NIEHS National Institute of Environmental Health Sciences

Environmental Factor

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April 2012

NIEHS Spotlight

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NIEHS/NTP Director Linda Birnbaum, Ph.D., will receive the National Research Center for Women & Families 2012 Health Policy Hero Award.

Sills elected president of the Society of Toxicologic Pathology

When the Society of Toxicologic Pathology gathers in June for its annual symposium, its new president will be NTP/NIEHS pathologist Robert Sills, D.V.M., Ph.D.

Researchers call for changes in policy and reproductive healthcare

In a new clinical opinion paper, NIEHS- and EPA-funded children's health specialists advocate for a proactive approach for preventing harmful environmental exposures.

NIEHS and EPA convene leaders in children's environmental health research

More than 150 scientists, experts, and stakeholders involved in children's environmental health convened March 6-7 on the NIH campus in Bethesda, Md.

Science Notebook

The importance of calcium entry in mammalian reproduction

A team of scientists from NIEHS and Penn is the first to show calcium ions entering the egg from the outside are needed for key events that propel the egg to the two-cell stage.

Reduced vaccine effectiveness tied to PFC exposure Video

NIEHS grantee Philippe Grandjean, M.D., has shown that higher levels of exposure to perfluorinated compounds are associated with reduced immune response in children.

Hormones and Cancer highlights NIEHS/NTP paper

The journal Hormones and Cancer is highlighting a new paper by NIEHS and NTP scientists as one of nine available free at the journal's website.

Grantee with Midas touch speaks at NIEHS

With an NIEHS Small Business Innovation Research grant, a company is developing equipment for extracting valuable metals from acid rock drainage waste water.

Science showcases grantee and NIEHS/NTP tox efforts

A feature in the March 2 issue of Science, "LIFE SCIENCE TECHNOLOGIES: Animal-Free Toxicology," highlights NIEHS/NTP predictive toxicology initiatives.

NIEHS Spotlight

PEPH meeting strengthens community-engaged research networks

The two-day NIEHS Partnerships for Environmental Public Health meeting March 7-8 included a variety of activities designed to promote grantee interactions.

Korach receives Society for Endocrinology Dale Medal

NIEHS senior research Ken Korach Ph.D., is this year's winner of the Dale Medal, the highest accolade awarded by the Society for Endocrinology.

Birnbaum inspires women with talks at TWU and UNC Video

In March, NIEHS/NTP Director Linda Birnbaum, Ph.D., was doubly honored as a role model with talks at Texas Woman's University and the University of North Carolina.

Grantee recognized by WSU

Veteran NIEHS grantee Michael Smerdon, Ph.D., received the Eminent Faculty Award during the annual Showcase celebration March 30 at Washington State University.

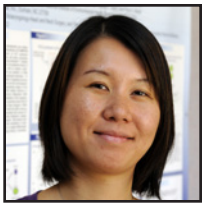
Enthusiasm for science reigns at SOT Video

The cool San Francisco weather and heavy rain didn't dampen the enthusiasm of the more than 7,000 scientists who attended the annual meeting March 11-15.

Science Notebook

Guest speaker helps NIEHS gauge the potential of microbiome research

Developmental biologist John Rawls, Ph.D., spoke March 1 at NIEHS on the relationship of intestinal tract flora balance and risk of obesity, an important public health challenge.



Lai discusses DNA methylation at WSA Scholars seminar

NIEHS scientist Anne Lai, Ph.D., was one of three honored presenters at the 2nd Annual NIH Women Scientist Advisors Committee Scholars seminar March 2 in Bethesda, Md.

Fire retardant study named paper of the year by ES&T Video

An NIEHS-funded study by grantee Heather Stapleton, Ph.D., was selected as top science paper of 2011 by the journal Environmental Science & Technology.

Early-life infection may lead to adult memory loss

NIEHS grantee Staci Bilbo, Ph.D., studies the influence of the neonatal environment on the immune system and its impact on the adult brain.

Study suggests possible therapy for arsenic toxicity

One of the first large-scale genomic studies conducted in a developing country suggests a possible route for preventing disease in people exposed to arsenic.

NIEHS Spotlight

NIEHS seminar encourages science outreach

The NIEHS Office of Science Education and Diversity welcomed Institute staff to Rodbell Auditorium Feb. 28 for a unique training seminar titled “Outreach 101.”

Seminar series marks ATSDR/ Superfund collaboration

Staff of the Agency for Toxic Substances and Disease Research gathered Feb. 15 for a talk by NIEHS Superfund Research Program researcher Staci Simonich, Ph.D.

NIEHS hosts annual meeting of Environmental Stewards

NIEHS welcomed representatives of North Carolina’s public and private sectors to the 10th annual North Carolina Environmental Stewardship Initiative (ESI).

Adelman balances science and parenthood for NIH tenure

NIEHS researcher Karen Adelman, Ph.D., recently received tenure for her work on how the environment impacts gene expression.

Upcoming presentation on data integration at HHS Video

NIEHS will welcome Todd Park April 5 for a presentation on the U.S. Department of Health Human Services Health Data Initiative.

Science Notebook

Small business explores new approaches in reproductive toxicology

NIEHS grantees Paul Turek, M.D., and Constance John, Ph.D., of MandalMed Inc., are developing a human-cell based testis model to study reproductive toxicology.

PEPH kicks off webinar series

The NIEHS Partnerships in Environment Public Health program presented the first installment of its environmental health and education webinar series Feb. 28.

High-throughput screening finds surprising properties for antioxidants Video

NIH researchers from two institutes and one center have demonstrated that some anti-oxidants damage DNA and kill cells instead of protecting them.

This month in EHP Audio

This month EHP takes on the issue of assigning actual dollar values to ecosystem services as a step toward better managing them and thus preserving human health.

Wilson honored by Columbia University

NIEHS lead researcher Samuel Wilson, M.D., will present the 19th annual Granville H. Sewell Distinguished Lecture in Environmental Health April 18 at Columbia University.

NIEHS Spotlight

Conference explores best practices of community-engaged research

NIEHS co-hosted the South Atlantic National Research Conference, “Engaging the Community for Research Success: What Scientists and IRBs Need to Know.”

Inside the Institute

Spring cleaning day for the NIEHS lake

Although it wasn’t officially spring yet when NIEHS employees picked up litter around the campus lake March 13, it was a great time for a lakeshore clean sweep.

Science Notebook

Rodbell lecture to feature Keith Yamamoto

Video

Biochemist Keith Yamamoto, Ph.D., will present the 2012 Rodbell Lecture, “Cell-, Gene-, and Physiology-Specific Regulation by the Glucocorticoid Receptor,” April 10 at NIEHS.

Staff and grantees at upcoming workshop

NTP Host Susceptibility Group leader Jef French, Ph.D., NIEHS grantees, and several NIEHS research associates will be among the presenters April 18-19.

Extramural Research

Extramural papers of the month

- Air pollution linked to cognitive decline
- Predicting sudden changes in pollution patterns
- Epigenetic interactions between flame retardant exposure and autism mutation
- Early BPA exposure and asthma development

Intramural Research

Intramural papers of the month

- Researchers find novel binding target for rotenone
- Novel role for a DNA polymerase in repairing damaged bases in *C. elegans*
- (Bi)sulfite oxidation prompts neutrophils to produce free radicals
- Synthetic estrogen induces feminization in male mice via ERalpha

Calendar of Upcoming Events

- **April 3 (offsite event)**, 1:00-2:00 p.m. — PEPH webinar titled “Examining and Communicating the Health Implication of Arsenic in our Food System,” featuring Margaret Karagas, Ph.D., and Laurie Rardin

- **April 5**, in Rodbell Auditorium, 10:00-11:00 a.m. — Seminar on U.S. Department of Health and Human Services technology, with Todd Park speaking on “The Health Data Initiative: Unleashing the Power of Open Data and Innovation to Improve Health”

- **April 9**, in Keystone 1003, 2:00-3:00 p.m. — Seminar on “Assessing the Impact of Research,” by Kristi Holmes, Ph.D., and Cathy Sarli

- **April 10**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Rodbell Lecture with Keith Yamamoto, Ph.D., exploring “Cell-, Gene-, and Physiology-Specific Regulation by the Glucocorticoid Receptor”

- **April 16**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Laboratory of Molecular Genetics Fellows Invited Guest Lecture, featuring Reuben Harris, Ph.D.

- **April 16**, in Rodbell Auditorium, 2:30-3:30 p.m. — Spirit Lecture, “From Stem Cells to Complex Patterning in the Embryo,” presented by Gail Martin, Ph.D.

- **April 23-24**, in Rodbell Auditorium, 9:00 a.m.-4:30 p.m. — NTP Neuropathology Symposium

- **April 24 (offsite event)**, at the U.S. Environmental Protection Agency in Research Triangle Park, N.C., 8:00-2:30 — Genetic and Environmental Mutagenesis Society spring meeting, “Emerging Environmental Issues”

- **April 26**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Laboratory of Toxicology and Pathology Seminar Series with Michael Kasten, M.D., Ph.D., topic TBA

- **April 26**, in Keystone 1003, 2:00-3:00 p.m. — Seminar with Paige Lawrence, Ph.D., topic TBA

- **April 27 (offsite event)**, at the U.S. Environmental Protection Agency in Research Triangle Park, N.C., 7:45-5:00 — 2012 NIEHS Biomedical Career Fair

- **April 30**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Laboratory of Molecular Genetics Fellows Invited Guest Lecture, featuring Kenneth Marians, Ph.D., speaking on “Mechanisms of Replication Fork Restart”

- View More Events: NIEHS Public Calendar

NIEHS Spotlight

GuLF STUDY marks recruitment milestone

Nearly two years after the Deepwater Horizon oil spill in the Gulf of Mexico, more than 10,000 cleanup workers and volunteers have enrolled in the Gulf Long-term Follow-up (GuLF) STUDY.

The study is a national effort conducted by NIEHS to determine if the oil spill led to physical or mental health problems. Recruitment continues, with the goal of reaching the GuLF STUDY's target goal of 55,000 participants, which would make it the largest health study of its kind.

"Ten thousand people have stepped forward to help find answers for their community and for the health concerns that linger after the oil spill," said Dale Sandler, Ph.D., chief of the NIEHS Epidemiology Branch and principal investigator of the study. "I encourage anyone who helped in the cleanup effort to make the call today to enroll in the GuLF STUDY. We want to hear everyone's story. Everyone is important to this study."

For more information, people can call the toll-free number at 1-855-NIH-GULF (1-855-644-4853) or visit the GuLF STUDY website at http://www.niehs.nih.gov/gulfstudy/.

Sandler and her team have held a string of community meetings in towns affected by the oil spill, in conjunction with media tours to raise awareness of the GuLF STUDY among people in the region. (Photo courtesy of Steve McCaw)

A continuing presence on the front lines of the oil spill

NIEHS was in the Gulf at the beginning of the oil disaster that occurred on April 20, 2010, and offered safety training to more than 150,000 cleanup workers. Now, some of these workers have concerns about their health as a result of participating in the cleanup. The GuLF STUDY was designed to answer some of these questions and will generate important data that may help guide policy decisions on health care and services in the Gulf region. Findings may also influence responses to future oil spills.

The GuLF STUDY staff reached out to the 150,000 people who took the cleanup worker safety training, but volunteers have been hard to find. Many have moved to new residences or changed telephone numbers, so the study has been using a range of approaches to invite people to join the study, including billboards, radio and TV, Facebook and Twitter, and community meetings. Individuals may be eligible for the study if they:

- Are at least 21 years old
- Did oil spill cleanup work for at least one day
- Supported the cleanup effort in some way or completed oil spill worker training

When volunteers join the GuLF STUDY, they are asked to complete a survey over the telephone. Most participants will also get a medical exam at home, and provide blood, urine, and other samples. When the medical visit is complete, participants will receive a gift card worth $50.

"We are grateful to have the support of more than 100 community and professional groups across the Gulf that represent workers who believe in the GuLF STUDY and who have endorsed it," said Sandler. "The study was developed to make participation as easy and convenient as possible and participation is confidential. We protect the identity of every participant."

GuLF STUDY is a registered trademark, held by the National Institute of Environmental Health Sciences.

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National Research Center honors Birnbaum

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., will receive the 2012 Health Policy Hero Award May 11 during the annual awards luncheon of the National Research Center for Women & Families (NRC), held at the historic Cosmos Club in Washington, D.C. Katharine Weymouth, publisher of The Washington Post, will serve as the emcee for the program, which is held each year on the Friday before Mothers Day.

Notifying Birnbaum of the award, NRC president Diana Zuckerman, Ph.D., wrote, "We'd be honored to honor you for your outstanding leadership at the National Institute of Environmental Health Sciences and the National Toxicology Program. We are inspired by your work on behalf of all Americans, as groundbreaking research, prevention, and intervention efforts make our homes and communities safer across the country."

With her message of promoting environmental public health through translation of research into primary prevention, Birnbaum is a natural choice for NRC's 2012 Health Policy Hero Award. (Photo courtesy of Steve McCaw)

Women at the forefront of public health and human rights

Birnbaum joins a select group of influential women who have been so honored for their contributions to public health, including last year's winner, Margaret Hamburg, M.D., commissioner of the U.S. Food and Drug Administration; Catherine DeAngelis, M.D., former editor in chief of JAMA; and two members of Congress, Rep. Rosa DeLauro and Sen. Chuck Grassley.

During the awards luncheon, the NRC will also honor what it calls Foremothers, influential women in public health over the age of 70, for their lifetime achievements on behalf of women and families. This year's honorees are Joan Claybrook, former president of Public

Citizen; economist Alice Rivlin; and Beatrix Hamburg, M.D., a leading children's health advocate. Previous honorees have included Eunice Kennedy Shriver; Dorothy Height, a national leader in the civil rights and women's movements; lawyer, administrator, activist, and author Mary Frances Berry; and children's author Judith Viorst.

A mission of advocacy and education

The NRC is dedicated to improving the health and safety of adults and children, by using research to encourage more effective programs and policies. The organization achieves its mission by gathering, analyzing, critiquing, and explaining scientific and medical research.

The NRC Cancer Prevention and Treatment Fund focuses on preventing cancer by reducing exposure to carcinogens and other risk factors, reducing the risk of recurrence, and improving the quality of medical care. The group prides itself on translating research results into everyday language, and then sharing that for free with the public, the media, opinion leaders, and policymakers.

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Sills elected president of the Society of Toxicologic Pathology

By Eddy Ball

When the Society of Toxicologic Pathology (STP) gathers in June for its annual symposium, its new president will be NIEHS/NTP pathologist Robert Sills, D.V.M., Ph.D., a diplomate of the American College of Veterinary Pathologists, and fellow of the International Academy of Toxicologic Pathology. In March, Sills who is chief of NIEHS and NTP pathology and the Cellular and Molecular Pathology Branch, was chosen as president elect by the STP membership.

In conjunction with his interdisciplinary research activities in the NIEHS/NTP, Sills holds adjunct positions in pathology at the University of North Carolina at Chapel Hill School of Medicine and in the College of Veterinary Medicine at North Carolina State University. (Photo courtesy of Steve McCaw)

"We [at NIEHS and NTP] have been honored with my selection as president elect of the Society of Toxicologic Pathology, which, personally, is very humbling, "Sills said when he learned of the election results. The STP, which consists of 1,200 members in more than 20 countries, is a nonprofit association of pathologists and other scientists. Its principal aim is the advancement of pathology as it pertains to changes elicited by pharmacological, chemical, or environmental agents, and factors that modify these responses.

The STP's 31st annual symposium, "Mechanisms of Toxicity," will take place June 24-28 in Boston. Featured events include a free pre-event NTP symposium June 23, as well as an awards ceremony and annual business meeting where Sills will be officially installed.

An active research and professional development agenda

Sills' research activities include the study of molecular mechanisms of carcinogenesis, neuropathology, and the inclusion of biologic-based interdisciplinary research in NIEHS/NTP studies.

Sills has served on the STP Executive Council and editorial board of the STP journal Toxicologic Pathology. He chaired STP annual meeting sessions on the human genome, implications for toxicologic pathology and carcinogenesis, and a session on cellular and molecular neurocarcinogenesis: toxicologic pathology of the nervous system. Also, he co-chaired a session of the STP annual meeting on cancer, the Scientific Program Planning Committee of the STP annual meeting on toxicologic neuropathology, and the International Life Sciences Institute seminar series on current issues in neuropathology.

Along with his affiliation with STP, Sills is very active in professional organizations as a member of the American College of Veterinary Pathologists, American Association for Cancer Research, and the American Veterinary Medical Association. He is the associate editor for the environmental pathobiology section of the journal Veterinary Pathology. Also, he has served on advisory committees, including the joint Food and Agriculture Organization of the United Nations/World Health Organization expert committee on food additives, International Agency for Research on Cancer, and U.S. Food and Drug Administration advisory committee.

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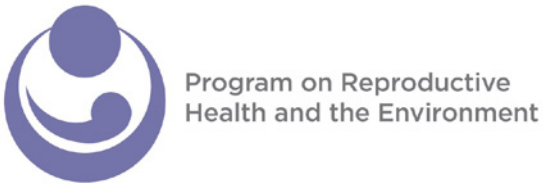
Researchers call for changes in policy and reproductive healthcare

By Eddy Ball

In a new clinical opinion paper, NIEHS- and U.S. Environmental Protection Agency (EPA)-funded children's health specialists advocate for a proactive approach for preventing harmful environmental exposures, by engaging reproductive health professionals in prevention efforts within and beyond the clinics.



Published online in March by the American Journal of Obstetrics and Gynecology, the article surveys trends in recent reproductive environmental health science research. The review considers the developmental origins of human disease, low-dose and coexposure toxicology, and epigenetic modification of gene expression triggered by exposures during windows of susceptibility.

The authors combined findings from what they describe as "this new science," to build a compelling argument for concerted action by reproductive health practitioners, institutions, and professional groups to improve individual health and drive policy change.

First author Patrice Sutton (Photo courtesy of UCSF)

Considering the rise in reproductive adversity linked to environment

The team set the stage for their analysis, by referencing findings of increases in reproductive and developmental adversity, ranging from declines in fertility and fecundity to increases in such childhood diseases as autism and certain types of cancer. The scientists also point to the alarming rise in the number of obese children and adolescents who will be at higher risk for developing diabetes and cardiovascular disease as they age.

"Because these and other barometers of reproductive health and capacity have changed at a relatively rapid pace," the authors contend, "they are unlikely to be explained by changes in genetic makeup." An important contributor to reproductive adversity, according to the researchers, is widespread human exposure to environmental chemicals. Over the past 70 years, there has been a 16-fold increase in U.S. production and use of chemicals that are largely unregulated and untested.

The research team cited data from the National Health and Nutrition Examination Survey indicating virtually all pregnant women have measured levels of a wide range of trace metals and chemicals in their bodies that have been documented to be harmful to human reproduction and development. These exposures range from lead and mercury to pesticides and endocrine-disrupting compounds, and many of them may act synergistically to impair health and cause disease.

Lead researcher Linda Giudice was one of several clinician researchers involved in the study. (Photo courtesy of UCSF)

According to the authors, studies have repeatedly linked exposures to these chemicals and compounds during critical windows of human development to adverse outcomes in human and animal studies. The associations are strong enough, they argue, to justify immediate precautionary measures to reduce or prevent exposures among vulnerable populations, such as pregnant women and children.

The researchers also point to statements and recommendations by professional organizations, such as the National Academy of Sciences, Endocrine Society, and American Academy of Pediatrics, on the links between environmental exposures and disease, as support for the need for timely action to prevent harm.

PRHE Director Woodruff is the lead on NIEHS grants to support research on the effects of environmental exposures during pregnancy. (Photo courtesy of UCSF)

Translating environmental health science into prevention

"Obstetricians, gynecologists, and other reproductive health professionals can play a groundbreaking role, by intervening in critical stages of human development," the authors conclude, "to translate the new science into healthier pregnancies, healthier children, and healthier future generations."

The authors call for changes in patient evaluation and education practices, increased advocacy by professional organizations, and better-informed institutional purchasing practices, especially with regard to food, with the goal of reducing exposures among pregnant women and children to harmful chemicals in the environment.

Led by senior author Linda Giudice, M.D., Ph.D., distinguished professor and chair of the department of obstetrics, gynecology, and reproductive sciences at the University of California, San Francisco (UCSF), the team included researchers in her department, as well as ones affiliated with the UCSF Program on Reproductive Health and the Environment (PRHE). PRHE members included Research Scientist Patrice Sutton, first author; second author Tracey Woodruff, Ph.D., PRHE director; and third author Joanne Perron, M.D., a postdoctoral fellow in the program.

Also participating in the study were scientists and clinicians from the UCSF Pediatric Environmental Health Specialty Unit and Kaiser Permanente North Valley network, and the American Congress of Obstetricians and Gynecologists. In addition to major funding from NIEHS and EPA, the research team also received support from the New York Community Trust.

Citation: Sutton P, Woodruff TJ, Perron J, Stotland N, Conry JA, Miller MD, Giudice LC. 2012. Toxic environmental chemicals: the role of reproductive health professionals in preventing harmful exposures. Am J Obstet Gynecol; doi: 10.1016/j.ajog.2012.01.034 [Online 8 March 2012].

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Perron, who has 20 years of experience treating women with reproductive disorders, has written about the effects of pesticides and air pollution on reproductive health and child development. (Photo courtesy of UCSF)

NIEHS and EPA convene leaders in children's environmental health research

By Ryan Campbell

More than 150 scientists, experts, and stakeholders, involved in children's environmental health, convened March 6-7 at the Centers for Children's Environmental Health and Disease Prevention Research annual meeting, to share scientific strategies, discuss new research approaches, and highlight late-breaking science in the field. The meeting held on the National Institutes of Health (NIH campus) and sponsored by NIEHS and the U.S. Environmental Protection Agency (EPA), provided an opportunity to foster collaborations, develop new partnerships, and enhance the overall children's environmental health network.

Speakers included many leading authorities in the field of children's environmental health, beginning with NIEHS Director Linda Birnbaum, Ph.D., and EPA Director of the Office of Children's Health Protection and Environmental Education Peter Grevatt, Ph.D. Together, they opened the meeting with complementary messages that highlighted institute and agency priorities. Birnbaum challenged grantees to continue their record of success, by expanding their research and exploring other exposures and diseases.

Other presenters highlighted research findings, and discussed the challenges of quantifying exposure from conception through childhood and linking these to disease endpoints. They addressed

Birnbaum's opening remarks brought the work of the Children's Centers into context with the overall NIEHS environmental health mission. She took the opportunity to discuss and preview the Institute's nearly completed 5-year strategic plan. (Photo courtesy of NIH)

topics including assessing how lifestyle habits and contaminant exposures in parents may lead to disease in children, and understanding the role of environment in children's airway diseases. In addition, researchers shared ways to improve genetic screening methods, novel exposure assessments techniques, such as analyzing children's teeth for signs of metal exposure, and topics that have received attention in the news, such as bisphenol A in food containers and arsenic in rice and rice products.

Partnerships with communities and non-governmental organizations were an ongoing theme throughout the meeting. A session in communication, outreach, and translation demonstrated the importance of community-academic partnerships, to implement change that can improve the health of communities exposed to environmental contaminants. A children's advocacy panel discussion, featuring representatives from many well-known organizations, such as the March of Dimes Foundation, American Lung Association, and Children's Environmental Health Network, described resources and experiences relevant to advancing children's environmental health.

Meeting participants also had an opportunity to share their research results and discuss collaboration opportunities, during a poster session and breakout discussions. These sessions tackled the challenges of sharing environmental health data, using genome-wide association studies in neurodevelopment, implementing quality control standards in the analyses of epigenetic markers in human studies, and conducting children's environmental health research in daycare and school settings.

Kimberly Gray, Ph.D., leads the NIEHS Children's Centers program. The centers focus on children's exposure to environmental agents, such as pesticides, metals, air pollution, and endocrine disruptors. (Photo courtesy of NIH)

Grevatt discussed EPA's priorities of integrating federal mandates with the best possible science, ensuring safe chemical management, and implementing effective community-based programs. (Photo courtesy of NIH)

Andrea Baccarelli, M.D., Ph.D., spoke about epigenetic mechanisms in relation to fetal growth and perinatal outcomes, cardiovascular function, obesity, and neurocognition. He is an associate professor of environmental epigenetics in the department of environmental health at the Harvard School of Public Health. (Photo courtesy of NIH)

Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, was also on hand to welcome experts from the fields of reproductive health, pubertal development, metabolism, early life exposures, and epigenetic changes, as well as key researchers in environmental technologies. (Photo courtesy of NIH)

Communications resources

Children's Center directors and investigators were able learn about how to maximize communication and research translation efforts from NIEHS and EPA experts.

- Christie Drew, Ph.D., DERT Program Analysis Branch chief, spoke about how NIEHS measures success by tracking publications, following grantee career trajectories in the NIEHS CareerTrac database, and using the Evaluation Metrics Manual. This information is used to inform Congressional staff, government management staff, and communities.

- Ed Kang of the NIEHS Office of Communications and Public Liaison, and Kelly Widener, assistant center director for research communications for the EPA National Center of Environmental Research, emphasized the importance of understanding target audiences, increasing Web page development, and webinar participation. Social media channels, including Facebook, Twitter, and YouTube, were also highlighted as useful communication tools.

- Mary Gant, NIEHS congressional liaison, conveyed the importance of working closely with Congress, and knowing its staff members and their political affiliations. Performing background research on Congress, tailoring briefings to congressional staff, and preparing concise and meaningful briefings were recommended best practices.

A full agenda, list of meeting presenters, and abstracts are available at: http://www.niehs.nih.gov/news/events/pastmtg/2012/children/index.cfm

The Natcher Conference Center on the NIH campus proved to be an ideal meeting location for the hundreds of scientists and other key stakeholders visiting from across the country. (Photo courtesy of NIH)

(Ryan Campbell is a contractor with MDB, Inc. supporting the NIEHS Division of Extramural Research and Training.)

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PEPH meeting strengthens community-engaged research networks

By Dustin Russell

NIEHS Partnerships for Environmental Public Health (PEPH) grantees assembled March 7-8 at the National Institutes of Health (NIH) in Bethesda, Md., for their annual meeting titled "Strengthening a dynamic environmental public health network for tomorrow: Advancing science through critical reflection." The two-day meeting included a variety of activities designed to promote grantee interactions, foster group learning, and, most importantly, spark dialogue about issues related to research translation, capacity building, and communication.

Looking for more photos from the 2012 PEPH annual meeting? Check our Facebook page at: www.facebook.com/nih.niehs

Linda Birnbaum, Ph.D., NIEHS/NTP director, opened the meeting by emphasizing the Institute's continued engagement with communities to advance environmental public health. "I am extremely supportive of all of our activities that involve the community," she said. "We cannot do environmental health work unless the community is involved from the get-go."

Myra Marie Tetteh, program coordinator for the Community Outreach and Education Core at the University of Michigan, is one of many grantees engaged in community outreach and education. (Photo courtesy of Liam O'Fallon)

PEPH grantees, including Pam Miller, founder of Alaska Community Action on Toxics, and Sacoby Wilson, Ph.D., environmental health scientist from the University of Maryland, then took the stage to highlight community partnerships addressing health issues related to populations that are overburdened and disproportionately affected by environmental contamination. Presenters offered models for successful partnerships addressing environmental health concerns in low-income and minority communities, the workplace, and among tribal populations. They illustrated challenges within the realm of community-engaged research and offered innovative approaches to resolving these challenges.

In addition to traditional scientific and poster presentations, the meeting featured training sessions on PEPH evaluation metrics, innovative environmental health outreach tools, such as theatrical performances, materials development, and a healthy hospitals initiative.

Networking is a critical component of every successful PEPH meeting. Collman is pictured, left, with Marie Lynn Miranda, Ph.D., dean of the School of Natural Resources and Environment at the University of Michigan. (Photo courtesy of Liam O'Fallon)

Breakout sessions highlight trust building, communication

Nine interactive breakout sessions further illuminated important lessons and recommendations on how greater effectiveness can be achieved within the PEPH program and for community-engaged research as a whole.

Trust building emerged as a major theme across the breakout groups. Participants identified the early involvement of community partners as essential to ensuring that researchers and community participants have a mutual understanding of the project and its goals, as well as the roles and responsibilities of each partner, thereby developing a greater sense of trust. In addition, the formation of equitable, long-term partnerships was recognized as central to fostering trust.

Multidirectional education and training surfaced as a second central theme in the breakout sessions. Participants noted that researchers, communities, and Institutional Review Boards all need specialized training to implement community-engaged research approaches more effectively.

Participants cited the value of communication training for researchers, to equip them with knowledge and tools to effectively incorporate input and communicate findings to the community in ways that acknowledge cultural, linguistic, and literacy variation among communities. Similarly, communities can become valuable agents of data collection that help to define environmental health concerns in particular communities. Attendees agreed that translation strategies must consider and utilize new and various channels of communication, such as multimedia and social media, to amplify environmental health messages.

Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training (DERT), closed the meeting by thanking the participants for their enthusiastic participation. She noted, "PEPH continues to be a participatory program at every level." She also said that community-engaged research will continue to evolve, as researchers and communities come together to share ideas and experiences. "Through active feedback," she concluded, "the power of our network can only increase."

A popular component of the PEPH meeting was the option for participants to attend training sessions to hear about the latest evaluation and communication techniques. Kristi Pettibone, Ph.D., from the DERT Program Analysis Branch, facilitated a discussion about the new PEPH Evaluation Metrics Manual. (Photo courtesy of Liam O'Fallon)

Liam O'Fallon, right, is the lead for PEPH, which serves to foster dynamic connections on common approaches and strategies among environmental health researchers and practitioners. Pictured with O'Fallon is Jennifer Runkle, Ph.D., from Emory University. (Photo courtesy of Liam O'Fallon)

For more information on PEPH and to read project highlights, visit www.niehs.nih.gov/PEPH.

(Dustin Russell is a contractor with MDB, Inc. supporting the NIEHS Division of Extramural Research and Training.)

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Korach receives Society for Endocrinology Dale Medal

By Eddy Ball

NIEHS senior researcher Kenneth Korach Ph.D., is this year's winner of the Dale Medal, the highest accolade awarded by the Society for Endocrinology (SfE). As part of his award, Korach delivered an acceptance lecture for the Dale Medal, "Estrogen receptor insensitivity: basic and clinical consequences in hormone and endocrine physiology," March 20 at the annual SfE meeting in Harrogate, England.

Korach's nomination emphasized the importance of his work with rodent models. "These models have completely transformed our understanding of the many and unexpected roles for estrogens, not only in female reproductive biology, but also that they have equally important roles in the male." (Photo courtesy of Steve McCaw)

In his letter of congratulations to Korach, SfE General Secretary Paul Stewart, M.D., wrote, "Each year, the Society of Endocrinology awards the Dale Medal to a member of the scientific community in recognition of outstanding studies, which have changed our understanding of endocrinology in a fundamental way."

SfE criteria for the Dale Medal include an international reputation in high-quality science in high-impact journals. The research findings are always of major significance in a translational way, as well, and the awardees are researchers widely recognized among their peers for outstanding research capabilities of world-class stature, recognized and frequently cited by others.

Contributions to the understanding of sex hormone action

Korach joined NIEHS in 1976, where he currently heads the Receptor Biology Group investigating estrogen hormone action in numerous tissues by the generation of estrogen-receptor knockout mouse models with an application toward understanding the basic mechanisms of estrogen's influence on physiological processes and disease. He is past director of the NIEHS Environmental Disease and Medicine Program and current chief of the Laboratory of Reproductive and Developmental Toxicology, and a member of the Senior Biomedical Research Service within the U.S Public Health Service.

In addition to the Dale Medal, Korach is the recipient of NIH outstanding performance and merit awards, the Medical College of Georgia Distinguished Alumnus Award, the Edwin B. Astwood Award from The Endocrine Society, the Keith Harrison Lecture Award from the Endocrine Society of Australia, the Transatlantic Medal from the Society for Endocrinology in the United Kingdom, and the Firkin Oration Research Award from the Australian Society for Medical Research.

An editor and past editor in chief of the journal Endocrinology, Korach holds adjunct professorships at North Carolina State University, the University of North Carolina at Chapel Hill School of Medicine, and in the department of pharmacology and cancer biology at Duke University Medical Center.

After completing his Ph.D. in endocrinology from the Medical College of Georgia, where he characterized biochemical properties of estrogen receptors in the pituitary and hypothalamus, Korach was a postdoctoral biological chemistry and Ford research Fellow at Harvard Medical School with the late professor Lewis Engel, Ph.D.

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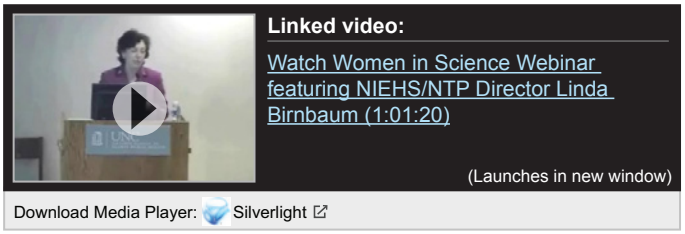
Birnbaum inspires women with talks at TWU and UNC

By Eddy Ball

In March, NIEHS/NTP Director Linda Birnbaum, Ph.D., was doubly honored as a role model with talks at Texas Woman's University (TWU) and the University of North Carolina at Chapel Hill (UNC).

Birnbaum spoke March 1 as one of three distinguished women scientists making keynote presentations before an audience of women scientists in training at the inaugural seminar of the Ann Stuart and Ray R. Poliakoff Celebration of Science series at TWU in Denton, Texas. The next day, she returned to Chapel Hill, N.C., to address a similar group of students at the UNC Gillings School of Global Public Health Center for Environmental Health and Susceptibility, as its 2012 Women in Science speaker (see text box).

The future of environmental health



In her talk at TWU, Birnbaum focused on the evolution of NIEHS and NTP during her three years as director, and her vision for the Institute's future as the world's premier research center for the environmental health sciences.

Setting the stage for a review of emerging paradigms in the understanding of environmental health and exciting new directions in research at NIEHS and NTP, Birnbaum challenged her audience to think divergently about the role of environment in human health, especially in terms of the developmental origins of disease and the complex causes of complex diseases.

"It's not enough to simply acknowledge that the environment has an effect on people's health," she told her young colleagues. "We also need to recognize that our old assumptions about toxicants and how they affect our bodies are being changed by modern science."

Inspiring women at UNC

In her presentation March 2 at the 2012 spring seminar series at UNC, Birnbaum wove together a personal narrative on work/life balance with an overview of NIEHS and NTP environmental public health initiatives. Speakers typically give a scientific seminar to the larger scientific community at UNC, as well as meet informally with young female scientists to discuss issues related to women in science.

In the invitation to Birnbaum, the series host, UNC professor Regina Carelli, Ph.D., described her as the perfect person to represent and promote women in science. "You have been such a positive role model for me over the years," Carelli wrote. "It would be wonderful for me to be able to share your wisdom with young women scientists at Carolina."

Birnbaum rose to the occasion with a talk titled "You *Can* Have It All," tracing her scientific career from its roots in middle school in Teaneck, N.J., where she enjoyed the support of great parents, great teachers, and, later on, great mentors. "Having it all is a very individual thing," she began. "For me, it's fulfilling my love of science, keeping involved with the community, and of course my family." And, she added, having as much fun at it as possible.

The talk traced Birnbaum's career with family and work photos, from her high school science projects to her current position as leader of NIEHS and NTP, where she transitioned into the scientific segment of her talk. As she did in her talk at TWU, Birnbaum concluded her talk at UNC by recognizing Rachel Carson, one of the many remarkable women who have shaped modern science. Carson also helped set the stage for women to work toward the goal of having it all — balancing career with family, community, and the sheer joy of living life and work fully.

Understanding that chemicals can act like hormones and drugs, to disrupt the control of development and function at very low doses to which the average person is exposed, and that susceptibility to disease persists long after exposure, Birnbaum explained, has led NIEHS and NTP into new directions of research. She pointed to new initiatives in the areas of low dose exposures, windows of exposure, advanced toxicology screening, the effects of mixtures, routes of exposure, emerging hazards, human health effects of climate change, disaster response, and clinical research as the basis for public health and prevention efforts.

Following a data-rich discussion of new approaches to environmental public health innovative research initiatives and the Institute's strategic plan for the next five years, Birnbaum concluded with a look back at Rachel Carson, the woman whose eloquence inspired the environmental movement with her 1962 book, "Silent Spring." Birnbaum concluded by saying, "We've really come a long way…women and research. It's been thrilling to be a part of it all."

Birnbaum ended her talk with a caveat — "The dire prediction of a silent spring has not come true, but the job is not yet done."

The Celebration of Science Series at TWU

The program began with a forum with students titled "Women in Science: Challenges and Promises," which helped set the stage for the keynote presentations. Along with Birnbaum's talk, Shana Kelley, Ph.D., a professor in the department of pharmaceutical sciences at the University of Toronto, addressed "Using Nanotechnology to Diagnose Disease," and Kimberly Orth, Ph.D., a professor in the department of molecular biology at the University of Texas Southwestern Medical Center, explored "Black Spot, Black Death, Black Pearl: The Tales of Bacterial Effectors."

An evening reception gave students the opportunity to talk with their distinguished guests.

According to TWU, the Ann Stuart and Ray R. Poliakoff Celebration of Science Series has a two-decade funding commitment for the departments of biology, and chemistry and biochemistry, to develop a sustained program of promoting and celebrating the wonders, truths, and mysteries of science.

The series was started with a $200,000 gift from Stuart, the chancellor of TWU, and Poliakoff, her late husband, announced April 1, 2011 during dedication of the leading-edge Ann Stuart Science Complex. Both Stuart, who holds a Ph.D. in English, and Poliakoff were first-generation graduates of public higher education, and both often said it was their education that enabled them to pursue the opportunities that enriched their lives.

Keynote speakers joined their hosts in the state-of-the-art 80,000-square-foot, $26.4 million Ann Stuart Science Complex. Shown, left to right, are Robert Neely, Ph.D., TWU provost and vice president for academic affairs, Stuart, Kelley, Birnbaum, Orth, and Richard Sheardy, Ph.D., professor and chair of the TWU department of chemistry and biochemistry. (Photo courtesy of Kristina Bowman)

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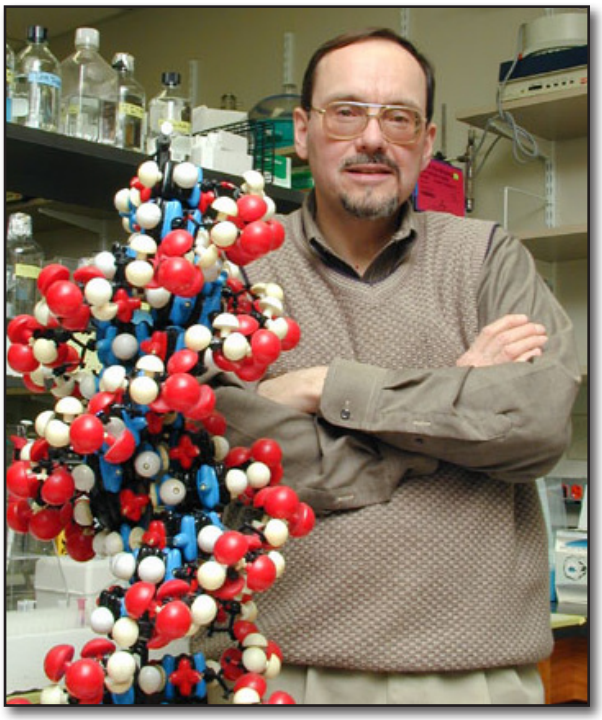
Grantee recognized by WSU

By Eddy Ball

Veteran NIEHS grantee Michael Smerdon, Ph.D., received the Eminent Faculty Award during the annual Showcase celebration March 30 at Washington State University (WSU). Smerdon, a regents professor of biochemistry and biophysics, is the 12th recipient of the highest honor his university bestows on faculty members, according to a Feb. 27 WSU press release.

For more than 30 years, Smerdon has been an NIH grantee, and he currently holds two NIEHS grants overseen by NIEHS Health Scientist Administrator Les Reinlib, Ph.D., "Repair of carcinogen damaged DNA in human chromatin" and "DNA repair in a hormone responsive gene." NIEHS first supported Smerdon as a junior investigator with a Young Environmental Scientist Grant Award from 1978 to 1981, following completion of his postdoctoral fellowship in pathology at Washington University School of Medicine.



Smerdon is a pioneer in the area of DNA repair and chromatin packaging. When he was a postdoc and junior investigator, his papers were among fewer than 20 published each year on the subject (see graph). By 2010, there were nearly 400 papers published on DNA and chromatin each year. (Photo courtesy of WSU)

"We are proud to have sponsored Dr. Smerdon for any years," Reinlib said. "He is a shining example of an investigator producing insights that will lead to a comprehensive understanding of ways that environmental chemicals or harmful radiation attack DNA and our ability to defend ourselves against these agents."

Smerdon's Eminent Faculty Award is the latest in a long list of honors for teaching, research, and service. Smerdon was elected a fellow of the American Association for the Advancement of Science in 2010, he received the Science and Engineering Alumni Leadership Award in 2003 from St. Cloud State University, his alma mater, and he has been recognized several times for faculty excellence. In 2001, he was selected for the prestigious NIH Method to Extend Research in Time (MERIT) Award, a special award of up to 10 years of research funding to select leaders in their field.

In a comment posted with the WSU press release, former Smerdon trainee Feng Gong, Ph.D., now an assistant professor at the University of Miami, wrote, "I am excited to hear that Mick will receive the 2012 Eminent Faculty Award. In addition to his numerous scientific contributions to the field of DNA repair, Mick is also a great mentor. He will continue to be a great source of inspiration for all his students in the years to come."

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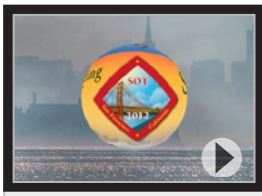
Enthusiasm for science reigns at SOT

By Robin Mackar

The cool San Francisco weather and heavy rain didn't dampen the enthusiasm of the more than 7,000 scientists who attended the annual Society of Toxicology (SOT) Meeting March 11-15.



Linked video:

Watch SOT President Jon Cook's invitation to the meeting and hear his description of all it had to offer (02:28)

(Launches in new window)

Download Media Player: Flash

NIEHS Deputy Director Rick Woychik, Ph.D., welcomed SOT President Jon Cook, Ph.D., to the NIEHS/NTP/EHP exhibit. (Photo courtesy or Hui Hu)

"The energy level at SOT was very high," said NIEHS/NTP Director Linda Birnbaum, Ph.D. "Not only does the annual meeting provide a chance to hear and see the newest findings in the world of toxicology, but also offers many opportunities to catch up with colleagues and friends and, sometimes, you can even find time to make some new acquaintances." As a past president of SOT, Birnbaum is well known and a popular draw at the meeting.

When not giving talks or meeting up with colleagues, Birnbaum could be found at the exhibit catching up on emails. (Photo courtesy of Hui Hu)

A few highlights

NIEHS/NTP staff led more than 110 science-related activities at the meeting, including talks and posters highlighting new findings, symposia, keynote lectures, demos of databases, exhibitor-hosted sessions, continuing education classes, and meetings with Superfund directors and grantees, as well as shared information about funding opportunities and recruited postdocs.

One of the busiest spots at the meeting was the combined NIEHS/NTP and Environmental Health Perspectives (EHP) exhibit. In addition to it being the hub for information about all NIEHS/NTP programs and activities, the exhibit served as a place for attendees to get hands-on experience with NTP databases. Scott Auerbach, Ph.D., of the NTP Biomolecular Screening Branch, formally introduced the DrugMatrix® and ToxFX® toxicogenomic database and analysis tools, at an exhibitor-hosted session on Monday that was very well attended.

Auerbach also gave demos at the booth. Laura Hall, Asif Rashid, and Hui Gong, from the NTP Program Operations Branch, presented a poster and walked many attendees through some of the upgrades and new information on the Chemical Effects in Biological Systems (CEBS) database. "We were all very pleased at the interest shown in our databases," Hall said. As a first-timer at the meeting, she also admitted being a little overwhelmed by the breadth of the meetings' offerings.

Another hot spot at SOT was the NIEHS Division of Extramural Research and Training (DERT) research funding and resource room, where Carol Shreffler, Ph.D., Annette Kirshner, Ph.D., and other DERT staff discussed federal research funding opportunities. According to Kirshner, "The grant writing brown bag session was a big hit with first-time grant writers."

The numerous continuing education sessions chaired by NIEHS/NTP staff were also very well attended, ranging from sessions on harmonized guidance for risk assessment and techniques for assessing chemical mixtures to nanotechnology.

Birnbaum continued to be a huge draw at all the sessions she participated in, especially the annual "Meet the Directors" special symposium. She provided a budget update and spent much of her time talking about the strategic planning process taking place at NIEHS. Birnbaum shared the stage with leaders from other agencies, including former NIEHS/NTP leader Chris Portier, Ph.D., who now heads the Agency for Toxic Substances and Disease Registry.

Hall and her colleagues showed more than 50 people how to use the CEBS database. (Photo courtesy of Asif Rashid)

2012 award recipients with ties to NIEHS/NTP

- **Grantee Donna Zhang, Ph.D.**, associate professor in the department of pharmacology and toxicology in the College of Pharmacy at the University of Arizona, is the recipient of the SOT 2012 Achievement Award. Zhang has made several seminal observations in the Nrf2-Keap1 field that are establishing new paradigms for understanding its roles in toxicology. This work has been supported, in part, through a highly competitive Outstanding New Environmental Scientist award from NIEHS, as well as awards from the National Cancer Institute and the American Cancer Society.

- **Former NTP Deputy Director John Moore, D.V.M.**, was presented the 2012 SOT Founders Award in recognition of his outstanding leadership in fostering the role of toxicological sciences in safety decision-making. Moore also previously served as director of toxicology research and testing at NIEHS.

- **Grantee and former councilor Martin Philbert, Ph.D.**, dean and professor of toxicology at the University of Michigan School of Public Health, is the recipient of the 2012 SOT Public Communications Award, in recognition of his major contributions in broadening public awareness on toxicological issues, and disseminating the message of toxicology and its impact in our society. Philbert has served on the National Advisory Environmental Health Sciences Council of NIEHS and continues to advise several federal agencies on a variety of issues surrounding emerging nanotechnologies.

- **Consultant Xuemei Huang, M.D., Ph.D.**, was honored with the 2012 Translational/Bridging Travel Award. Huang is associate professor in the departments of neurology, neurosurgery, pharmacology, radiology, kinesiology, and bioengineering at the Penn State Hershey Medical Center and Penn State University, as well as the director of the Hershey Brain Analysis Research Laboratory for Neurodegenerative Disorders. She is a member of a number of professional groups related to toxicant exposures and, since 2007, has served as a consultant to NIEHS.

SOT leaders among us

NIEHS/NTP is also proud to have two elected SOT leaders representing the Institute. Dori Germolec, Ph.D., immunology discipline leader for the NTP, and Michael Waalkes, Ph.D., chief of the NTP Laboratories Branch, serve as SOT councilors. Both commented about how pleased they were with the meeting.

"NIEHS was very well represented at the SOT, with wonderful presentations from the director on down to numerous postdoctoral fellows," Waalkes said with a sense of pride. "Toxicology continues to shine at the Institute."

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison.)

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The database demos were quite popular. Auerbach was kept busy throughout the conference. (Photo courtesy of Denise Lasko)

NIEHS seminar encourages science outreach

By Ian Thomas

The NIEHS Office of Science Education and Diversity (OSED) welcomed Institute staff to Rodbell Auditorium Feb. 28 for a unique training seminar titled "Outreach 101." Featuring key presenters from the NIEHS Office of Communications and Public Liaison (OCPL), the U.S. Environmental Protection Agency (EPA), and the University of North Carolina at Chapel Hill (UNC), the three-hour event treated attendees to a number of fun and interactive techniques designed to enhance interest in science education.

"A lot of people still don't know what environmental health science is," said Ericka Reid, Ph.D., the OSED lead specialist for education outreach and diversity. "Whether it's through basic outreach at a middle school science fair or a formal presentation at a national research conference, the job of our office is to work with the public to teach them how their overall health is directly linked to the world around them."

As the NIEHS primary outreach arm for science education in the local, state, and national communities, OSED continually partners with students, teachers, parents, and fellow scientists to raise awareness about the Institute and its mission.

Reid emphasized the importance of communicating the environmental health paradigm and the effects that the many components of the environment have on human health, as well as tailoring the message to the diverse audiences that OSED targets. (Photo courtesy of Steve McCaw)

The interactive key

A common theme throughout the afternoon was the notion of an interactive educational experience between students and those who conduct outreach.

"As anyone who has ever stepped foot into a classroom knows, you can't just walk in and lecture," explained Kelly Leovic, manager of the EPA Science, Technology, Engineering, and Math (STEM) and environmental outreach programs in Research Triangle Park, N.C. "Whether it's by using games, educational demonstrations, or just some really cool props, you have to have hands-on activities in order to get students engaged in learning."

"Competitions are always a great way to get people to plug in, particularly when you're dealing with kids in middle and high school," added Rachel Clark, Leovic's colleague at EPA who led a quick round of Environmental Jeopardy for the crowd in attendance.

Schelp's focus in outreach is community engagement, especially at meetings of the NIEHS Public Interest Partners and at community forums. (Photo courtesy of Steve McCaw)

A message of clarity

In addition to fostering more interaction among students, teachers, and administrators, attendees also learned the value of conveying their message with not only clarity, but simplicity.

"As scientists, it's very easy for us to confuse people with the same terminology and concepts we use around our peers," said Dana Haine, K-12 science education manager of the Environmental Resource Program at UNC. "That's why it's crucial for us, as scientists and educators, to know our audience, so that we can tailor our message in a way that everyone can understand."

While Haine emphasized the importance of message clarity with regard to the spoken word, Ed Kang of OCPL stressed the need for it with the written word as well.

Along with talks by outreach specialists, the program included small working groups. Michelle Heacock, Ph.D., left, one of several NIEHS trainees involved in education and outreach, talked with Debbie Wilson, coordinator of the NIH Summer Internship Program at NIEHS. (Photo courtesy of Steve McCaw)

"As communicators, we use words that have meaning for our audience," said Kang. "Whether we're crafting a research paper or writing an email to a friend, it's important that we think about not only what we want to say, but who we want to say it to, in order to ensure that the key points of our message are understood."

A partnership for success

"Ultimately, environmental health outreach has to be a two-way conversation, not a one-sided lecture," explained John Schelp, OSED special assistant for community engagement and outreach. "That means working with our partners in the community to find out what they need and how they need it, because, in the end, we're all just trying to help people live healthier lives."

Bono Sen, Ph.D., science education and outreach program manager for the NIEHS journal Environmental Health Perspectives, has drawn upon the talents of NIEHS postdoctoral fellows for staffing workshops for teachers and high school students. (Photo courtesy of Steve McCaw)

As part of their outreach efforts, Clark, above, and Leovick coordinate the EPA-RTP Speakers Bureau, a database organizations can search to find and request speakers on a wide variety of environmental science and related topics. (Photo courtesy of Steve McCaw)

Outreach 101 presenters

- **Kelly Leovic, EPA**
  "Developing an Effective and Sustainable Outreach Program: Best Practices"
- **Dana Haine, UNC**
  "Effective Communication Strategies: The Spoken Word"
- **Rachel Clark, EPA**
  "K-12 Classroom: Engaging Your Audience"
- **Ed Kang, NIEHS**
  "Effective Communication Strategies: The Written Word"

(Ian Thomas is a public affairs specialist for the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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Seminar series marks ATSDR/Superfund collaboration

By Rebecca Wilson

More than 50 staff members from the Agency for Toxic Substances and Disease Registry (ATSDR) gathered Feb. 15 in Atlanta, and online, for a presentation by Staci Simonich, Ph.D. Simonich, an NIEHS-funded Superfund Research Program (SRP) researcher, shared findings from her work tracking air pollution from China to the west coast of the United States.

CDC
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Simonich's presentation was the latest in a seminar series that connects SRP researchers with government regulators and researchers in sister agencies of the U.S. Department of Health and Human Services (HHS).

ATSDR is a unit of the Centers for Disease Control and Prevention (CDC). Like NIEHS, which is one of 27 institutes and centers of the National Institutes of Health, ATSDR and CDC are part of HHS.

Simonich's talk, "What Goes Around Comes Around: Chasing Polycyclic Aromatic Hydrocarbons from the Beijing Olympics to the U.S. West Coast," detailed sources and environmental detection methods for more than 150 polycyclic aromatic hydrocarbons (PAHs), an airborne contaminant of major importance in ATSDR field work. After her presentation, Simonich received a tour of the ATSDR facility, met with airborne contamination experts about their research needs, and discussed opportunities for collaboration.

Simonich holds a joint appointment in the department of chemistry and department of environmental and molecular toxicology at Oregon State University, where she heads a research lab supported by NIEHS SRP funding. (Photo courtesy of Oregon State University)

Forming interagency partnerships to advance public health

The SRP ATSDR seminar series began in 2007, when University of North Carolina at Chapel Hill SRP researcher Frederick Pfaender, Ph.D., was invited to ATSDR to give a seminar about the role bioavailability plays in determining pollutant exposure. The presentation was so well received that other researchers were invited to present in 2008, and a series was launched. Since then, 16 investigators have presented their research to an ever-growing audience of regulators and researchers.

"The SRP seminar series at ATSDR has become a signature communication tool that provides SRP grantees a window into the ATSDR and an understanding of the challenges it faces," said Beth Anderson, program analyst for the SRP. "At the same time, it is a venue to advance the use and utility of the SRP research findings. It is a nice match for both the SRP and the ATSDR."

SRP researchers report that they have benefited from giving seminars, as well. "I very much enjoyed my conversations during my visit," said Kelly Pennell, Ph.D., of her 2011 visit and presentation. "I felt like it brought some practical aspects to my research." Pennell, a researcher at the University of Massachusetts Dartmouth, researches how gaseous pollutants seep into buildings and pollute the air inside.

These seminars have also led to long-term collaborations. Clement Furlong, Ph.D., of the University of Washington, presented his research about the neurological effects of exposure to organophosphates in 2008. Organophosphates are found in pesticides used in commercial farming practices, and exposure to them can cause neurological damage. The seminar allowed Furlong to collaborate with scientists at ATSDR and they now work together to develop biomarkers to test for exposure. One biomarker assay has been created and three more are under development. Furlong said they plan to collaborate on a poster, presenting their research at a conference this summer.

An additional seminar is planned for the fall of 2012. Abstracts from previous seminars are available on the SRP/ATSDR seminar series Web page.

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

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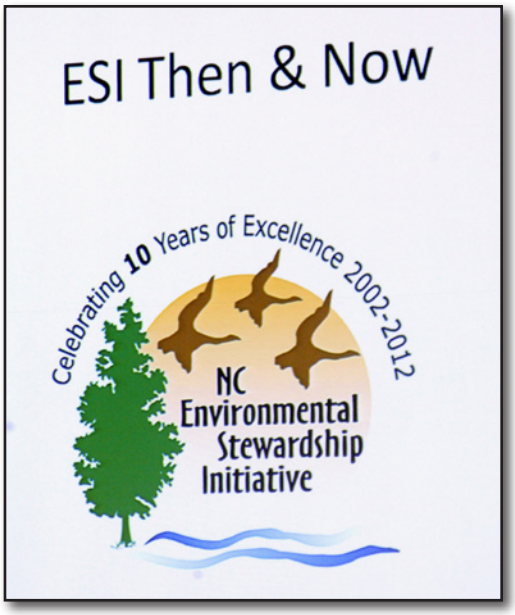
NIEHS hosts annual meeting of Environmental Stewards

By Ian Thomas

NIEHS welcomed key representatives of North Carolina's public and private sectors to Rodbell Auditorium March 23 for the 10th annual convening of the state's Environmental Stewardship Initiative (ESI) members. Launched in 2002 by the N.C. Department of Environment and Natural Resources (NCDENR), ESI is a voluntary program designed to foster partnerships among the government and business communities, to promote the state's overall commitment to environmental sustainability.



2012 marked the 10th anniversary of the ESI. (Photo courtesy Steve McCaw)

"Our mission here at NIEHS shares some very common, fundamental goals with the ESI program," explained Scott Merkle, head of the NIEHS Health and Safety Branch. "Preserving and protecting public health is one of the main pillars of environmental stewardship and we see that link, firsthand, every day in the research that we conduct."

A unified forum for innovation

Throughout the day, attendees took part in a number of testimonials, talks, and interactive panels, designed to stimulate discussion on a number of key environmental issues, such as policy and legislation, techniques for building sustainability practices, and green technology.

"Environmental stewardship becomes a real challenge once you've been at it a while," said Raymond Price of Smithfield Foods, a long-time ESI steward. "Everybody knows about recycling and composting, but once that low-hanging fruit is gone, it's meetings like these that help us generate new ideas for keeping that forward momentum of progress."

Dan Miller of the U.S. Navy's Fleet Readiness Center East in Cherry Point, N.C. agreed.

"ESI membership offers companies the unique opportunity to be part of an established system of like-minded organizations, all of whom pool their ideas and resources for the collective betterment of everyone involved," said Miller.

Merkle discusses the numerous benefits NIEHS has gained from its six-year participation in ESI. (Photo courtesy Steve McCaw)

Speaking the language

While a common theme of this year's meeting was advocating environmental stewardship for the sake of protecting the environment itself, another theme focused on showing businesses and corporations why things like energy reduction, pollution prevention, water conservation, and waste elimination make smart financial sense, as well.

"Ten years ago, the original goal of ESI was to simply help people take the journey from noncompliance, to compliance, to beyond compliance, with regard to their business practices," said Bill Ross, former secretary for NCDENR, who now works as an environmental consultant in the private sector. "However, today, part of environmental stewardship is learning how to speak the language of business. As a general rule, if you can show someone how integrating certain practices into their business model can impact their bottom line, they'll usually listen to what you have to say."

Building a connection

"At the end of the day, sustainability and stewardship is about a lot more than facilities, animal welfare, or water conservation," added Price. "It's about building partnerships in our communities and recognizing that we're all connected to the same environment. The joy of programs like ESI is that they constantly provide us with new ways and insights on how best to do that."

(Ian Thomas is a public affairs specialist for the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

Attendees listen to testimonials from ESI stewards and discuss their own experiences with sustainability practices. (Photo courtesy Steve McCaw)

Ross, right, leads attendees in an ESI rendition of the North Carolina toast. (Photo courtesy Steve McCaw)

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Adelman balances science and parenthood for NIH tenure

By Ian Thomas

NIEHS lead researcher Karen Adelman, Ph.D., was awarded the prestigious honor of tenure by the NIH Central Tenure Committee, for her exemplary work with the Laboratory of Molecular Carcinogenesis. A native of Buffalo, N.Y., Adelman was one of eight recently tenured NIH scientists to be recognized in the March-April 2012 issue of the NIH Catalyst.

"I can't say enough wonderful things about my lab members and the people at NIEHS," said Adelman. "From the moment I arrived here, everyone, from the Director on down, has shown tremendous support for my work and the ideas I was passionate about."

The NIH tenure track process involves the rigorous evaluation of an intramural scientist and their work, in order to determine their overall worthiness of the long-term salary, personnel, and resource commitment that accompanies the tenure appointment.

In her spare time, Adelman is an avid hiker and amateur photographer. (Photo courtesy Steve McCaw)

A well-traveled career

Having earned her Ph.D. in molecular and cellular genetics from the Universite de Paris VI, Adelman spent 5 years as a postdoctoral researcher at Cornell University, before arriving at NIEHS in 2005. As head of the NIEHS Transcriptional Responses to the Environment Group, she and her team study the environment's impact on gene expression in Drosophila, or fruit flies, and mice.

"We've learned a lot about the various mechanisms of development and immune response by studying these areas in the fly system," explained Adelman. "Now the challenge comes in shifting those experiments toward the mammalian model and, therefore, that much closer to human application."

Throughout her career, Adelman has been recognized with a number of awards, including the 2006 Rising Star Early Career Award and a 2010 NIH Director's Award.

A focus on family

In addition to her duties as a full-time scientist, Adelman has also managed to balance the responsibilities of a home life. As the mother of two young children, she notes that effective time management skills have been crucial to her success with both roles.

"Bedtime is a wonderful thing," Adelman joked. "Another nice thing about working here at the Institute is that they're pretty flexible with my time and, as a mom, you can get a lot of work done between the hours of 8:00 p.m. and midnight."

Still, Adelman is quick to point out that none of it would be possible without help on the homefront.

"My husband is a phenomenal partner," she added. "We do everything as a team and that's been a huge supporter in allowing me to pursue my career. There's no way I could pull any of this off without him."

Balancing the future

With the tenure-track behind her, Adelman is excited for the challenges that lay ahead, as well as the research benefits and freedoms that come with tenure. However, proud as she may be of her career, Adelman freely admits that, for her, true happiness comes from not only success on the bench, but also at home.

"I'm so incredibly thankful to have had the kind of career in science that I've enjoyed, but still have such a wonderful family to come home to," said Adelman. "It's been an incredible challenge to balance those two aspects of my life but, difficult as that is at times, it's all doable if you're committed to making it work."

(Ian Thomas is a public affairs specialist for the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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Upcoming presentation on data integration at HHS

By Eddy Ball

NIEHS will welcome Todd Park April 5 for a presentation on the U.S. Department of Health Human Services (HHS) Health Data Initiative. Park, who has served as HHS chief technology officer since 2009 and was appointed U.S. Chief Technology Officer in March, will give a talk titled "The Health Data Initiative: Unleashing the Power of Open Data and Innovation to Improve Health" beginning at 10:00 a.m. in Rodbell Auditorium.

Park has brought his extensive private sector experience to bear on advancing the multifaceted Health Data Initiative. Park is often described as the HHS entrepreneur-in-residence. (Photo courtesy of Todd Park)

Park will discuss the rapid growth and success of the Health Data Initiative in making the troves of data available at HHS much more accessible to the public, putting it in the hands of innovators across the country who have developed novel and powerful applications for serving millions of Americans. The initiative maintains a constantly evolving, centralized Health.Data.gov platform for delivering new datasets and tools, along with supporting a community of data users and providers through social networking, as part of the HHS and Institute of Medicine commitment to open government.

Linked video:

Watch Park's interview with PBS News Hour's Hari Sreenivasan (05:03)

(Launches in new window)

Download Media Player: Flash

Looking forward to the Health Data Initiative Forum III, the third annual Health Data Palooza, June 5-6 in Washington, D.C., organizers are utilizing public-private partnerships and extensive outreach programs to make it easier than ever for consumers, employers, healthcare providers, researchers, advocates, journalists, local leaders, and others to access HHS data sources to improve individual and public health.

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Conference explores best practices of community-engaged research

By Robin Arnette and Brant Hamel

NIEHS and the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP) sponsored the South Atlantic National Research Conference (SANC), "Engaging the Community for Research Success: What Scientists and IRBs Need to Know," March 21-22 at the Raleigh Convention Center in North Carolina. The conference brought together more than 550 registered participants, which included principal investigators, research and clinical personnel, institutional officials, deans, vice-chancellors, human subject protection professionals, legal counsel, institutional review board (IRB) members, community health advocates, and public health officials.

The purpose of SANC was to gain a better understanding of ethical, regulatory and policy issues involved in conducting community-engaged research in national and international settings; to learn best practices in community-engaged research; and to provide a forum for researchers, regulators, and community representatives to learn from one another, network, and form partnerships. The two-day gathering included keynote and plenary sessions, and twenty eight break-out sessions.

Packenham welcomed conference attendees and introduced several speakers. As director of the OHRC, she works to establish a culture of protecting human participants in research studies. (Photo courtesy of John Maruca)

NIEHS advocates protection of human research participants

The NIEHS Office of Human Research Compliance (OHRC), which falls under the Clinical Research Program, Division of Intramural Research, developed the vision and theme for SANC, and served as host and major organizer. The OHRC is responsible for managing a comprehensive human research protection program at the Institute, and does so by establishing educational and training programs, offering suggestions during protocol development, providing guidance on federal and state regulations, conducting daily administration of the NIEHS IRB, and serving as liaison with the National Institutes of Health Office of Subjects Human Research Protections.

Joan Packenham, Ph.D., director of the OHRC and vice chair of the NIEHS IRB, said the conference was a great way to raise awareness about the responsibilities and challenges of conducting successful community-engaged research.

"Hosting this conference was an important part of what we do to equip community-engaged research stakeholders with useful information," Packenham said. "The speakers have been outstanding, and the conference has been a perfect forum to spur dialogue."

NIEHS has a long-standing commitment with community-based participatory research through the Division of Extramural Research and Training (DERT). DERT has funded research centers through its Partnerships for Environmental Public Health (PEPH), a program that brings together scientists, community members, educators, health care providers, and public health officials, in the shared goal of conducting research that is fully integrated with the community.

Norris and Packenham fielded questions following Norris' presentation. (Photo courtesy of Steve McCaw)

Research subjects or research partners?

During the conference, keynote speaker Keith Norris, M.D., executive vice president for research and health affairs at Charles R. Drew University of Medicine and Science, said a vital feature of community-engaged research is that researchers must build a true partnership with the community they are studying and consider them as participants in a shared program of research, not as research subjects. Norris noted that researchers must be willing to engage the community on its own ground and include community members in all aspects

of research, from conception to communication of results. He used the analogy that a truly successful community-engaged research program is like a marriage that involves a full and equal commitment of both parties to a common goal.

Community-level ethical considerations

Several of the conference speakers emphasized that communities may have serious concerns about how research results impact the reputation of the community and how such results are reported. Communities also want to see that results and knowledge obtained from studies come back to the research participant and to the community at-large, not just published in journals. According to Elmer Freeman, executive director of the Center for Community Health Education Research and Service in Boston, participants have insisted that results get reported in the popular press or in local news, in addition to traditional academic publishing.

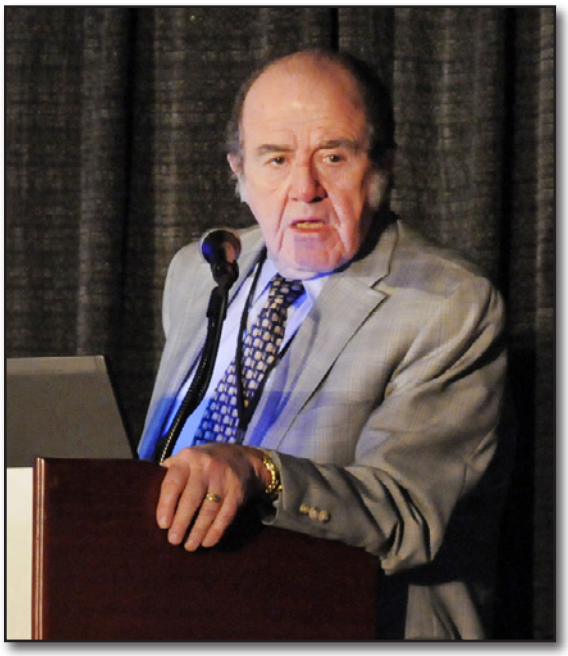
Communication is key to success

Many cultures have unique considerations that may affect how participants are recruited and the study is conducted. Ruth Ellis, M.D., a staff clinician in the Laboratory of Malaria Immunology and Vaccinology at the National Institute of Allergy and Infectious Diseases, noted that failing to treat the community as a partner in research could lead to a failure to recruit and retain subjects or to assess the true impact of innovations. In the worst case, Ellis said a loss of community trust could shut down the entire research program, which actually occurred due to a breakdown in communication between researchers and local residents in Jakarta, Indonesia.

Does the Belmont Report provide considerations for community risks and benefits?

Robert Levine, M.D., is a professor of medicine and lecturer in pharmacology at Yale School of Medicine and special consultant to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Levine was instrumental in crafting the 1978 Belmont Report, and structured his talk around whether the Belmont Report and the Common Rule of 1991 spoke to the fundamental issues of truly community-engaged research. He conceded that the Belmont's ethical principles could be seen as the necessary predecessor to the more ambitious goals of community-engaged research, where researchers and participants, who are no longer considered subjects and subordinates, ultimately reach consensus about objectives, study design, and results.

Ivor Pritchard, Ph.D., senior advisor to the director in OHRP, delivered a thought-provoking talk encouraging participants to critically consider how to best engage an IRB in community-engaged research proposals. (Photo courtesy of Steve McCaw)



Levine said, "Belmont marked a great advance over letting black men die miserably of syphilis in Tuskegee, but today's generation needs genuine community engagement to overcome the memories of Tuskegee, the legacies of racism, sexism, and imperialism, socioeconomic hierarchy, and the distrust of government." (Photo courtesy of Steve McCaw)

Feedback from conference attendees

Based on conference evaluations, attendees have overwhelming agreed that the conference was needed and provided an important opportunity for learning and discussion. Many have requested that OHRC sponsor another conference to continue the dialogue.

(Brant Hamel Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Laboratory of Signal Transduction.)

Many in the conference audience raised their hands in response to questions from Pritchard. (Photo courtesy of Steve McCaw)

Stephen Thomas, Ph.D., director of the University of Maryland Center for Health Equity, led an interactive discussion on the ethical considerations of community-engaged research in minority communities. (Photo courtesy of Steve McCaw)

With several networking breaks, meeting attendees had lots of opportunities to talk. (Photo courtesy of Steve McCaw)

NIEHS/NTP Director Linda Birnbaum, Ph.D., and Edward Emmett, M.D., from the Hospital of the University of Pennsylvania, discussed their experiences and successes in communicating research findings with local communities. Birnbaum noted that NIEHS has a history of supporting community-engaged research, saying, "You cannot conduct environmental health research unless the community is involved from the very inception." (Photo courtesy of Steve McCaw)

David Resnik, J.D., Ph.D., bioethicist and chair of the NIEHS IRB, posed several questions during the two-day conference. (Photo courtesy of Steve McCaw)

Thomas moderated a panel discussion titled, "Community Voices," which talked about the ethical considerations of community-engaged research in minority and disadvantaged communities. Seated from left to right, Elaine Hart-Brothers, M.D., Alan Richmond, Missy Brayboy, Melvin Jackson, Freeman, and Edgar Villanueva. Panelist Tony Locklear is not pictured. (Photo courtesy of Steve McCaw)

Science Notebook

The importance of calcium entry in mammalian reproduction

By Robin Arnette

The intricate steps that a fertilized egg takes in route to becoming an embryo are true marvels of nature. Reproductive biologists explain the phenomenon by saying the merging of an egg and sperm triggers signals deep inside the egg that allow it to begin cell division. These signaling events are known as egg activation, but new research suggests that some of the cues that induce egg development actually occur elsewhere.

Scientists from NIEHS, led by Carmen Williams, M.D., Ph.D., and the University of Pennsylvania are the first to show that calcium ions entering the egg from the outside are needed for key events that propel the egg to the two-cell stage. The Williams team published the results online Feb. 27 in the Proceedings of the National Academy of Sciences. Since calcium is a common ingredient in solutions used for *in vitro* fertilization, the work has significant implications for assisted reproductive procedures.

Simonich holds a joint appointment in the department of chemistry and department of environmental and molecular toxicology at Oregon State University, where she heads a research lab supported by NIEHS SRP funding. (Photo courtesy of Steve McCaw)

Back and forth

According to Williams, during fertilization of a mammalian egg, the sperm delivers a protein called phospholipase C (PLC), which causes the egg to release calcium from internal storage areas to the egg's cytoplasm. Since too much calcium in the cytoplasm is toxic to the egg, excess calcium is either pumped back into storage or out of the egg. The back and forth movement of calcium from storage or outside the cell into the cytoplasm is known as oscillation, and PLC keeps it going for 4-6 hours.

"The signaling that happens as a result of calcium entry occurs directly under the plasma membrane, rather than the entire inside of the egg," Williams said. "Our work shows that the calcium being pumped back into the egg from the outside helps spur egg activation."

Williams said she became interested in signaling as a result of calcium entry, after hearing about the work of NIEHS researcher James Putney, Ph.D. Putney studies store-operated calcium entry (SOCE), one of the pathways that calcium uses to re-enter a cell. Williams' work determined that SOCE probably happens at fertilization, but it isn't necessary. There are other unidentified channels that permit calcium reuptake and generate signals. Putney was pleased with Williams' findings.

"It is exciting to see that the process of calcium entry, so extensively studied in simple cell lines, plays such a fundamental role in the complex signaling underlying egg fertilization," Putney said.

Williams said this study wasn't possible without the technical expertise of visiting fellow and lead author on the paper Yi-Liang Miao, Ph.D. Miao only had five minutes to microinject mouse sperm into mouse eggs, load the eggs into a device that measures calcium levels, and record. He also had to figure out the proper buffer solution for the experiments. He needed something that had the correct pH, kept all of the ingredients in solution, and wasn't toxic to the eggs. It took several months, but he developed a buffer that worked.

Williams holds dual appointments in the Laboratory of Reproductive and Developmental Toxicology and the Clinical Research Program at NIEHS. (Photo courtesy of Steve McCaw)

What's in the media?

This research sets the stage for a new way of thinking when it comes to handling eggs for human *in vitro* fertilization. Williams explained that after eggs are removed from a woman, they are placed into a solution called culture medium that normally contains calcium. She also noted that many reproductive specialists freeze eggs and embryos and need to add chemicals, such as the cryoprotectant dimethyl sulfoxide (DMSO), to prevent the eggs from forming ice crystals. She urged these practitioners to pay attention to what's in the media.

"We've demonstrated that calcium and other chemicals in the media may impact the egg's ability to receive signals from the outside, or may let calcium leak in too soon, which is also a problem," Williams maintained.

Eggs depend on calcium to receive signals from the outside world and to communicate with other parts of the cell. Thanks to the Williams research team, we now know how important this abundant mineral can be.

Citation: Miao YL, Stein P, Jefferson WN, Padilla-Banks E, Williams CJ. 2012. Calcium influx-mediated signaling is required for complete mouse egg activation. Proc Natl Acad Sci U S A; doi:10.1073/pnas.1112333109 [Online 27 February 2012].

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Reduced vaccine effectiveness tied to PFC exposure

By Nancy Lamontagne

NIEHS grantee Philippe Grandjean, M.D., has shown that higher levels of exposure to perfluorinated compounds (PFCs) are associated with reduced immune response in children. The study is one of the first to link childhood exposure to PFCs with immune system deficiency and the results point to the importance of assessing the immunotoxic potential of PFCs. In addition, the immunotoxic effects of PFCs and other environmental contaminants might help explain vaccination failures that have puzzled scientists.

As described in their paper published in the Journal of the American Medical Association (JAMA), Grandjean and his colleagues studied the immunotoxic effects of PFCs by evaluating about 600 children from the Faroe Islands, located between Scotland and Iceland. The people of these islands

frequently eat marine food, which exposes them to a wide variety of contaminants, including PFCs, which accumulate in the marine food chain. PFCs are highly persistent in the environment and are widely used in food packaging and textiles, because of their stain-resistance and water-repellant properties.

Grandjean and his colleagues have studied the health effects of marine contaminants in the Faroe Islands people since the 1980s. In addition to PFCs, the researchers have investigated methylmercury and polychlorinated biphenyls. (Photo courtesy of Philippe Grandjean)

"We've worked with this community for 25 years and have been very successful in conducting population studies," says Grandjean, an adjunct professor of environmental health at the Harvard School of Public Health in Boston. "We have a record of doing something that is useful to the community and also useful to science."

The investigators assessed prenatal exposure by measuring PFCs in the mother's serum during pregnancy and later checked for the compounds in samples from the children at age 5. They used the antibody response to childhood immunizations as an indication of how well a child's immune system was functioning, taking measurements of antibody concentration just before the last booster shot at age 5 and again two years later. The children with elevated exposure to PFCs showed lower antibody responses to childhood immunizations.

Grandjean presented his research Feb. 16 at the NIEHS National Advisory Environmental Health Sciences Council meeting (see story), where NIEHS/NTP Director Linda Birnbaum, Ph.D., described his work as potentially paradigm changing. (Photo courtesy of Steve McCaw)

"When the PFC exposure doubled, the child lost about half of the antibody concentration and the risk of not being protected, even after four vaccinations, increased by a factor of two to four at age 7," says Grandjean, who is also head of environmental medicine research at the University of Southern Denmark, Odense.

The researchers will continue to examine immune system dysfunction associated with PFC exposure, including responses to infectious disease. There are problems with vaccine effectiveness around the world, and Grandjean says that immunotoxicity needs to be examined to ensure vaccinations are effective both on individual and population levels. He also says that the impact of environmental contaminants on the immune system could possibly play a role in noncommunicable diseases, such as cancer, and autoimmune diseases, such as type 1 diabetes.

Citation: Grandjean P, Andersen EW, Budtz-Jorgensen E, Nielsen F, Molbak K, Weihe P, Heilmann C. 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. JAMA 307(4):391-397.

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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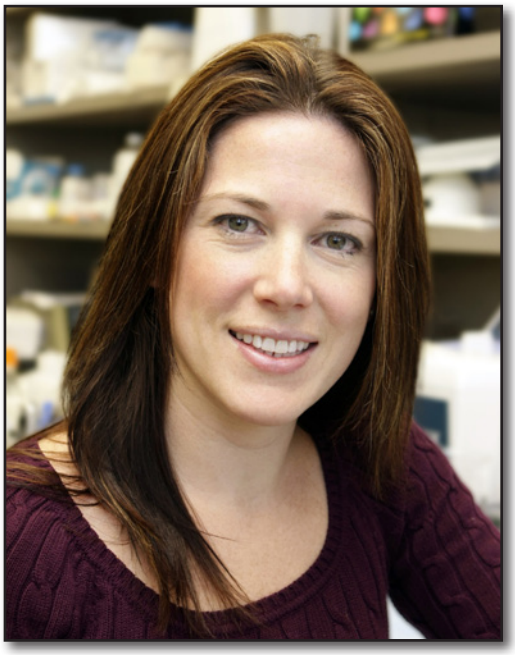
Hormones and Cancer highlights NIEHS/NTP paper

By Eddy Ball

The journal Hormones and Cancer is highlighting a new paper by NIEHS and NTP scientists as one of nine available free at the journal's website. The bimonthly journal is beginning its third year, as a publication of the Endocrine Society, with an updated cover design and new leadership for its mission of advancing basic and clinical research on hormonally influenced cancers of endocrine glands.

In a message of congratulations to the paper's first author, NIEHS postdoctoral fellow Shannon Whirledge, Ph.D., incoming Editor-in-Chief Carol Lange, Ph.D., wrote, "Hormones and Cancer has selected your recent paper for its high significance to our field and made it available as a free download." As such, the paper forms part of the important first impression the journal makes on potential subscribers and prospective members of the Endocrine Society, who receive open access as part of their membership.

Whirledge, who is a member of the NIEHS Molecular Endocrinology Group headed by lead researcher John Cidlowski, Ph.D., co-authored the paper with Cidlowski, the senior author, and lead researcher Darlene Dixon, D.V.M., Ph.D., head of the NTP Molecular Pathogenesis Group, the second author.

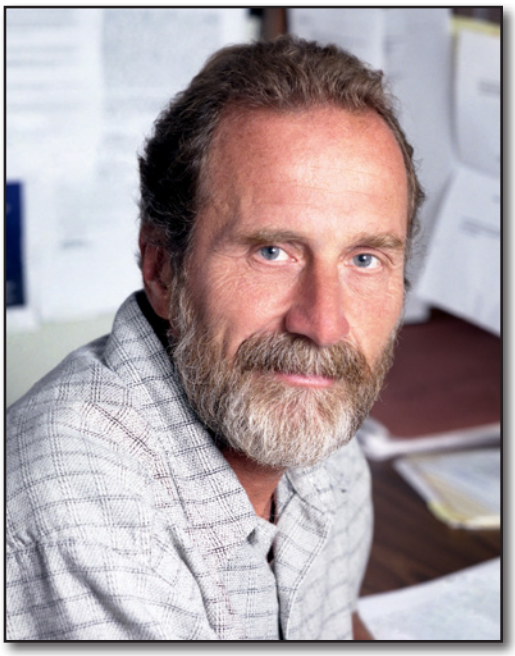


The Hormones and Cancer paper is Whirledge's second publication as a member of the NIEHS Molecular Endocrinology Group and as first author. (Photo courtesy of Steve McCaw)

Linking glucocorticoids to cellular proliferation in uterine fibroids

According to the study, it is reported that women over age 45 have more than a 60 percent lifetime risk of developing uterine fibroids, or leiomyomas, benign tumors of the uterus that are the leading cause for hysterectomies in the U.S. Fibroids pose a significant public health concern, due both to their prevalence and associated symptoms, including heavy bleeding, pain, infertility, and complications during pregnancy and labor.

Although estrogen has been clearly linked to fibroid development and growth, Whirledge and her colleagues suspected that other factors, including the steroid hormone glucocorticoid receptor (GR) binding, are involved. "We hypothesized that glucocorticoids might also block estrogen-regulated gene expression or biological functions important for leiomyoma growth," they wrote, "[with] the potential to improve current strategies in the development of treatment for uterine leiomyomas."



Among his many honors for his research, Cidlowski has received the Edwin B. Astwood Award by the Endocrine Society. He has been with NIEHS since 1995. (Photo courtesy of Steve McCaw)

In vitro results suggest potential efficacy of *in vivo* intervention

Using immortalized human uterine leiomyoma cells and uterine smooth muscle cells supplied by Dixon, the team performed a series of detailed experiments to determine expression of GR and estrogen

receptor, gene expression, and cell proliferation. The researchers were able to identify gene expression changes differentially regulated with treatment by both the synthetic glucocorticoid dexamethasone (Dex) and estrogen (E2) that may play a role in an antagonistic relationship. Dex and E2 had significant effects on the expression of genes involved in inflammatory and cell proliferation pathways. By interfering with cell phase progression, Dex treatment decreased cell proliferation, a key to stemming the aberrant growth characteristic of fibroids, and cotreatment with E2 did not reverse the effect.

Dixon's group studies rodent reproductive tissue and tissue samples taken from cycle-staged, premenopausal women that are part of the NIEHS/George Washington University Uterine Fibroid Study. (Photo courtesy of Steve McCaw)

"This study provides the first evidence that glucocorticoid and estrogen antagonism acts not only in a global manner, but also in a cell-specific manner in the uterus, specifically a uterine tumor in which many questions remain regarding the regulation of its endocrinology," the researchers explained. "The clinical implications of the current findings are significant and have the potential to improve current strategies in the development of treatment for uterine leiomyomas."

Looking ahead to clinical applications of their findings, the research team said that translating their discoveries into a therapeutic intervention will require further study to better understand the molecular processes involved in glucocorticoid antagonism and whether the findings can be replicated in an intact uterine environment.

Citations:

Lange CA. 2012. Hormones and Cancer: A Bright Future. Horm Cancer. Apr;3(1-2):1-2.

Whirledge S, Dixon D, Cidlowski JA. 2012. Glucocorticoids Regulate Gene Expression and Repress Cellular Proliferation in Human Uterine Leiomyoma Cells. Horm Cancer; doi: 10.1007/s12672-012-0103-0 [Online 7 February 2012].

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Grantee with Midas touch speaks at NIEHS

By Eddy Ball

As his company develops equipment for extracting metals from toxic acid rock drainage (ARD), with the potential for turning hazardous waste water into copper, zinc, and other valuable metals or useful compounds such as iron sulfate, NIEHS grantee Patrick James, Ph.D., has taken to heart the environmental concept of sustainability.

As James told his audience during a talk at NIEHS March 9, "Our paradigm is to treat ARD as a resource, not a waste." If the equipment ultimately performs as expected — and early results are very promising — James' company, Blue Planet Strategies, LLC, (BPS) could become instrumental in cleanup efforts at orphaned legacy mines, extend the profitable life of mines in the U.S., and possibly make James and his partners wealthy men.

The host of James' talk was NIEHS Superfund Research Program (SRP) Health Scientist Administrator Heather Henry, Ph.D. Most of the people in James' audience were NIEHS grant administrators managing opportunities with the NIH Small Business Innovation Research (SBIR)/Small Business Technology Transfer (SBTT) program. Funded by a set-aside portion of an agency's extramural budget, the program fosters research and development projects that further the agency's mission and show a potential for commercialization.

Following the presentation, Henry, left, and James stayed to answer questions from the audience. James noted that U.S. Geological Service estimates indicate there are 450,000 contaminated legacy mining sites in the U.S. alone. (Photo courtesy of Steve McCaw)

SBIR funds startup

SBIR funding would help get the prototype off the ground, the developers reasoned, but it would still need private sector demand to fully develop extraction potential. "If it's not economically viable," James explained, "it's not going to get out the door." So developers set about enhancing a proprietary method for extraction, using a single-electrode, two-step electrowinning/electroplating procedure that would cost less to operate than the value of materials it reclaimed from wastewater.

Because of regulatory and legal concerns, Blue Planet decided to use samples from operating mines that were similar in composition to waste water at the Summitville Superfund site. That approach would simultaneously demonstrate the procedure's potential for toxic metal remediation and its value for the private sector.

The equipment was originally developed around copper extraction. Recent upgrades have greatly expanded its range of utility, and initial tests on ARD targeted iron sulfate recovery, because iron is a common ARD contaminant present in large amounts, but is not of sufficient value, in itself, to warrant recovery of the metal, James explained.

In initial efforts, the cost of production was $350 per ton, while market value of the extracted ferrous sulfate was $700 per ton. Ferrous sulfate is a high-value product widely used in a variety of industrial processes, including textile manufacturing, water treatment, printing, and agriculture.

James said he hopes to reduce production cost to around $200 per ton as the equipment is scaled to increase the treatment volume to as much as 2,000 gallons per minute.

Sustainability

The private sector has a compelling interest in the extraction technique for turning what is currently waste into additional revenue and extending the lives of existing mines in the U.S., where the purest ores are quickly becoming depleted. "Because of high closure costs, nobody wants to shut down mines," James explained. Furthermore, getting permits for new mines takes years, and the costs are also enormous.

"So they're very, very interested," James said. Augmenting existing processing facilities with BPS technology will enable the use of vast quantities of waste quality ore for copper production, while consuming about half as much energy as conventional processing. The augmentation would be economically viable, as long as copper stays above $2 per pound. The process could double the life as well as the production capacity of existing mines, thus reducing the need for imported ore and new mine development.

James is hoping that with a proven prototype, his new technology will find its place in Superfund cleanup, once legal and regulatory issues are worked out. As an entrepreneur, he is also striving to achieve a healthy return on his company's investment of time, ingenuity, and capital.

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Science showcases grantee and NIEHS/NTP tox efforts

By Eddy Ball

A feature in the March 2 issue of Science, "LIFE SCIENCE TECHNOLOGIES: Animal-Free Toxicology: Sometimes, in Vitro is Better," highlights NIEHS/NTP predictive toxicology efforts. The article discusses work by NIEHS grantee Thomas Hartung, M.D., Ph.D., toward mapping what he calls the toxome, the Tox21 consortium, and alternative testing.

National Toxicology Program
U.S. Department of Health and Human Services

Along with efforts well underway in Europe, writes Jeffrey Perkel in the Science article, animal-free toxicology in the U.S. is demonstrating that, sometimes, *in vitro* is better than trying to subject tens of thousands of chemicals to time-consuming and expensive animal testing. The goal of these initiatives is to identify the biomolecular changes triggered by toxic exposure that lead ultimately to the pathological outcomes, or apical endpoints, measured in traditional animal studies.

Prior to joining Johns Hopkins, Hartung was head of the European Center for the Validation of Alternative Methods of the European Commission from 2002 to 2008. (Photo courtesy of Johns Hopkins)

Mapping perturbed pathways as a guide to high-throughput screening

Hartung, a Doerenkamp-Zbinden professor and chair for evidence-based toxicology at the Johns Hopkins University Bloomberg School of Public Health, has embarked on a six-year NIEHS funding quest to map the biomolecular pathways perturbed in response to toxicity by endocrine disruption that will mark one important step forward toward the gargantuan task. "Mapping the entirety of these [toxicity] pathways (i.e., the Human Toxome)," Hartung wrote in his grant description, "will be a large-scale effort, perhaps on the order of the Human Genome Project."

Using gene expression microarrays and mass spectrometry-based metabolomics, Hartung's team is testing human breast cancer cell lines, exposed to some 53 endocrine-disrupting compounds, to chart gene expression and metabolomic changes in protein production.

Consortia to develop predictive toxicology and reduce animal testing

In addition to funding such researchers as Hartung, NIEHS/NTP is also a part of two forward-thinking interagency consortia working to expand use of *in vitro* testing and reduce reliance on animals. The newest, known as Tox21, is a partnership among NIEHS/NTP, the NIH Chemical Genomics Center (NCGC), the U.S. Environmental Protection Agency, and the U.S Food and Drug Administration, to develop predictive toxicology using high-throughput screening.

Tox21 has set its sights on screening 10,000 plus compounds on an NCGC robotics platform. The information that high-throughput screening yields will help identify toxicity pathways that will be the basis for more targeted assays.

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) also administers a partnership known as the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). With representatives from U.S. federal regulatory and research agencies that require, use, generate, or disseminate toxicological information, ICCVAM is charged with promoting the validation and regulatory acceptance of new alternative test methods that may reduce, refine, and replace animal use for safety testing of various chemicals, medicines, and consumer products.

NICEATM ICCVAM
Advancing Public Health and Animal Welfare

To date, ICCVAM has contributed to the regulatory approval of more than 49 alternative methods. Replacing animals with *in vitro* testing to ensure consumer and worker safety isn't always possible. But when they can't replace animals, alternative methods strive to use many fewer animals and to make safety testing with animals less harmful, painful, and stressful.

Everyone Perkel interviewed for his story conceded that the challenges are enormous, and that progress toward realizing predictive toxicology and reducing animal testing, as much as possible, will take several years. Still, the effort is receiving government support from such agencies as NIEHS/NTP and private sector involvement is growing.

Citation: Perkel, JM. 2012. LIFE SCIENCE TECHNOLOGIES: Animal-Free Toxicology: Sometimes, in Vitro is Better. Science 335(6072):1122-1125.

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Guest speaker helps NIEHS gauge the potential of microbiome research

By Melissa Kerr

Developmental biologist John Rawls, Ph.D., spoke March 1 at NIEHS on the relationship of intestinal tract flora balance and risk of obesity, an important public health challenge that affects one-third of adults and nearly a fifth of children and adolescents in the U.S. Rates of overweight and obesity have increased steadily in recent years, suggesting a link to other environmental factors, in addition to the usual suspects of sedentary lifestyle and increased food intake.

At the beginning, Rawls introduced the theme that would run throughout his talk. "One of my main goals in life is to try and come up with novel approaches to treat obesity and prevent it as well," he said. "Collectively, our nation needs to lose about 4.6 billion pounds."

"It's a very complex ecosystem," Rawls said of the bacteria community in the human gut. (Photo courtesy of Steve McCaw)

Hosted by Health Scientist Administrator Lisa Chadwick, Ph.D., Rawls' talk on "Microbial and developmental regulation of vertebrate energy balance" also gave his audience an opportunity to consider how similar lines of research on the trillions of microbes that colonize humans might advance the NIEHS mission of discovering the ways environment affects people, in order to promote healthier lives (see text box).

Rawls is an assistant professor in the department of cell and molecular physiology and the department of microbiology and immunology at the University of North Carolina (UNC) at Chapel Hill School of Medicine, where he conducts research in the areas of microbiology and gastroenterology. In 2004, Rawls published the first in a series of papers on the development of germ-free zebrafish as a model organism for microbiome research. His current research is supported by three grants funded by the National Institute of Diabetes and Digestive and Kidney Diseases.

Helena Davis was one of several NIEHS Division of Extramural Research and Training staff members who attended the talk. (Photo courtesy of Steve McCaw)

Making science transparent

Rawls explained that he uses zebrafish in his work because of the transparency of its tissues during development, its size and rapid development, and the extent to which its biology is evolutionarily conserved in mammals. This optical transparency, Rawls said, permits real-time *in vivo* imaging of host tissues and their microbial inhabitants. The small size of the zebrafish enables high-throughput screening.

Through these experiments, he hopes to come to an understanding of how gene transcription is affected by different microbial populations, using comparative studies of zebrafish that are germ-free, conventionally raised, and conventionalized — colonized with defined microbiota after being conceived germ-free.

Some of Rawls' work identified certain intestinal microbes that could influence a host's ability to promote fat storage. The unique ability of scientists to observe zebrafish tissue has revealed that certain gene transcriptions are modified by microbial interactions, specifically expression of a circulating inhibitor of lipoprotein lipase called angiopoietin-like 4 (Angptl4).

Chadwick, who hosted the talk remotely, presented a concept clearance, "Microbiome/Environment Interactions," during the February meeting of the National Advisory Environmental Health Sciences Council at NIEHS. (Photo courtesy of Steve McCaw)

Microbes seem to play a role in the regulation of Angptl4 in the intestine, promoting fat storage in the host. Thus, there is potential for using Angptl4 as a target for obesity intervention.

Branching out

Along with research into gut microbial ecology and regulation of host nutrient metabolism, Rawls is also exploring the morphogenesis of white adipose tissue (WAT), which is used by the body as sites of energy storage, as well as regulators of energy balance and inflammation. "It matters how we store fat and it matters how adipocyte tissue is built," said Rawls.

As he explained, the origin of these tissues, or adipogenesis, is not well understood. Also, the role of environmental factors and diet in the development of adipocytes is not yet clear. Rawls' group is the first to use zebrafish as a model organism for studying WAT development.

Rawls argued that understanding WAT development could lead to novel approaches for obesity intervention and prevention. Although he readily admits there are more ideas than information about WAT development, Rawls' group is gaining insights from their model into the dynamics of vascularization and patterns of what he described as temporal oscillation between increases in their size of cells and their number. Vascular architecture, he said, determines growth of WAT, and the pattern of antagonism between increases in size and number of cells seems to influence inflammation and insulin sensitivity.

Advancing understanding of the microbiome

The microbiome consists of the collection of microorganisms that live on and in a human being. Within a person, there are around 160 bacterial species and anywhere from 10-100 trillion microorganisms — 10 times the number of human cells.

As part of her work in the NIEHS Division of Extramural Research and Training, Chadwick is the Institute's representative for the Human Microbiome Project, a large program funded by the NIH Common Fund. One of the goals of this program is to develop a reference microbiome that would consist of information from many different body sites within a healthy individual. This information, and other studies funded by this program, is helping us better comprehend the relationship between microbial balance and disease development.

In addition, Chadwick administers the NIEHS extramural research program investigating how the microbiome interacts with the environment. NIEHS is interested in how the function of the microbiome may be permanently altered by exposure to environmental chemicals, particularly during early life exposures when the microbiome is being colonized. It has also been discovered that some environmental chemicals can be metabolized by an individual's microbiome. "Everyone has a slightly different microbiome, so you can imagine that this could be a factor in why people respond differently to the same exposure," said Chadwick. NIEHS would like to know more about this process, and the range of chemicals that are metabolized in this way.

Rawls' research is clearly related to Chadwick's planning for future initiatives. Previous experiments have shown that the microorganisms within a person's intestines have an impact on the host's metabolism of dietary nutrients, and, because of the import role of the gut in immunity, the microbiome can influence health throughout the body.

"This is kind of a new area for [NIEHS] and I wanted to bring someone to talk about it. Dr. Rawls' work is particularly interesting, because he uses zebrafish as a model, one which is also frequently used in toxicology studies," said Chadwick.

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

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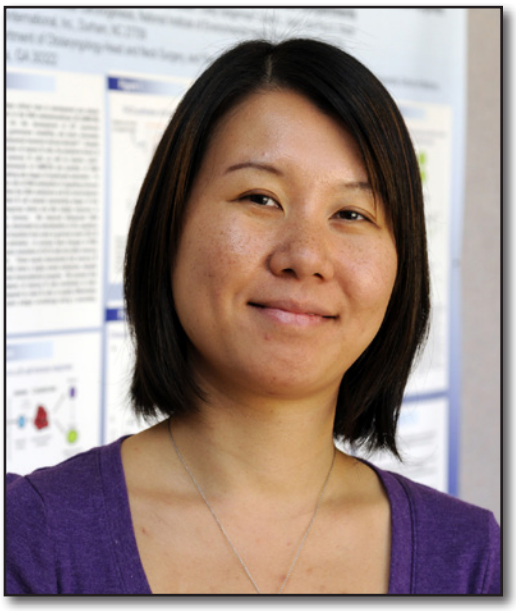
Lai discusses DNA methylation at WSA Scholars seminar

By Ian Thomas

NIEHS scientist Anne Lai, Ph.D., was one of three honored presenters at the 2nd Annual NIH Women Scientist Advisors Committee (WSA) Scholars Seminar March 2 in Bethesda, Md. Held in Wilson Hall on NIH's main campus, the series features talks from female recipients of the Fellows Award for Research Excellence (FARE).



WSA Scholar Lai (Photo courtesy of Steve McCaw)

"Winning the WSA scholar award itself was a wonderful honor, but I was thrilled for the chance to give a talk to so many of my fellow women scientists," said Lai. "It is always a great feeling when your research is recognized, but it's particularly nice when that recognition comes from such a closely knit group of one's peers."

A postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis, Lai was named a 2012 FARE winner for her paper, titled "Dynamics of DNA methylation during B lymphocyte activation and differentiation," a study which examined the impact of epigenetic events on the immune system (see story).

"We set out to better understand how DNA methylation can influence immune response," Lai explained. "By tracking the distribution of a specific epigenetic mark in B lymphocytes throughout the course of an infection, we discovered a number of DNA methylation reprogramming events that occurred after immune activation. It is these events that we believe may have an important role in shaping a memory immune response."

A native of Hong Kong, China, Lai's family immigrated to California when she was 11 years old. Raised in Los Angeles, Lai completed her undergraduate studies at the University of California, Berkeley before moving to North Carolina, where she earned a Ph.D. in immunology at Duke University and began postdoctoral work at NIEHS.

"Anne has done an amazing job as a member of my group," said Paul Wade, Ph.D., Lai's principal investigator. "Her body of work as a whole speaks for itself, but it's always nice to see someone who works as hard as she does get the recognition for it that she deserves."

Launched in 1993, the WSA committee was founded to examine and recognize the achievements of women scientists in intramural research. At present, there is at least one WSA representative for each of NIH's 27 institutes and centers (see text box).

Other presenters included Yurong Song, Ph.D., a postdoctoral fellow with the National Cancer Institute Center for Cancer Research, and Shruti Naik, a research fellow with the National Institute of Allergy and Infectious Diseases.

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor)

Duties and activities of WSA members

Like their fellow WSA members, the NIEHS/NTP representatives, biostatistician Grace Kissling, Ph.D., and chemist Suramya Waidyanatha, Ph.D., have the following duties to perform:

- Hold regular meetings with her Scientific Director in order to advise him/her about issues relevant to women scientists. Attend Lab/Branch Chief meetings to serve as a representative of women scientists.
- Inform the Institute's women scientists on issues that will affect them, such as tenure track and staff scientist policy decisions, and solicit their opinions.
- Organize meetings for the women scientists, to discuss issues of general concern, or to present programs of general interest.
- Serve, or designate an alternate woman scientist, from her own IC, another IC, or even from the extramural community, to serve on tenure-track, tenured scientist, or lab/branch chief IC search committees.
- Attend WSA committee meetings once a month where issues such as pay equity, family life, and work-related hazards are discussed.
- Subcommittees may be established to deal with specific issues, such as monitoring resource allocations, awards, or handling arrangements for lectures.

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Fire retardant study named paper of the year by ES&T

By Eddy Ball

An NIEHS-funded study by grantee Heather Stapleton, Ph.D., was selected as top science paper of 2011 by the journal Environmental Science & Technology (ES&T). Published by ES&T May 18, 2011, the paper examined levels of flame retardant chemicals in infant and toddler products. It attracted immediate attention from the media, including a feature on the CBS Evening News and coverage by the New York Times and others.

According to Kellyn Betts, who wrote an article about Stapelton's winning paper for ES&T, the study prompted California to amend its fire retardant statute to exempt some children's products, a potentially important step in reducing exposures nationwide. Stapleton's mentor and longtime colleague, NIEHS/NTP Director Linda Birnbaum, Ph.D., described the paper as groundbreaking.

In addition to this year's win, Stapleton also authored the ES&T top paper of 2005. (Photo courtesy of Duke University)

The study, "Identification of Flame Retardants in Polyurethane Foam Collected from Baby Products," found that infant products contain high levels of several flame retardant chemicals, which are suspected to have potential to disrupt thyroid hormone signaling important in normal development (see story). Stapleton and her colleagues tested levels in polyurethane foam in car seats, changing tables pads, mattresses, and other infant and toddler products, and found retardants in 80 of 101 products tested at levels as high as 12 percent by weight of foam.

"This paper was a real wake up call," Birnbaum said. "Some of these chemicals are very persistent in the environment and may have the potential to cause a variety of adverse health effects."

Stapleton, who is an assistant professor of environmental chemistry at Duke University, received an NIEHS Outstanding New Environmental Scientist award in 2008 (see story), providing early career support for setting up her lab. She holds two grants from NIEHS — "Children's exposure to flame retardants: Effects on thyroid hormone regulation" and "Deiodinase activity as a biomarker of response to brominated flame retardants."

Citations:

Betts K. 2012. Fire Retardants Abound in Baby Products: ES&T's Top Science Paper 2011. Environ Sci Technol; doi:10.1021/es300730d [Online 5 March 2012].

Stapleton HM, Klosterhaus S, Keller A, Ferguson PL, van Bergen S, Cooper E, Webster TF, Blum A. 2011. Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol 45(12):5323-5331.

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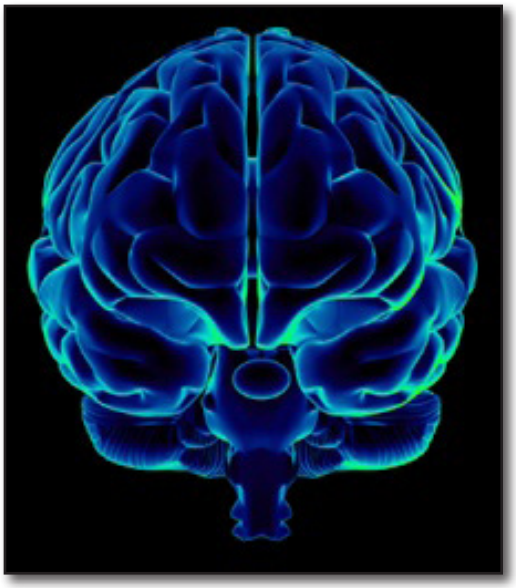
Early-life infection may lead to adult memory loss

By Robin Arnette



Lance, a 30-year-old law student, is studying for the bar exam. As he sifts through volumes of cases in a secluded corner of the law library, he's a little anxious. It will be his third attempt to pass the test. Lance works as hard as his classmates, but he just can't seem to hold all of the pertinent legal details in his head.

According to research performed in rodents, Lance's memory problems may be the result of an infection he had early in life. NIEHS grantee Staci Bilbo, Ph.D., studies the influence of the neonatal environment on the immune system and its impact on the adult brain. During her talk March 8 at NIEHS, Bilbo said rat pups that suffered bacterial infections *in utero*, and experienced a second immune challenge later in life, displayed severe memory impairments as mature rats.

Bilbo explained that this early-life infection doesn't just impact memory. She argued that it is a vulnerability factor that primes animals, particularly humans, to exhibit any number of disorders, such as multiple sclerosis, depression, and even addiction.

Learning and the immune response

Bilbo said microglia, one type of immune cell in the brain, is a major player in later-life brain function and behavior. Microglia cells produce interleukin-1beta (IL-1beta), a signaling molecule that is critical for normal brain development. To understand the role of microglia in later-life effects, Bilbo and her team exposed postnatal day four rats — equivalent to a preterm human infant in the second or third trimester — to *E. coli*, a common infection in developing fetuses. When the rats reached adulthood, Bilbo examined their learning ability using a standard conditioning program.

On the first day, the rats were placed into a new environment and allowed to explore. They were then separated into two groups. The control group received an injection of saline, while the other received bacterial lipopolysaccharide (LPS), a substance meant to stimulate the immune system. On day two, both sets of rats were placed in the same surroundings as the previous day and were given a mild foot shock. When placed in the same terrain on day three, the saline-treated rats had learned that a shock was imminent and froze in their tracks. Members of the LPS group, however, didn't remember the shock and explored their environment as if nothing had ever happened.

"The neonatal exposure to *E. coli* allowed the brain to upregulate all of the genes it needed to respond to the infection," Bilbo said. "But, if it had LPS on top of that, the microglia in the brain produced too much IL-1beta, allowing the rat to over respond when it encountered a second immune challenge."

Bilbo is an assistant professor in the department of psychology and neuroscience at Duke University. She presented a talk titled "Programming Innate Immunity: Implications for Brain Behavior Throughout the Lifespan.". (Photo courtesy of Steve McCaw)

NIEHS Laboratory of Toxicology and Pharmacology scientist Jau-Shyong Hong, Ph.D., right, who examines microglial response to brain injury, invited Bilbo to the Institute to talk about her work. (Photo courtesy of Steve McCaw)

A mother's love

Other scientists have shown that mother rats impact the brains of their offspring through licking, grooming, and nursing. The researchers mimicked this behavior, by separating the moms from their pups for 15 minutes a day and then placing them back with their babies. As a result, the moms increased their amount of care, and the pups grew up to have enhanced learning capabilities and decreased microglial activities in response to LPS.

Bilbo wondered if she could prevent the effect of early infection by augmenting rodent maternal care. She used the same separation protocol on early-infected pups, and found she could prevent microglial sensitization.

"The extra licking blocked an over response by the microglia, so we believe the entire process is epigenetically induced," Bilbo remarked.

After the lecture, NIEHS Laboratory of Molecular Genetics researcher Michael Resnick, Ph.D., left, asked Bilbo how her work relates to studies being done on post-traumatic stress disorder (PTSD) in troops returning from Iraq and Afghanistan. (Photo courtesy of Steve McCaw)

Huiming Gao, M.D., Ph.D., a postdoctoral fellow in the NIEHS Laboratory of Toxicology and Pharmacology, took copious notes during the seminar and said, "Bilbo's results not only help us better understand brain and immune system development, but also neurodegenerative diseases and mental illnesses."

It's unclear whether attorney-to-be Lance suffered an infection as a developing fetus or if he had a nurturing mother. Nonetheless, Bilbo's research offers an intriguing explanation for his poor memory and a new direction in understanding the influence of the immune system.

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Study suggests possible therapy for arsenic toxicity

By Angela Spivey

One of the first large-scale genomic studies conducted in a developing country suggests a possible route for preventing disease in people exposed to arsenic, by improving metabolism of the metal with nutrients or compounds that target a process called methylation. The study also showed that genetic differences may partially explain why some people exposed to arsenic get sick, while others exposed to the same levels do not.

The study, funded by NIEHS and the Superfund Research Program, identified small genetic variants that increase risk for skin lesions in people exposed to arsenic. The variants are found near the enzyme for metabolizing the chemical into a less toxic form, providing strong evidence that efficient metabolism of arsenic through methylation is protective.

The team was led by Habibul Ahsan, M.D., senior author of the study and Louis Block professor of epidemiology at The University of Chicago (UC). NIEHS Outstanding New Environmental Scientist (ONES) awardee Brandon Pierce, Ph.D., also of UC, was first author.

The Environmental Factor has featured stories on studies led by Ahsan in the past — one on arsenic and risk of death in 2010 (see story) and another on arsenic and smoking in 2011 (see story). Pierce was a co-author on the first one and Graziano was a co-author on both. (Photo courtesy of Habibul Ahsan)

Understanding differences in host susceptibility

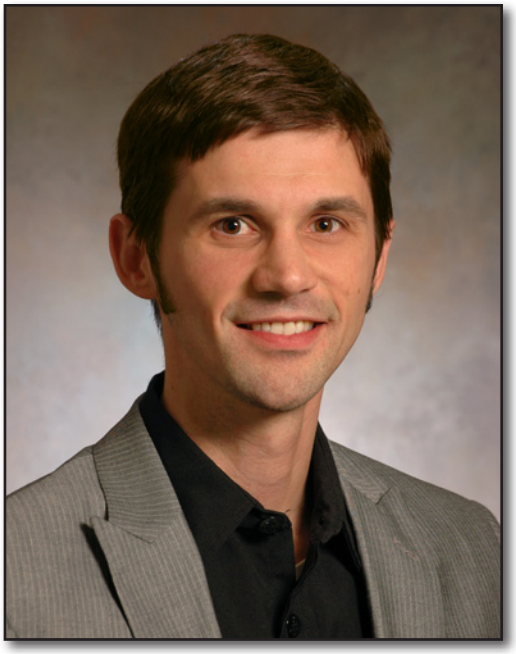
"Whatever the source of exposure, different individuals vary with respect to their susceptibility to the toxicity of arsenic," said Ahsan. "Now that we understand the molecular basis of some of this disease risk, it is conceivable to think of incorporating this information into testing and evaluating, or potentially coming up with successful biomedical interventions."

"This current study shows if you're a better methylator, you're at a lower risk for disease," said co-author Joseph Graziano, Ph.D., professor of environmental health sciences and director of the Superfund Research Program at the Mailman School of Public Health at Columbia University.

Nutrition may be a protective factor

The findings open the possibility of interventions using compounds that boost methylation, such as folic acid, a strategy currently being tested by co-author Mary Gamble, Ph.D., associate professor of environmental health sciences at Columbia.

The researchers conducted the study with participation from almost 3,000 people in Bangladesh exposed to arsenic for decades through their drinking water. About half the country's population has been accidentally exposed to arsenic, due to the installation of tube wells to tap groundwater sources in the 1970s.



As a ONES awardee, Pierce will receive five years of new investigator support from NIEHS (see story). He and Ahsan have collaborated on a series of studies on arsenic in a Bangladesh cohort. (Photo courtesy of Brandon Pierce)

An unbiased search of the genome

In this genome-wide association study, the researchers genotyped the participants to look for small genetic changes known as single nucleotide polymorphisms (SNPs). They identified several SNPs that were common among three groups of people — those with high levels of the most toxic arsenic metabolite, dimethylarsinic acid, people who had skin lesions, and people with reduced expression of the arsenic metabolizing enzyme.

The study also shows that such large-scale genomic studies are possible in a rural population of a developing country and, therefore, have potential for translational impact.

"Many genomic signals that we see are not robust enough or do not pertain to a large population," Ahsan said. "But, in this study, the finding is robust and the impact is massive." The study was published online Feb. 23 in PLoS Genetics.

Citation: Pierce BL, Kibriya MG, Tong L, Jasmine F, Argos M, Roy S, Paul-Brutus R, Rahaman R, Rakibuz-Zaman M, Parvez F, Ahmed A, Quasem I, Hore SK, Alam S, Islam T, Slavkovich V, Gamble MV, Yunus M, Rahman M, Baron JA, Graziano JH, Ahsan H. 2012. Genome-wide association study identifies chromosome 10q24.32 variants associated with arsenic metabolism and toxicity phenotypes in Bangladesh. PLoS Genet 8(2):e1002522.

(Angela Spivey is a contract science writer for the NIEHS Superfund Research Program.)

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Small business explores new approaches in reproductive toxicology

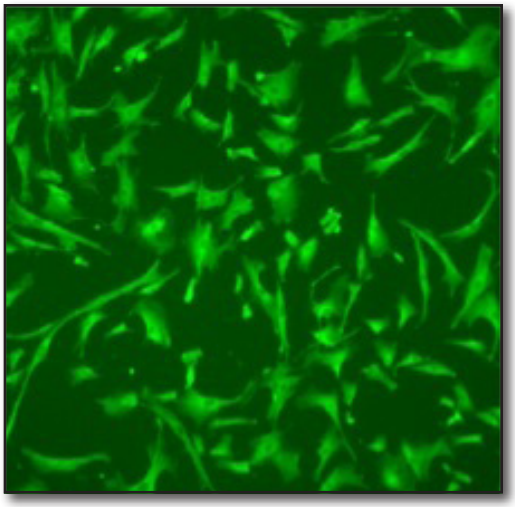
By Nancy Lamontagne

NIEHS grantees Paul Turek, M.D., and Constance John, Ph.D., of MandalMed Inc., are developing a human-cell based testis model to study reproductive toxicology. Such a system could provide information not available from animal studies, because of differences in how humans and animals respond to environmental exposures.

Turek and John are supported by an NIEHS Small Business Innovation Research grant, which funds projects with commercial potential. John, the chief executive officer of MandalMed Inc., estimates that it may take three to four years to develop a product for testing the toxicity of potential drugs in the development of sperm. "Hopefully the model can be used as an FDA-approved adjunct to animal testing during drug development," she said.

Turek, who is MandelMed's chief medical officer and also has a male fertility clinic in San Francisco, added, "We could discover information that tells us more about how testicular cancer or infertility begins."

NIEHS currently supports a number of projects to develop three-dimensional human tissue culture systems to more accurately reflect *in vivo* responses to toxicant exposures in human tissues and organs. These models are developed using multiple cell types that replicate tissue functions more accurately than traditional cell culture systems using a single cell type. Through funding of both university and small business grants, the NIEHS has supported the development of human models of skin, eye, liver, and lung, to evaluate biological responses to a range of toxicant exposures. These efforts address goals of the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods to refine, reduce, or replace animal use in toxicology testing.



Cultured human Sertoli cells, shown in this fluorescence image at 100X magnification, are a key part of the testis model. (Photo courtesy of Constance John)

Creating a functioning testis model

To create a model of the testis, the researchers will culture three types of cells in a hollow fiber. Sertoli cells, also called nurse cells, are a key component, because they support the stem cells that eventually develop into sperm, create the blood-testis barrier, and reduce the body's immune responses to sperm. To make the model functional, the researchers will induce stem cells to differentiate into sperm inside the hollow fibers. Turek says that their work will likely provide insight that will be useful for other applications of stem cells.

Turek is the chief medical officer of MandalMed, based in San Francisco. (Photo courtesy of Paul Turek)

If the researchers succeed in creating a functioning testis model, they can begin to examine reproductive toxicology. This will involve examining the effects of molecules, on the various cell types involved, over the 70 days it takes for sperm to develop. The analysis will take time but will provide high-quality information. "We don't really know what the toxicology will look like," Turek said. "We hypothesize that most effects will be on the nurse cells."

Human challenges

Scientists have successfully produced artificial sperm, using cells from mice and other animals, but have failed to produce artificial sperm using cultured human cells. To overcome this challenge, Turek gathered experts in the various cell types and processes of spermatogenesis to be part of the research team working on the artificial testis.

John, the founder and chief executive officer of MandalMed, thinks that a functioning model of the testis could have great commercial value. (Photo courtesy of Constance John)

John has worked extensively with human Sertoli cell cultures, which are commercially available for research applications from MandalMed's distributor Lonza in Walkersville, Md. The team also includes Renee Reijo Pera, Ph.D., of Stanford University,

who has characterized genes required to coax human embryonic stem cells into the precursors of sperm; Chuen-yan Cheng, Ph.D., of the Population Council's Center for Biomedical Research in New York, who has shown that cadmium can destroy the blood-testis barrier; and Juan Aréchaga, Ph.D., who runs the Laboratory for Stem Cells, Development, and Cancer at the University of the Basque Country in Spain and is an expert in peritubular myoid cells, which make up the walls of the channels in the testis where sperm develop.

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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PEPH kicks off webinar series

By Eddy Ball

The NIEHS Partnerships in Environmental Public Health (PEPH) program presented the first installment of its environmental health and education webinar series Feb. 28. The webinar, moderated by NIEHS Program Analyst Jerry Phelps, featured three scientific presentations exploring the theme of "Connecting Environmental Exposures to Chronic Inflammation and Diseases."

According to organizers, the webinars strive to promote interactions among PEPH grantees, and increase awareness of emerging issues and approaches in environmental public health. The PEPH umbrella unites researchers in basic and clinical research, community-based participatory research, education, outreach, and environmental justice in the pursuit of improved public health.

Shown with his wife and co-author, Janice, Dietert translated his research in a 2010 book directed to parents and pediatricians, "Strategies for Protecting Your Child's Immune System: Tools for Parents and Parents-To-Be." (Photo courtesy of Cornell University)

Inflammation 101: How Is the Immune System Involved in Inflammation?

Starting off the program was NIEHS Health Scientist Administrator Michael Humble, Ph.D., who discussed the first line of the body's defense against environmental exposures, including skin, mucus, and saliva, and the second line, innate and adaptive immunity. The immune system, Humble explained, is responsible for differentiating what is "self" and normal from things that are foreign, such as bacteria, virus, fungus, and parasites.

Innate immunity is all about immediate repair, Humble explained, with its mobilization of macrophages, initiation of inflammation, and recruitment of the adaptive immune response. "The real goal is to keep the host alive long enough for the adaptive immune response to develop," he said. But if inflammation, which is normally closely regulated within the body, becomes excessive or prolonged, it sets the stage for disease.

Humble organized a 2010 state-of-the-science workshop on autoimmune diseases. (Photo courtesy of Steve McCaw)

Air Pollution Morbidity: Confounding Effects of Chronic Inflammation

NIEHS Health Scientist Administrator Sri Nadadur, Ph.D., opened his talk with a review of major air pollution events, such as the one in Donora, Penn. in 1948, and the London killer smog of 1952 that inspired the Clean Air Act of 1963 and the creation of the U.S. Environmental Protection Agency in 1970, which established National Ambient Air Quality Standards. In this early period following the wake-up calls from Donora and London, Nadadur explained, air pollution was regarded as primarily a threat to respiratory health.

Nadadur oversees grants for nanomaterial research, as well as for work on air pollution. (Photo courtesy of Steve McCaw)

As research advanced, concern spread to air pollution's effects on cardiovascular health among susceptible populations and then, by the early 21st century, to links with diabetes mellitus, obesity, and deficits in reproductive and neurological development. According to Nadadur, recent research has associated air pollution exposure with oxidative stress leading to systemic inflammation and laying the foundation for development of chronic diseases and cancer.

Inflammation and Effects of Chronic Disease

The final speaker of the webinar, Rodney Dietert, Ph.D., of Cornell University, placed chronic inflammation and related diseases into a policy and economic context. Dietert set the theme for his talk by saying, "The combination of approaches we are using in public health [at the current time] are really not sustainable relative to chronic disease."

He also referred to findings by the Harvard School of Public Health and World Economic Forum report, The Global Economic Burden of Non-communicable Diseases. "Over the next 20 years," he said, "the estimated cost of chronic disease is some 48 percent of global GDP [gross domestic product], and already chronic diseases are the leading killers worldwide."

Dietert proceeded to build a compelling case for fundamentally rethinking approaches to chronic diseases, to incorporate the role of environmental exposures during critical windows of maturation. He called for a new approach in the categorization, diagnosis, and treatment of autoimmune disease, with a new functional paradigm to better address the underlying immune dysfunction that is the cause of most chronic disease.

"We also should have outcome-based safety testing [to] give us information about those diseases that are the most significant public health threats," he told the audience. He also called for concerted efforts to both manage symptoms and correct the underlying immune dysfunction at the cellular level, to reduce risk for additional immune-based chronic disease across a lifetime and cancer risk in target tissues.

PEPH webinar series continues

The PEPH webinars are free and open to the public, but pre-registration is required. To register for the webinars, visit https://www2.gotomeeting.com/register/198613834.

Upcoming seminars include the following:

- **April 3:** Examining and Communicating the Health Implication of Arsenic in our Food System
- **April/May:** Mapping and Environmental Public Health: Visualizing Health Disparities and the Effects of Pollution
- **May:** Health Impact Assessments and Community Engagement
- **June:** Science-based Decision Making
- **July:** Hydraulic Fracturing

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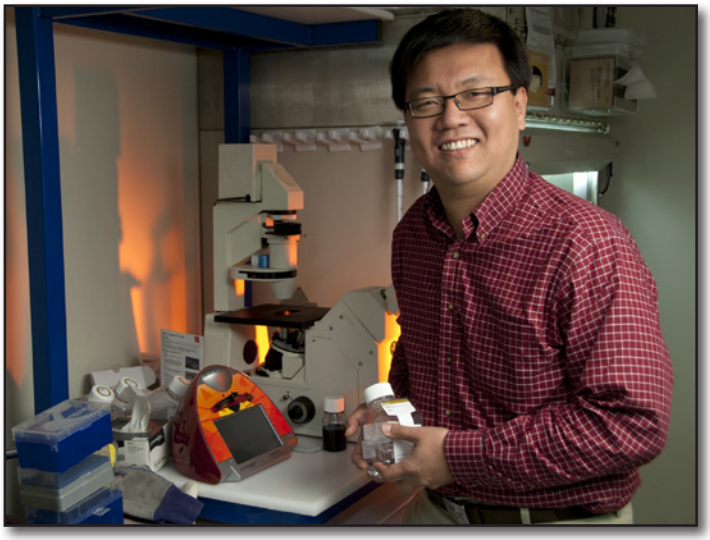
High-throughput screening finds surprising properties for antioxidants

By Larry Thompson

Antioxidants have long been thought to have anti-aging properties, primarily by protecting a person's genetic material from damaging chemicals. The story, however, now appears to be much more complicated.

National Institutes of Health researchers from two institutes and one center have demonstrated that some anti-oxidants damage DNA and kill cells instead of protecting them. The findings, published March 19 in the Proceedings of the National Academy of Sciences, also suggest that this surprising capability may be good for treating cancer, but may prove cautionary when using antioxidant-based medicines to treat other disorders, such as diabetes.

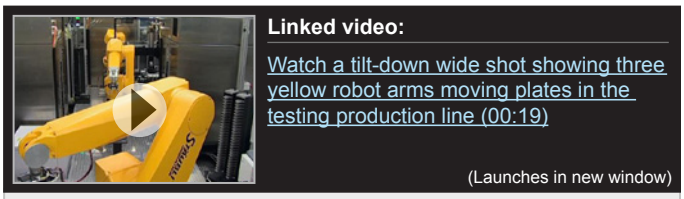


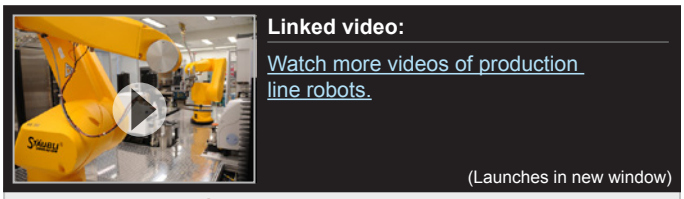
Myung's laboratory investigates genome instability, which is a characteristic of cancer and many genetic disorders, by examining the mechanisms of DNA repair and replication, as well as their roles in the production and suppression of gross chromosomal rearrangements. (Photo courtesy of NHGRI)

An unexpected discovery

"It's an unexpected discovery," said Kyungjae Myung, Ph.D., a senior researcher in the Genetics and Molecular Biology Branch of the National Human Genome Research Institute (NHGRI), and the senior author on the report.

"This report demonstrates the ability of the high throughput screening program to generate findings that may impact on human health," said co-author Raymond Tice, Ph.D., chief of the NIEHS/NTP Biomolecular Screening Branch. "In this case, the technology is helping to identify potential drug candidates for treating cancer."





Many people attempt to boost their levels of antioxidants by eating fruits and vegetables, nuts and grains, or by taking supplements. By adding antioxidants to the diet, many people hope to slow down the process that some believe contributes to the normal process of aging.

DNA repair

Myung did not set out to challenge this anti-aging strategy. His lab studies DNA repair, the enzyme systems within a cell that fix mistakes and other damage accumulating routinely in DNA as cells live and divide. Researchers know that naturally occurring defects in DNA repair can lead to a number of disorders, including cancer.

Myung's group sought a new way to easily identify chemicals that damage DNA and then use those chemicals to study cellular repair mechanisms, a basic research question. Using a laboratory-grown cell line from human kidneys, the team developed a novel laboratory test that readily shows when a chemical exposure damages DNA.

With the test developed, Myung's team formed collaborations with two other NIH research groups. The first was with what is now the NIH National Center for Advancing Translational Sciences (NCATS). Over the last several years, a team lead by Christopher Austin, M.D., head of the NCATS labs, has developed high-throughput chemical screening systems using robotics. Austin agreed to use Myung's test to screen thousands of chemicals for their ability to damage DNA. But what chemicals should they test?

Tice is the lead coordinator for the NTP High Throughput Screening (HTS) Initiative and plays a key role in the efforts of the Tox21 community. (Photo courtesy of Steve McCaw)

Tox21 — testing chemicals faster and more efficiently

In 2008, NCATS (then part of NHGRI), NIEHS/NTP, and the U.S. Environmental Protection Agency (EPA) formed the Tox21 initiative to develop high-throughput screening tests that measure cellular harm caused by environmental chemicals. The Tox21 team created a library of some 2,000 compounds and agreed to test them against Myung's assay. The NHGRI researchers also added a commercially available chemical collection to the screening runs for a total of some 4,000 chemicals.

The screening runs produced surprises, identifying 22 antioxidants that damaged DNA. Three of the antioxidants — resveratrol, genistein, and baicalein — are currently used or being studied as an anti-aging intervention, as well as a treatment for several disorders, including heart disease, type 2 diabetes, osteopenia and osteoporosis, and chronic hepatitis.

Not only did the antioxidants damage the DNA, the researchers found, but, in dividing cells such as in tumors, the antioxidants could be lethal, killing the disease-causing cells. Despite their ability to damage DNA, the chemicals did not cause genetic mutations, making them particularly good candidates for improved cancer drugs.

Cool biology — new research avenues

"This is what's cool about biology," Austin said. "Just when we think we understand something, it turns out to be more complex than we thought. Not only did the NHGRI team produce a novel way to measure DNA damage, but their test has given us insights into the effects of chemical compounds that were not seen in more conventional strategies."

The discovery opens up several new lines of research. As a first step, the collaborators are dramatically expanding the number of compounds — more than 300,000 — to be screened with the new test. The Tox21 team also has decided to include the test in its standard screen for biological harm produced by environmental chemicals.

Citation: Fox JT, Sakamuru S, Huang R, Teneva N, Simmons SO, Xia M, Tice RR, Austin CP, Myung K. 2012. High-throughput genotoxicity assay identifies antioxidants as inducers of DNA damage response and cell death. Proc Natl Acad Sci U S A; doi:10.1073/pnas.1114278109 [Online 19 March 2012].

Findings about compounds that damage DNA, but may treat cancer

The clinical implications for these findings are more complicated. This initial discovery is only in lab-grown cell lines, not even in intact organisms. The relevance for humans has yet to be demonstrated.

Still, there is plenty of work already underway. Other research teams have launched various studies of these DNA-damaging antioxidants in various diseases. For example, 44 studies are currently listed in www.clinicaltrials.gov for resveratrol, which is found in many foods, including red grapes and wine, peanuts, and chocolate. The studies focus on treating Alzheimer's disease, type 2 diabetes, obesity, inflammation, colon cancer, multiple myeloma, and testing other anti-aging strategies, among others. The newly reported study does not suggest that resveratrol in red wine is harmful, because the dose is probably too low to be significant, Myung said.

Researchers also have launched 43 studies on genistein, including trials to treat cancers of the prostate, pancreas, bladder, breast, kidney, and skin (metastatic melanoma) and as adjunct treatments for rare diseases, such as cystic fibrosis.

Even though the antioxidants damaged the DNA, the researchers reported that the chemicals did not cause genetic mutations — another surprise. "Because they don't cause genetic mutations, antioxidants may be useful for treating cancer," Myung said. "Standard chemotherapy mutates the tumor's DNA, speeding its evolution and sometimes allowing it to escape the toxic treatment intended to kill it. This leads to multidrug resistance in some cancer patient's disease."

To test whether the antioxidants might help, the NHGRI team borrowed some multidrug resistant cancer cells from Michael Gottesman, Ph.D., a National Cancer Institute researcher and NIH Deputy Director for Intramural Research. Although these cells are very resistant to anticancer drugs, treatment with resveratrol appeared to sensitize the cancer cells, leading to their death. "Resveratrol," Myung said, "could prove useful in treating multidrug resistant cancers."

The findings do raise concerns about using antioxidants to treat disorders, as treatment with high doses may cause unexpected DNA damage that leads to other problems. "Clearly," Myung said, "much more study will be needed."

(Larry Thompson is the communications director for the National Human Genome Research Institute.)

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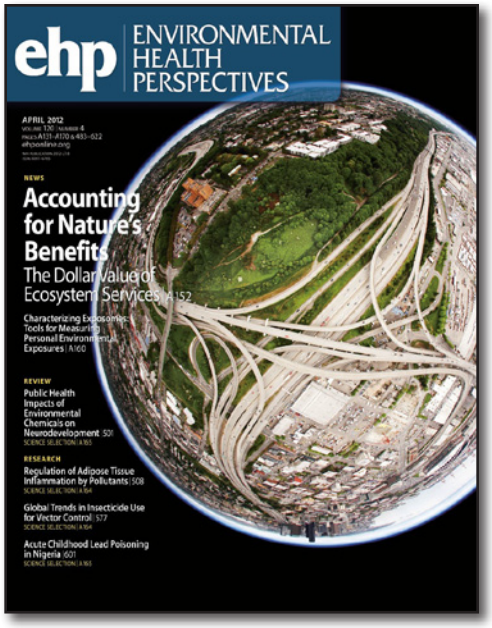
This month in EHP

By Ian Thomas

A widespread underappreciation of the human health benefits and other services provided by ecosystems means these services often are not factored into decisions about natural resource management. In its feature story this month, Environmental Health Perspectives (EHP) takes on the issue of assigning actual dollar values to ecosystem services, as a step toward better managing them and, thus, preserving human health.

http://twitter.com/ehponline

A second story examines new tools for capturing information about individual exposomes, the compilation of things an individual is exposed to over a lifetime. The tools were discussed at a recent workshop of the National Academies' Emerging Science for Environmental Health Decisions committee.



In this month's Researcher's Perspective Podcast, host Ashley Ahearn interviews guests Fay Johnston and Sarah Henderson about their latest work estimating global mortality attributable to smoke from landscape fires.

Featured commentaries, reviews, and research this month include the following:

- Public Health Impacts of Environmental Chemicals on Neurodevelopment
- Regulation of Adipose Tissue Inflammation by Pollutants
- Global Trends in Insecticide Use for Vector Control
- Acute Childhood Lead Poisoning in Nigeria

(Ian Thomas is a public affairs specialist in the NIEHS Office of Communications and Public Liaison and a regular contributor to the Envirnomental Factor.)

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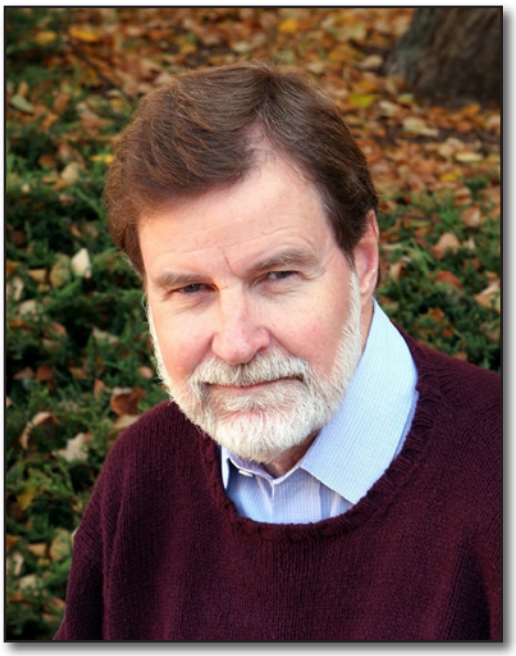
Wilson honored by Columbia University

By Eddy Ball

NIEHS lead researcher Samuel Wilson, M.D., will present the 19th annual Granville H. Sewell Distinguished Lecture in Environmental Health April 18 at Columbia University. Wilson, who heads the DNA Repair and Nucleic Acid Enzymology Group in the Laboratory of Structural Biology, will address "Implications of genetic toxicology in public health."



Wilson is a scientist who regularly publishes in high-impact journals. He is also widely regarded as a high-quality mentor of the next generation of biomedical researchers. (Photo courtesy of Steve McCaw)

Under his leadership, Wilson's group has made a number of contributions over the years to the understanding of mechanisms of DNA synthesis and, in particular, synthesis by the repair enzyme DNA polymerase beta. He and his colleagues identified the kinetic mechanism of this enzyme, its primary and three-dimensional structures, and its biological role in base excision DNA repair. This DNA repair pathway protects cells against endogenous DNA lesions, including single-strand breaks.

Wilson, who served as NIEHS deputy director from 1996 to 2007 and acting director from 2007 to 2009, has received many honors for his research. Along with election as a fellow of the American

Association for the Advancement of Science in 2009, Wilson has given a number of keynote and named lectures in the U.S. and abroad. He has edited several books and authored or co-authored more than 365 peer-reviewed research articles.

Joining a select group of leaders in environment health science

Inaugurated in 1993, the lecture series was established in memory of Granville Sewell, Ph.D., who directed the educational programs in environmental health sciences at Columbia for more than 20 years prior to his death in 1992. Sewell was a pioneer in global environmental health. With his background in engineering and economics, Sewell emphasized the social context for environmental problems and their remedies in projects across Asia, the Middle East, and Africa.

Wilson joins a group of distinguished scientists who have been honored by the Sewell lectureship for their accomplishments in environmental science. They range from bioethicist Peter Singer; entomologist E.O. Wilson, Ph.D.; and microbiologist Rita Colwell, Ph.D., to former Director of the U.S. Environmental Protection Agency Carol Browner and James Hansen, Ph.D., director of the National Aeronautics and Space Administration Goddard Institute for Space Studies. Topics have ranged from acid rain and cholera to remote global sensing and climate change.

Along with Wilson, two other Sewell lecturers have had ties to NIEHS. NIEHS grantee Kirk Smith, Ph.D., spoke in 2011 on "Cooking and Climate: The Unfinished Health Agenda of Incomplete Combustion" and, in 2000, former NIEHS Scientific Director Carl Barrett, Ph.D., explored "New Approaches to the Study of Environmental Causes of Disease."

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Rodbell lecture to feature Keith Yamamoto

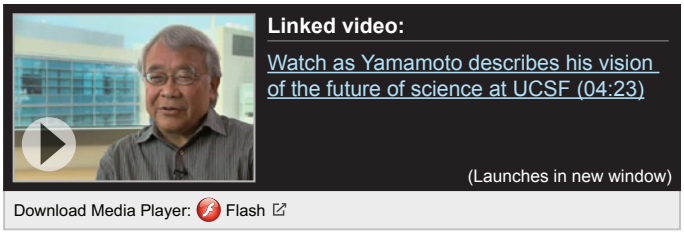
By Eddy Ball

Biochemist Keith Yamamoto, Ph.D., will present the 2012 Rodbell Lecture, "Cell-, Gene-, and Physiology-Specific Regulation by the Glucocorticoid Receptor," April 10 at NIEHS. The presentation, which begins at 11:00 a.m. in Rodbell Auditorium, will be hosted by NIEHS Laboratory of Molecular Carcinogenesis chief Trevor Archer, Ph.D., and NIEHS Laboratory of Signal Transduction chief John Cidlowski, Ph.D.

As part of his commitment to the future of science, Yamamoto served on the Board on Life Sciences Committee on A New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution, which presented its report to Congress in 2010. (Photo courtesy of UCSF)

Yamamoto is a professor of cellular and molecular pharmacology at the University of California, San Francisco (UCSF), where he also serves as vice chancellor for research and executive vice dean of the School of Medicine. His research is focused on signaling and transcriptional regulation by intracellular receptors (IR), which mediate the actions of several classes of essential hormones and cellular signals. The Yamamoto lab employs biochemical, cellular, molecular, genetic, and structural approaches in mammals, *C. elegans*, and yeast to investigate IR functions and mechanisms.

In the course of his 39-year career at UCSF, Yamamoto has published more than 170 peer-reviewed studies in high-impact journals, edited three books, written some 20 science and public policy articles, and given many distinguished, honorary, and keynote lectures. He has been active in service at UCSF and nationally, and he has served on the editorial boards of 18 major journals. His long list of honors includes an NIH MERIT Award, major fellowships, and this year's Endocrine Society Edwin B. Astwood Award.



Now in its 13th year, the Rodbell Lecture is one of two named talks in the annual NIEHS Distinguished Lecture Series. It honors former NIEHS Scientific Director and Nobel Laureate Martin Rodbell, Ph.D., who presented the first talk in the series shortly before his death in 1998. Rodbell shared the 1994 Nobel Prize in Physiology or Medicine with Alfred Gilman, Ph.D., for the discovery of G-proteins, signal transducers that transmit and modulate signals in cells to control fundamental life processes.

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Staff and grantees at upcoming workshop

By Eddy Ball

An innovative interagency program sponsored by NIEHS opens its 2012 workshop series with an exploration of "Biological Factors that Underlie Individual Susceptibility to Environmental Stressors, and Their Implications for Decision-Making" April 18-19 in Washington, D.C. NTP Host Susceptibility Group leader Jef French, Ph.D., NIEHS grantees, and several NIEHS research associates will be among the presenters.

French is scheduled to present a talk on his work using a mouse model, "Using In Vivo Animal Models to Explore Individual Variability in Toxicity." (Photo courtesy of Steve McCaw)

The workshop, which is part of the National Academies' Emerging Science for Environmental Health Decisions series, is free and open to the public. Registrations are now being accepted for attendees at http://www.surveygizmo.com/s3/788909/Individual-Variability-Registration and for the live webcast at http://www.tvworldwide.com/events/nrc/120418/.

Why individuals may respond differently to environmental exposure

The workshop will focus on the endogenous and biological factors that influence individual variability in response to environmental exposures, such as genetics and epigenetics, physiology, life stage, and other biological differences. Presenters will explore new and innovative approaches for characterizing individual variability, as well as approaches for and challenges to communicating the relationships among individual variability, disease susceptibility, and public health.

Sponsored by NIEHS, the program holds three workshops per year on the use of new discoveries, tools, and approaches for guiding environmental health decisions. The workshops provide a public venue for communication among government, industry, environmental groups, and the academic community.

The April workshop is the tenth in the series, which began in July 2009 with a workshop on "Use of Emerging Science and Technologies to Explore Epigenetic Mechanisms Underlying the Developmental Basis for Disease." Past presentations are archived online, and videos are available for several recent workshops.

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Extramural papers of the month

By Nancy Lamontagne

- Air pollution linked to cognitive decline
- Predicting sudden changes in pollution patterns
- Epigenetic interactions between flame retardant exposure and autism mutation
- Early BPA exposure and asthma development

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

Air pollution linked to cognitive decline

NIEHS grantees report that a faster decline in the cognitive function of older women is associated with long-term exposure to particulate matter (PM) air pollution at levels typical of many areas of the United States. This is one of the first studies to examine the role of PM in cognitive decline over time.

The researchers evaluated exposures to both coarse and fine PM in relation to cognitive decline in the Nurses' Health Study Cognitive Cohort, which included more than 19,000 U.S. women 70 to 81. The investigators performed baseline and follow-up cognitive testing that examined general cognition, verbal memory, category fluency, working memory, and attention. They also used geographic information system (GIS)-based models to estimate exposures over several intervals, including the preceding month and the previous seven to 14 years.

The study showed that higher levels of long-term exposure to both coarse and fine PM are associated with significantly faster cognitive decline. The researchers estimate that a 10-microgram per cubic meter increase in long-term PM exposure was cognitively equivalent to aging by approximately two years. If the findings are confirmed in other studies, reducing air pollution could offer a way to lessen age-related cognitive decline and, because cognitive decline often precedes the development of dementia, a way to reduce the future population burden of dementia.

Citation: Weuve J, Puett RC, Schwartz J, Yanosky JD, Laden F, Grodstein F. 2012. Exposure to particulate air pollution and cognitive decline in older women. Arch Intern Med 172(3):219-227.

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Predicting sudden changes in pollution patterns

An NIEHS grantee and her colleague have developed a technique for forecasting major short-term changes in how oil spills will move in the ocean. The method, which is also applicable to harmful algal blooms and volcanic ash clouds, offers a tool for minimizing the impact of environmental disasters.

Over the last decade, the researchers have developed mathematical methods to describe hidden patterns in the way that air and water move, known as Lagrangian coherent structures (LCSs). The new technique uses these mathematical methods to detect LCS cores, which unite incoming flow from opposite directions and eject the resulting mass of water or air. LCS cores emerge before a sudden shape change in the contamination pattern and, thus, allow the forecast of dramatic changes that were previously considered unpredictable.

As a demonstration, the researchers showed that the method could have forecast the tigertail and coastal spread instabilities that occurred in the Deepwater Horizon oil spill. They developed high-precision forecasts of the location and time of these major instabilities, by detecting two strong LCS cores four to six days before the instabilities were observed.

Citation: Olascoaga MJ, Haller G. 2012. Forecasting sudden changes in environmental pollution patterns. Proc Natl Acad Sci U S A; doi: 10.1073/pnas.1118574109 [Online 12 March 2012].

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Epigenetic interactions between flame retardant exposure and autism mutation

NIEHS grantees studying the effects of flame retardant exposure on a mouse model of autism susceptibility found that the offspring of exposed mice had an increased risk for neurodevelopmental deficits associated with reduced sociability and learning. The work provides insight into the epigenetic interface of gene-environment interactions that are involved in the social and cognitive behaviors associated with neurodevelopmental disorders.

The researchers examined the effects of the flame retardant BDE-47 on the offspring of mice genetically modified to have a Mecp2 gene mutation (Mecp2(308)). Mutations in the epigenetic factor methyl-CpG binding protein 2 (MECP2), cause Rett syndrome, an X-linked autism spectrum disorder.

The study results showed gene-environment interactions occurred in the female, but not the male, offspring of the mice with the Mecp2 mutation. BDE-47 exposure had a negative impact on pup survival and learning in adult females. Female mice receiving perinatal exposure to the flame retardant had significantly lower DNA methylation levels in the adult brain, and these methylation levels correlated with decreased social behavior. However, the Mecp2 mutation reversed a social novelty-learning defect brought on by BDE-47 exposure, in a way that corresponded to increased levels of the methyltransferase Dnmt3a gene, which is required for learning and memory in the mouse brain.

Citation: Woods R, Vallero RO, Golub MS, Suarez JK, Ta TA, Yasui DH, Chi LH, Kostyniak PJ, Pessah IN, Berman RF, Lasalle JM. 2012. Long-lived epigenetic interactions between perinatal PBDE exposure and Mecp2(308) mutation. Hum Mol Genet; doi:10.1093/hmg/dds046 [Online 15 February 2012].

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Early BPA exposure and asthma development

An NIEHS-supported grantee and colleagues report that prenatal bisphenol A (BPA) exposure promotes the development of allergic asthma in a mouse model. They also provide evidence that one reason the mice are susceptible during the prenatal period might be because BPA-metabolizing enzymes have not yet developed.

The mice received BPA in their drinking water beginning at one week before pregnancy. To separate the effects from prenatal BPA exposure and early-postnatal exposure, the researchers transferred some pups after birth from their BPA-exposed mother to an unexposed mother or vice versa. Half of the pups were sensitized with an experimental allergen and then later challenged by inhalations of the allergen. The researchers found that the pups exposed to BPA prenatally only, or prenatally and through breast milk, developed asthma after the allergic challenge. Pups that received only postnatal exposure did not develop asthma.

To look for a possible mechanism for BPA's enhancement of asthma development, the investigators assessed the expression of Ugt2b1, an enzyme that metabolizes BPA. They found that the enzyme was not detectable in mouse fetuses and newborn pups, but its levels increased by day five and approached adult levels by day 25. Whether this mechanism is at work in humans must still be studied.

Citation: Nakajima Y, Goldblum RM, Midoro-Horiuti T. 2012. Fetal exposure to bisphenol A as a risk factor for the development of childhood asthma: an animal model study. Environ Health 11:8.

(Nancy Lamontagne is a science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

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Intramural papers of the month

By Brant Hamel, Sonika Patial, Jeffrey Stumpf, and Ian Thomas

- Researchers find novel binding target for rotenone
- Novel role for a DNA polymerase in repairing damaged bases in *C. elegans*
- (Bi)sulfite oxidation prompts neutrophils to produce free radicals
- Synthetic estrogen induces feminization in male mice via ERalpha

Researchers find novel binding target for rotenone

Previous epidemiology studies have shown that chronic exposure to rotenone, a common pesticide, can reproduce Parkinsonism in rodents and increase the risk of Parkinson's disease in humans. In a new study from the NIEHS Laboratory of Toxicology and Pharmacology, scientists discovered a novel mechanism that explains how this process works.

The investigators transfected COS7 cells with cytoplasmic subunits of the human phagocyte NADPH oxidase (PHOX), p47(phox) and p67(phox), and the membrane subunits, gp91(phox), the catalytic subunit of PHOX,

and p22(phox). Their data suggests that the binding of rotenone to gp91(phox) causes a conformational change that allows p67(phox) to bind to the rotenone/gp91(phox) complex. This binding creates a functional oxidase that generates superoxide. Also, the scientists observed that, in response to rotenone, superoxide production in p47(phox)-deficient macrophages still occurs, which means p47(phox) is not required for this mechanism.

This study clarifies that PHOX is a novel target of rotenone and demonstrates a distinct mechanism by which the pesticide rotenone triggers inflammation-mediated excessive production of free radicals. Oxidative stress-related damage to cellular proteins and nucleic acids may be an important mechanism of pesticide-induced degeneration of nerve tissue.

Citation: Zhou H, Zhang F, Chen SH, Zhang D, Wilson B, Hong JS, Gao HM. 2012. Rotenone activates phagocyte NADPH oxidase by binding to its membrane subunit gp91phox. Free Radic Biol Med 52(2):303-313.

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Novel role for a DNA polymerase in repairing damaged bases in *C. elegans*

With genomes being constantly bombarded with DNA damaging agents, organisms require proteins that protect the nucleotide alterations that disrupt cellular function. NIEHS researchers identified a wrinkle in a canonical DNA repair pathway that, in many organisms, requires the specialized DNA polymerase pol beta. The study shows the involvement of another specialized DNA polymerase, pol theta, in a critical step in base excision repair.

Base excision repair is a major pathway to clear DNA damage and to avoid cancer-causing lesions. After recognition of the damage, the combined actions of a damage-specific glycosylase and AP endonuclease excise the damaged base and prepare the DNA for a polymerase to replicate the small gap, resulting in a repaired DNA template.

The researchers used the roundworm *C. elegans* to study base excision repair. *C. elegans* is used for developmental biology because the fate of every cell is known, making it an important model organism to understand basic life processes. This study shows that base excision repair in *C. elegans* requires replication by pol theta and that this model organism does not have a gene for pol beta. Although the overall function of pol theta is not well understood, these results suggest pol theta as a viable alternative to pol beta in base excision repair.

Citation: Asagoshi K, Lehmann W, Braithwaite EK, Santana-Santos L, Prasad R, Freedman JH, Van Houten B, Wilson SH. 2012. Single-nucleotide base excision repair DNA polymerase activity in C. elegans in the absence of DNA polymerase beta. Nucleic Acids Res 40(2):670-681.

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(Bi)sulfite oxidation prompts neutrophils to produce free radicals

New research from scientists at NIEHS have determined that the toxicity of (bi)sulfite in patients suffering from asthma and other pulmonary disorders may result from its ability to induce the production of highly reactive free radicals, such as the sulfate and sulfite anion radical in neutrophils. These free radicals can then oxidize proteins inside of the cell and cause cellular damage.

(Bi)sulfite can be formed in the lung by the hydration of sulfur dioxide, a major air pollutant released by the combustion of fossil fuels. It is also used as a preservative and anti-browning agent in many foods. Using electron spin resonance (ESR) spectroscopy, NIEHS researchers demonstrated that the ability of neutrophils to create these compounds was dependent on the myeloperoxidase (MPO) enzyme. MPO is a very abundant protein — almost 5 percent of cell weight. It is secreted from active neutrophils and is known to catalyze the formation of cytotoxic oxidants involved in inflammatory disorders.

Using specific inhibitors of MPO, researchers could not detect radical formation, thus implicating MPO as necessary for the generation of (bi)sulfite-derived free radicals. Researchers hope that the elucidation of this mechanism will lead to future studies to examine the deleterious effects of (bi)sulfite in respiratory disorders.

Citation: Ranguelova K, Rice AB, Khajo A, Triquigneaux M, Garantziotis S, Magliozzo RS, Mason RP. 2012. Formation of reactive sulfite-derived free radicals by the activation of human neutrophils: An ESR study. Free Radic Biol Med; doi:10.1016/j.freeradbiomed.2012.01.016 [Online 2 February 2012].

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Synthetic estrogen induces feminization in male mice via ERalpha

In a new study, NIEHS scientists found that estrogen receptor alpha (ERalpha) is responsible for mediating the toxic effects of diethylstilbestrol (DES), a potent synthetic estrogen, on the seminal vesicles of male mice inducing feminization. The harmful effects of DES exposure on the development of the male rodent reproductive tract were well known. The results of this study, however, show that the developing male reproductive tract expresses estrogen receptors and is highly sensitive to the toxicological effects of exogenous estrogens through ERalpha.

The authors injected DES at postnatal days 1-5 in wild-type (WT), ERalpha or ERbeta knockout male mice. DES exposure led to a dramatic reduction in the weight of the seminal vesicles and induced the expression of lactoferrin, an estrogen-inducible uterine secretory protein. It also decreased the expression of seminal vesicle secretory protein IV in WT and ERbeta knockout mice. However, these effects were not seen in ERalpha knockout mice, suggesting that ERalpha mediates DES-induced feminization in male mice.

Although the risk of DES exposure in humans during development is relatively low, the results imply that genistein and bisphenol A, two other estrogenic compounds to which humans are widely exposed, could have similar effects.

Citation: Walker VR, Jefferson WN, Couse JF, Korach KS. 2012. Estrogen receptor alpha (ERα) mediates diethylstilbestrol (DES)-induced feminization of the seminal vesicle in male mice. Environ Health Perspect; doi:10.1289/ehp.1103678 [Online 24 January 2012].

(Brant Hamel Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Laboratory of Signal Transduction. Sonika Patial, D.V.M., Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction. Jeffrey Stumpf, Ph.D., is an IRTA fellow in the NIEHS Laboratory of Molecular Genetics. Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

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Inside the Institute

Spring cleaning day for the NIEHS lake

By Eddy Ball

Although it wasn't officially spring yet when NIEHS employees picked up litter in and around the campus lake March 13, it was a great time for a lakeshore clean sweep.

The weather, with clear skies and temperature approaching 70 degrees, was just right for the effort, which was organized by the NIEHS Environmental Awareness Advisory Committee (EAAC). And, as the EAAC announcement noted, it was still winter, which meant inactive reptiles and less vegetation to hide the trash.

Over the winter, winds had blown the occasional piece of waste from picnic tables, trashcans, and careless hikers into the undergrowth and water, so a small group of volunteers donned outdoor clothing and took trash bags down to the shore to get the job done. The EAAC provided some gloves and rubber boots for the volunteers.

Joining NIEHS Health and Safety Branch (HSB) Environmental Specialist Bill Steinmetz were HSB Hazardous Waste Specialist Carranza Smith, biologist Bill Willis, and Deputy Associate Director of Management Chris Long. Photographer Steve McCaw and son Patrick stopped by to take a few photos and help out with policing the entire shoreline, including the U.S. Environmental Protection Agency (EPA) side.

Patrick McCaw, left, works with Long, as they look for litter. Long dressed appropriately for the task and brought along the right tool for the job. (Photo courtesy of Steve McCaw)

By the time they finished, the grounds were pristine. It's a tribute to the environmental awareness of NIEHS and EPA employees that the volunteer lake stewards collected less than one large trash bag of plastic bottles, pieces of Styrofoam, fishing bobbers, and a golf ball, which Steinmetz said the volunteers kept for future reuse.

Most of the lake's residents and visitors seemed to have little interest in what was happening on shore. (Photo courtesy of Steve McCaw)

As Willis looked on, Steinmetz took advantage of rubber boots and used a long branch to extend his reach farther into the water. (Photo courtesy of Steve McCaw)

Others, including the ones who built this dam, kept a low profile. (Photo courtesy of Steve McCaw)

Part of the reward for a job well done was the chance most people don't have every day — to get a perspective of NIEHS headquarters from the shoreline on the other side of the lake. (Photo courtesy of Steve McCaw)

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