signed into law by President Gerald Ford in 1976, and was intended to restrict or ban the use of toxic chemicals. “However, more than three decades later, TSCA has not lived up to that promise,” Chairwoman Boxer said. “TSCA does not include sufficient protections for pregnant women, infants, children, and others who are particularly vulnerable to chemical exposures. [There is] growing consensus that now is the time to act to transform America’s toxic chemical policies.” She added, “EPA is stepping up to the plate on the need to reform our toxics laws.”

EPA and GAO leaders offer compelling arguments for updating legislation

EPA Administrator Jackson testified on her agency’s principles for TSCA reform, which were announced earlier this fall. These modernizations address the risks of dangerous toxic chemicals. Jackson said, “Standards should be driven solely by scientific evidence of risks.” She also expressed a desire to place “the legal obligation on producers to conduct testing” and to expand EPA’s “authority to take risk management actions when chemicals do not meet safety standards.”
According to Stephenson, the Government Accountability Office placed the chemical program on its list of “high risk” programs requiring executive branch and congressional attention. In his remarks Stephenson summarized a GAO report that identified “significant shortcomings with TSCA,” and recommended “broadening EPA’s authority to develop sufficient information to support critical decisions regarding how to protect human health and the environment from toxic chemicals.”

**Birnbaum points to a new testing paradigm for moving forward**

As the final witness, Birnbaum talked at length about the progress in environmental health science and the importance of partnerships between agencies. “TSCA reform can be built upon vastly improved and less expensive toxicological testing methods. The NTP is laying the foundation for this testing paradigm in partnership with the National Human Genome Research Institute and the EPA.”

Birnbaum closed her testimony with a salient acknowledgement that encapsulated the hearing’s presentations. “Over the past 33 years, we’ve significantly expanded our understanding of chemical exposures and health. It only stands to reason that TSCA would, at some point, be updated to account for scientific progress. We must have the ability to harness new technologies and our growing knowledge. We are poised to move forward, and new tools will provide for research and development to create the comprehensive testing our citizens deserve under a revitalized TSCA.”

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison and a contributor to the *Environmental Factor.*

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**Dearry Represents NIEHS and NIH in Copenhagen**

*By Eddy Ball*

As high-profile talks by politicians and demonstrations in the streets took center stage at the United Nations Climate Change Conference (COP15) at the Bella Center in Copenhagen Dec. 7–18, hundreds of scientists, including Allen Dearry, Ph.D., of the NIEHS Office of the Director, shared their data and projections in meetings and seminars held outside the range of the spotlights and cameras.

As part of his visit to Copenhagen as NIEHS representative, Dearry made a presentation Dec. 11 at the U.S. Center at COP15 as the NIH member of the U.S. National Science & Technology Council Subcommittee on Disaster Reduction (SDR). Dearry’s talk, titled “Maximizing Public Investment: Disaster Risk Reduction Meets Climate Change Adaptation,” presented a compelling case for enhancing disaster resilience by charting a 10-year agenda of science and technology activities to produce a dramatic reduction in the loss of life and property from natural and technological disasters.

**Climate change will impact public health and public safety**

Dearry’s presentation drew attention to the impact of Hurricane Katrina as one example of the human health effects of natural disasters and paralleled the findings of NIEHS-supported climate change health studies published in The Lancet just before COP15 (see story). Both helped to reinforce the NIEHS message that
climate change has important public health implications. Mitigating climate change can produce important public health co-benefits that will help offset the costs of intervening as quickly and comprehensively as possible.

As U.S. Department of Health and Human Services (HHS) Secretary Kathleen Sibelius said when The Lancet papers were published, “We are learning that the health of our planet and the health of our people are tied together. It’s difficult for one to thrive without the other.”

**Climate change presents “grand challenges” for disaster risk reduction**

Near the beginning of his talk, Dearry referred to the U.S. presidential science advisor, John Holdren, on the need to take a proactive role in developing adaptation strategies to meet the extreme events scientists expect as a result of climate change. Dearry pointed to what the SDR identified as the “grand challenges” ahead:

- Providing hazard and disaster information where and when it is needed
- Understanding the natural processes that produce hazards
- Developing hazard mitigation strategies and technologies
- Recognizing and reducing vulnerability of interdependent critical infrastructure
- Assessing disaster resilience using standard methods
- Promoting risk-wise behavior

**Efforts to make the world more disaster resilient**

AsDearry explained, scientists and policy makers committed to disaster resiliency continue to gather resources and information, such as that available through PreventionWeb as part of the Hyogo Framework — a 10-year global blueprint for disaster risk reduction efforts during the decade 2005–2015. The blueprint, adopted by 168 countries that met in Kobe, Hyogo, Japan, offers guiding principles, priorities for action, and practical means for achieving disaster resilience for vulnerable communities.

The goal of such disaster resilient efforts, Dearry concluded, is three-fold — to help communities at risk understand the hazards they face and know when an event is imminent, minimize property losses and lives at risk in future natural hazard events, and ensure that disaster-resilient communities experience minimum disruption to life and economy after a hazard event has passed.

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Collegium Ramazzini Elects Birnbaum as Fellow

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., received notification in December of her election as a fellow of the Collegium Ramazzini headquartered in Carpi, Italy. The letter from Collegium Ramazzini Secretary General Morando Soffritti, M.D., praised Birnbaum for her “scientific stature and authority” and “commitment to the public’s health.”

Birnbaum described her election as “a great honor” and said she looks forward to working with this prestigious group.

Birnbaum recognized for international distinction in environmental health

With 180 fellows in 30 countries, the Collegium Ramazzini is an international scientific society that examines critical issues in occupational and environmental health, with a view towards action to prevent disease and promote health. The fellows are professionals of clear personal distinction and integrity, distinguished by their contributions to occupational and environmental health.

Birnbaum is one of the select group of current and former NIEHS scientists who are Collegium Ramazzini fellows. They include former NIEHS Director Ken Olden, Ph.D., NTP Associate Director John Bucher, Ph.D., and Superfund Research Program Director William Suk, Ph.D., as well as several other outstanding current and former NIEHS scientists -- Carl Barrett, Ph.D., David Hoel, Ph.D., James Huff, Ph.D., George Lucier, Ph.D., Ronald Melnick, Ph.D., John Moore, Ph.D., Walter Rogan, Ph.D., and Raymond Shapiro, Ph.D. Former NIEHS Director David Rall, M.D., Ph.D., was both a fellow and the recipient of the annual Ramazzini Award in 1989.

Among the several fellows who are NIEHS grantees is Philip Landrigan, M.D., who serves as Collegium Ramazzini president.

The Collegium Ramazzini carries on the legacy of the father of occupational medicine

Founded in 1982, the Collegium derives its name from Italian physician and University of Modena Professor Bernardino Ramazzini (1633–1714), who authored one of the founding and seminal works of occupational medicine and played a substantial role in its development. His book, De Morbis Artificum Diatriba (Diseases of Workers), outlined the health hazards of chemicals, dust, metals, repetitive or violent motions, odd postures, and other disease-causative agents encountered by workers in 52 occupations.

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Superfund Research Program Continues Strategic Planning Process

By Thaddeus Schug

As part of a comprehensive strategic planning effort aimed at gathering input for future program direction, the Superfund Research Program (SRP) organized a series of informational meetings, Web-based seminars, and a Web-based questionnaire.

The program held face-to-face meetings in New Orleans and New York during November and conducted its first Web-based meeting on Dec. 7. About fifty people participated in the latest meeting, including representatives of the U.S. Environmental Protection Agency (EPA) and Agency for Toxic Substances and Disease Registry (ATSDR), as well as local, state, and non-profit organizations, universities, and environmental groups.

Two areas of interest that several participants raised were the need for SRP to address aspects of cumulative risks, and the importance of partnering with other relevant federal agencies to leverage its resources.

Four additional meetings will take place in January (see text box).

Planning design promotes full participation by stakeholders and public

SRP encourages feedback from the public, environmental health researchers, and other interested community members, as well as its sister Superfund agencies, the EPA and ATSDR. SRP staff will use the information gathered at these sessions to develop a long-term strategic plan to direct programmatic focus and enhance the impact of the SRP program.

As SRP Program Administrator Heather Henry, Ph.D., described the process, “The multi-format meetings promote exchange of ideas through different avenues and provide opportunity for stakeholders to voice their perspectives [to SRP planners].” The meetings involve moderated discussions framed by the seven questions that make up the program’s online questionnaire. The questions focus on future direction of the program with regard to science, training, translation, outreach, and grant mechanisms.

Planners will post comments and transcripts online

Following the comment period that continues through the end of January 2010, SRP will post feedback gathered from the meetings and the online questionnaire on its Web site. SRP will use this information, along with recommendations made by the SRP External Advisory Panel (see Oct. 2009 story) to draft a strategic plan, which it has scheduled for release in the summer of 2010.

SRP Will Hold Four Meetings in January

- Jan. 5, at the NIEHS Keystone Building 530 Davis Drive, Room 1003, Durham, N.C. 27713 — 2:00–3:30
- Jan. 25, Web-based meeting, 2:00–4:00 — Register in advance
- Jan. 28, at the Agency for Toxic Substances and Disease Registry, 4770 Buford Highway NE, F-61, Atlanta, Ga. 30341-3717, 1:30–3:30

Visitors planning to attend meetings in person should contact Janet Cakir. Visitors to federal facilities need to present two forms of identification (with photo) at the campus or building entrance.
According to SRP program administrators, the strategic plan will chart a course for the program to meet the program’s goals.

**SRP will build on two decades of success to shape the program’s future**

During the Web seminar titled “Superfund Research Program Strategic Planning - Your Input for Future Directions,” SRP Director William Suk, Ph.D., explained, “The main goals of the SRP are to clearly establish the relationship between exposure and disease, develop efficient and cost-effective cleanup strategies, and conduct science that contributes to human health risk assessment and decision-making for remediation that reduces the risk of exposure and improves public health.”

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction.)

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**Stokes Helps Build Pacific Rim Partnerships for Advancing Alternative Testing**

*By Eddy Ball*

With talks and meetings scheduled in Korea and Japan, Rear Admiral William Stokes, D.V.M., a U.S. Public Health Service Commissioned Corps officer, an Assistant Surgeon General, and the director of the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), faced a busy schedule when he traveled in Asia during November. His visits there were part of an ongoing quest to build global partnerships to advance alternatives to animal testing.

Stokes represented NICEATM, which is the participating U.S. national validation organization for a memorandum of cooperation signed earlier this year by Linda Birnbaum, Ph.D., as director of the NIEHS and NTP along with representatives of Europe, Canada, and Japan which established the International Cooperation on Alternative Test Methods (ICATM). While the memorandum was a major step forward (see May 2009 eFactor article), Stokes said, “Greater international cooperation will hasten progress on new safety testing methods that will help further reduce, refine, and replace animal use while ensuring human safety.

**Korea is the newest Asian partner in the global effort**

During his stop in Seoul, Korea, Stokes delivered a keynote address at the inaugural International Symposium of the Korean Center for the Validation of Alternative Methods (KoCVAM). Recently established as part of the National Institute of Food and Drug Safety (NIFDS) in Korea’s Food and Drug Administration (KFDA), KoCVAM held its symposium in conjunction with the Sixth Congress of the Korean Society for Alternatives to Animal Experiments (KSAAE) at Seoul National University on Nov. 3.
Following an opening address by Dong Sup Kim, Ph.D., president of the KSAAE, and a congratulatory address by Seung-Hee Kim, Ph.D., director general of NIFDS, Stokes spoke on “Validation and Regulatory Acceptance of Alternative Methods for Safety Testing: Recent Progress and Future Directions.” He emphasized the need for high quality scientific validation studies for proposed new safety test methods as a prerequisite for regulatory acceptance and use — highlighting new technologies and scientific advances that are expected to support the future development of more predictive safety tests to reduce use of animals.

While in Seoul, Stokes joined Japanese partner, Hajime Kojima, Ph.D., director of the Japanese Center for the Validation of Alternative Methods (JaCVAM), for a visit to the KFDA, where they met with Kim and Sang Yong Lee, Ph.D., deputy commissioner of the KFDA. They also participated in a KoCVAM colloquium, where they discussed several areas of potential collaboration and made plans to communicate regularly and work toward conducting joint validation studies and test method evaluations in the future.

Stokes speaks at Japanese alternative methods meetings

Stokes was just as busy during his next stop in Japan, where he was an invited speaker at the International Workshop on Skin Safety Evaluation of Cosmetics and Chemicals, held at the International Conference Center in Kyoto on Nov. 5. Later in his visit, Stokes delivered the keynote plenary lecture for the 22nd Annual Meeting of the Japanese Society for Alternatives to Animal Experiments (JSAAE), held at Osaka University on Nov. 13-15.

At the Skin Safety workshop, Stokes addressed “Current Validation and Regulatory Acceptance Status of Local Lymph Node Assays (LLNA): Alternative Test Methods for Assessing the Allergic Contact Dermatitis Potential of Chemicals and Products.” In this talk, he reviewed the recent evaluation of the validation status of several new versions and applications of the LLNA by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

Afterwards, Stokes met with Director General Masahiro Nishijima, Ph.D., of the National Institute of Health Sciences (NIHS) in Tokyo and with Kojima and JaCVAM staff to discuss ongoing joint validation and evaluation activities with NICEATM and ICCVAM.
On the final leg of his trip, Stokes enjoyed a warm reception by an audience of 300 scientists at the JSAAE meeting Nov. 13. Stokes explored the topic of “Advancing Laboratory Animal Welfare and Public Health Science: The Role of Innovative Refinement, Reduction, and Replacement Strategies.” The theme of the meeting was “The 3Rs: Refinement and then Reduction and Replacement,” emphasizing refinement as a way to achieve immediate benefit for the welfare of animals that must still be used.

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NIEHS Welcomes John Balbus as New Advisor for Public Health

By Laura Hall

NIEHS recently announced the appointment of John Balbus, M.D., as the Institute’s senior advisor for public health. Assigned to the NIEHS Bethesda office, he will act as a liaison to those with an interest or involvement in the many aspects of the NIEHS mission — external constituencies, stakeholders, and advocacy groups. Balbus began his new position at NIEHS on Dec. 7.

“I am pleased to welcome John to our NIEHS team,” said NIEHS/NTP Director Linda Birnbaum, Ph.D. “His wealth of experience in public health from environmental health research to service on federal advisory boards makes him a great advocate for NIEHS who will understand the concerns of those outside our Institute.”

Balbus is well suited to represent NIEHS. His long-standing interest in and numerous research papers on air and water pollution, nanotechnology, lead and mercury exposure, asthma, toxicogenomics, and climate change mesh well with the mission and research of NIEHS.

His education and experience make him well fitted to the role of advisor and liaison. Balbus is board-certified in Internal Medicine and Occupational Medicine. As an associate professor at the George Washington University School of Public Health, he founded the Center for Risk Science and Public Health, practiced clinical occupational and environmental medicine, and was involved with public health education.

Balbus became chief health scientist at the Environmental Defense Fund in 2002, maintaining academic appointments at the John Hopkins Bloomberg School of Public Health and at George Washington University.
He has served as a member of several federal advisory committees, including EPA’s Science Advisory Board and Children’s Health Protection Advisory Committee and the National Academy of Sciences Board on Environmental Studies and Toxicology. He continues to serve on the Institute of Medicine Roundtable on Environmental Health Sciences, Research, and Medicine and as chair of the Monitoring and Surveillance work group for the National Conversation on Public Health and Chemical Exposures.

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

**Androphy and Burr Appointed to Senior Posts at NIEHS**

*By Eddy Ball*

During the final weeks of 2009, NIEHS announced the appointments of Deputy Ethics Counselor Bruce Androphy, J.D., and Administrative Management Branch Chief Matt Burr to senior posts at the Institute.

With his appointment in the Office of the Director, Androphy will provide on-site consultation for NIEHS personnel to achieve the highest level of compliance with NIH ethics guidelines. As Chief of the Administrative Management Branch in the Office of Management, Burr will lead the efforts of the Institute’s integrated administrative officers and staff, who provide support to employees across the Institute.

**Androphy brings 20 years of government ethics experience**

Prior to joining NIEHS, Androphy served for nearly three years as the first executive director of the Tennessee Ethics Commission, established in 2006 in response to the Tennessee Waltz bribery scandal. In that role, he oversaw the Commission staff, was responsible for the Commission’s operations and mission, and advised the Commission members. He dealt extensively with members of the Tennessee state legislature and legislative lobbyists (see Androphy in action in a March 2007 YouTube video).

Before assuming his position in Tennessee, Androphy was general counsel to the New York State Ethics Commission, where he worked for almost 17 years. As general counsel, he was involved in issues surrounding state-sponsored scientific research. He is a member of the Council on Governmental Ethics Laws (COGEL), an international government ethics society that includes NIEHS as a member organization.

A graduate of the University of Pennsylvania, Androphy received his law degree from George Washington University National Law Center in Washington, D.C.
Burr worked at several NIH offices and institutes

Burr has been at NIH in Bethesda since 1991, serving in a variety of extramural and intramural program positions. Early in his career, he entered the NIH Management Intern Program, which allowed him to gain broad administrative experience at four Institutes and the NIH Office of the Director.

Burr later served as a grants management analyst for the National Cancer Institute (NCI) before beginning his career as an administrative officer with NCI’s clinical research program. During the past decade, he served as deputy chief of the Administrative Services Branch at the National Eye Institute, as co-director of the Office of Intramural Management at the National Human Genome Research Institute (NHGRI), and most recently as Chief of the Administrative Services Branch at NHGRI.

Burr has also served on a number of NIH-wide committees and is a past recipient of the NIH Director’s Award. A native of Maryland, Burr is a graduate of the University of Maryland at College Park.

Seminar Reviews Public Health Role of Congressional Oversight

By Brian Chorley

During an invited lecture on Dec. 15 at NIEHS, Paul Jung, M.D., discussed his experience as a public health investigator for the U.S. House Committee on Energy and Commerce and outlined public health aspects of the congressional oversight process. Jung is a commander in the U.S. Public Health Service Commissioned Corps. Hosted by NIEHS/NTP Director Linda Birnbaum, Ph.D., his talk was titled “Inspecting the Sausage: Congressional Oversight and Environmental Health.”

When he opened his talk, Jung explained his title by referring to the famous Otto von Bismarck quote comparing legislation to sausages — “It’s better not to see them made.” He then compared the messy process of making laws to the more streamlined process of oversight, which strives to ensure that once Congress enacts laws, they function as intended to serve the general good.

Jung’s committee has oversight for much more than energy and commerce

Despite what the name implies, the Committee on Energy and Commerce oversees a broad jurisdiction. To reflect this, Jung lightheartedly suggested the committee change its name to the “Committee on...”
Health Care, Medicare, Pharmaceuticals, Health, Communications, Wireless Services, Internet, Consumer Protection, Nuclear Regulation, and College Football Bowl Championship Series.”

The Committee has been active for over 200 years and is one of the oldest in the House of Representatives. The first article of the constitution gives authority for legislative oversight, and the Committee may use a variety of legal tools including subpoenas, depositions, witness immunity, and even jail time to get the information it needs to carry out its mandate.

Oversight produces direct benefits for consumers

Jung cited some recent cases where the committee influenced procedural change without the need for new federal regulation — using health care examples familiar to the NIEHS research community, including manufacturing with the plastic component bisphenol A (BPA), the operations of the U.S. Environmental Protection Agency’s Integrated Risk Information System (IRIS), and food-related applications of the brominated flame retardant Deca.

In the case of BPA, the simple act of congressional inquiry resulted in a reexamination of both manufacturing practices and federal action concerning BPA levels in food. Jung explained that the U.S. Food and Drug Administration (FDA) currently mandates that BPA — a common component of infant formula can linings — be detected at levels higher than 5 parts per million (ppm). There is mounting evidence, however, that levels below this cutoff could have harmful effects in developing infants and children.

According to Jung, this standard of detection is similar to “measuring the speed of a person’s pitch with a speed gun that only measures it if it’s greater than 100 miles per hour” — a speed that is difficult for even the best of pitchers.

Following the Committee’s inquiry into the use of BPA in infant formula, Jung continued, all four companies agreed to voluntarily remove BPA from their can linings. In addition, the FDA agreed to reassess the BPA threshold.

A long-time advocate of improving public health, Jung stated that the Committee on Energy and Committee is and will continue to be a powerful congressional tool to influence health policy and regulation.

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

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Fellow Receives Lab Animal Medicine Award

By Omari J. Bandele

NIEHS Postdoctoral Fellow Coralie Zegre-Cannon, D.V.M., recently received first-place honors at the 60th annual American Association of Laboratory Animal Science (AALAS) National Meeting held Nov. 8-12 in Denver. Zegre-Cannon received the award for her poster presentation, “Evaluation of Route of Administration and Dosage of Tramadol as an Analgesic in the Rat.”

The AALAS is the premier forum for the exchange of information and expertise in the care and use of laboratory animals. The AALAS National Meeting is the largest gathering of laboratory animal professionals in the world.

Zegre-Cannon works in the NTP Laboratory Animal Management (LAM) Group led by Angela King-Herbert, D.V.M. Her work involves the study of pain management in laboratory animal medicine. Zegre-Cannon identified the optimum dosage and route of administration of tramadol — an analgesic used in human and veterinary medicine — that produces the most effective analgesia in rats. These studies have led to additional evaluation of tramadol in a rat surgical model.

“The first place award was a big surprise for all of us but very welcome,” stated King-Herbert.

In the spring of 2010, Zegre-Cannon will present her work at the American College of Laboratory Animal Medicine (ACLAM) Forum. She also plans to submit a manuscript of her findings to the Journal of the American Association for Laboratory Animal Science (JAALAS).

(Award-winning Postdoctoral Fellow Coralie Zegre-Cannon (Photo courtesy of Steve McCaw)

Friends and Colleagues Remember Pioneering Woman Scientist

By Eddy Ball

Former NIEHS investigator and environmental attorney Carol Ann Masters Schiller, Ph.D., J.D., D.A.B.T., died Dec. 5 in Raleigh at age 68, following a seven-year battle with the rare neurological disease progressive supranuclear palsy (PSP). Surviving are her husband Marvin Schiller, J.D., Ph.D., a son and daughter, and three grandchildren, all of Raleigh.

When she learned of Schiller’s death, NIEHS/NTP Director Linda Birnbaum, Ph.D., echoed the sentiments of Schiller’s friends and colleagues at NIEHS. “Carol was a leader in the field of toxicology and environmental health, marrying her scientific excellence with her legal expertise,” Birnbaum observed. “She was really not only the first, but also one of a kind.”
Schiller was the first woman to receive tenure in the intramural research program at NIEHS

In the course of her work at NIEHS in the Laboratory of Organ Function and Toxicology, Schiller performed seminal research on dioxin, a highly toxic component of Agent Orange. As recently as July 2009, a study on the effects of dioxin on vascular endothelial growth factor cited Schiller’s 1984 findings on dose-related effects of the chemical in mouse strains.

In recognition of her exemplary work, in 1977 she became the first woman scientist to achieve tenure at NIEHS, joining a handful of others in NIH and helping to pave the way for women scientists who would follow. She also served as an advocate for eliminating inequities in the hiring and promotion of women at NIEHS and NIH, in her role as coordinator of the Institute’s Federal Women’s Program.

Her interests took Schiller from the bench to the bar and beyond

Refusing to limit herself to the field of biochemistry, Schiller in 1984 completed a law degree at the University of North Carolina at Chapel Hill (UNC-CH). She earned the respect of her professors, one of whom described her as a “Renaissance Woman.”

A member of the American Society of Biochemists and Society for Toxicology (SOT) since 1979, Schiller gained board certification as a toxicologist in 1985. She also chaired the SOT Legislative Affairs and Regulatory Assistance Committee from 1988 to 1992.

Schiller devoted a lifetime to environmental science and justice

Prior to joining NIEHS in 1975, Schiller completed her Ph.D. at the University of Texas Southwestern Medical School in 1970. She completed a postdoctoral fellowship at the University of Toronto Department of Medicine and served as a research associate in the Department of Biochemistry and Nutrition and the Department of Medicine at UNC-CH.

After earning her J.D. and certification as a toxicologist, Schiller received a Science and Engineering Congressional Fellowship from the American Chemical Society and American Association for the Advancement of Science. She served as an advisor on environmental issues and legislation in the office of New Jersey Senator Frank Lautenberg.

In 2004, Schiller retired as a partner in the Raleigh law firm Schiller & Schiller PLLC. In 2008, the School of Medicine at UNC-CH established the Carol Masters Schiller Distinguished Scholar in Neurology in her honor.

Schiller leaves behind a legacy of scientific research

Schiller’s family also established the Carol Masters Schiller PSP Research Fund at UNC-CH to receive memorial gifts in her honor. Similar in several ways to Parkinson’s disease, PSP may have links to environmental factors, such as exposure to chemicals, which Schiller’s research fund may help scientists better understand.

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Library Hosts Visitors from Russian

By Eddy Ball

As part of their Sister Cities sponsored visit to Durham, a delegation of librarians from Kostroma, Russia spent several hours on Nov. 20 at the NIEHS Library with Library and Information Services Branch Chief Dav Robertson and his colleagues. Robertson described the group’s visit as “a chance for us to reach out to the Durham community” and “an opportunity for them [the visitors] to learn about the ways we provide personalized, specialized services to our scientists here at NIEHS.”

In addition to their tour of the library, the librarians and their coordinator, retired Durham County public librarian Anne Berkley, attended an overview of NIEHS research presented by John Peterson, a public information specialist with the NIEHS Office of Communications and Public Liaison, and a lab tour conducted by NIEHS Reproductive Medicine Group Biologist Wendy Jefferson, Ph.D.

Delegation tours Durham-area libraries

The visitors participated in the independent Open World Leadership Center at the Library of Congress, which enables emerging European leaders to experience American-style democracy at the local level. During their visit, members of the delegation stayed with families in the Durham area who volunteered their hospitality to the Sister Cities of Durham program.

With the objective of learning about public access to government information in various types of libraries, the Russians visited libraries at Duke University, the University of North Carolina at Chapel Hill, Riverside High School, Durham County Library, the State Library of North Carolina, and the North Carolina State Archives in Raleigh. Organizers chose NIEHS as the only special library included on the tour.

The delegates also met with the staff of Representative David Price’s Durham office and officials of the Durham Chamber of Commerce, and visited Durham City Hall.

Now in its tenth year, Open World strengthens international communication

Since its establishment in 1999, the Open World program has served more than 12,000 participants hosted in all 50 states. Delegates range from politicians and non-profit directors to journalists and government administrators.
According to Robertson, the delegation’s experience at NIEHS sparked interest in a possible future exchange involving visits to NIEHS and the neighboring Environmental Protection Agency by people from Kostroma who have an interest in environmental issues.

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NIEHS Is Accepting Applications for Extramural Director

By Eddy Ball

NIEHS began accepting applications for the director of its Division of Extramural Research and Training (DERT) on Dec. 7, with a deadline of Feb. 27, 2010.

The acting incumbent performs a high-level leadership role at the Institute, overseeing operations organized into seven branches and centers and composed of 56 full-time federal employees. DERT is currently responsible for awarding approximately 874 research grants for a total of $388 million.

Candidates must have an M.D., Ph.D. or a doctoral degree in a discipline relevant to environmental health sciences and have a strong publication record and a proven track record of administrative experience and scientific program development.

A search committee headed by Robert Croyle, Ph.D., director of the Division of Cancer Control and Population Sciences at the National Cancer Institute (see related story), will review the applications of qualified candidates.

Interested individuals may access information about duties, qualifications, and application procedures online at the NIEHS jobs website or directly at USAJOBS.

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Kahn Gives Hans L. Falk Memorial Lecture

By Robin Arnette

Each year scientists from the NIEHS Division of Intramural Research (DIR) set aside one of the distinguished guest lectureships to honor their first Scientific Director Hans L. Falk, Ph.D. The lecture series features investigators who have made significant contributions to environmental health sciences research. This year’s speaker, C. Ronald Kahn, M.D., presented “Genes and Environment in the Epidemic of Diabetes and Obesity.” DIR Deputy Scientific Director Bill Schrader, Ph.D., hosted the Dec. 8 event.

Kahn noted that the average number of new cases of diabetes in the U.S. increases by one million people each year. The factor that bridges both diabetes and obesity is insulin resistance — a condition in which fat, muscle, and liver cells don’t use insulin properly. Insulin resistance is also a problem for a group of disorders collectively known as metabolic syndrome (see text box).

Although he believes that genes play a vital role in these illnesses, Kahn considers the environment to be more of a factor. “While 30,000 genes may be involved, there must be 300,000 or three million environmental impact factors,” he maintained. “The environment will interact with these genes in subtle, sometimes overt, ways.”

Identifying the relationship between genes and the environment

In a non-diabetic, insulin turns off glucose production in the liver and stimulates glucose uptake in muscle tissue and fat, resulting in lower blood glucose levels. However, in a person with type 2 diabetes or metabolic syndrome, the liver, muscle, and fat are insulin resistant, which means insulin no longer turns off hepatic glucose production, and fails to stimulate glucose uptake in muscle and fat. As a result, glucose levels in the blood increase, and cells have altered metabolism.

Metabolic syndrome is a cluster of risk factors

- glucose intolerance or type 2 diabetes
- central obesity
- hypertension
- dyslipidemia (abnormal concentrations of lipids or lipoproteins in the blood)
- accelerated atherosclerosis (plaque buildup within arteries)
- hepatic steatosis (fatty liver)
- gall stone formation
- reproductive dysfunction

The condition is associated with negative health outcomes

- Alzheimer’s disease
- impaired longevity
- increased incidence of some cancers
To study the interaction between genes and the environment in insulin resistance and metabolic syndrome, Kahn’s lab used multiple mouse models, three of which he discussed in the lecture — a tissue specific knockout mouse lacking insulin signaling in the liver, two natural strain variants, and a single normal mouse strain with a modified essential amino acid in its diet.

The liver insulin-resistant knockout (LIRKO) mice constituted the tissue specific knockout model. Because the LIRKO mouse had an inactivated insulin receptor gene in its liver, the liver couldn’t sense insulin and behaved like the liver of a diabetic animal. The LIRKO mice exhibited a diabetic glucose tolerance curve, but normal blood cholesterol levels. When Kahn modified the environment by switching the diet of LIRKO mice from low fat to high fat, they developed extensive atherosclerosis and experienced a dramatic increase in serum cholesterol, from 70 to 700 milligrams per deciliter (mg/dl).

In the second group of studies, Kahn investigated the difference between C57Bl/6 mice and 129/Sv mice subjected to a high fat diet or to genetic defects in insulin signaling. In both cases, the C57Bl/6 mice demonstrated more severe insulin resistance and, in the case of the genetic defects, resulted in 90 percent of the C57Bl/6 mice developing diabetes within six months. Only 10 percent of the 129/Sv mice manifested the disease. A Gene Network Analysis determined that one of the most important differences was the inflammatory response genes in the adipose tissue of C57Bl/6 mice, which exhibited increased expression with age or high-fat diet, while the inflammatory genes of 129/Sv mice didn’t show an increase. This finding is important because inflammation and the response to inflammation is part of what creates insulin resistance.

To answer whether changing a single nutrient could impact insulin resistance and obesity, Kahn split C57Bl/6 mice into three feeding groups over a 12-week period: low fat, high fat and high fat with double the amount of the amino acid leucine. Mice that ingested the double amount of leucine had improved insulin signaling and glucose tolerance, as well as reduced inflammation and fat.

Kahn concluded, “If one little amino acid can do this much to metabolism, think of what the other three million things in the environment can do regarding signaling and metabolic syndrome.”

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Grantee Explores Right-to-Know in Community-Based Participatory Research

By Negin Martin

On Dec. 1, NIEHS welcomed grantee Julia Brody, Ph.D. as the latest speaker in the Keystone Science Lecture Series sponsored by the NIEHS Division of Extramural Research and Training (DERT). Brody discussed the policy and ethical considerations involved in deciding how and when to report test results to individuals and communities participating in personal exposure assessment studies and what information should be included.

According to Brody, sharing results with communities can help people learn about sources of exposure, so they can take action — both in their own lives and through the democratic process. Positive outcomes of informing participants about exposure data include raising environmental literacy, expanding subjects’ right-to-know, and building trust.

At the same time, researchers must consider the possibility that data could lead to emotional stress, unnecessary or counterproductive interventions, and stigma.

Providing participants’ results builds awareness, trust, and pride

“In traditional clinical ethics, experts decide what to report to study participants, often limiting information to findings that are medically relevant to the individual,” Brody said. “In our studies of emerging contaminants, we don’t know yet what the health implications will be, but we respect our participants’ right to learn their results, consistent with the human research ethics criteria of autonomy, beneficence, and justice.”

As Brody explored this ethical dilemma, she reviewed the approach and findings her team of investigators published in an American Journal of Public Health study in 2007, a Journal of Health and Social Behavior study in 2008, and a review in Environmental Health earlier this year. She proposed strategies for reporting exposure results to maximize benefit and minimize negative outcomes for participants.

Presentation of the report also plays an important role in establishing trust and improving environmental knowledge in a community, Brody explained. Researchers should present their results clearly, take the time to describe what is known, and clearly outline the limitations of the study.
Brody shared her own experiences reporting exposure data to individuals as part of her NIEHS-funded research. In her studies, she found that people wanted to know about their individual results. Volunteers expressed pride in participating in a study that helped their communities, and they were generally surprised by the findings, which showed that indoor pollution builds up from everyday consumer products.

**Research advances outpace ethical guidelines**

Brody explained that recent studies have discovered increasing levels of potentially harmful pollutants in people and raised public awareness of related health risks. Referring to several examples of the “flood of personal exposure information,” Brody noted that the ability to detect chemicals in tissue samples and the environment has advanced faster than the development of ethical guidelines and methods for interpreting and communicating results.

Brody is the executive director of the Silent Spring Institute. Established in 1994, Silent Spring is a collaborative effort between scientists and activists to identify environmental factors that influence women’s health and contribute to breast cancer.


(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.)
Slight Nerve Effect with Elemental Mercury Exposure from Fillings

By Laura Hall

On Dec. 4, Alfred Franzblau, M.D., discussed the effect of chronic low-level elemental mercury (Hg) exposure on dental professionals. In his study, researchers measured urine mercury concentrations and nerve function in 2,974 volunteers and found a very slight, but significant deleterious effect on sensory nerves. The University of Michigan (UM) professor’s talk was titled “The Impact of Low-Level Mercury Exposure on Peripheral Nerve Function.”

“I’ve got a bunch of mercury fillings, but I’m not going to rush around and get them taken out,” said Franzblau. “I’m not worried about it. The effect is so small that I’m reassured about mercury amalgam effects for adults.”

However, Franzblau said that this small nerve effect in adults raises some concern about elemental mercury exposure in more susceptible groups, such as children. In particular, the fetus with its developing nervous system could be at risk from maternal exposure. Also, exposure from organic mercury is not eliminated from concern with this study.

Dental amalgams are most common Hg exposure

Restorative tooth fillings, dental amalgams, are the most common source of elemental mercury exposure for the general population. Franzblau pointed out that the amalgams are 50 percent Hg — one large filling alone may contain as much as one gram of Hg. Previous studies have shown that the amount of Hg in the urine increases linearly with the number of fillings a person has.

In addition to exposure from their own fillings, dentists and dental hygienists are occupationally exposed to Hg when they make the amalgams used for their patients.

Mercury is a nerve poison

Franzblau explained that mercury occurs naturally and exists in various forms that are all poisonous to the nervous system. The indicator, or biomarker, for human exposure from elemental mercury is the urine mercury concentration. In contrast, the hair is used as the biomarker for organic mercury exposure such as that caused by eating contaminated fish.
Nerve damage measurements
Franzblau used measurements of nerve conduction to determine nerve damage.

Scientists tested the median nerve by sending an electric signal down the nerve between electrodes placed on the index finger and farther down the arm. The ulnar nerve was similarly measured by using the fifth finger. Reduced amplitude, the size of the electronic signal peak, and longer latency, the time for the signal to travel in milliseconds, indicate nerve damage.

The median nerve is the nerve affected in carpal tunnel syndrome, a common cause of hand discomfort and functional impairment.

Mercury concentration in dental professionals
The dental professionals had a mean urine Hg concentration of 3.63 microgram per liter, which is approximately twice the urine Hg concentration that women in the general population have. The 1,748 women tested for urine Hg in another study, the National Health and Nutrition Examination Survey (NHANES), had a mean concentration of 1.55 microgram per liter.

The study used information from the NHANES investigations on urine mercury concentration and other parameters as a control to represent the general population.

It combined data collected for 10 years at the American Dental Association (ADA) annual meetings on the dental professionals. The data collected by Franzblau and his colleagues at the UM, ADA, and SmartHealth, Inc. allowed this study to be the largest of its kind, enabling them to see the slight adverse effect.

Slight nerve damage
Increased urine Hg resulted in very slight but significant nerve damage. The study results showed that for every one microgram per liter increase in urine Hg of the dental professionals, the median sensory nerve latency increased by 0.006 milliseconds. Increasing Hg exposure resulted in slower nerves, but the amplitude of the nerve signal was unaffected.

Franzblau and clinical occupational medicine
Franzblau studies occupational musculoskeletal, neurological, and respiratory disease. NIEHS/NTP Director Linda Birnbaum, Ph.D., introduced Franzblau as her long-time colleague who “has broad experience in occupational medicine and epidemiology and has done a lot of work with carpal tunnel syndrome.”

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor.)
A new NIH-funded study involving data from more than 20,000 individuals has uncovered several DNA sequences linked to impaired pulmonary function. The research, an analysis that combined the results of several smaller studies, provides insight into the mechanisms involved in reaching full lung capacity. Published online in Nature Genetics, the findings may ultimately lead to a better understanding of lung function and diseases such as asthma and chronic obstructive pulmonary disease (COPD) — the fourth leading cause of death in the United States.

“We have known for a while that genetic factors put some people at risk for lower lung function — a factor in COPD and a risk for early mortality. But, we did not know which specific genetic regions were involved,” said Stephanie London, M.D., Dr.P.H., NIEHS senior investigator and a senior author on the paper. “These findings point to specific gene regions.”

Findings may also offer insight into other diseases
Impaired lung function is a hallmark of COPD and other lung diseases. But it is also linked to mortality from a wide range of other diseases, including cardiovascular disease and cancer. So knowing some of the genes involved is a first step toward understanding the relationship between lung function and mortality, as well as developing new interventions to manage lung diseases.
Leveraging our investment in collecting these samples has led to new findings and will help focus future research efforts,” said James P. Kiley, Ph.D., director of the Division of Lung Diseases at the National Heart, Lung, and Blood Institute (NHLBI).

The researchers used data from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium. CHARGE is an ongoing study — a group of groups — that combines genome-wide association study (GWAS) results from several population-based studies. Pooling data from many studies gives much greater power to find the specific genes involved than looking at any one study alone.

**The study analyzed data from participants in four earlier large-cohort studies**

The GWAS approach involves measuring hundreds of thousands of genetic variants, in thousands of individuals, in hopes of finding novel genetic variations associated with specific diseases or conditions.

This meta-analysis provided data from more than 20,000 participants. The individual studies included three US-based population studies supported by the NHLBI — the Artherosclerosis Risk in Communities, the Cardiovascular Health Study, and the Framingham Heart Study — and the Rotterdam Study in the Netherlands.

The researchers focused on finding genetic commonalities in DNA that lead to some people having lower lung function than others of the same age, gender, race, size, and smoking history.

One way researchers determine airflow obstruction is by using a machine called a spirometer to measure how much air a person breathes in and out, as well as how fast it is blown out, or expired. Spirometry is an important tool used to diagnose asthma, pulmonary fibrosis, cystic fibrosis, and COPD, as well as the impact of environmental exposure on lung health. In disease, the ratio between forced expiratory volume (FEV1) and forced vital capacity (FVC) — an indicator of airflow obstruction — is abnormally low.

**Research has potential applications in environmental public health**

“This is a beautiful example of how modern genomic approaches can unearth valuable new insights from previous research,” said NIEHS/NTP Director Linda Birnbaum, Ph.D. “It sets us on a course for learning much more about how lung diseases develop and how environmental triggers like smoking and air pollution work in combination with genes.”


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

**First author Dana Hancock, Ph.D., is a postdoctoral fellow in the NIEHS Genetics, Environment and Respiratory Disease Group headed by London. She recently received an NIH Fellows Award for Research Excellence. (Photo courtesy of Steve McCaw)**
Increased Risk of Parkinson’s Disease with PON1 Gene Variant and Pesticide Exposure

By Laura Hall

University of California, Los Angeles (UCLA) researchers report that study participants with two copies of a common gene variant showed an increased risk of Parkinson’s disease (PD) when exposed to pesticides used in agriculture. NIEHS partially funded the epidemiologic study that focused on the paraoxonase 1 (PON1) gene, which codes for an enzyme that metabolizes organophosphate pesticides.

“Our research suggests that the impact of organophosphate exposure depends on the activity of a detoxifying enzyme produced by the body,” said senior author Beate Ritz, M.D., Ph.D. Ritz, professor and vice chair of the UCLA Epidemiology Department, co-directs the NIEHS-funded UCLA Center for Gene-Environment Studies in Parkinson’s Disease.

The authors assessed pesticide exposure in a new way and showed that understanding gene-environment interaction is necessary to explain PD etiology.

PD etiology

PD is a progressive neurological movement disorder. Both genetic and environmental factors probably cause PD but usually are studied separately. The insecticides measured in the UCLA study — the organophosphates diazinon, chlorpyrifos, and parathion — are neurotoxic and implicated in PD by earlier studies.

Pesticide exposure

The UCLA study used participants from three rural California counties known for extensive agricultural pesticide application. A large percentage of participants were exposed to the pesticides from living near agricultural areas.

After application, pesticides can drift in the air, be volatilized, and settle in water or soil. Humans and pets can bring pesticides into houses on clothing and fur. Although organophosphate pesticides have short half lives of a few days on foliage, other studies have shown they can concentrate 10 to 100 times higher indoors than outdoors and persist for months in the soil.

New approach to assess exposure

The authors used a novel, improved approach to determine agricultural exposure from different organophosphate pesticides. They assessed participant pesticide exposure using a geographic information system (GIS) tool, data from California Pesticide Use Reports, land-use maps, and geocoded residential historical locations. This approach allowed time-specific average exposure estimates for each participant and each study pesticide. The researchers determined agricultural exposure to diazinon, chlorpyrifos, and parathion between 1974 and 1999 separately for each subject.

“Studying genetics alone or environment alone is like looking through only one eye — you have limited depth perception,” explained Ritz. “What you observe is simpler because there are only two dimensions, but it is not an accurate representation of the world.” (Photo courtesy of Georges Mollon)
“This GIS tool for determining exposure to pesticides is a vast and important improvement over the more traditional method of asking study participants to recall past exposure — a notoriously biased method of collecting exposure data that has been used by almost all previous studies of pesticides,” Ritz explained.

**Genetic variant and increased risk of PD**

The genetic variant studied is fairly common in the Caucasian population. The variant has a methionine substitution for leucine at the amino acid position 55 of the PON1 protein. This substitution is known to decrease the protein’s ability to metabolize certain pesticides. In the study group, 14 percent of the pesticide-exposed subjects and 10 percent of the control subjects had the genotype with two copies of the methionine PON1 variant — the MM PON1-55 genotype.

Individuals with the variant genotype have an increased risk of Parkinson’s disease with exposure to specific insecticides. Participants with the MM PON1-55 genotype and exposed to diazinon or chlorpyrifos showed a twofold increased risk of Parkinson’s disease (PD) compared to exposed subjects with wildtype genotype or only one variant copy or non-pesticide exposed subjects. The authors found no increased risk of PD with parathion exposure regardless of genotype.

**Finding susceptible subpopulations**

“Our findings highlight the importance of considering gene variants when studying the risk of environmental exposures,” said first author Angelika Manthripragada, Ph.D., now an epidemiologist at the U.S. Food and Drug Administration. “More research is needed to examine the combined effect of environmental exposures with other PON1 gene mutations or variants of other genes involved in xenobiotic metabolism to gain further insight into PD etiology.”

The authors pointed out that human genetic variations can cause some individuals to be more vulnerable to environmental exposures. Identifying these vulnerable subpopulations raises awareness of the potential need to protect these groups.

*Citation: Manthripragada AD, Costello S, Cockburn MG, Bronstein JM, Ritz B. 2010. Paraoxonase, agricultural organophosphate exposure, and Parkinson disease. Epidemiology 21(1):87-94.*

(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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**Group Gathers for Asbestos and Related Fibers Meeting**

*By Rebecca Wilson*

NIEHS scientists, federal partners, representatives from industry, and members of the academic community gathered in Chapel Hill, NC, Dec. 16–17 to discuss the state of the science on asbestos and develop recommendations for future work.

The NIEHS, U.S. Environmental Protection Agency (EPA), Agency for Toxic Substances and Disease Registry (ATSDR), and NIEHS Superfund Research Program (SRP) sponsored the two-day meeting.
NIEHS/NTP Director Linda Birnbaum, Ph.D., opened the public session of the meeting by stressing the importance of moving beyond the traditional definition of asbestos. She pointed to three central questions participants should strive to better understand:

- What do researchers know about the modes and mechanism of actions of all fiber characteristics on health outcomes?
- What characteristics of these fibers drive the health effects of exposure?
- What future research is necessary to answer remaining data gaps?

More interdisciplinary training and low dose research needed

The workshop began with six small working-group sessions, with each addressing specific aspects of research or health endpoints in depth. The topics included pulmonary and non-pulmonary health effects, the role of gene mutation, factors affecting disease susceptibility, and exposure anomalies.

After they summarized the state of the science in these areas during a plenary presentation of key findings, workshop participants met in four interdisciplinary groups to address confidence areas, data gaps, and research needs. Among the recommendations was a nearly unanimous call for graduate students to be trained in interdisciplinary research methods to interact with scientists from a wide range of disciplines.

When discussing data gaps and research needs, researchers expressed a need for studies conducted at ever-lower doses, in response to industrial exposure patterns seen since OHSA began regulating asbestos in the 1970s. Most laboratory and environmental exposure case studies involve high doses, far above the levels encountered in modern occupational settings. However, even at low doses, asbestos may cause health problems.

While most research to date has involved diseases of the heart and lungs, workshop participants stressed the need to investigate endpoints beyond these two systems. This is important because, as Birnbaum pointed out, “If you only look where you’ve always looked, that’s all you’re ever going to find.”

Meeting conclusions will be published

Writing groups will compile notes and materials from the workshop into a consensus document for publication in a peer-reviewed journal. In addition, scientists attending the workshop prepared six white papers in advance of the meeting that they will submit for publication in a peer-reviewed journal as a set of state-of-knowledge review articles.

(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.)
In her discussion of pleural endpoints, Brown University’s Agnes Kane, M.D., Ph.D., described the anatomical differences among species that make extrapolation of data from asbestos experiments to humans so challenging. “There’s a lot more we don’t know about these [asbestos and related mineral fiber] diseases than we do know.” (Photo courtesy of Steve McCaw)

Among several scientists from NIEHS and NTP at the meeting was Scott Masten, Ph.D., above, who participated in planning the workshop. (Photo courtesy of Steve McCaw)

Columbia University Professor of Radiation Oncology Tom Hei, Ph.D., joked about the graying of his colleagues in asbestos research. “We do need fresh blood in the community,” he said. (Photo courtesy of Steve McCaw)

NIEHS attendees included, left to right, Health Scientist Administrators Mike Humble, Ph.D., Heather Henry, Ph.D., and Acting Deputy Director Steve Kleeberger, Ph.D., who is a respiratory biologist. (Photo courtesy of Steve McCaw)

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This Month in EHP

By Eddy Ball

The January issue of *Environmental Health Perspectives (EHP)* is sure to catch the attention of sleep-challenged readers with its cover stories on light exposure, circadian rhythm, and sleep — “What’s in a Color? The Unique Human Health Effects of Blue Light” and “Lose Sleep, Gain Weight: Another Piece of the Obesity Puzzle.”

The stories examine some of the human health effects unique to the influence of blue light on regulation of the body’s inner circadian clock, as well as the connection between chronic lack of restorative sleep and a host of metabolism-related health problems, including obesity and metabolic syndrome.

Also appearing in EHP this month are several new studies:

- **Aerosolized Nanomaterials in Environmental Studies** — exploring the potential for laboratory workers to be exposed to airborne engineered carbonaceous nanomaterials during routine material handling

- **Summer Heat and Mortality: How Hot Is Too Hot?** — examining 10 years of all-cause mortality data (1997–2006) for New York City residents to identify the most appropriate criteria for triggering health alerts

- **Concentrations of the Active Metabolite of Tamiflu in Wastewater Samples** — investigating levels of the flu-medication metabolite in sewage treatment plant wastewater and describing a sewage treatment method that may reduce environmental contamination and help prevent the emergence of drug-resistant influenza strains

- **Childhood Brain Tumors and Insecticide-Metabolism Genes** — analyzing population-based case–control data to assess whether childhood brain tumors are associated with select functional genetic polymorphisms

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Dan Littman Will Give Next Distinguished Lecture

By Eddy Ball

The NIEHS 2009–2010 Distinguished Lecture Series will feature a talk January 19 by Dan Littman, M.D., Ph.D., on the “Role of Environmental and Intrinsic Factors in the Differentiation of Inflammatory T Cells.” Hosted by NIEHS Laboratory of Respiratory Biology Principal Investigators Anton Jetten, Ph.D., and Donald Cook, Ph.D., Littman’s lecture begins at 11:00 a.m. in the Rodbell Auditorium at NIEHS.

Littman is the Helen L. and Martin S. Kimmel Professor of Molecular Immunology and professor of Pathology and Microbiology at the New York University (NYU) School of Medicine. He is also an investigator in the Howard Hughes Medical Institute Program in Molecular Pathogenesis of the Skirball Institute of Biomolecular Medicine at the NYU Langone Medical Center.

Expert in the field of T lymphocyte development and retroviral pathogenesis

His laboratory investigates the molecular events underlying T lymphocyte differentiation and activation, and how the human immunodeficiency virus (HIV) causes systemic depletion of helper T cells. In both areas, he studies the functions of T cell surface molecules and their interactions with intracellular signal transducing components.

In addition, his lab has been in the forefront of studies determining the role of several transcription factors, including the retinoid-related orphan receptor ROR-gt, in T cell lineage determination and the potential of ROR-gt as a target in the treatment of autoimmune disease. Littman consistently publishes in top tier journals and is frequently invited to present his work at international meetings.

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Researchers Map the First Human Epigenome

A comparison of the epigenomes of embryonic stem cells and fibroblasts shows a pattern of methylation unique to stem cells according to a study supported by NIEHS. The novel methylation pattern may help to explain how stem cells maintain their pluripotent state.

The research team developed a high-throughput method to determine the methylation status of every cytosine molecule in the genome and to layer the resulting epigenomic map onto the genome it regulates. The technique was then applied human fibroblasts and human embryonic stem cells to determine if the epigenomes differed between differentiated cells that perform a specific job and cells that have the potential to become any cell type. The results showed that the fibroblasts had a high degree of expected CG-methylation, but the stem cells showed a surprising result. Their methylation pattern exhibited non-CG methylation, which previously had been considered a laboratory artifact.

To confirm the results, the experiments were repeated in a second embryonic stem cell line and in fibroblasts reprogrammed into induced pluripotent stem cells. Both of these cell-types exhibited the same high level of non-CG methylation.

This study provides the first complete high-resolution map of an epigenome superimposed on the human genome. This knowledge could be extremely valuable for understanding and developing treatments for diseases.


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Metal and Diesel Exhaust Linked to Respiratory Symptoms in Children

Perinatal exposure to metals from heating oil combustion and diesel exhaust particles in ambient air is associated with respiratory disorders in young inner city children, according to an NIEHS-funded study. The study is among the first to link metal exposure with respiratory symptoms in young children.

The study was conducted with children living in the South Bronx and Northern Manhattan. Pollutant levels and the presence of respiratory symptoms were compared. The research team found that exposures to the metals vanadium
and nickel are risk factors for wheezing in young children. Residential oil combustion for heating is a major source of these metals. Elemental carbon, which is an indicator of exposure to diesel exhaust, was found to be linked to increased coughing, but only during the traditional cold and flu season, defined as September through April.

The findings increase the understanding of the effects of specific pollutants on the respiratory health of young children. The results are of special concern because the levels of nickel found in the air in the study areas are among the highest in the U.S., as are the rates of pediatric asthma. The children in this study will be followed to see if these effects persist and are associated with increased rates of respiratory diseases at later ages.


Spatial Epidemiology of Abused Drugs

Using wastewater samples from urban and rural areas in Oregon, researchers discovered patterns of illicit drug use that mimic those found in human epidemiologic studies. This study demonstrates the utility of wastewater-derived measurements of community drug-use and the potential for such measurements to more accurately represent the levels and distribution of drug abuse.

The research was co-funded by the National Institute on Drug Abuse and an NIEHS center grant to Oregon State University.

The researchers used single day samples from 96 municipalities representing 65 percent of the population of Oregon. The samples were analyzed for methamphetamine, 3,4 methylenedioxyamphetamine (MDMA), and a metabolite of cocaine. The wastewater-derived drug load was consistent with expected drug-use patterns.

The cocaine metabolite was significantly higher in urban areas and below detection in many rural areas, whereas methamphetamine was found in all areas with no differences between urban and rural samples. MDMA was found in measurable levels in less than half of the municipalities, with higher amounts in urban areas.


Traffic and Childhood Asthma

A study conducted by NIEHS grantees at the University of Southern California estimates that nine percent of all childhood asthma cases in Long Beach and six percent in Riverside are attributable to traffic proximity. The study also found that ship emissions from the Los Angeles-Long Beach port complex contributed greatly to asthma exacerbations. The researchers estimated that 21 percent of yearly asthma-related bronchitis is caused by elevated nitrogen dioxide levels from ships.
Although there is an extensive body of research on the effects of traffic proximity on asthma risk, this study is one of a few that estimated the number of cases, the so-called burden of disease, associated with traffic in specific high risk communities. The researchers conclude that the traditional methods of estimating the burden of air pollution-related diseases highly underestimated the true effect. The results show that more than 2,200 cases of childhood asthma in Long Beach and Riverside are linked to living within 75 meters of a major road or highway. In addition, the severity of the asthma is greater, resulting in more frequent visits to a clinic or emergency room.

Unlike regional air pollutants, local traffic-related pollutants are not currently regulated. The authors conclude that traffic-related health effects should have a central role in planning, positioning, and expansion of transportation corridors.


(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 Laura Hall and Omari Bandele

- Initiation of Repair of Random DNA Double Strand Breaks Requires RAD50
- New Pathway for Viral Regulation of the Cell Cycle Through TGF-ß
- Methoxyacetic Acid Disrupts Endogenous Estrogen Receptor Signaling
- Structural Studies Reveal Specificity of mRNA Regulatory Proteins

Initiation of Repair of Random DNA Double Strand Breaks Requires RAD50

DNA double-strand breaks (DSBs) are important sources of genome stability and disease. Researchers from NIEHS and Indiana University-Purdue University Indianapolis found a way to track early events in repairing DSBs caused by gamma irradiation in yeast using pulsed field gel electrophoresis (PFGE).

They showed that the initial step in repair of random DSBs involved resection — the removal of one of the strands at a DSB end. This step depends on the MRX complex composed of the Mre11, Rad50, and Xrs2 proteins. Yeast lacking Rad50 or Mre11 were slow in generating resected ends — a key step in DSB repair in most organisms.

While much is known about DSB mechanisms based on model systems employing a unique DSB, little is known about the random breaks created by environmental agents, especially gamma radiation commonly used in cancer radiation treatment. The authors incorporated circular chromosomes into yeast cells, then irradiated them to cause DSBs that changed the chromosomes to a linear form that that could be detected with PFGE.
Surprisingly, the subsequently resected linear chromosomes with single-stranded DNA tails were less mobile in the gel than those without a tail. This mobility shift provided a unique opportunity to examine repair by tracking the appearance of the tails and disappearance of the linearized chromosome as repair was completed.


New Pathway for Viral Regulation of the Cell Cycle Through TGF-β

NIEHS researchers have shown that the cytokine, transforming growth factor beta (TGF-β), enhanced respiratory syncytial virus (RSV) replication by inducing cell cycle arrest in human lung epithelial cells. Furthermore, RSV infection induced the expression of TGF-β enhancing its own replication.

Blocking TGF-β with TGF-β antibody or inhibitor, or using a TGF-β receptor signaling inhibitor, prevented the RSV-induced cell cycle arrest. This effect, resulting from signaling cytokine or receptor blockage, suggests a TGF-β autocrine pathway.

RSV, a single stranded RNA virus, is a common cause of severe respiratory infections in children and is associated with the development and exacerbations of asthma. Previous genetic studies have shown an association between asthma phenotype and TGF-β, a cytokine or cell signaling protein involved in regulation of the cell cycle.

TGF-β is also involved in fibrosis, inhibiting inflammation and regulating immune function. Aberrant expression of TGF-β in the lung leads to fibrosis, airway remodeling, and mucus hypersecretion like that found in asthma. The NIEHS study shows a connection between RSV and TGF-β, which suggests a mechanism to explain how RSV infections can lead to the development and exacerbations of an asthma phenotype.


Methoxyacetic Acid Disrupts Endogenous Estrogen Receptor Signaling

A collaborative study by researchers from NIEHS and the German Cancer Research Center in Heidelberg, Germany demonstrates that methoxyacetic acid (MAA), a short-chain fatty acid, exerts antiestrogenic effects by reducing the levels of endogenous estrogen receptor-alpha (ERα). The authors also show for the first time that MAA reduces estrogen-induced expression of ERα target genes.

MAA is the primary metabolite of ethylene glycol monomethyl ether (EGME), an industrial solvent. Exposure to EGME is associated with reproductive toxicity in humans and animals, which is attributed to MAA. Using human cells and mice as models, Korach and colleagues sought to gain insight into the
molecular mechanisms of MAA activity on the estrogen-signaling pathway. They report that the MAA-induced antiestrogenic effects observed in the study are similar to those seen with other members of the short-chain fatty acid family, which suggests a common mechanism of action.

The effects of MAA on endogenous ER are consistent with the reproductive abnormalities reported following EGME exposure in humans and animals. These results suggest that MAA-induced attenuation of endogenous ERα signaling may likely contribute to these toxicities.


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**Structural Studies Reveal Specificity of mRNA Regulatory Proteins**

Researchers from NIEHS and the University of Wisconsin recently provided the first structural explanation for the unique specificity of a PUMILIO/fem-3 binding factor (PUF) protein for distinct RNA targets. This study suggests that PUF protein-induced base flipping may be a common mechanism utilized to distinguish specific RNA targets.

Hall and colleagues utilized the RNA-binding domain of a _Caenorhabditis elegans_ PUF protein, FBF-2, to capture protein-RNA complexes. The FBF protein is a founding member of the PUF family of mRNA regulatory proteins. It regulates multiple mRNAs that are critical for stem cell maintenance and germline development.

The authors used six different RNA sequences, including four natural mRNAs to probe these interactions. Through structural and biochemical experiments, the group determined that the positions of flipped and specifically recognized bases within target sequences contribute to FBF-2 sequence specificity.

Together with other PUF protein structural studies, this work provides a model of PUF protein specificity for RNA and its evolution.


(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the Environmental Factor. Omari J. Bandele, Ph.D. is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

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CFC Has Banner Year at NIEHS

By Eddy Ball

By the time organizers completed the accounting in early December, the 2009 Combined Federal Campaign (CFC) at NIEHS exceeded its goal by more than $20,000, with a total of $91,392 in pledges. Following its kickoff on Sept. 28, the campaign continued through Nov. 20.

The numbers represent a 24 percent increase over pledges for the 2008 campaign and is the third highest amount ever pledged at the Institute — exceeded only by the campaigns in 2001, when the terrorist attack at the World Trade Center inspired record giving, and in 2005, as NIEHS and the nation responded to the devastation in the aftermath of Hurricanes Katrina and Rita along the Gulf Coast.

Organizers praised the level of participation

A total of 178 employees pledged to the 2009 CFC, representing 26 percent of the Institute’s full-time equivalency. Of that number, 73 percent, 130 employees, utilized the online pledge system. Employees Cheryl Thompson and Robin Mackar, working with contractors Paul Cacioppo and Jason Suter, developed the user-friendly NIEHS Web site that proved so popular.

“Even in difficult economic times,” said CFC Co-chair Rachel Frawley, “NIEHS employees consistently show their generous spirit, acknowledge the benefits that they have, give back to their communities, and support more than 2500 non-profit organizations.”

The 2009 CFC benefited from the talent and support of volunteers Institute wide

The record level of pledging is a testament to the concerted efforts of the co-chairs for the 2009 CFC campaign — Veronica Godfrey Robinson and 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 tailgating 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. The 2009 kickoff events took advantage of the catchy campaign statement “I Can... Now More Than Ever,” free samples from a chili cook-off contest, and a football motif to boost employee turnout at events at the Rall Building and Keystone.
Frawley and Godfrey Robinson both emphasized the team effort that led to the successful campaign. They pointed to support from NIEHS Deputy Associate Director in the Office of Management Chris Long and NIEHS/NTP Director Linda Birnbaum, Ph.D., who sent a series of all-hands e-mails to encourage employee participation.

In her final campaign message to employees, Birnbaum wrote, “How exciting for our Institute! Thank you to everyone who volunteered to assist with this year’s campaign. I personally appreciate your hard work and dedication. I especially thank those who contributed to CFC. Your contributions will help make a difference and for that you should be proud. I am certainly proud of our entire NIEHS family. Let’s keep up the great work!”

Director’s Awards Ceremony Recognizes Employee Achievements

By Eddy Ball

NIEHS employees, friends, and family turned out in force on Dec. 17 in Rodbell Auditorium to watch as NIEHS/NTP Director Linda Birnbaum, Ph.D., presented Director’s Awards to employees who made meritorious contributions to the NIEHS mission in 2009. NTP Deputy Program Director for Science Nigel Walker, Ph.D., served as the master of ceremony at the event.

NIEHS Acting Deputy Director Steve Kleeberger, Ph.D., Deputy Associate Director for Management Chris Long, Acting Scientific Director John Pritchard, Ph.D., and Interim Director of DERT Gwen Collman, Ph.D., announced the Merit Awards for members of their divisions and offices.

Program Analyst and NIEHS Awards Coordinator Diane Crawford organized the event and contacted the winners prior to the ceremony. Following the ceremony, employees and guests enjoyed refreshments and music at the annual NIEHS International Day holiday reception in the NIEHS cafeteria.

NIH MERIT AWARD WINNERS

Office of the Director (OD)
• Tonya Stonham
• Linda Lindley
• David Fargo

Cross-divisional Collaboration (OD)
• Laurie Johnson, Gwen Collman Rachel Gross, Pat Mastin, Michael Loewe, Margarita Roque. Dorothy Duke, Benny Encarnacion and Susan Hart

Office of Management (OM)
• Nancy Powell, Marcus Bell, Diane Crawford, and Ellen Moul
• Heather Nicholas, Charlie Tate, and Rob Levine

Lin Lindley, above, was one of a record number of winners of 2009 NIH Merit Awards honored at the ceremony. (Photo courtesy of Steve McCaw)
Cross-Divisional Collaboration (OM)
- Rhonda Carroll, Vickie Englebright, Frank Williams, Jack Field, Steve Herndon, Versal Mason, Kyle Hawkins, Clyde Hasty, Scott Merkle, Fred Carter, Megan Tozer, Amanda Thompson, Chris Long, Margarita Roque, Debra Del Corral, Mitch Williams, Josee Crowell, Deitra Lunney, Paula Pier, Charlie Tate, Kathryn Woods, and Karen Hunter

Division of Intramural Research (DIR)
- Dori Germolec
- Jack Taylor, Dale Sandler, Lisa DeRoo, Clare Weinberg, Stephanie London, and Paula Juras
- Terry Lewis, Craig Wladyka, Joan Packenham, Edith Lee, and Jane Lambert
- Danica Andrews, Laura Wharey, Stella Sieber, Rickie Fannin, and Kevin Gerrish
- Paul Foster and Dori Germolec
- Deepa Rao, Darlene Dixon, Mark Hoenerhoff, Ron Herbert, Arun Pandiri, Susan Elmore, Mark Cesta, Gordon Flake, Greg Travlos, and David Malarkey

Division of Extramural Research and Training (DERT)
- Jerry Heindel
- Jerry Phelps, Donald Ellis, Pam Clark, Wanda Boggs, James Ray Williams, Aaron Nicholas, Lisa Edwards, Michelle Victalino, Dwight Dolby, Donna Roach, Carolyn Mason, Barbara Gittleman, Natasha Hurwitz, and Carolyn B. Winters
- Linda Bass, Gwen Collman, Dorothy Duke, Margarita Rogue, Chip Hughes, Claudia Thompson, Christie Drew, Pat Mastin, and Bill Suk
- Caroline Dilworth, Sri Nadadur, Ted Outwater, Kathy Ahlmark, Sharon Beard, Mike Humble, Heather Henry, Jennifer Collins, Cindy Lawler, Kimberly McAllister, Liam O’Fallon, Elizabeth Maull, David Balshaw, Martha Barnes, Helena Davis, Kimberly Gray, Astrid Haugen, Jerry Heindel, Annette Kirshner, Jerry Phelps, Les Reinlib, James Remington, Daniel Shaughnessy, Carol Shreffler, Beth Anderson, Fred Tyson, and Lisa Chadwick
- Sally Eckert-Tilotta, Linda Bass, Rose Anne McGee, Leroy Worth, and Michelle Victalino
- Chip Hughes, Ted Outwater, Sharon Beard, James Remington, and Kathy Ahlmark
- Annette Kirshner, Kimberly Gray, Linda Bass, Gwen Collman, Cindy Lawler, and Aaron Nicholas

Unsung Hero Awards
- Rose Anne McGee, Mary Gant, Stephen Cannon, Bill Jirles, Jennie Foushee and Judy Hanson

Peer Awards
- A’tondra Carree, Lisa Edwards, and Fran Wagstaff
Fellows Awards For Research Excellence (FARE)

- Thaddeus Schug, Ryan Dackor, Jim Aloor, Jeffrey Sunman, Andrew Kraft, Abee Boyles, Ritu Rana, Jeremy Smyth, Omari Bandele, Li Qian, Xueqian Wang, David Draper, Aparna Purushotham, Dana Hancock, Erica Lannan, Andres Larrea, Hideki Nakano, Rongqin Ren, Ramendra Saha, and Jeffrey Stumpf

FARE winners gathered for a group photo. With each getting a $1,000 travel award, individually and collectively, the trainees received the most lucrative honors at the event. (Photo courtesy of Steve McCaw)

Staffers Complete Clear Writing Workshop

By Eddy Ball

NIEHS employees enjoyed an opportunity during the first week of December to look at their writing from the distinctive perspective of veteran communications consultant Ginny Redish, Ph.D. Redish is the president of Redish & Associates in Bethesda, who combines her training in linguistics and cognitive psychology with decades of experience helping government agencies and private businesses communicate more effectively in the new world of electronic publishing.

Organized by the NIEHS Office of Communication and Public Liaison (OCPL), the two-day sessions, Dec. 1–2 and Dec. 3–4, drew 30 employees from throughout the Institute to the interactive, hands-on training. Along with staff from OCPL, the National Toxicology Program (NTP), Division of Extramural Research and
Training (DERT), and Office of Management (OM), postdoctoral fellows from several Division of Intramural Research (DIR) labs attended the workshops.

**OCPL plans to offer more workshops in the future**

OCPL Director Christine Bruske Flowers said her office has a waiting list of people eager to attend the next workshop series. “As more and more communication takes place on the internet,” she explained, “more scientists and administrators are coming to realize their writing strategies need to evolve to take advantage of the new medium and produce Web content that works.”

**Participants comment on the workshop experience**

“Dr. Redish’s writing workshop was a great educational experience. Its highly interactive style was effective,” commented DIR Postdoctoral Fellow Omari Bandele, Ph.D. “I am already implementing the tips that she provided. This type of workshop could be beneficial to all postdoctoral fellows.”

“I found this among the best courses I’ve taken at NIEHS, ever, in my 31 years here!” added OM staffer and Grapevine editor Dick Sloane. “Redish emphasized simplicity many times, even when writing for a technical audience. The idea is to get our ideas across efficiently and quickly for readers who usually have little time to spend looking for the message.”

Veteran OCPL Public Information Specialist John Peterson offered an insider’s take on the experience. “No matter how much training and experience writers have,” he said, “they can always benefit by learning fresh ways to make their writing clearer.”

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Trainees Celebrate the Holiday Seasons

By Eddy Ball

A group of the Institute’s youngest scientists accepted an invitation to leave their pipettes behind on December 11 and enjoy a holiday party sponsored by the NIEHS Trainee Assembly (NTA) and the Office of Fellows Career Development (OFCD). Emceed by OFCD Director Diane Klotz, Ph.D., the mood was lighthearted as the trainees decorated cookies, enjoyed seasonal snacks, joked with each other, and socialized.

NIEHS Scientific Director John Pritchard, Ph.D., and Deputy Scientific Director Bill Schrader, Ph.D., dropped in to wish everyone a happy holiday with family and friends.

Fellow Jim Aloor, Ph.D., didn’t let the laughter and noise distract him from the serious business at hand — decorating his cookie for the contest. (Photo courtesy of Steve McCaw)

While a handful of task-oriented trainees worked on their cookies, Postdoctoral Fellows Andres Larrea, Ph.D., left, and Jill Hesse, Ph.D., opted for a round of rock-paper-scissors. (Photo courtesy of Steve McCaw)

Like his fellow trainees, Post-baccalaureate Fellow Zachary Zalinger, above, enjoyed the group’s half-hearted attempts at answering quiz questions from Klotz and Schrader. (Photo courtesy of Steve McCaw)
The e-Factor, which is produced by the Office of Communications and Public Liaison, is the staff newsletter at the National Institute of Environmental Health Sciences. It is published as a communication service to NIEHS employees. We welcome your comments and suggestions. The content is not copyrighted. It can be downloaded and reprinted without permission. If you are an editor who wishes to use our material in your publication, we ask that you send us a copy for our records.

- Director of Communications: Christine Bruske
- Writer-Editor: Eddy Ball
- Science Editor: Robin Arnette

NTA Co-Chair Raj Gosavi, Ph.D., left, smiled at the holiday antics as he sat with Research Fellow Jakub Kwintkiewicz, Ph.D.

Friends and lab mates Mercy Arana, Ph.D., left, and Danielle Watt, Ph.D., joined in the fun from the sidelines. (Photo courtesy of Steve McCaw)

The trainees had a lot of fun decorating their cookies, but only one of them could be a prize winner. One of the entries, second row right, showed a distinctive “South Park” influence. (Photo courtesy of Steve McCaw)

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