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December 2009

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Science Notebook

Cellular Effects of Mutated DNA Polymerases

DNA polymerase is responsible for DNA replication, a process that allows all living organisms to precisely copy their genetic material so that the information can be passed on to the next generation. But what happens when the polymerase has a mutation in its sequence? ...read more

REST's Repressive Activities Determine Neuronal Cell Development

On November 13, Distinguished Lecturer Gail Mandel, Ph.D., came to NIEHS to talk about her research, which is defining the gene regulatory mechanisms involved in cell differentiation and specialization. ...read more

NIEHS Science Awards Day Celebrates Intramural Research Achievements

On the first Thursday in November, NIEHS traditionally holds an event that honors outstanding scientific achievements among the Institute's intramural community. On November 5, researchers and trainees left their laboratories and offices to discuss science and listen to oral presentations during the 7th Annual Science Awards Day. ....read more

NIEHS Spotlight

NTP Staff Recognized by Environmental Mutagen Society

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Bay Area Forum Bridges Research and Community

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Dearry Speaks at One Health Summit

The newly formed One Health Commission — a collaborative group of health science experts representing human, animal and ecosystem disciplines — held a groundbreaking summit on November 17 at the National Academy of Sciences (NAS) in Washington, D.C. ....read more

NIH Women in Science Receive Recognition

The NIH Office of Research on Women's Health (ORWH), in collaboration with the NIH Coordinating Committee on Research on Women's Health (CCRWH), has published *Women in Science at the National Institutes of Health, 2007–2008*. ....read more

Science Notebook

Chromium Linked to Telomere Damage

On November 10, Patricia Opresko, Ph.D., an assistant professor at the University of Pittsburgh, presented "Links Between Telomere Instability, Environmental Genotoxins and Human Disease" for the Keystone Science Lecture Series at NIEHS. Opresko is an NIEHS 2006 Outstanding New Environmental Scientist (ONES) grantee. ....read more

Arsenic Biomethylation Required for Oxidative DNA Damage

According to GreenFacts.com, inorganic arsenic occurs naturally in the earth's crust and results from man-made activities such as mining, smelting and coal-fired power plants. Inorganic arsenic is known to be carcinogenic to humans and is a common contaminate in drinking water. ...read more

This Month in EHP

This month, *Environmental Health Perspectives (EHP)* investigates the potential threat of lead exposure in tap water. The focus article, "Out of Plumb: When Water Treatment Causes Lead Contamination," examines how lead gets into treated water and what water utilities and residents are doing about it. ...read more

C. Ronald Kahn To Give Falk Lecture

The NIEHS 2008–2009 Distinguished Lecture Series continues on December 8 with the annual Hans L. Falk Memorial Lecture. The lecturer this year is C. Ronald Kahn, M.D., Sc.D., who will speak on "Genes and Environment in the Epidemic of Diabetes and Obesity." ...read more

NIEHS Spotlight

NIEHS Booth Wins Best Exhibit at APHA Meeting

Several NIEHS employees represented the Institute at the American Public Health Association's (APHA) 137th Annual Meeting and Exposition at the Pennsylvania Convention Center in Philadelphia on November 7–11. Myra Westmoreland, Mary Collins, Martha Dimes and Rita Hanson were on hand at the NIEHS exhibit to meet attendees and answer questions about NIEHS. Little did they know that the exhibit would win first prize out of the many exhibit booths representing "non-profit organizations." ....read more

Inside the Institute

Tvermoes Excels in Ford Ironman World Championship

On October 10, Brooke Tvermoes, Ph.D., a postdoctoral fellow in the Comparative Genomics Group, finished fifth in her age class in the Ford Ironman World Championship in Kailua-Kona, Hawaii. ...read more

North Carolina Central Students Get Short Course on Toxicology Testing

On November 19, a group of students from the Biology and Cancer Research Program at North Carolina Central University (NCCU) visited the NIEHS to attend a public meeting of the National Toxicology Program's (NTP) Board of Scientific Counselors Technical Reports Review Subcommittee. ...read more

Extramural Research

Extramural Update

Ever wish there was a grant program that allows expansion of your currently funded NIEHS grant, and at the same time, allows you to bring in new collaborators to improve the translational or transdisciplinary nature of the research? If so, take a look at ViCTER, "Virtual Consortium for Translational and/or Transdisciplinary Environmental Research," a new grant program developed at NIEHS. ...read more

Extramural Papers of the Month

- Chronic Glucocorticoid Use Raises Risk of Bladder Cancer
- Discovery in Aflatoxin Formation
- Bacterial Toxin Linked to Parkinson's
- Social Isolation Speeds Breast Tumor Growth

Intramural Research

Intramural Papers of the Month

- Zinc Finger RNA-Binding Protein Zfp3612 Critical in Hematopoiesis
- Alternative Mouse Model for Asthma Reveals Novel Pathways
- Calcium Sensing Protein is Specialized for Digital Signaling
- Polymerase Stalling Controls Inflammatory Gene Expression

Calendar of Upcoming Events

- **December 3**, in Rall D450, 10:00–11:00 — Laboratory of Molecular Carcinogenesis Seminar Series with Charles Loftin, Ph.D., speaking on “COX-2 Dependent Inflammation in Cardiovascular and Adipose Tissue”
- **December 7–10 (Offsite Event)** at Lowes Miami Hotel, 8:00–5:00 — pptoxII – Role of Environmental Stressors in the Developmental Origins of Disease
- **December 8**, in Rodbell Auditorium, 10:00–11:00 — Annual Falk Lecture featuring C. Ronald Kahn, M.D., presenting “Genes and Environment in the Epidemic of Diabetes and Obesity”
- **December 9 (Offsite Event)** in 103 Bryan Research Building at Duke University — Seminar on “Regulation and Function of Store-Operated Calcium Entry” by James Putney, Ph.D.
- **December 9–10**, in Rodbell Auditorium, 8:30–5:00 — NTP Board of Scientific Counselors Meeting
- **December 17**, in Rall D450, 10:00–11:00 — Laboratory of Molecular Carcinogenesis Seminar Series with John Cidlowski, Ph.D., speaking on “The Complex Lives of the Glucocorticoid Receptors in Health and Disease”
- **December 17**, in Rodbell Auditorium, 1:00–2:30 — Director’s Award Ceremony
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

NIEHS and *The Lancet* Address Public Health Impacts of Climate Change

By Robin Mackar

Strategies to reduce greenhouse gases also benefit human health, according to studies published in the medical journal *The Lancet*. *The Lancet* series was unveiled on November 25 by key researchers and public health officials who gathered in the United States and Britain via satellite simulcast. NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., and NIEHS Associate Director Christopher Portier, Ph.D., took a lead role in the U.S. portion of the event held at the National Press Club in Washington, D.C.

Linda Birnbaum (Photo courtesy of Steve McCaw)

The Lancet series highlights case studies on four climate change topics — household energy, transportation, electricity generation and agricultural food production. Researchers say cost savings realized from improving health will offset the cost of addressing climate change and, therefore, should be considered as part of all policy discussions related to climate change. The studies were commissioned to help inform discussions at the U.N. Framework Convention on Climate Change in Copenhagen in December 2009.

More than 120 people attended the Washington event. U.S. Assistant Secretary for Health Jon Kim Andrus, M.D., participated by providing opening remarks for the press conference that immediately followed the meeting (please see event agenda).

Chris Portier (Photo courtesy of Steve McCaw)

"We are learning that the health of our planet and the health of our people are tied together. It's difficult for one to thrive without the other," said U.S. Department of Health and Human Services Secretary Kathleen Sebelius in a video message to the two continents. "Climate change is not a problem that one country or one organization can solve on its own. It's a problem that affects us all."

"These papers demonstrate there are clear and substantive improvements for health if we choose the right mitigation strategies for reducing greenhouse gas emissions," said Birnbaum. "We now have real-life examples of how we can save the environment, reduce air pollution and decrease related health effects; it's really a win-win situation for everyone."

Each study in the series examines the health implications of actions in high- and low-income countries designed to reduce the release of carbon dioxide and other greenhouse gases.

- The household energy paper demonstrated that introducing low-emission stove technology, specifically replacing biomass stoves in India, could improve respiratory health.

- The transportation study showed that cutting emissions by reducing motor vehicle use and increasing walking and cycling would bring substantial health gains by reducing heart disease and stroke by 10-20 percent, dementia by 8 percent, and depression by 5 percent.

- The electricity study demonstrated that changing methods of generation to reduce carbon dioxide, such as using wind turbines, would reduce particulate air pollution and yield the greatest potential for health-related cost savings in China and India.

Margaret Chan, Director General World Health Organization (via satellite). (Photo courtesy of Susan Hornyak)

- The food production study showed that the food and agriculture sector contributes about 20 percent of the global greenhouse gas emissions, and that a 30 percent reduction in consumption of saturated fats from animal sources would reduce heart disease by about 15 percent while also reducing greenhouse gas emissions.

Funding for *The Lancet* Health and Climate Change series was provided by NIEHS, and British partners including the Academy of Medical Sciences, the British Department of Health, the Economic and Social Research Council, the London School of Hygiene and Tropical Medicine, the National Institute for Health Research, the Royal College of Physicians, and the Wellcome Trust.

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

NIEHS Director Linda Birnbaum, and panelists Kirk Smith, Roger Glass and Rita Colwell. (Photo courtesy of Susan Hornyak)

Assistant Secretary for Health, HHS, Howard Koh (Photo courtesy of Susan Hornyak)

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NIEHS Awards Recovery Act Funds for BPA Research, Brings Researchers Together

By Robin Mackar

On October 6, researchers who received funds from the American Recovery and Reinvestment Act of 2009 to study the health effects of the chemical bisphenol A (BPA) gathered in North Carolina to meet with scientists from academia and government already working on the compound. The purpose of the meeting was to launch an integrated research initiative to produce data that will allow for a comprehensive assessment of possible human health effects due to BPA.

Jerry Heindel, Ph.D., the health scientist administrator at NIEHS who oversees much of the Institute's portfolio on BPA said, "Having the key players talking to one another as they begin new research efforts will stimulate collaboration, create opportunities to share resources, and encourage researchers to develop reliable and reproducible methods that will allow for a comprehensive assessment of the human health effects of BPA."

BPA is a chemical primarily used to produce polycarbonate plastics and epoxy resins, which are used to coat the lining of canned foods. Humans are exposed to BPA when the chemical leaches from polycarbonate tableware, canned foods, food storage containers, water bottles and baby bottles. BPA exposure has been linked to a variety of physiological problems in animal studies such as infertility, weight gain, behavioral changes, early onset puberty, prostate and mammary gland cancer, and diabetes.

Director of the NIEHS and National Toxicology Program (NTP), Linda Birnbaum, Ph.D., said, "We know that many people are concerned about bisphenol A, and we want to support the best science we can to provide the answers. Bringing the key BPA researchers together at the onset of new funding will maximize the impact of our expanded research effort."

NIEHS will invest approximately $30 million over two years on BPA-related research, including existing grants, the newly awarded Recovery Act grants and supplements, in-house research and NTP projects. The NTP effort is part of a

Awardees

The 10 Recovery Act NIH Grand Opportunities grants focusing on BPA research have been awarded to:

- Scott M. Belcher, University of Cincinnati
- Kim Harley and Brenda Eskenazi, University of California, Berkeley
- B. Paige Lawrence, University of Rochester
- Gail S. Prins, University of Illinois at Chicago; Shuk-Mei Ho, University of Cincinnati; and Kevin P. White, University of Chicago
- Beverly Sharon Rubin and Andrew S. Greenberg, Tufts University, Boston
- Ana Soto, Tufts University, Boston
- Shanna H. Swan and Bernard Weiss, University of Rochester
- Frederick vom Saal, University of Missouri, Columbia and William Allen Ricke, University of Rochester School of Medicine and Dentistry, Rochester
- Cheryl L. Walker, University of Texas M. D. Anderson Cancer Center, Houston; Shuk-Mei Ho, University of Cincinnati; and Michael A. Mancini, Baylor College of Medicine, Houston
- Robin Marjorie Whyatt, Columbia University Health Sciences, New York City

larger five-year commitment to collaborate with the U.S. Food and Drug Administration's National Center for Toxicological Research, to examine long-term health outcomes resulting from developmental exposures.

"Without the support of the American Recovery and Reinvestment Act, we would not have been able to expand on this research that is of such concern to so many people," Birnbaum noted. "Through this effort we will be able to provide a better perspective of the potential threat that exposure to bisphenol A poses to public health."

The newly funded two-year animal and human studies will focus on a number of health effects including behavior, obesity, diabetes, reproductive disorders, prostate development, breast and uterine cancer, asthma, cardiovascular diseases and transgenerational or epigenetic effects.

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

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Expert Panel Recommends Listing Formaldehyde as Known Human Carcinogen

By Robin Mackar

On November 4, a 10-member independent scientific expert panel convened by the National Toxicology Program (NTP) voted unanimously to list formaldehyde as a "known human carcinogen" in the upcoming 12th NTP Report on Carcinogens (RoC). Currently, formaldehyde is listed in the 11th RoC as "reasonably anticipated to be a human carcinogen." The vote came after three days of presentations, public comments and lengthy discussions of the body of literature on this widely used chemical.

Expert Panel Chair Kenneth E. McMartin, Ph.D., and NTP RoC Group Director Ruth Lunn, Dr.P.H., absorb all of the information presented and discussed during the RoC formaldehyde expert panel meeting in North Carolina. (Photo courtesy of Steve McCaw)

"The decision to change the listing status of formaldehyde is based on sufficient evidence in human epidemiology studies, as well as in animal studies, and the fact that a substantial number of U.S. residents are frequently exposed to detectable concentrations of formaldehyde," said Kenneth E. McMartin, Ph.D., chair of the expert panel. McMartin is a member of the Department of Pharmacology, Toxicology and Neuroscience at Louisiana State University Health Sciences Center in Shreveport.

Formaldehyde is a high production chemical with a wide variety of uses. In the United States, formaldehyde is predominantly used to produce industrial resins that are used as adhesives and binders in wood products. It can be found in products such as particle board, glues, permanent press fabrics, paper product coatings, fiberboard and plywood. Formaldehyde is also commonly known for its use as a preservative in medical laboratories and mortuaries.

The panel reviewed numerous key epidemiological studies of workers exposed to formaldehyde in different occupational settings. The studies were deemed sufficient evidence to indicate a causal relationship between exposure to formaldehyde and cancer in humans. Taken together, these human studies revealed three types of cancers, including nasopharyngeal carcinoma, sinonasal adenocarcinoma and myeloid leukemia. "Chance, bias and confounding factors are unlikely to explain the observed excess in these cancers," McMartin noted.

Expert panel members Stephen M. Rappaport, Ph.D., and Lisa Peterson, Ph.D., listen intently as epidemiological studies are discussed. (Photo courtesy of Steve McCaw)

The expert panel noted that in the case of myeloid leukemia, there is evidence of genetic damage in lymphocytes in the blood of formaldehyde-exposed people. These studies and toxicity studies in animals suggest that formaldehyde can produce effects at sites other than the nose and sinus that receive the initial contact of the colorless, strong-smelling gas.

"Having studies linking formaldehyde to not just relatively rare nasal cancers, but to a form of leukemia, which is a more common cancer, is an additional public health concern," said Ruth Lunn, Dr.P.H., director of the Report on Carcinogens Center.

Paul Demers, Ph.D., and Anneclaire DeRoos, Ph.D., carefully consider the comments made during the public comment portion of the meeting. (Photo courtesy of Steve McCaw)

Formaldehyde is one of eight substances under consideration by the NTP for possible listing in the 12th RoC. Next, the NTP will solicit public comment on the expert panel's listing recommendation and scientific justification through the Federal Register, and finalize the background document, taking into consideration the panel's recommended edits and public comments. Following additional internal government review, the NTP will draft its listing recommendation for the 12th RoC and scientific information supporting the recommendation, solicit public comment on the listing recommendation, and convene a meeting of the NTP Board of Scientific Counselors to peer review the science supporting the listing recommendation.

Information about this meeting, and the review of formaldehyde or any other RoC nominated chemical, is available online.

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

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NIEHS Awards Recovery Act Funds for Research on Health and Safety of Nanomaterials

By Robin Mackar

NIEHS plans to increase its investment in understanding the potential health, safety and environmental issues related to tiny particles that are used in many everyday products such as sunscreens, cosmetics and electronics. The Institute will award approximately $13 million over a two-year period, through the American Recovery and Reinvestment Act, to bolster the NIEHS's ongoing research portfolio in the area of engineered nanomaterials (ENMs).

ENMs are very tiny materials about 100,000 times smaller than a single strand of hair. They represent a significant breakthrough in material design and development for industry and consumer products, including stain-resistant clothing, pesticides, tires and electronics, as well as in medicine for purposes of diagnosis, imaging and drug delivery.

"We currently know very little about nanoscale materials' effects on human health and the environment," said Linda Birnbaum, Ph.D., director of the NIEHS and the National Toxicology Program (NTP). "Nanomaterials come in so many shapes and sizes, with each one having different chemical properties, and physical and surface characteristics. They are tricky materials to get a handle on. The same properties that make nanomaterials so potentially beneficial in drug delivery and product development are some of the same reasons we need to be cautious about their presence in the environment."

The new awards focus on ensuring that the Institute has reliable and reproducible methods and models to assess exposure, exposure metrics, and biological response to nanomaterials. This research is also essential for the harmonization of research results and forming a scientifically sound basis for hazard assessment, as well as the safe design and development of ENMs.

"There are inconsistencies in the biological effects of ENMs reported in the scientific literature, and a major reason for this is lack of detailed characterization of the physical and chemical properties of the ENMs used in these studies," said Sri Nadadur, Ph.D., program administrator at the NIEHS. "One of our goals is to identify three or four reliable and reproducible test methods using the same ENMs by investigators across different labs."

The NIEHS is establishing an integrated program that will narrow its focus to identify the best methods to evaluate the health effects of nanomaterials through use of cell cultures and animal systems. "Recovery Act funds have allowed us to expand our efforts in this important area," said Sally Tinkle, Ph.D., senior science advisor at the NIEHS. "We want to be sure that we come away with some better tools to assess the health and safety of nanomaterials." The NIEHS effort focused on nanomaterials supports the goals identified by the National Nanotechnology Initiative Strategy for Nanotechnology-related Environmental, Health and Safety Research.

The NIEHS also used Recovery Act funds to support efforts under its Superfund Research Program to determine ways to apply nanotechnology to better detect and evaluate effects on human health, and clean up Superfund chemicals in the environment. The Superfund Worker Education Training Program also provided Recovery Act funding targeting health and safety training.

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

Awardees

The 10 Recovery Act NIH Grand Opportunities grants focusing on engineered nanomaterial safety have been awarded to:

- James Christopher Bonner, North Carolina State University, Raleigh
- Edward David Crandall, University of Southern California, Los Angeles
- Alison Cory Pearson Elder and Gunter Oberdorster, University of Rochester, N.Y.
- Andrij Holian, University of Montana, Missoula
- Andre Elias Nel, University of California, Los Angeles
- Galya Orr, Battelle Pacific Northwest Laboratories, Richland, Wash.
- Christopher D. Vulpe, University of California, Berkeley
- Paul K. Westerhoff, Arizona State University, Tempe
- Frank A. Witzmann and Somenath Mitra, Indiana University, Indianapolis
- Robert M. Worden, Michigan State University, East Lansing

The three Recovery Act Nanotechnology NIH Challenge Grants have been awarded to:

- Kent E. Pinkerton, University of California, Davis
- Timothy R. Nurkiewicz, West Virginia University, Morgantown
- Wynne K. Schiffer, Feinstein Institute for Medical Research, Manhasset, N.Y.

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NTP Staff Recognized by Environmental Mutagen Society

By Robin Mackar

Mike Shelby, Ph.D., of the National Toxicology Program (NTP) was recognized by his peers at the 40th annual meeting of the Environmental Mutagen Society (EMS), October 24–28, in St. Louis. Shelby was publicly thanked and received an award for his service as a longstanding editor of the journal, *Mutation Research*.

Shelby received a plaque from Elizabeth Perill, a publisher at Elsevier, at the EMS meeting banquet. Perill said, "On behalf of Elsevier and the editors, I would like to extend our warm appreciation to Mike Shelby for his contributions of 30 years, not only to *Mutation Research*, but to the field of mutation research as author, reviewer and editor. We wish him well in his future endeavors." Shelby will retire as co-editor of the journal at the end of this year.

NTP's Mike Shelby is recognized by Elsevier Publisher Elizabeth Perill for his long-term service as a co-editor of ***Mutation Research****. (Photo courtesy of the Environmental Mutagen Society)*

The mission of the EMS is to promote critical scientific knowledge and research into the causes and consequences of damage to the genome and epigenome to inform and support national and international efforts to ensure a healthy, sustainable environment for future generations.

Shelby was appreciative of the award and said, "It's amazing how fast three decades can go by when you are doing something you enjoy. I've seen the journal and the entire field grow tremendously and am thrilled that I was part of the effort." Shelby has been working in the mutagenesis area since he received his Ph.D. in radiation mutagenesis and DNA repair from the University of Tennessee at Knoxville. After serving as a research associate in the Biology Division at Oak Ridge National Laboratory, Shelby joined NIEHS in 1977. He started the NTP Center for the Evaluation of Risks to Human Reproduction in 1998.

Ray Tice, Ph.D., of the NTP, was also recognized by EMS. Tice was the 32nd recipient of the society's prestigious Alexander Hollaender Award. This award is conferred in recognition of outstanding contributions in the application of the principles and techniques of environmental mutagenesis to the protection of human health, and for dedicated service to the EMS.

Ray Tice, Chief of the Biomolecular Screening Branch, receives a prestigious award from the Environmental Mutagen Society. (Photo courtesy of the Environmental Mutagen Society)

Tice was recognized "for his contributions to the development and application of the Comet and Micronucleus assays to environmental mutagenesis, biomonitoring and regulatory testing." While accepting the award, Tice said, "I am very honored to receive this award, especially because of my personal and professional interactions with Dr. Hollaender in the 1980s."

Tice plans to donate the cash award to the EMS Hollaender Fund, which supports workshops and training courses in countries where environmental mutagenesis and health issues are major concerns. "The Hollaender Courses have been, and continue to be, a unique contribution of the EMS to the international scientific community," Tice remarked. Tice is the third NTP member to receive this award. Errol Zeiger, Ph.D., received it in 1987, followed by Mike Shelby in 1988.

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

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NTP Scientists Qualify for Toxicology Certification

By Eddy Ball

Two National Toxicology Program (NTP) scientists — Scott Auerbach, Ph.D., and Matt Stout, Ph.D. — recently took an important step along toxicology's professional ranks by satisfying requirements for Diplomate of the American Board of Toxicology (D.A.B.T.) certification. ABT certification often offers an advantage in the job market and career advancement, and it has been associated with higher levels of compensation.

In an announcement to NTP colleagues, Acting Chief of the Toxicology Branch Paul Foster, Ph.D., congratulated Auerbach and Stout for "their hard work and effort [that] has now reaped a wonderful reward."

The American Board of Toxicology was established in 1979 to advance standards in the field of toxicology and to confer recognition upon those members of the profession who, measured against such standards, demonstrate competence. Certification requirements include a combination of education and experience and a three-part examination.

Auerbach is a molecular toxicologist in the Host Susceptibility Branch headed by Acting Chief Jef French, Ph.D. He is a former NIEHS/NTP postdoctoral intramural research and training award (IRTA) fellow who earned a Ph.D. in pharmacology from the University of Washington, Seattle.

Stout is a toxicologist in the NTP Program Operations Branch headed by Acting Chief Cynthia Smith, Ph.D. He was an NIEHS postdoctoral IRTA fellow in applied toxicology and carcinogenesis in the NTP Toxicology Branch. Stout received a Ph.D. in toxicology from the University of North Carolina at Chapel Hill.

Diplomates hold initial ABT certification for 5 years and must demonstrate that they actively practice toxicology, engage in continuing education, and maintain expert knowledge in their field prior to pursuing recertification.

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Scott Auerbach (Photo courtesy of Steve McCaw)

Matt Stout (Photo courtesy of Steve McCaw)

Bay Area Forum Bridges Research and Community

By Ed Kang

November 18-19, NIEHS Director Linda Birnbaum, Ph.D., participated in a series of events dedicated to discussing breast cancer and the environment, including the annual meeting of the Breast Cancer and the Environment Research Centers (BCERC) and a public forum in Sausalito, Calif. These Bay Area events helped to amplify the voices of area women affected by breast cancer.

Expert panelists engaged in open discussion on breast cancer at the Bay Area public forum — the latest in a series of community-based participatory events. Seated, left to right, are Birnbaum, Collman, Barlow, Reynolds, Rizzo and Das. (Photo courtesy of Ed Kang)

Highlighting her activities with partners and grantees, Birnbaum headlined a rousing, and at times, emotional public forum convened at the historic Cavallo Point Lodge. Attendees were mostly members of a concerned community struggling with a disease Birnbaum labeled in her opening remarks as "our common enemy — an equal opportunity killer." Introduced by Robert Hiatt, M.D., Ph. D., director of Population Sciences at the University of California, San Francisco (UCSF) Comprehensive Cancer Center, Birnbaum spoke of the "state of the science" of breast cancer research, and also joined a distinguished panel in initiating a frank and open discussion about community needs in ongoing breast cancer research.

Moderated by noted television reporter, Ysabel Duron, a breast cancer survivor and inductee into the National Association of Hispanic Journalists' Hall of Fame, the panel of speakers featured leaders in various disciplines. Joining Birnbaum and Hiatt on the dais were Gwen Collman, Ph.D., interim director of the Division of Extramural Research and Training (DERT) at NIEHS; Janice Barlow, M.S.N., executive director of Zero Breast Cancer; Rupali Das, M.D., chief of the Exposure Assessment Section in the Environmental Health Investigations Branch of the California Department of Public Heath; Peggy Reynolds, Ph.D., senior research scientist at the Northern California Cancer Center; and Jeanne Rizzo, R.N., president and CEO of the Breast Cancer Fund. The combined influence of these renowned experts shed light on different aspects of breast cancer from basic research to advocacy to education and prevention.

The public forum at the Cavallo Point Lodge, a former military base turned hotel, brought together scientists, sufferers and survivors to talk frankly about environmental connections to breast cancer and prevention strategies. (Photo courtesy of Ed Kang)

Public participation is always encouraged at these kinds of meetings and other forums. "It provides an opportunity for feedback," Barlow said. "It does change the direction of the research and the relevance to the community; plus, when [the community is] involved from the beginning, it has an influence on the questions that are being asked." Birnbaum added, "We need input from communities in setting science agenda and in fostering positive partnerships. Together with my Institute's partners and grantees, we will solidify our coalition in the national effort to keep the science moving forward."

Birnbaum's closing comments summarized the discussion with partners, grantees, community leaders and advocates. "I look forward to the day when I can stand here with all of our partners to say, 'We did it. We know how it happens, and we can stop it.' That day will come. Until then, we will continue the hard work." In borrowing a familiar concept, she added, "Knowledge is power," a simple but powerful adage that in the context of cancer and disease prevention takes on deliberate new meaning.

The next NIEHS community forum will be in West Harlem, N.Y. in January 2010.

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

One of Birnbaum's many activities included a stop at the Breast Cancer Fund, a group committed to identifying and eliminating environmental causes of breast cancer. (Photo courtesy of Ed Kang)

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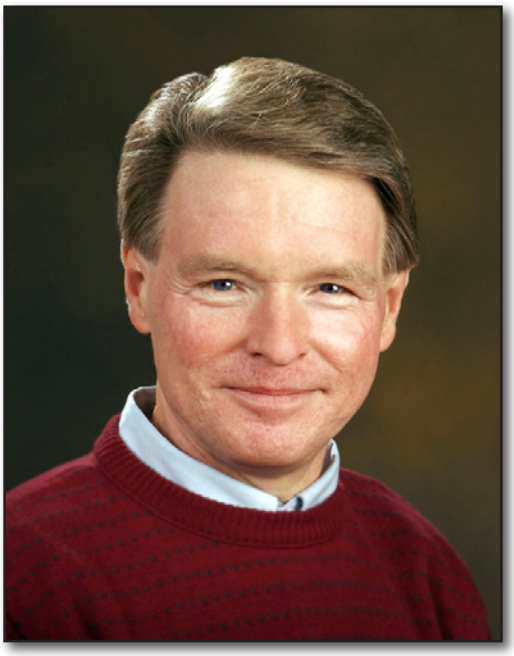
Dearry Speaks at One Health Summit

By Thaddeus Schug

The newly formed One Health Commission — a collaborative group of health science experts representing human, animal and ecosystem disciplines — held a groundbreaking summit on November 17 at the National Academy of Sciences (NAS) in Washington, D.C. Allen Dearry, Ph.D., a senior advisor at NIEHS, gave an oral presentation at the summit that was designed to raise awareness of the importance of transcending institutional and disciplinary boundaries to improve health outcomes for all species. Dearry's presentation, "NIEHS Perspective on One Health," emphasized a need to bridge the gap between scientific disciplines and institutions to monitor, diagnose, treat, prevent and control the spread of disease.



Allen Dearry (Photo courtesy of Steve McCaw)

Dearry illustrated how environmental events, such as habitat destruction, pollution and climate change, can alter biological systems and heighten the risks of emerging transmittable diseases between animal and human populations. He noted that collaborative efforts between NIEHS and the National Science Foundation (NSF) have been successful in understanding and forecasting potential public health problems. "For example," Dearry said, "using in-water sensors, genomics and modeling systems, researchers were able to predict development of red tide outbreaks on the Massachusetts coast and alert health officials, thereby reducing economic and health-related impacts."

Dearry concluded his presentation by outlining the challenges and opportunities facing the One Health Commission. He said it was important to overcome institutional and disciplinary barriers and to improve

communication between the public and medical health communities. He also mentioned that the One Health Commission should aim to develop a concrete research agenda, but pointed out that One Health offers opportunities to provide more holistic approaches to health programs and the potential to integrate institutional resources to solve health issues.

(Photo courtesy of the National Academy of Science)

Other presenters included keynote speaker Rajiv Shah, M.D., under secretary for research, education and economics at the U.S. Department of Agriculture; Roger Mahr, D.V.M., chief executive officer of the One Health Commission; Rear Admiral Ali Khan, M.D., acting director of the National Center for Zoonotic, Vector-Borne and Enteric Diseases, Centers for Disease Control and Prevention; Joshua Sharfstein, M.D., principal deputy commissioner of the U.S. Food and Drug Administration; and Angela Kreps, president and chief executive officer of the Kansas Bioscience Organization. Rear Admiral Bill Stokes, D.V.M., director of the NIEHS National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), also attended the summit as a representative of NIEHS.

An audio webcast and photos of Dearry's presentation and panel participation are available at the NAS Office of News and Public Information.

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

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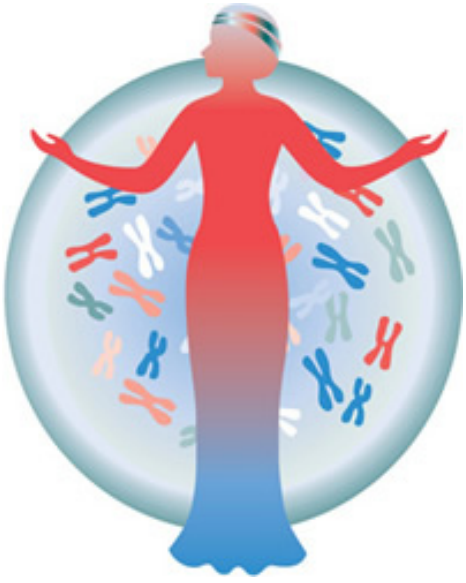
NIH Women in Science Receive Recognition

By Omari J. Bandele

The NIH Office of Research on Women's Health (ORWH), in collaboration with the NIH Coordinating Committee on Research on Women's Health (CCRWH), has published *Women in Science at the National Institutes of Health, 2007–2008*. The book, inspired by the brochure *National Institutes of Health: Women in Science*, celebrates the leadership and accomplishments of talented female scientists from throughout the NIH. Fifteen NIEHS women scientists are included in the book.


(Image courtesy of the NIH Office of Research on Women's Health)

The ORWH, established within the NIH Office of the Director in 1990, works to ensure that research conducted and supported by the NIH adequately addresses issues regarding women's health. The office also seeks to increase opportunities for females in the biomedical sciences by identifying and eliminating barriers to success for women in these careers.

The purpose of *Women in Science* is to inspire young women and men to pursue careers in science. The female scientists highlighted in this book represent a diverse range of accomplishments, backgrounds, positions and

career paths. They provided insight about their profession including descriptions of influential events that shaped their career path and the contribution of their mentors to their success. These scientists also offered perspectives on how they have balanced professional and personal responsibilities — a challenge frequently mentioned by young women considering research careers.

One of these featured NIEHS women, Marilyn Diaz, Ph.D., a principal investigator and head of the Somatic Hypermutation Group in the Laboratory of Molecular Genetics, was delighted to be part of the book. "While women scientists share many of the challenges associated with a career in science with their male counterparts, some challenges, however, uniquely or more severely affect them," Diaz said. "I hope that by sharing my views and experiences as a scientist, younger women will take comfort in knowing many have walked the same path and dealt with similar issues." Another highlighted NIEHS scientist, Katarzyna Bebenek, Ph.D., a staff scientist for the Replication Fidelity Group in the Laboratory of Molecular Genetics, added, "This book will be a true source of inspiration for young people."

Women in Science celebrates the remarkable achievements of these NIH researchers and accentuates the need for increased representation of women in the sciences.

To download an electronic copy or order a hard copy of *Women in Science at the National Institutes of Health, 2007-2008*, go to the ORWF Web site.

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

NIEHS Researchers Featured in *Women in Science*

Donna D. Baird, Ph.D., principal investigator, Epidemiology Branch

Katarzyna Bebenek, Ph.D., staff scientist, Laboratory of Molecular Genetics

Leesa J. Deterding, Ph.D., staff scientist, Laboratory of Structural Biology

Marilyn Diaz, Ph.D., principal investigator, Laboratory of Molecular Genetics

June K. Dunnick, Ph.D., toxicologist, Toxicology Branch

Dori Germolec, Ph.D., biologist, Toxicology Branch

Joyce A. Goldstein, Ph.D., principal investigator, Laboratory of Pharmacology

Traci M. T. Hall, Ph.D., principal investigator, Laboratory of Structural Biology

Gaylia Jean Harry, Ph.D., principal investigator, Laboratory of Molecular Toxicology

Freya Kamel, Ph.D., staff scientist, Epidemiology Branch

Stephanie J. London, Ph.D., principal investigator, Epidemiology Branch

Lisa G. Rider, M.D., deputy chief of the Environmental Autoimmunity Group, Clinical Research Program

Dale P. Sandler, Ph.D., principal investigator and chief, Epidemiology Branch

Christina T. Teng, Ph.D., molecular biologist, Biomolecular Screening Branch

Clarice R. Weinberg, Ph.D., principal investigator and chief, Biostatistics Branch

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NIEHS Booth Wins Best Exhibit at APHA Meeting

By Robin Arnette

Several NIEHS employees represented the Institute at the American Public Health Association's (APHA) 137th Annual Meeting and Exposition at the Pennsylvania Convention Center in Philadelphia on November 7–11. Myra Westmoreland, Mary Collins, Martha Dimes and Rita Hanson were on hand at the NIEHS exhibit to meet attendees and answer questions about NIEHS. Little did they know that the exhibit would win first prize out of the many exhibit booths representing "non-profit organizations."

NIEHS and EHP staff members in front of the award-winning exhibit. Shown, left to right, are Myra Westmoreland (NIEHS), Mary Collins (EHP Contractor), Rita Hanson (EHP) and Martha Dimes (EHP). (Photo courtesy of Rita Hanson)

The 2009 APHA meeting had more than 12,000 attendees, 1,000 scientific sessions, and 600 companies, associations and programs in the Exhibit Hall. Members of the APHA Exhibit Advisory Council judged the best booth in each size category based on color, organization, creativity, eye appeal and design. They chose the NIEHS booth as the best in the 10 feet-by-20 feet category.

Even before the win, several dignitaries stopped by to admire the artwork. "APHA Executive Director Georges C. Benjamin, M.D., FACP, FACEP (Emeritus) and U.S. Surgeon General Regina Benjamin, M.D., M.B.A., stopped by our booth," Westmoreland noted. "It was an honor to meet both Dr. Benjamins."

U.S. Surgeon General Regina Benjamin stopped by to admire the NIEHS exhibit. (Photo courtesy of Myra Westmoreland)

Bernie Birnbaum, son of NIEHS and NTP Director Linda Birnbaum, Ph.D., showed off the blue ribbon with pride. (Photo courtesy of Bernie Birnbaum)

The NIEHS first-place ribbon on display. (Photo courtesy of Rita Hanson)

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Science Notebook

Cellular Effects of Mutated DNA Polymerases

By Robin Arnette

DNA polymerase is responsible for DNA replication, a process that allows all living organisms to precisely copy their genetic material so that the information can be passed on to the next generation. But what happens when the polymerase has a mutation in its sequence? Does this genetic mistake produce abnormalities during replication and cause further harm to cells?

Wang holds the Klaus Bensch Endowed Professorship in Experimental Pathology at the Stanford University School of Medicine. (Photo courtesy of Steve McCaw)

According to Stanford University School of Medicine's Teresa Shu-Fong Wang, Ph.D., cell lines that express a mutated polymerase experience chromosome chaos. Wang presented an NIEHS Distinguished Lecture on October 26 titled "The Perils of Bad DNA Polymerases: Chromosome Chaos." Bill Copeland, Ph.D., a principal investigator in the Laboratory of Molecular Genetics and a fellow expert in DNA replication, hosted the seminar.

Host Bill Copeland leads the Mitochondrial DNA Replication Group. (Photo courtesy of Steve McCaw)

Biochemistry and yeast genetics were Wang's specialty for many years, so she applied that expertise to human genetics and cell biology in her latest research. Wang explained the impetus for her work by saying, "I wanted to know what kind of chromosome chaos a bad or mutant DNA polymerase would cause, besides making genetic mistakes in the genome."

To address the question, Wang generated cell lines expressing either a mutated DNA polymerase α (Polα), the principal initiation polymerase, or a mutated DNA polymerase δ (Polδ), a key elongation polymerase in normal human fibroblasts, cancerous p53-deficient HeLa cells and p53-proficient U2OS cells. Both mutations in these polymerases were in the evolutionarily conserved N-terminal region — not in the catalytic domain.

Wang said in normal human fibroblasts, expression of either polymerase compromised the S-phase progression in the cells. Polα-mutant expressing cells, in response to S-phase progression delay, were unable to maintain mitotic arrest with weak expression of mitotic checkpoint proteins BubR1 and Mad2. As a result, the cells experienced mitotic slippage and arrested in G1 as tetraploids, having four sets of chromosomes.

In contrast, the Polδ-mutant expressing cells were able to maintain mitotic arrest in response to S-phase progression delay with proficient levels of BubR1 and Mad2. These cells had a normal number of chromosomes known as ploidy. Wang added, "These studies suggested that the mitotic checkpoint played a key role in preventing mitotic slippage that could result in polyploidy in replication-stressed cells."

In Polα-mutant expressing HeLa or U2OS cells, the Polα-mutant protein was unable to interact with And-1, a sister chromatid cohesion related factor. The Polα-mutant expressing cells exhibited mitotic and cohesion defects, resulting in chromosome chaos. The Polδ-mutant expressing HeLa or U2OS cells induced dramatic deregulation of centrosome duplication, resulting in chromosome chaos. The cause of the centrosome duplication deregulation was due to the upregulation of cyclines E and A — proteins that control cell cycle progression — when cells experienced replication stress.

Samuel Wilson, M.D., center, one of many DNA replication experts in the audience, listened intently to Wang's seminar. Wilson is head of the DNA Repair and Nucleic Acid Enzymology Group and was former Acting Director of NIEHS. (Photo courtesy of Steve McCaw)

Wang concluded her talk with an important take home message. "In normal human cells, replication delay requires mitotic checkpoint to prevent mitotic slippage that will result in polyploidy of chromosomes. In cancerous cells, proper assembly of an initiation complex is a pre-requisite of the sister chromatid cohesion establishment, failure of which will result in chromosome chaos," she urged. "Defects in the replication elongation process will upregulate cyclins E and A to push the cells to go through S-phase, resulting in deregulation of centrosome duplication."

Wang used cell biology techniques to demonstrate that mutations in replicative DNA polymerases outside of the catalytic domain can cause a variety of chromosome abnormalities. Copeland, who completed his postdoctoral fellowship with Wang at Stanford, was familiar with her forward-thinking approach to science. He added, "Dr. Wang's ability to apply her previous experiences as a biochemist and yeast geneticist in cell biology demonstrates that she is not hesitant to take on new challenges."

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REST's Repressive Activities Determine Neuronal Cell Development

By Thaddeus Schug

On November 13, Distinguished Lecturer Gail Mandel, Ph.D., came to NIEHS to talk about her research, which is defining the gene regulatory mechanisms involved in cell differentiation and specialization. Mandel, a recent inductee into the National Academy of Sciences, presented a seminar titled "Repression Mechanisms and Neuronal Phenotype." The lecture was co-hosted by NIEHS Principal Investigators Serena Dudek, Ph.D., and Paul Wade, Ph.D.

Mandel, a senior scientist at the Oregon Health and Science University (OHSU) Vollum Institute in Portland and an investigator with the Howard Hughes Medical Institute, said, "Understanding what makes a neuron

different from all other types of cells is key to establishing how cell identity is established and maintained." She explained that identifying the key regulatory proteins in cells should help efforts to reprogram mature cells into stem cells or other cell types. Reprogramming could someday allow the recapitulation of disease processes from patients' tissue or the creation of new tissues, such as insulin-producing cells from the pancreas.

Gail Mandel (Photo courtesy of Bruce Forster)

Mandel became interested in neuronal development while investigating proteins that control gene expression of the sodium channel in neurons. She expected to find an activating protein, but, "Instead, I found that nervous system gene expression is sustained in a very unusual way," she continued. Mandel demonstrated that neuronal specificity is defined not by an activator, but by the absence of an inhibitor protein that she found in 1995 and named RE1-silencing transcription factor or REST. When REST is absent in neuronal cells, neuronal genes are expressed. REST's presence in nonneuronal cells represses neuronal genes. Employing several genetic techniques, her group has revealed that REST silences 2,000–4,000 neuronal genes in nonneuronal cells, making it a master regulator of neuronal identity.

Utilizing gene trap reporter mouse models and embryonic stem cells, Mandel's group has established how the REST repressor complex is regulated during normal development. She said that REST's repressive activities are important during nervous system development, when stem cells differentiate into the various cells that ultimately make up the nerves, spinal cord and brain. REST is present in cells slated to become neurons, yet it keeps neuron genes turned off. At some point, REST disappears when the cell matures and neuron genes are expressed.

"REST keeps DNA less compact in developing neuronal cells than in nonneuronal cells, where REST acts on DNA like a clamp, like a much stricter parent," she commented. Mandel is studying REST repression mechanisms and how REST vanishes at the right time in development to allow nerve cells to form and express their genes.

Mandel concluded her presentation by discussing how REST regulates the expression of a family of micro RNAs (miRNA). She noted that in nonneuronal cells and neural progenitors, REST inhibits the expression of miR-124a , a brain-specific miRNA, allowing the persistence of nonneuronal transcripts. As progenitors differentiate into mature neurons, REST leaves the miR-124a gene loci, and nonneuronal transcripts are degraded selectively. She concluded that the combined transcriptional and posttranscriptional consequences of REST action maximize the contrast between neuronal and nonneuronal cell phenotypes.

Co-host Dudek noted that both she and Wade independently nominated Mandel to be an NIEHS Distinguished Lecturer, a rarity that speaks to the quality of Mandel's work. "Mandel's research is impressive because it encompasses such a broad spectrum of interest in molecular biology," Dudek said.

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

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NIEHS Science Awards Day Celebrates Intramural Research Achievements

By Negin P. Martin

On the first Thursday in November, NIEHS traditionally holds an event that honors outstanding scientific achievements among the Institute's intramural community. On November 5, researchers and trainees left their laboratories and offices to discuss science and listen to oral presentations during the 7th Annual Science Awards Day. The event, sponsored by the NIEHS Office of the Scientific Director, was created to celebrate the research conducted by intramural scientists at NIEHS.

John Pritchard, Ph.D., acting scientific director, opened the ceremonies by welcoming participants and acknowledging the efforts put forth by the event organizer and moderator Joel Abramowitz, Ph.D. Awardees were nominated by their NIEHS peers, and a panel of outside judges formed the Board of Scientific Counselors that selected the winner of the 2009 Paper of the Year. The Outstanding Staff Scientist and Early Career Award winners were determined by a group of extramural scientists at local universities and research institutes. The Mentor of the Year was selected by the NIEHS Trainees Assembly (NTA).

Lead author Stephanie Nick McElhinny (center) and her mentor Tom Kunkel (left) were recognized for publishing the Paper of the Year. Gordenin (right), also a co-author on the Paper of the Year, was selected as the Outstanding Staff Scientist. (Photo courtesy of Steve McCaw)

Scientist of the Year, Laboratory of Reproductive and Developmental Toxicology Chief Ken Korach, presented an impressive body of research about the signaling pathways of estrogen receptor isoforms. (Photo courtesy of Steve McCaw)

Dmitry Gordenin, Ph.D., the 2009 Outstanding Staff Scientist from the Laboratory of Molecular Genetics, presented the first scientific seminar titled "Amplifying risk of genome instability." Gordenin and Michael Resnick, Ph.D., the primary investigator in the study, used versatile yeast genetics to investigate the source and mechanism of chromosomal instability and its role in evolution and population dynamics.

The morning and afternoon sessions of oral presentations featured eight selected seminars from abstracts submitted by trainees and staff. Presenters did a superb job of communicating their research accomplishments and future goals in short 10 minute talks. Participants also got a chance to review 87 posters and talk with scientists about an impressive array of environmental health research presented by NIEHS trainees.

The Early Career Award recipient Raja Johti Ph.D., from the Biostatistics Branch, described the multi-level regulatory components of transcription factors and how they contributed to cell response variability within a uniform population.

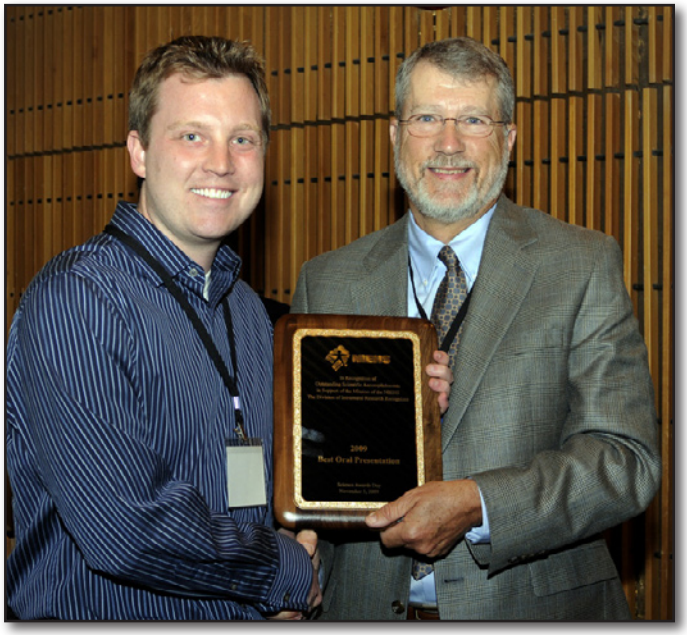
Kenneth Korach, Ph.D., chief of the Laboratory of Reproductive and Developmental Toxicology, was selected as the 2009 Scientist of the Year. Korach's seminar focused on his comprehensive research on the estrogen receptor and its role in regulating reproductive health. Nominations for Scientist of the Year can come from lab chiefs, program directors or the Scientific Director. Nominations are then reviewed by a committee of extramural scientists.

The final segment of the ceremony was dedicated to recognizing accomplishments and presenting awards.

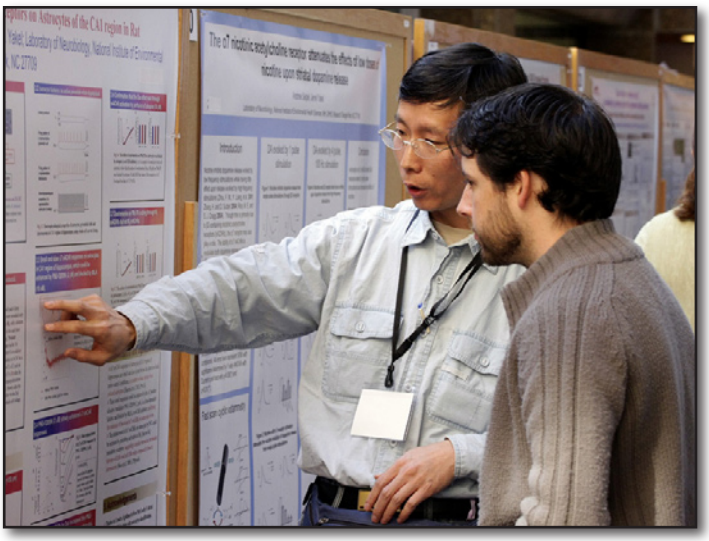
(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences. She recently completed a postdoctoral fellowship with the NIEHS Membrane Signaling Group.)

Abramowitz (left) presented Jothi (right) with the Early Career Award. (Photo courtesy of Steve McCaw)

Dudek (left), who was voted as Mentor of the Year by the NIEHS Trainees Assembly, posed with Christopher Geyer (right), a postdoctoral fellow in the Laboratory of Reproductive and Developmental Toxicology. (Photo courtesy of Steve McCaw)



Best Oral Presentation Award winner Simons (left) accepted his award from Acting Scientific Director Pritchard (right). (Photo courtesy of Steve McCaw)



Visiting fellow Jianxin Shen (left) explains details about the functional role of alpha7 nicotinic acetylcholine receptors in hippocampal signaling to another Laboratory of Neurobiology fellow Ezequiel Marron (right) (Photo courtesy of Steve McCaw)

Researchers filled Rodbell Auditorium to listen to the Annual Science Award Day oral presentations. (Photo courtesy of Steve McCaw)

2009 Science Day Awards

- Scientist of the Year - Kenneth S. Korach, Ph.D., Laboratory of Reproductive and Developmental Toxicology chief, presenting "Estrogen receptor insensitivity: Physiological consequences"
- Early Career Award - Raja Jothi, Ph.D., Biostatistics Branch, presenting "Seeing the forest for the trees: A systems level understanding of differential cell-fate outcome"
- Outstanding Staff Scientist - Dmitry Gordenin, Ph.D., Laboratory of Molecular Genetics, speaking about "Amplifying risk of genome instability"
- Mentor of the Year - Serena Dudek, Ph.D., Laboratory of Neurobiology
- Best Poster Presentation in Environmental Biology - Nisha A. Cavanaugh, Ph.D., Laboratory of Structural Biology, presenting a poster tilted "How sweet it is: Ribonucleotide discrimination by DNA polymerase beta"
- Best Poster Presentation in Environmental Diseases and Medicine - Daniel A. Gilchrist, Ph.D., Laboratory of Molecular Carcinogenesis, presenting a poster titled "NELF globally regulates Pol II stalling and potentiates the drosophila innate immune response"
- Best Poster Presentation in Environmental Toxicology - Brooke Tvermoes, Ph.D., Laboratory of Molecular Toxicology, presenting a poster titled "The effects of cadmium exposure on calcium homeostatis and signaling pathways"
- Best Oral Presentation - Stephen B. Simons, Ph.D., Laboratory of Neurobiology, presenting "Switching off plasticity: Are your neurons getting enough calcium?"
- Paper of the Year - From the Laboratory of Molecular Genetics and Laboratory of Structural Biology, S.A. Nick McElhinny, D.A. Gordenin, C.M. Stith, P.M.J. Burgers and T.A. Kunkel for "Division of Labor at the Eukaryotic Replication Fork", Molecular Cell 30: 137-144, 2008

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Chromium Linked to Telomere Damage

By Laura Hall

On November 10, Patricia Opresko, Ph.D., an assistant professor at the University of Pittsburgh, presented "Links Between Telomere Instability, Environmental Genotoxins and Human Disease" for the Keystone Science Lecture Series at NIEHS. Opresko is an NIEHS 2006 Outstanding New Environmental Scientist (ONES) grantee. ONES is a program that funds early career scientists for five years to investigate the influence of the environment on human disease. Opresko's research focuses on understanding telomere biology and the mechanisms of telomere loss.

"Telomeres are really starting to become big business," explained Opresko. "I think in a public health setting, we need to be aware of this so we can properly educate the public." (Photo courtesy of Steve McCaw)

During her talk, Opresko discussed telomere biology, the role of Werner syndrome helicase protein (WRN) and the deleterious effects of hexavalent chromium, Cr(VI), on telomeres. Human exposure to Cr(VI) occurs mainly as an occupational hazard in the welding industry where exposure is associated with respiratory problems and increased risk of lung disease. Cr(VI) is also found in pigments, anti-corrosive agents and sometimes at toxic waste sites.

Dan Shaughnessy, Ph.D., health science administrator for the Exposure Biology Program, part of the Genes, Environment and Health Initiative, introduced ONES grantee Patricia Opresko. (Photo courtesy of Steve McCaw)

Opresko explained that a telomere is a series of repetitive DNA elements at the end of a chromosome. Telomeres become shortened with each cell division, partly due to the inability of the DNA replicating enzyme to copy DNA at the tip of the telomere. Opresko said that this shortening mechanism normally limits the number of times cells can divide and this process is believed to be responsible for cellular aging and a limited lifespan. Sperm, egg and stem cells have an enzyme called telomerase that replaces the lost telomere sequence, while other cells of the body, called the somatic cells, do not show telomerase activity.

Fu-Jun Liu, Ph.D., a postodoctoral associate in Opresko's lab, has looked at the effects of the environmental pollutant Cr(VI) and found that it causes replicative stress chromosome breaks due to replication or stalling fork breaks (see *Environmental Factor* article). WRN, which unwinds and separates double-strand DNA allowing the DNA to be copied or repaired, is involved in the recovery from this Cr(VI) damage.

These studies are "the first molecular evidence that WRN protects against replicative stress induced by environmental pollutants," said Opresko. "I think this is a real strength of the ONES program and the NIEHS strategic plan, to try to use environmental agents to inform about biological pathways."

In addition, Opresko and Liu found that Cr(VI) exposure causes telomere damage. Guanine residues of the telomeric repeats are particularly susceptible to oxidative stress caused by Cr(VI). The studies show that Cr(VI) induces chromatid breaks, telomere defects and telomere loss. Cr(VI) induces telomeric defects presumably by interfering with telomeric replication.

In Werner syndrome, a premature aging disease caused by mutations in the WRN gene, the number of sister chromatid exchanges increases relative to normal and is confined specifically to the telomeres. WRN appears to play a role in preventing exchanges, by regulating the recombination of the telomeres. Opresko is currently conducting studies to investigate if Cr(VI) exposure induces more telomeric defects in cells lacking WRN.

Opresko's talk was the third seminar in the Keystone Science Lecture Series hosted by the Division of Extramural Research and Training (DERT). (Photo courtesy of Steve McCaw)

The research on Cr(VI) and telomere damage has led Opresko to examine the mutagenesis rate of replicating telomeres using an assay she generated in her lab. Opresko has found that under normal conditions this rate is very low. She plans to use this system to see which proteins are important in telomere replication.

Understanding the role and interactions of the genetic and environmental factors that affect telomere biology may help scientists understand aging and diseases such as Werner syndrome. Doing so may also help to identify groups or individuals that may particularly be at risk from certain occupational or other environmental exposures.

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

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Arsenic Biomethylation Required for Oxidative DNA Damage

By Eddy Ball

According to GreenFacts.com, inorganic arsenic occurs naturally in the earth's crust and results from man-made activities such as mining, smelting and coal-fired power plants. Inorganic arsenic is known to be carcinogenic to humans and is a common contaminate in drinking water. NIEHS researchers have found that biomethylation of arsenic compounds, previously considered to be a detoxification mechanism, actually appears to cause oxidative DNA damage and to increase arsenic carcinogenicity. The findings were published in an online article titled "Requirement of Arsenic Biomethylation for Oxidative DNA Damge," which recently appeared online in the *Journal of the National Cancer Institute*.

Michael Waalkes (Photo courtesy of Steve McCaw)

Michael Waalkes, Ph.D., of the National Cancer Institute, is currently on detail at NIEHS. Waalkes and several other colleagues, including Ronald Mason, Ph.D., a principal investigator in the NIEHS Laboratory of Pharmacology, compared methylation-competent and methylation-deficient cell lines exposed to arsenic. Exposure of methylation-competent cells, but not methylation-deficient cells, was followed by a sharp rise in oxidative damage. After the peak of oxidative DNA damage (ODD), methylation-competent cells acquired the *in vitro* characteristics of cancer cells. The methylation-deficient cells exhibited the same characteristics, but at a much later time.

Ron Mason (Photo courtesy of Steve McCaw)

Biomethylation is a mechanism of metabolizing arsenic in the body whereby one or more methyl groups is attached to the inorganic arsenic. Methylation-competent cells have this biomethylation ability. The *in vitro* characteristics of cancer, the cancer phenotype, used in this study included enhanced cellular invasiveness, cell proliferation, and activity of certain enzymes. These attributes are all commonly increased in cells that develop cancer from arsenic exposure.

The authors treated arsenic exposed methylation-competent rat liver epithelial cells with selenite, an arsenic biomethylation inhibitor. Selenite treatment abolished arsenic-induced ODD and the *in vitro* cancer phenotype, which indicated that biomethylation, not inorganic arsenicals, are likely to be key factors for ODD formation.

Oxidative DNA radicals that cause ODD were detected using immuno-spin trapping (IST), a method that converts the DNA radicals induced by reactive oxygen species, which normally last only milliseconds or less, to stable DNA-nitrone adducts that last months or years. The DNA is then extracted from the cells and immuno-chemically quantified. IST, a methodology developed by Mason at NIEHS, avoids the artifacts and indirect quantitation found in other methods used to measure DNA radicals.

A human urothelial cell line, UROtsa, stably transduced with mouse arsenite methyltransferase (As3mt), an enzyme which adds a methyl group to inorganic arsenical, made the cells arsenic methylation-competent. These cells showed more ODD and developed the cancer phenotype more quickly than the parent cell line that was methylation-deficient. Mutations of the human version of this gene are known to affect arsenical methylation.

Mice have been engineered to lack the As3mt gene. “Although inorganic arsenicals have not yet been tested for carcinogenic effects in these genetically altered mice, this clearly should be a high priority,” the authors write.

Citation: Kojima C, Ramirez DC, Tokar EJ, Himeno S, Drobna Z, Syblo M, Mason, RP, Waalkes MP. 2009. Requirement of arsenic biomethylation for oxidative DNA damage. J Natl Cancer Inst Advance Access published November 23, 2009, doi:10.1093/jnci/djp414

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

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This Month in EHP

By Eddy Ball

http://twitter.com/ehponline

This month, *Environmental Health Perspectives (EHP)* investigates the potential threat of lead exposure in tap water. The focus article, "Out of Plumb: When Water Treatment Causes Lead Contamination," examines how lead gets into treated water and what water utilities and residents are doing about it. December's Spheres of Influence feature, "Communication Gap: The Disconnect Between What Scientists Say and What the Public Hears," looks at ways to maintain the integrity and accuracy of reported data while presenting new findings in terms that are meaningful to the public.

Other highlights in the issue include the following topics:

- **Nanotechnology and in Situ Remediation** – Using nanoremediation — the manipulation of reactive nanoscale (1–100 nm) materials to transform and detoxify pollutants — to reduce the cost and time required to decontaminate large-scale sites and eliminate the need for treatment and disposal of extracted contaminants

- **Cadmium-Induced Breast Cell Transformation** – Analyzing the role of the environmental pollutant cadmium in the pathogenesis of breast cancer and the basal-like phenotype

- **The Melamine Incident: Food and Feed Safety** – Factors that contributed to melamine contamination of infant formula in China and recommendations to manage future food-safety incidents and protect public health

- **Well Water, Pesticides and Parkinson's Disease** – Adding further evidence of a link between the consumption of pesticide-contaminated well water and Parkinson's disease

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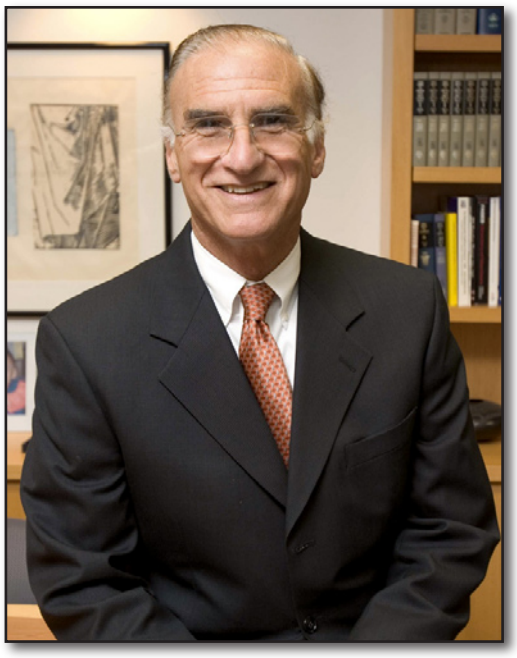
C. Ronald Kahn To Give Falk Lecture

By Eddy Ball



Falk Lecturer C. Ronald Kahn (Photo courtesy of C. Ronald Kahn and the Joslin Diabetes Center)

The NIEHS 2008–2009 Distinguished Lecture Series continues on December 8 with the annual Hans L. Falk Memorial Lecture. The lecturer this year is C. Ronald Kahn, M.D., Sc.D., who will speak on "Genes and Environment in the Epidemic of Diabetes and Obesity." The lecture will begin at 11:00 a.m. in the Rodbell Auditorium. Kahn is senior investigator and head of the Section on Obesity and Hormone Research, the Mary K. Iacocca Professor of Medicine at Harvard Medical School, and Vice Chairman of the Board of the Joslin Diabetes Center in Boston.

Kahn has been recognized internationally for his pioneering work in the field of diabetes, including seminal discoveries that have defined the molecular and cellular mechanisms of insulin action, and have yielded critical information about insulin resistance in obesity and diabetes.

His principal research interests involve understanding the molecular mechanism of action of insulin and related growth factors at a molecular level and defining the defects that underlie human diabetes mellitus at a molecular and physiologic level. The Kahn lab has also found interesting links between SIRT1-3 and the control of metabolism and longevity.

The annual Hans L. Falk Memorial Lecture Series was initiated by scientists and friends of Hans Falk, Ph.D., the first scientific director at NIEHS, to showcase scientists who have made distinguished contributions to environmental health sciences. Falk was an internationally known environmental health science authority, and one of the founding members and shaping forces at NIEHS.

During his visit, Kahn will meet with investigators, students and fellows to discuss issues of common interest. He will also deliver a second lecture on Wednesday, December 9, when he will present his own current research in a seminar designed for specialists in his field.

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Extramural Update

Virtual Consortium for Translational/Transdisciplinary Environmental Research (ViCTER)

Ever wish there was a grant program that allows expansion of your currently funded NIEHS grant, and at the same time, allows you to bring in new collaborators to improve the translational or transdisciplinary nature of the research? If so, take a look at ViCTER, "Virtual Consortium for Translational and/or Transdisciplinary Environmental Research," a new grant program developed at NIEHS. The announcement can be found at: http://grants.nih.gov/grants/guide/pa-files/PAR-10-030.html.

Jerry Heindel (Photo courtesy of Steve McCaw)

The purpose of the ViCTER program is to foster transdisciplinary collaboration and promote translational research efforts between and among basic (technology and mechanism oriented), clinical (patient-oriented) and population-based researchers and other individuals with expertise relevant to environmental health. The program fosters the gathering of those who study a particular environmental stressor(s) of interest.

The ultimate goal of ViCTER is to accelerate the exchange of knowledge and resources among collaborators to improve human health in those areas where environmental factors are known or expected to influence the development or progression of disease. Each virtual consortium will consist of an NIEHS-funded researcher (lead applicant), who will serve as the principal investigator (PI) and overall coordinator of the consortia, and two new collaborators.

For purposes of this program, translational research is defined as research that involves scientists and public health professionals from the same or multiple disciplines working interactively on a common problem to stimulate the bidirectional flow of information across the spectrum from *in vitro* systems to rodent models, higher models (sheep/primate), human epidemiological or clinical research, research dissemination and public health action.

Transdisiplinary research is defined as research that involves scientists and public health professionals from multiple disciplines working interactively on a common problem to develop novel cross-disciplinary methods, insights and research approaches that would not have occurred with a traditional uni-disciplinary investigation.

ViCTER will allow you to expand the scope of your own research to include new perspectives, such as basic mechanistic, clinical, epidemiological, computational, engineering and/or health risk communication approaches, expanding the translational and/or transdisciplinary nature of the grants with the goal of improving their impact on public health.

If you have a current NIEHS-funded R01 and will have at least two years of funding remaining on the grant on July 1, 2010, you can submit a Competitive Revision to develop and implement a ViCTER. Eligible PIs can request $100,000 direct costs per year remaining on the parent grant to expand the scope of the original project. In addition, new collaborators can request $75,000 direct costs per year to develop one or two new aims that would improve the transdisciplinary or translational nature of the overall project.

The deadline for receipt of application is **January 13, 2010**.

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Extramural Papers of the Month

By Jerry Phelps

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

Chronic Glucocorticoid Use Raises Risk of Bladder Cancer

The most recent study by NIEHS grantee Margaret Karagas at Dartmouth University reports that chronic use of glucocorticoid drugs is a risk factor for bladder cancer. The findings appear in the *British Journal of Cancer*.

Glucocorticoids are often prescribed for immunosuppressive therapy for organ transplant patients, asthma sufferers, or people with an autoimmune disorder such as rheumatoid arthritis. The study matched 786 bladder-cancer patients to 1,083 control subjects. The risk of bladder cancer was three-fold higher for people who had taken glucocorticoids for more than five years.

These results raise the possibility of an increased risk of bladder cancer from long-term use of glucocorticoids and a potential role of immunological effects in bladder cancer etiology.

Citation: Dietrich K, Schned A, Fortuny J, Heaney J, Marsit C, Kelsey KT, Karagas MR. 2009. Glucocorticoid therapy and risk of bladder cancer. Br J Cancer 101(8):1316-1320.

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Discovery in Aflatoxin Formation

A *Nature* article by NIEHS grantee Craig Townsend reports advances in the understanding of how the fungal toxin aflatoxin is synthesized, opening new avenues that might lead to possible methods to prevent the formation of the toxin and its harmful effects.

Aflatoxin is produced by molds in the *aspergillus* family. They are ubiquitous and are found in many crops such as corn, rice, wheat and peanuts. The toxin is consumed directly by eating contaminated crops or by drinking milk from cows fed contaminated food stuffs. The toxin is a known human carcinogen causing liver cancer.

Using x-ray crystallography, the research team determined the three-dimensional structure of an enzyme in the polyketide synthase family, which is a component of the multi-step process of toxin synthesis. They discovered a region known as the product template domain responsible for producing a precursor of the toxin. The researchers hope to further their discoveries and possibly develop a method to prevent the formation of aflatoxin.

Citation: Crawford JM, Korman TP, Labonte JW, Vagstad AL, Hill EA, Kamari-Bidkorpeh O,Tsai SC, Townsend CA. 2009. Structural basis for biosynthetic programming of fungal aromatic polyketide cyclization. Nature 461(7267):1139-43.

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Bacterial Toxin Linked to Parkinson's

NIEHS-funded researchers in Alabama discovered that a common soil bacterium produces a metabolite that disrupts a protein degradation pathway associated with Parkinson's disease. This finding suggests that exposures to metabolites from common bacteria may contribute to the development of Parkinson's disease.

Parkinson's disease is a progressive neurodegenerative disorder involving the loss of dopamine producing neurons from the substantia nigra region of the brain. For the past several years, scientists have speculated that environmental causes of the disease are more important than genetics because studies in twins suggest that genetic predisposition is only possibly responsible for the disease occurrence. A clinical hallmark of the disease is misfolding and accumulation of proteins, such as α-synuclein, in inclusions called Lewy Bodies.

In the current study, funded through an exploratory R21 grant, Alabama scientists discovered that a common *streptomyces* bacterium found in soil produces a natural proteosome inhibitor that blocks protein degradation and causes gradual degeneration of all neuronal cells examined. Dopamine neurons were particularly vulnerable to the metabolites effects. The studies were carried out in a Parkinson's disease model using the nematode *C. elegans.*

Citation: Caldwell KA, Tucci ML, Armagost J, Hodges TW, Chen J, Memon SB, Blalock JE, DeLeon SM, Findlay RH, Ruan Q, Webber PJ, Standaert DG, Olson JB, Caldwell GA. 2009. Investigating bacterial sources of toxicity as an environmental contributor to dopaminergic neurodegeneration. PLoS One 4(10):e7227.

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Social Isolation Speeds Breast Tumor Growth

A socially-isolated and stressful environment may speed up the growth of breast tumors according to NIEHS-supported researchers at the University of Chicago. The effects are believed to be caused by changes in gene expression in mammary glands.

Previous human epidemiologic studies have shown a link between cancer and stress. The current study was conducted in a strain of laboratory mice genetically susceptible to breast cancer. Mice are generally very social animals and social isolation is recognized as a severe stressor for them. Mice were randomly assigned to be isolated at a very early age. The isolated mice developed larger and more breast cancers than the group-housed mice.

Gene expression changes in mammary tissue were also measured in the mice. Genes involved in metabolism were turned on and off in the isolated mice in a very reproducible manner. Certain metabolic pathways and changes are known to contribute to the increased growth of breast cancer. The isolated mice also had much higher stress hormone levels than their group-housed counterparts.

These findings are preliminary, but suggest that reducing stress and increasing social activity may be important factors in the prevention and treatment of breast cancer in women.

Citation: Williams JB, Pang D, Delgado B, Kocherginsky M, Tretiakova M, Krausz T, Pan D, He J, McClintock MK, Conzen SD. 2009. A model of gene-environment interaction reveals altered mammary gland gene expression and increased tumor growth following social isolation. Cancer Prev Res (Phila Pa). 2(10):850-61.

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

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Intramural Papers of the Month

By Laura Hall and Thaddeus Schug

Zinc Finger RNA-Binding Protein Zfp3612 Critical in Hematopoiesis

A collaborative effort of researchers from several institutions led by NIEHS scientists generated mice completely deficient in the zinc finger protein 36, C3H type-like 2 (Zfp36l2). The knock-out (KO) mice died within two weeks and showed very low levels of all types of blood cells, the hematopoietic cells.

The authors found that the definitive multi-lineage and lineage-committed hematopoietic progenitors that occur in the yolk sac of developing embryos from day 11.5 and in fetal liver from day 14.5 were significantly decreased in KO mice compared to wild type. The results indicated that Zfp36l2 played a critical role in the development of the hematopoietic system.

Zfp36l2 is a member of a family of proteins containing zinc fingers — protein domains that bind a zinc ion which help stabilize protein folds. Many zinc finger protein families exist in the mammalian genome and their members can bind to DNA, RNA, other proteins and lipids and are involved in many different cellular processes.

Another member of the ZFP36 family, tristetraprolin, is able to destabilize certain messenger RNAs (mRNAs) by binding to adenine-uridine-rich elements located in the 3' untranslated region. Destabilizing the mRNA coding for a protein prevents the protein from being made, a form of post-transcriptional regulation. The authors suggest that Zfp36l2 may also regulate mRNA encoding proteins critical to hematopoiesis in a similar way.

Citation: Stumpo DJ, Broxmeyer HE, Ward T, Cooper S, Hangoc G, Chung YJ, Shelley WC, Richfield EK, Ray MK, Yoder MC, Aplan PD, Blackshear PJ. 2009. Targeted disruption of Zfp3612, encoding a CCCH tandem zinc finger RNA-binding protein, results in defective hematopoiesis. Blood 114(12):2401-2410.

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Alternative Mouse Model for Asthma Reveals Novel Pathways

To understand some of the physiological factors initiating allergic asthma, researchers from NIEHS and the Children's Hospital of Pittsburgh compared two models of allergic sensitization in mice. They found that allergic sensitization through the airway, using ovalbumin (OVA) as an allergen, together with low-dose lipopolysaccharide (LPS) as an adjuvant, induced a very different immune response than the traditional mouse model of asthma, which relies on intraperitoneal injections of OVA together with the adjuvant, aluminum hydroxide.

Following these two types of sensitization, both groups of mice were challenged with aerosolized OVA. Although mucus production in the lung was similar in both groups, airway levels of eosinophils and T helper (Th)2 cell cytokines were significantly higher in mice sensitized through the peritoneum. However, these mice had low levels of airway neutrophils and did not develop allergen-induced airway hyperreactivity (AHR).

In contrast, mice sensitized through the airway displayed only modest Th2 responses, but had high levels of neutrophils and Th17 cells in the lung, and exhibited robust AHR. The pro-inflammatory Th17 cells released the cytokine IL-17 into the airway, which in turn led to neutrophil recruitment and AHR. Neutrophils, which are white blood cells associated with inflammation, are also increased in lungs of humans with severe asthma.

The findings in this paper suggest that Th17 and Th2 responses act synergistically to promote airway neutrophilia and AHR. Blocking neutrophil recruitment to the lung prevented AHR in the mice, suggesting that a similar approach might also be an effective therapy in humans.

Citation: Wilson RH, Whitehead GS, Nakano H, Free ME, Kolls JK, Cook DN. 2009. Allergic sensitization through the airway primes Th17-dependent neutrophila and airway hyperresponsiveness. Am J Respir Crit Care Med 180(8):720-730.

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Calcium Sensing Protein is Specialized for Digital Signaling

Many cells utilize calcium as an important second messenger. Physiological receptor activation induces repetitive intracellular calcium release events, called calcium oscillations, a regenerative process that involves the release of calcium from the endoplasmic reticulum (ER).

Researchers at NIEHS demonstrate how these "digital" calcium release events are sufficient to cause two transmembrane ER proteins, STIM1 and STIM2, to aggregate and migrate toward the plasma membrane. The proximity of these STIM proteins to the plasma membrane is crucial for the activation of store-operated calcium entry (SOCE), a calcium entry process dependent on calcium channels made up of the Orai proteins. Importantly, a sustained oscillatory calcium response is dependent on SOCE to replenish ER calcium stores.

The group combined intracellular calcium measurements, using fluorescent calcium indicators, with total internal reflection fluorescence microscopy (TIRFM) to simultaneously monitor agonist-induced oscillatory calcium responses and the movement of STIM proteins, respectively. The researchers reported that STIM1, not STIM2, was necessary for activating SOCE and sustaining intracellular calcium oscillations.

The study also provides remarkable evidence that during calcium oscillations, the movement of STIM1 proteins is coordinated with transient calcium release events. By this manner, the transient drops in ER calcium stores are digitally encoded by STIM1 and may activate SOCE with a similar time course. Thus, under physiological conditions, this arrangement provides a clearly defined and unambiguous signaling system, translating a digital calcium release signal into calcium influx that can signal to downstream effectors.

Citation: Bird GS, Hwang SY, Smyth JT, Fukushima M, Boyles RR, Putney JW Jr. 2009. STIM1 is a calcium sensor specialized for digital signaling. Curr Biol 19(20:1724-1729.

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Polymerase Stalling Controls Inflammatory Gene Expression

RNA Polymerase II stalling ensures a timely and coordinated activation of proinflammatory gene expression in immune cells. Using immune cells from both mice and *Drosophila*, researchers from NIEHS and Weil Medical College of Cornell University studied the kinetics of cytokine gene regulation in response to microbial stimulus. They determined that the key difference between rapid responding genes and slower activated genes is the step in the transcription cycle at which they are regulated.

Karen Adelman, Ph.D., lead author on the study and principal investigator in the Laboratory of Molecular Carcinogenesis, showed that in quickly activated genes, such as TNF alpha, RNA Polymerase II initiates transcription, but stalls near the promoter region, held back by the negative elongation factor (NELF). Upon macrophage stimulation, NELF is shed from the polymerase complex and the polymerase is released into the gene, thus promoting rapid synthesis of cytokine gene products. In contrast, both polymerase and NELF are absent in promoter regions of slow response genes such as IP-10. The investigators determined that recruitment of polymerase is the rate-limiting factor for transcription of these genes.

Adelman's group used chromatin immunoprecipitation (ChIP) and permanganate probing to establish the molecular mechanisms involved in polymerase stalling. The group concluded that there is a high degree of evolutionary conservation of the transcriptional regulatory mechanisms governing inflammatory gene expression from *Drosophila* to mammals.

Citation: Adelman K, Kennedy MA, Nechaev S, Gilchrist DA, Muse GW, Chinenov Y, Rogatsky I. 2009. Immediate mediators of the inflammatory response are poised for gene activation through RNA polymerase II stalling. Proc Natl Acad Sci USA 106(43):18207-18212.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*. Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction.)

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Inside the Institute

Tvermoes Excels in Ford Ironman World Championship

By Laura Hall

On October 10, Brooke Tvermoes, Ph.D., a postdoctoral fellow in the Comparative Genomics Group, finished fifth in her age class in the Ford Ironman World Championship in Kailua-Kona, Hawaii. The grueling non-stop triathlon consisted of a 2.4 mile swim in the Kailua Bay, a 112 mile bike ride across the Hawaiian lava desert, followed by a 26 mile 385 yard run along the coast of the Big Island. Tvermoes finished the race in 10:30:43.

Brooke Tvermoes posed with her husband, Nicolai Tvermoes, after the race. "I was essentially fifth in my age group in the world. Sometimes I have to pinch myself to make sure it's real," she said. (Photo courtesy of Brooke Tvermoes)

Even though she had trained all year in all sorts of weather conditions, the race was held on a day that tested her endurance. It was the hottest, most humid day they'd had in Hawaii on race day in 15 years, but Tvermoes was glad she participated. "It was amazing to be racing with the best Ironman athletes in the world. I was on the same course with the pros that we read about and watch on TV, and here they are just a few feet from me," Tvermoes said.

This triathlon is considered the most prestigious in the world. Tens of thousands compete for 1800 spots. Anyone who finishes the race in 17 hours has won the right to be called "Ironman." Tvermoes qualified for her spot in the race by winning her age group in the Ford Ironman Arizona race in November 2008, with a course record time of 10:05. She was the second amateur female to finish.

Tvermoes plans to continue to compete in Ironman triathlons because of the sense of accomplishment it brings her. When she crosses the finish line, she declares, "It's all worth it — all of it, all the hours of training, all the sacrifices you make to be there. The feeling is unbelievable." Tvermoes has advice for anyone interested in competing in triathlons — "You can do it. Start slowly and work into it." She also explained that being able to cope and adjust is important in triathlon competition. She maintained, "It's such a long day, something is bound to go wrong, and it's how you deal with those situations that makes or breaks your day."

Tvermoes excels in her work, as well as her sport. She won "Best Poster Presentation in Environmental Toxicology" on Science Awards Day on November 5.

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

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North Carolina Central Students Get Short Course on Toxicology Testing

By John Peterson

On November 19, a group of students from the Biology and Cancer Research Program at North Carolina Central University (NCCU) visited the NIEHS to attend a public meeting of the National Toxicology Program's (NTP) Board of Scientific Counselors Technical Reports Review Subcommittee. The visit — organized by William Stokes, D.V.M., director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and Special Assistant Debbie McCarley of NICEATM — allowed the group to get a first-hand look at the peer review of two widely-used chemicals.

Stokes invited NCCU Assistant Professor Antonio Baines, Ph.D., and eight graduate students in his toxicology course to attend the discussion of rodent bioassay studies conducted on ginseng and 1-bromopropane. The peer review is a critical step toward finalizing technical reports used by regulatory authorities worldwide for developing risk assessments and regulations for "safe" levels of chemicals in the environment.

Following the Board of Scientific Counselors meeting, Public Affairs Specialist John Peterson accompanied the students on a tour of two NIEHS laboratories. Kevin Gerrish, Ph.D., technical laboratory manager for the NIEHS Microarray Core, introduced the students to three commercially available microarray platforms that allow the investigators to explore the effects of environmental agents on gene expression and the regulatory mechanisms that influence gene expression. According to Gerrish, these platforms provide coverage for every model species used by NIEHS investigators in their research programs. "Research using microarrays generates vast quantities of data that require specialized software for higher-level analyses," said Gerrish.

The students were then escorted across the hall for an overview of the necropsy and histology laboratories. They examined whole-tissue samples taken from mouse heart, kidney, eyes, and brain, and viewed color diagrams that highlighted the sampling and trimming guidelines for tissue preparation. Biologist Natasha Clayton provided the students with a demonstration of sample preparation, processing and embedding, followed by a presentation of special staining techniques.

The visit concluded with lunch with NTP staff, including Raj Chhabra, Ph.D., D.A.B.T., and three NTP postdoctoral fellows. Baines indicated that the visit was highly informative and that he would like to continue to provide this educational opportunity to future NCCU graduate students.

(John Peterson is a public affairs specialist in the NIEHS Office of Communications and Public Liaison and a contributor to the *Environmental Factor*.)

The tour group enjoys the scenery at NIEHS. Shown, left to right, are John Peterson, NIEHS; Stephanie Farmer and Seema Chettri, NCCU; Debbie McCarley, NTP, NIEHS; Patience Hall, Samora Rugumamu, LaShaya Smith, Balagopal Nair and Antonio Baines, Ph.D., NCCU; William Stokes, D.V.M., NTP, NIEHS. (Photo courtesy of William Stokes)

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