

October/November 2013

## NIEHS Spotlight



### [Council has a busy two days](#)

NIEHS and NTP Director Linda Birnbaum, Ph.D., welcomed members to the 140th meeting of the National Advisory Environmental Health Sciences Council Sept. 10-11.



### [Capitol Hill events put spotlight on environmental connections to cancer](#)

NIEHS and NTP Director Linda Birnbaum, Ph.D., made presentations at two events about environmental factors and women's cancers Sept. 19 on Capitol Hill.



### [NIEHS collaborates with World Health Organization to address global environmental health issues](#)

The Institute reached an important milestone when the World Health Organization (WHO) designated it as a Collaborating Centre for Environmental Health Sciences.



### [NIEHS scientists, grantees participate at environment and health conference](#)

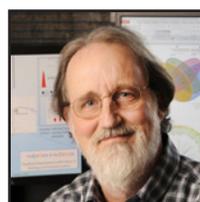
NIEHS scientists and other environmental health researchers from around the world gathered Aug. 19-23 in Basel, Switzerland, to discuss cutting-edge research.

## Science Notebook



### [Council science talk focuses on asthma](#)

In an address to council, Donald Cook, Ph.D., head of the NIEHS Immunogenetics Group, discussed the molecular links his team found between house dust and asthma.



### [Study links tanning gene to increased risk of testicular cancer](#)

Nearly 80 percent of white men carry a variant form of this gene, according to new work from scientists at NIEHS and Oxford University.



### [NIEHS holds high throughput toxicogenomics platforms workshop](#)

Leaders in the field of toxicogenomics met at NIEHS Sept. 16-17 to discuss the best methods for prioritizing approximately 1,000 genes for use in high-throughput platforms.



### [Scientists document arsenic spread to previously unpolluted aquifer in Vietnam](#)

Superfund researchers from Columbia University report clear evidence that human activity can increase the extent of naturally occurring arsenic in water.

## NIEHS Spotlight



### [Balbus briefs Congress on climate change and public health](#)

NIEHS Senior Advisor for Public Health John Balbus, M.D., participated in a briefing session Sept. 12 for Rep. Lois Capps, D-Calif., and her staff.



### [Miller delivers keynote at international conference on occupational health](#)

NIEHS Senior Medical Advisor Aubrey Miller, M.D., gave the keynote presentation Sept. 12 at the 17th National Congress of Occupational Health in Mexico City.



### [Bucher keynotes at meeting of hazardous waste specialists](#)

NTP Associated Director John Bucher, Ph.D., took the mission of NIEHS and NTP to the grass roots Sept. 25, with his keynote address at a meeting in St. Paul, Minn.



### [Advisors learn about the reinvention of ICCVAM](#)

Members of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) presented a new vision Sept. 14 to their external advisors.



### [Rutgers holds high school summer program](#)

Thanks, in part, to NIEHS funding, 46 high school students gained new insights into laboratory techniques and real-world applications of toxicology this summer.

## Science Notebook



### [Reducing lead contamination in urban soils](#)

SRP Program Administrator Heather Henry, Ph.D., organized a session on lead at the American Chemical Society (ACS) Meeting Sept. 8-12 in Indianapolis, Ind.



### [Bishop honored by Environmental Mutagenesis and Genomics Society](#)

Former NTP geneticist Jack Bishop, Ph.D., received the 2013 Alexander Hollaender Award Sep. 24 at the society's annual meeting in Monterey, Calif.



### [NIEHS celebrates National Postdoc Appreciation Week](#)

To say thank you, NIEHS celebrated its postdoctoral fellows Sept. 20 with a day full of events, including a general assembly meeting, a trivia contest, and a picnic.



National Institute of  
Environmental  
Health Sciences

### [Annual LSB retreat caps another successful year](#)

The NIEHS Laboratory of Structural Biology held its annual retreat on Sept. 12-13 at the Botanical Gardens of the University of North Carolina at Chapel Hill.



### [Superfund research grantee honored by American Chemical Society](#)

Barry Dellinger, Ph.D., will receive the 2014 American Chemical Society (ACS) Award for Creative Advances in Environmental Science and Technology.

## NIEHS Spotlight



### [Public health group announces launch of Canadian Environmental Health Atlas](#)

Simon Fraser University-based project coordinator Joanne Telfer announced Sept. 13 the official launch of the Canadian Environmental Health Atlas.



### [PEPH webinar highlights tribal efforts to address environmental justice and public health](#)

The NIEHS Partnerships for Environmental Public Health (PEPH) webinar Aug. 21 offered important insights into the tribal perspective on important topics.



### [NIEHS hosts local middle school students](#) ▶ Video

Eighteen Lowes Grove Middle School students visited NIEHS Sept. 30 to begin learning about cell biology as part of the newest Citizen Schools education outreach effort.



### [SRP grantees gather in Baton Rouge for annual meeting](#)

Hosted by Louisiana State University, the meeting featured discussion about new research, technology, communication, and community, as well as trainee awards.



### [NIEHS welcomes new chief information officer](#)

As the person in charge of information technology at NIEHS, Chief Information Officer Bernard Brown will play a vital role in advancing the Institute's mission.

## Science Notebook



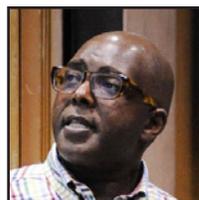
### [Former NIEHS postdoctoral fellows obtain NIH funding](#)

Archana Dhasarathy, Ph.D., and Sergei Nechaev, Ph.D., received an NIH grant to study the epigenetics of development and disease at the University of North Dakota.



### [New insight into how neonatal exposure to DES affects uterus function in mice](#)

A new study finds that mice exposed briefly to the synthetic estrogen immediately after birth had abnormal expression of the Six1 gene in the uterus when they became adults.



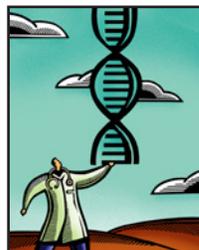
### [Penn State professor explores consequences of non-regulated mitochondrial transcription](#)

Pennsylvania State University Professor Craig Cameron, Ph.D., spoke Sept. 23 at NIEHS on "Human Mitochondrial Transcription."



### [NTP postdoc takes top prize at NCSOT meeting](#)

First-place winner in the President's Award for Research Competition was Yuanyuan (Laura) Xu, Ph.D., a fellow in the NTP Laboratories Inorganic Toxicology Group.



### [Upcoming GEMS meeting on cancer prevention and cure](#)

Research Triangle Park-based Genetics and Environmental Mutagenesis Society will hold its annual fall meeting Nov. 14 at the Sheraton Imperial Hotel in Durham.

## Inside the Institute



### [NIEHS celebrates Years of Service with 2013 honorees](#)

NIEHS and NTP Director Linda Birnbaum, Ph.D., recognized 48 Institute employees during the annual Years of Service awards ceremony held Sept. 4.

## Calendar of Upcoming Events

- **Nov. 2-6 (offsite event)**, at the Boston Convention and Exhibition Center and Westin Boston Waterfront Hotel in Massachusetts — American Public Health Association Annual Meeting and Exposition
- **Nov. 5 (offsite event)**, in Bioinformatics 1131 at the University of North Carolina at Chapel Hill, 11:00 a.m.-12:00 p.m. — Paul Wade, Ph.D., addressing “Gene Regulation by Chromatin”
- **Nov. 6-8 (offsite event)**, at NIH in Bethesda, Md. — NIH Research Festival
- **Nov. 7-8, in Rodbell Auditorium** — Nov. 7, 8:30 a.m.-4:15 p.m.; Nov. 8, 9:00 a.m.-12:00 p.m. — NIEHS Science Day presentations (Nov. 7-8) and awards (Nov. 8), culminating a week-long poster display in the Rall Building lobby and mall
- **Nov. 8 (offsite event)**, in the Levine Science Research Center, Room 247, Duke University, 12:00-1:00 p.m. — Integrated Toxicology and Environmental Health Program Fall 2013 Seminar Series, featuring Heather Patisaul, Ph.D., addressing “Brain Chemistry: Environmental Influences on Neuroendocrine Development and Behavior”
- **Nov. 13**, webinar, 1:00-2:30 p.m. — EPA/NIEHS Children’s Centers 2013 Webinar Series, <http://www.epa.gov/ncer/childrenscenters/webinar/2013/overview.html>
- **Nov 15 (offsite event)**, in the Levine Science Research Center, Room 247, Duke University, 12:00-1:00 p.m. — Integrated Toxicology and Environmental Health Program Fall 2013 Seminar Series, featuring a presentation by Sherine Chan, Ph.D., on “Environmental Toxicant Exposures, Mitochondrial Dysfunction, and Birth defects”
- **Nov. 18**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Keystone Science Lecture Series seminar on “Testing the Developmental Origins of Adult Diseases Hypothesis: The Durham Newborn Epigenetics Study,” by Cathrine Hoyo, Ph.D.
- **Nov 22 (offsite event)**, in the Levine Science Research Center, Room 247, Duke University, 12:00-1:00 p.m. — Integrated Toxicology and Environmental Health Program Fall 2013 Seminar Series, featuring a seminar on “Developmental Origins of Central Norepinephrine Neuron Diversity,” by Patricia Jensen, Ph.D.
- View More Events: [NIEHS Public Calendar](#)

## Science Notebook



### [This month in EHP](#)

The current issue of EHP, published Oct. 1, highlights the transgenerational impacts of chemical exposure and the Minamata Convention on Mercury. EHP will publish its combined November-December issue Dec. 2.

## Extramural Research

### [Extramural papers of the month](#)

- [DNA methylation in the human genome](#)
- [Genome-wide sequencing links aristolochic acid to cancer](#)
- [A better understanding of tissue growth and repair](#)
- [BPA linked with obesity in children](#)
- [Prenatal nitrate exposure and birth defects](#)
- [Mechanism for amyloid-beta accumulation in Alzheimer’s disease](#)
- [PBDE levels decrease in pregnant women after ban](#)
- [DNA methylation in children](#)

## Intramural Research

### [Intramural papers of the month](#)

- [Assessing cockroach allergen exposure via its structure](#)
- [Study finds pregnancy length varies by up to five weeks](#)
- [Role of arginine in polymerase beta-catalyzed nucleotidyl transfer reactions](#)
- [Redundancy in DNA repair mechanisms protects cells from UV-induced DNA damage](#)
- [Crystal structures reveal how flame retardants may disrupt estrogen metabolism](#)
- [Probiotics use during pregnancy may reduce diseases in children](#)
- [Dermatomyositis shares genetic background with other autoimmune diseases](#)
- [Identification of novel immune regulatory elements and epigenetic plasticity in memory lymphocytes](#)

# NIEHS Spotlight

## Council has a busy two days

By Ernie Hood

With almost all council members and *ex officio* members in attendance, NIEHS held its 140th meeting of the National Advisory Environmental Health Sciences Council Sept. 10-11. The council had a full agenda and got right to work.

NIEHS and NTP Director Linda Birnbaum, Ph.D., and Division of Extramural Research and Training (DERT) Director Gwen Collman, Ph.D., provided detailed accounts of Institute developments and accomplishments since the May council meeting. Council members also heard presentations on several topics, from a scientific talk on house dust and asthma ([see related article](#)) to progress reports on several important NIEHS initiatives.

### Budget outlook remains cloudy

Birnbaum said budget uncertainty continues to be a major issue, but predicted that the government would continue to operate under a series of continuing resolutions (CRs) beyond the end of the current fiscal year on Sept. 31.

“We are hopeful that they will not be one- or two-day or one-week CRs, but that we will end up with at least a one-month if not a two-month CR, while Congress tries to figure out how to deal with the budget,” Birnbaum said.

She noted that sequestration could continue or even expand in fiscal year 2014, which would bring challenges in fulfilling the Institute’s mission. Despite the prospect of dwindling resources, Birnbaum stressed that NIH will maintain its footing as the country’s leading medical research agency ([see text box](#)).

### Confirmation of DERT reorganization

DERT, which manages grant applications and awards for NIEHS, will be reorganized, according to



Among the many scientific advances Birnbaum shared with council, was a recent [publication on the Consortium Linking Academic and Regulatory Insights on BPA Toxicity program](#), which represents a new approach to synergizing academic and guideline-compliant research. The initiative involves several DERT and NTP scientists collaborating with colleagues at the FDA. “We are very optimistic that this is a new paradigm for how certain kinds of research questions can be addressed,” said Birnbaum. (Photo courtesy of Steve McCaw)



During her DERT Director’s Report, Collman welcomed Alfonso Latoni, Ph.D., the soon-to-be new chief of the DERT Scientific Review Branch (SRB), who will join NIEHS in November, after serving five years as deputy SRB chief at the National Institute on Aging. (Photo courtesy of Steve McCaw)

Collman. Beginning Oct. 6, DERT will have a total of eight branches — four newly organized branches, appearing first in the list below, and four existing branches:

- Genes, Environment, and Health Branch — Branch Chief Cindy Lawler, Ph.D.
- Population Health Branch — Branch Chief Claudia Thompson, Ph.D.
- Exposure, Response, and Technology Branch — Acting Branch Chief David Balshaw, Ph.D.
- Hazardous Substances Research Branch — Branch Chief, William Suk, Ph.D.
- Program Analysis Branch — Branch Chief, Christina Drew, Ph.D.
- Grants Management Branch — Branch Chief, Dorothy Duke
- Scientific Review Branch — Acting Branch Chief Patrick Mastin, Ph.D.
- Worker Education and Training Branch — Chief Joseph (Chip) Hughes

Collman also described Phase II of the DERT initiative to categorize the research grants portfolio according to how they align with the NIEHS strategic plan. The multi-project and training grants have already been completed, comprising more than 1,800 grants.

“Looking today at our portfolio helps us, in DERT, look for areas of heavy investment versus areas where perhaps there’s lighter investment, looking for gaps,”

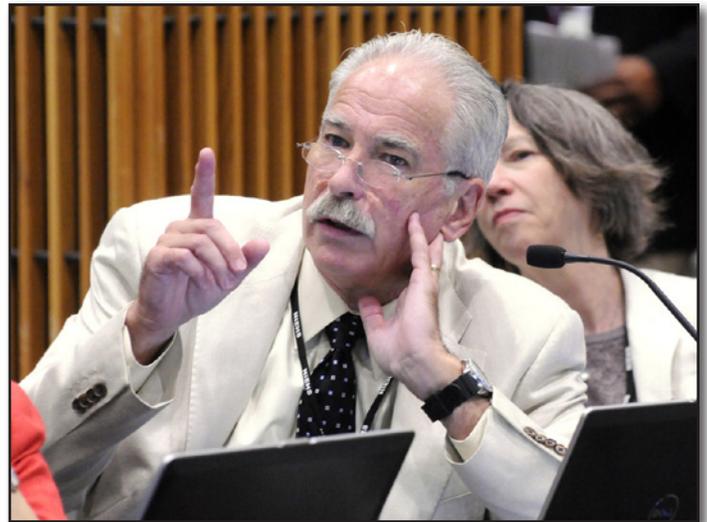
Collman said. “Using this kind of data when we’re doing program development, will help us look at initiatives in the future and how they line up with the strategic plan opportunities.”

### A plethora of updates

Former council member Grace LeMasters, Ph.D., from the University of Cincinnati College of Medicine, reported, by phone, on her participation in the [NIH Council of Councils](#), representing NIEHS. The Council of Councils advises the NIH director on matters related to policies and activities of the [Division of Program Coordination, Planning, and Strategic Initiatives](#), which plans and implements trans-NIH initiatives supported by the [Common Fund](#), and coordinates research related to AIDS, behavioral and social sciences, women’s health, disease prevention, and research infrastructure.



*Tilson contributed his ideas to the discussion on scientific data reproducibility, from the perspective of a journal editor. He has been at the helm of EHP for the past six years. (Photo courtesy of Steve McCaw)*



*Long-time council member Edward Postlethwait, Ph.D., from the University of Alabama School of Public Health, emphasized a point during council discussion. (Photo courtesy of Steve McCaw)*

The council was also updated on issues related to research reproducibility, by NTP Associate Director John Bucher, Ph.D., and Environmental Health Perspectives (EHP) Editor-in-Chief Hugh Tilson, Ph.D.; the [Centers for Children’s Environmental Health and Disease Prevention Research](#) program, by Health Scientist Administrator Kimberly Gray, Ph.D.; and the Toxicant Exposures and Responses by Genomic and Epigenomic Regulators of Transcription (TaRGET) Program, by Program Administrator Frederick Tyson, Ph.D.

On the meeting’s second day, council and NIEHS leadership conducted a mini-retreat. The discussion included whether NIEHS is getting what it needs from council, how council can engage in the implementation of the strategic plan, and council’s strategy ideas for funding the best quality science in the current fiscal reality.

The next council meeting is scheduled for Feb. 19-20, 2014.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)



*Ex officio council member Yvonne Maddox, Ph.D., shared the perspective of a sister institute during council proceedings. She is deputy director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. (Photo courtesy of Steve McCaw)*



*Council members, from left, Linda McCauley, Ph.D., R.N., of Emory University; Norbert Kaminski, Ph.D., of Michigan State University; and David Eaton, Ph.D., of the University of Washington, paid close attention to the council proceedings. (Photo courtesy of Steve McCaw)*



*Council member Howard Hu, M.D., Sc.D., of the University of Toronto, made several convincing comments during the council meeting. (Photo courtesy of Steve McCaw)*

## Impact of NIH on the nation's health and economy

During her remarks, Birnbaum mentioned a few examples of how NIH improves lives and helps drive the economy.

- Impact of medical research on Americans' health
  - Life expectancy gains worth approximately \$3.2 trillion annually.
  - Cardiovascular disease rates have fallen more than 60 percent in the past 50 years.
  - Cancer rates are falling about 1 percent per year. Each 1 percent drop saves almost \$5 billion.
  - HIV therapies enable people in their 20s with the infection to live to 70 years old and beyond.
- Impact of NIH-supported research on U.S. economy
  - In 2012, NIH funding:
    - Supported more than 402,000 jobs at 2,500 institutions and small businesses, nationwide.
    - Generated more than \$7.8 billion in new economic activity — nearly twice U.S. taxpayers' investment.
  - NIH as a foundation for the entire U.S. medical innovation sector:
    - Total employment impact of 7 million jobs
    - Exports equal \$90 billion in goods and services

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## Capitol Hill events put spotlight on environmental connections to cancer

*By Paula Whitacre*

The impact of environmental factors on cancer, especially women's cancers, received high-profile attention at two events Sept. 19 on Capitol Hill. In the afternoon, attendees took part in a roundtable discussion co-sponsored by the H. John Heinz III Center for Science, Economics and the Environment; Congressional Families Cancer Prevention Program of the Prevent Cancer Foundation; and Executive Women in Government. During the evening session, participants were treated to a panel and film presentation at the U.S. Capitol Visitor Center Orientation Theater.



*Drescher, left, listened to Birnbaum describe NIEHS funding used to study women's cancers. (Photo courtesy of April Bennett)*

NIEHS and NTP Director Linda Birnbaum, Ph.D., made presentations at both events, where she emphasized the role of environmental health research in understanding the causes of cancer.

### Cancer as the great equalizer

The roundtable, “Women’s Cancers: New Science, New Activism,” attracted a standing-room-only audience that featured actress and activist Fran Drescher, and included a number of wives of current and former legislators. Purposefully set up as a bipartisan briefing, the event co-chairs consisted of Susan Allen, Debbie Dingell, Diana Enzi, and Lisa McGovern. Allen, wife of former Governor and Republican Senator from Virginia George Allen, introduced Drescher to the audience.

After a misdiagnosis and, ultimately, successful treatment for uterine cancer 13 years ago, Drescher began to write and speak about her experience. The organization she founded, [Cancer Schmancer](#), which is also the title of her best-selling book, focuses on prevention, early detection, and policy change. Describing Cancer Schmancer’s Detox Your Home campaign, Drescher urged the audience to be mindful of toxins in, on, and around them, referring to food, personal care, and cleaning and gardening products.

Birnbaum highlighted NIEHS research on women’s cancers, including the Breast Cancer and Environment Research Program, co-funded with the National Cancer Institute; Sister Study; Fibroid Growth Study; and others. Stressing that “you can’t change your genes, but you can change your environment,” she pointed out that environmental factors may account for at least two-thirds of U.S. cancer cases.

“That’s why environmental health research is so important,” Birnbaum said. “It gives us vital information on how we could change our environment, to prevent disease and promote wellness.”

H. Kim Lyerly, M.D., a breast oncologist from the Duke University School of Medicine, discussed how environmental factors may influence not only cancer development, but also therapy.

“Laboratories around the world are making this connection,” Lyerly said. “Many forms of therapy that are preventing recurrences, and keeping you from having a metastases or expansion of a tumor, are also influenced by the same environmental signals that initiated cancer in heretofore normal cells.”

Dingell, a civic leader and wife of Rep. John Dingell, D-Mich., reminded the audience that efforts by congressional spouses on women’s health issues have borne results.

“Thirty years ago, we didn’t use the word breast, and women were not included in federally funded research,” she said. “We as [congressional] spouses have a platform that we can use to educate in our states and districts.”



*During the evening panel and film showing, Deutch, left, discussed the role of the private sector in reducing environmental hazards in consumer products. (Photo courtesy of Paula Whitacre)*

A screenshot of a video player interface. On the left is a logo for "Cancer Schmancer Movement" featuring a yellow circular graphic with a play button icon. To the right of the logo, the text reads "Linked video:" followed by a blue hyperlink: "Watch Drescher talk about Cancer Schmancer, and its goal of saving lives through prevention and early detection of cancer (04:38)". Below the video player area, there is a "Download Media Player" button with a red "Flash" icon and a small external link icon. At the bottom right of the video player area, it says "(Launches in new window)".

## The power of the marketplace

Later in the day, Birnbaum joined Rep. Ted Deutch, D-Fla., on a panel, followed by a screening of “Unacceptable Levels,” a documentary on the presence of environmental hazards in everyday life.

Deutch described legislation that he seeks to introduce in Congress, to establish a program that uses market forces to push known carcinogens out of household products. Drescher voiced support for what she called Deutch’s non-regulatory, revenue-earning, bipartisan initiative.

During this session, Birnbaum focused on NIEHS research on cancer, and talked about research related to lung cancer, asbestos, and pesticides. She explained why NIEHS has prioritized support for research into combined exposures.

She concluded by saying, “The choices we make regarding the foods we eat, exercise, and the chemicals we are exposed to, will make a difference in our wellness. We need to take ownership of those choices and make the necessary changes to have healthier lives.”



*Before the briefing, event hosts, co-sponsors, and presenters gathered for a photo in the Dirksen Senate Office Building. From left, are Lindi Harvey, director of the Heinz Center Bipartisan Initiative for the Prevention of Breast Cancer; Lisa McGovern, executive director of the Congressional Families Cancer Prevention Program; Conn Nugent, president of the Heinz Center; Birnbaum; Dingell; Drescher; Allen; Shoshana Grove, president of Executive Women in Government; Reta Jo Lewis, past president of Executive Women in Government; and Lyerly. (Photo courtesy of Heinz Center)*

(Paula Whitacre is a contract writer with the NIEHS office in Bethesda, Md.)

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# NIEHS collaborates with World Health Organization to address global environmental health issues

By Sheila Yong

NIEHS reached a significant milestone in its quest to improve global environmental health, when it was designated in September as a World Health Organization (WHO) Collaborating Centre for Environmental Health Sciences. John Balbus, M.D., NIEHS senior advisor for public health, will head the new center.

“This designation is important for NIEHS, because it enhances the Institute’s ability to develop effective partnerships and also provide leadership on global environmental health issues,” Balbus said. “Building on decades of collaboration with the World Health Organization, the Collaborating Centre will provide a focal point and resource for the Institute in fulfilling its strategic goals in global environmental health.”

## A partnership for environmental health

The most recent designation as a Collaborating Centre comes after three productive decades of partnership with WHO. The partnership began with a memorandum of understanding, and culminated in the first cooperative agreement in the early 1980’s, an effort overseen by William Suk, Ph.D.

This agreement, [commemorated](#) in recent highlights produced by WHO, played an important role in the development of WHO’s International Programme on Chemical Safety. It led to the publication of many Environmental Health Criteria documents on chemical hazards, the promotion of children’s environmental health as a global environmental health research priority ([see story](#)), and numerous other scientific workshops and capacity building initiatives. It also led to recent collaborations with WHO and the Pan American Health Organization (PAHO), such as the hosting of the 2011 PAHO biennial meeting of regional environmental health Collaborating Centres ([see story](#)).

The creation of the Collaborating Centre would not have been possible without the commitment and dedication of the NIEHS Global Environmental Health Working Group and Steering Committee, which includes staff from divisions and offices across the Institute with interest and expertise in global environmental health issues.

## Striving for a healthier global environment

Under the new designation, NIEHS will assist WHO in promoting international cooperation among environmental health research institutes around the world; promoting global awareness of emerging issues in environmental health, such as children’s environmental health, the developmental origins of health and disease (DOHaD), health implications of climate change, and household air pollution; and preparation of training materials, and support of education and training efforts in environmental and occupational health sciences.

The Collaborating Centre will kick off its activities with a satellite event, facilitating a network of WHO Collaborating Centres for Children’s Environmental Health, at the Pacific Basin Consortium for Environment



*Balbus will direct the activities of the new WHO Collaborating Centre for Environmental Health Sciences. (Photo courtesy of Steve McCaw)*

and Health; a satellite event on environmental exposures at the upcoming DOHaD annual conference; and a monthly webinar series on global environmental health in partnership with PAHO.

NIEHS and NTP Director Linda Birnbaum, Ph.D., believes the creation of the new Collaborating Centre comes at the right time.

“Modern health advances have led to longer life spans and a better standard of living, but environmental pollution threatens to take away those gains. NIEHS science is demonstrating the harm that comes from exposures to chemicals like endocrine disruptors and other developmental toxins, and how early life exposures to these can contribute to adult chronic diseases,” said Birnbaum. “We are also building our understanding of how climate change affects human health. By joining forces, NIEHS and WHO will ensure issues involving environmental health will stay in the forefront and help translate research findings into effective public health interventions to improve health around the world.”

(Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)

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## **NIEHS scientists, grantees participate at environment and health conference**

*By Joe Balintfy*

Environmental health researchers from around the world gathered in Basel, Switzerland, Aug. 19-23 to discuss cutting-edge research on topics including air pollution, endocrine disrupting chemicals, and childhood obesity.

The conference, Environment and Health – Bridging South, North, East and West, was a joint meeting of three societies — the International Society for Environmental Epidemiology, the International Society of Exposure Science, and the International Society of Indoor Air Quality and Climate — which resulted in more than 2,000 scientific contributions in nearly 140 sessions and symposia.

Grantees were quite prominent at this meeting, said Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training (DERT). There were also a number of Institute staff and scientists who gave talks, including Collman.

“This year, there were a few areas of emphasis that I think reflect how the science is changing, and how topics NIEHS has been pursuing, in terms of program development, are coming to fruition through discussion at this meeting.”



*“We always have a very strong presence in the area of children’s environmental health at the meeting,” said Collman. (Photo courtesy of Steve McCaw)*

## **Grappling with the concept of the exposome**

A pre-session workshop, and a symposium chaired by DERT Program Administrator David Balshaw, Ph.D., and Tuomo Karjalainen, D.M.D., Ph.D., European Commission Directorate-General for Research and Innovation, covered the exposome. The exposome is the measure of all the exposures of an individual in a lifetime and how those exposures relate to health.

The first session of the symposium, “International Efforts to Implement the Exposome,” was led by Collman, who gave an overview of the exposome concept and outlined several challenges in seeing it become a reality. The other speakers, experts from the U.S. and European Union, presented initial efforts to characterize the exposome.

Collman said, in regard to the exposome and measuring multiple chemical exposures, this was the first time, in a long time, she had heard people talking about both the challenges and the research data that comes from looking at multiple substances.

“That was very exciting, to see how investigators, who have access to very large scale epidemiologic studies and data that we have invested in collecting, are now using those datasets to measure multiple exposures and analyzing it all together, as opposed to just looking at one factor at a time,” Collman added.

## **Green topics and a green meeting**

NIEHS staff also chaired or led sessions on engineered nanomaterials, endocrine disrupting chemical studies, and childhood obesity and links to the environment.

“We always have a very strong presence in the area of children’s environmental health at the meeting,” said Collman. “There were four exciting presentations from those groups, and a lot of really good discussion in a standing-room-only room, which I think indicates that obesity is a major health outcome that environmental epidemiologists are now trying to get in the mix, to try to understand the causes of obesity.”

More than 1,700 people attended the conference and there were more than 1,200 posters presented. The conference also had the goal of being green and sustainable, with only regional and organic vegetarian food served. Collman noted that the meeting was a great place to learn what’s happening on the cutting edge.

“Organizers have done a really good job of keeping up with evolving issues in environmental health sciences, and really engaging those folks who are involved in epidemiologic research and exposure assessment to present and debate the new methods and new findings,” Collman said.

Next year’s conference is scheduled for Aug. 24-28 in Seattle.

(Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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*Balshaw is a program administrator in the DERT. (Photo courtesy of Steve McCaw)*

## Balbus briefs Congress on climate change and public health

*By Ernie Hood*

NIEHS Senior Advisor for Public Health John Balbus, M.D., participated in a briefing session Sept. 12 for Congressional staff, organized by Rep. Lois Capps, D-Calif. His talk, “Public Health in a Changing Climate: How Does Climate Change Impact Public Health Today, and What Can Be Done to Address It?” provided an overview of the links between climate change impacts and public health.

Capps provided opening remarks and an update on the status of the Climate Change Health Protection and Promotion Act (H.R. 2023), a bill she introduced early in 2013. There were several other speakers at the briefing whose talks touched on critical aspects of the bill.

In his presentation, Balbus summarized key health messages from the current draft of the National Climate Assessment, and noted the health sector components of the president’s Climate Action Plan.

“Current research findings show that climate change affects health in many different ways, some of which, like changes in pollen seasons, are having an impact now,” he told the panel. “Research also shows that reducing the use of fossil fuels lessens harmful exposures to air pollution and provides immediate benefits to our health.”



*“Climate change is not just an environmental issue,” Balbus emphasized to the congressional staffers. “It is clearly a public health issue.”  
(Photo courtesy of Steve McCaw)*

Balbus, who is the NIEHS lead for climate change and global health initiatives, was joined by speakers from other organizations, including the American Lung Association, the National Association of County and City Health Officials, and the American Academy of Pediatrics Council on Environmental Health.

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison.)

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## Miller delivers keynote at international conference on occupational health

*By Pamela Kidron*

NIEHS Senior Medical Advisor [Aubrey Miller, M.D.](#), gave the keynote presentation Sept. 12 at the 17th National Congress of Occupational Health in Mexico City. As a medical epidemiologist and a captain in the U.S. Public Health Service, Miller understands the importance of transdisciplinary collaboration when disasters strike.

“Disasters and emerging health threats are intensifying the need for occupational and environmental health professionals to work together,” Miller said. “Both areas of expertise are critical to understanding the aftereffects.”

## Environmental and occupational health crossovers

According to Miller, the 2010 Gulf oil spill is a perfect example of occupational and environmental experts working together. These specialists joined forces to form the Deep Water Horizon Research Consortia, a trans-NIH effort with university and community partners, to assess both the health of Gulf Coast residents and thousands of workers involved in the cleanup, as part of the [GuLF STUDY](#).

Disasters also have taught researchers that crossovers between occupational and environmental health are inevitable, Miller said. He recalled the 1990s asbestos situation in Libby, Mont., in which exposure to asbestos endangered the mining workers, and resulted in widespread contamination and disease in the community, as well as the distribution of contaminated vermiculite insulation from the mine into millions of homes across the United States.

## Testing chemicals with high-throughput technology

Miller mentioned that high-throughput screening (HTS) is one of the newest advances in environmental health. HTS is a new way to evaluate chemicals, aided by robotics and computers, to help determine potential toxicity and possible health effects. Currently, there are 80,000 chemicals in food and other products, with 1,500 new chemicals released every year. Yet, there is no toxicological or safety information for most of them.

Advances in HTS may soon allow researchers to become less dependent on slow, costly, and tedious methods, such as human and animal studies, in the effort to better understand the risks associated with new and existing chemicals in the workplace and environment.

## New advances in epigenetics

Miller also discussed the conceptual shift in the environmental health sciences in recent studies. The old dogma stated that chemicals act by overwhelming the body's defenses by brute force at very high doses. But, new advances in epigenetics demonstrate that even low exposures to chemicals can cause disease, and that susceptibility to disease can persist long after exposure.

This new doctrine says that chemicals can act like hormones and drugs to disrupt, even at low doses, the control of body functions and development. It is especially true of chemicals that are endocrine disruptors, which interfere with hormone action. Small amounts of hormones may have profound effects on developmental processes and normal health. There is growing evidence that some prenatal and early-life exposure can disrupt the endocrine system, leading to changes in development or risk for diseases in adulthood.

For example, there is concern that exposure to the chemical bisphenol A can result in changes during critical periods of development, and may even increase the risk for obesity later in life. Also, most cases of asthma now are thought to originate in early life, during gestation and early childhood, through exposure to contaminants in the environment, such as tobacco smoke, dust mites, and traffic-related pollutants.



*Miller is the NIEHS liaison to the U.S. Department of Health and Human Services, coordinating disaster response with sister agencies. "More and more, there is a growing need for occupational and environmental health expertise to conquer the disciplinary divides, and to join forces to perform needed research and advance the understanding of exposures, risks, and diseases related to toxic substances," he said. (Photo courtesy of Steve McCaw)*

## Environmental exposure in Mexico

Miller also discussed ongoing environmental research now being conducted in Mexico and Latin America. Currently, NIEHS researchers and collaborators are looking at the relationship between childhood asthma and air pollution in Mexico City, which has one of the highest ozone levels in North America. Also, in another study, early exposure to arsenic in drinking water has been linked to later development of COPD and lung cancer in Chile.

Additionally, several cases of malignant mesothelioma have been associated with erionite-rich areas in the Mexican state of Jalisco. Exposure to erionite, an asbestos-like mineral fiber, has previously been linked to very high rates of mesothelioma in Turkey, and was recently found along roads made from erionite-contaminated gravel in Dunn County, N.D.

(Pamela Kidron is a contract writer with the NIEHS office in Bethesda, Md.)

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## Bucher keynotes at meeting of hazardous waste specialists

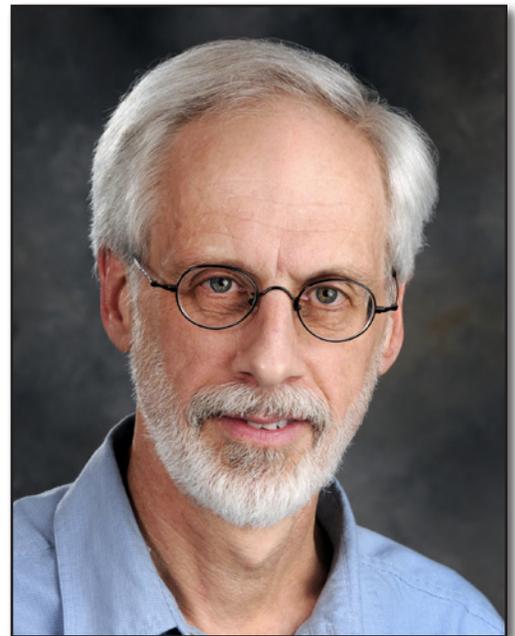
*By Eddy Ball*

NTP Associate Director John Bucher, Ph.D., took the mission of NIEHS and NTP to the grass roots Sept. 25, with his keynote address at a meeting in St. Paul, Minn., outlining “Current Issues and New Approaches in Environmental Health Research at NIEHS and NTP.”

Bucher spoke to members of the North American Hazardous Materials Management Association (NAHMMA), during the group’s [2013 annual conference](#), organized around the theme “Upstream Stewardship, Downstream Sustainability.”

As NAHMMA vice president and meeting organizer Jennifer Volkman explained in her invitation to Bucher, “Most of the attendees have a connection to household hazardous waste. They collect it and they educate consumers on alternatives, safe use, storage, and disposal of household products.” According to Volkman, NAHMMA members strive to provide the public with meaningful messages about hazardous household waste management, grounded in the best research available on environmental and health issues.

As a senior leader of the interagency group coordinating toxicological testing programs within the U.S. Department of Health and Human Services, Bucher is well-positioned to help NAHMMA members better understand how the research performed and coordinated by NIEHS and NTP relates to issues people may face on a daily basis in their own homes. For many of the attendees, Bucher’s talk was their first introduction to NIEHS and NTP and their roles in promoting public health.



*Bucher leads a staff of highly qualified toxicologists and pathologists, and oversees studies conducted by contractors and in-house researchers. He is a Diplomate of the American Board of Toxicology, one of the top credentials in the field. (Photo courtesy of Steve McCaw)*

## Showcasing the role of toxicology testing and research in public health

Following his overview of the mission and vision of NIEHS and NTP, Bucher moved into a discussion of key current concepts in environmental health science research. These topics included the Institute's emphases on the interactions of genes and the environment, the presumed involvement of epigenetic modifications in many environmentally associated diseases and dysfunctions, low-dose effects of some environmental exposures, and the developmental origins of disease.

Bucher pointed out that the prevalence of many diseases has increased much more quickly than would be predicted, based on evolutionary changes in DNA sequence. He then outlined possible ways epigenetic regulation of gene expression could be influenced by environmental exposures, as well as some of the tools to study these processes under development at NIEHS. Bucher discussed the findings from the 2011 workshop on "Environmental Chemicals in the Development of Diabetes and Obesity," sponsored by the NIEHS Office of Health Assessment and Translation, as examples of emerging areas of study. He also highlighted the extensive Institute-sponsored studies on understanding the potential human health effects of exposures to bisphenol A, a chemical that plays into many of the Institute's focus areas.

While NTP is probably best known for its gold-standard rodent assays and the rigorous methodology of its literature analysis programs, it has also established extensive interagency and cross-divisional collaborations. As an example, Bucher pointed to the current NTP polycyclic aromatic hydrocarbon (PAH) research program, as a subset of the Institute's larger extramural-funded research on PAH exposures and children's health, as well as the GuLF STUDY of health effects associated with oil spill clean-up.

Bucher emphasized the broad range of NTP Good Laboratory Practices-compliant research and testing programs — from complex occupational exposures, and food and drinking water contaminants, to nanoscale materials, persistent environmental contaminants, and radiofrequency radiation. He touched on activities, such as the Tox21 high throughput screening program, and the use of the diversity outbred mouse, as examples of how NTP is working to provide new and useful information in a more timely manner.

Bucher concluded his talk with a slide on "A New Vision for NIEHS and NTP," which includes increased emphasis on partnering with sister research agencies and regulatory bodies, improved integration across research disciplines, and utilization of the best individual and team science to address complex diseases and complex environmental impacts.



### North American Hazardous Materials Management Association

*NAHMMA has 10 regional chapters, more than 400 members, and hosts an annual conference. The association conducts specialized training for hazardous materials managers and technicians at its annual conference and through its regional chapters.*

#### By the numbers — substances studied by NTP

• Distinct test articles	2,553
• Chronic rodent bioassays	616
• Genetically modified mice-cancer	13
• Genetic toxicity	2,236
• Immunotoxicity	112
• Reproductive/developmental	242
• General and other toxicity	838
• Tox21 high throughput screening	8,307
TOTAL	14,917

As Bucher told the audience at the end of his talk, “We are working to improve our translation and communication of basic science findings into human health protection.” This theme dominated a lengthy discussion period following his talk, as NAHMMA members are involved, daily, in deciding what are hazardous materials, how best to handle and dispose of them, and how to communicate this information to the public.

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## Advisors learn about the reinvention of ICCVAM

By Robin Mackar

Over the past nine months, representatives from 15 federal agencies have been working together to reinvent how they do business. Members of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) presented Sept. 24 a new vision and direction to their external advisors, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM).

“We praise Dr. Birnbaum for stepping up to the plate and changing the way the committee will operate,” said SACATM member Ricardo Ochoa, D.V.M., Ph.D., president of Pre-Clinical Safety Inc. Ochoa was referring to an [editorial](#) written earlier this year by NIEHS and NTP Director Linda Birnbaum, Ph.D., in which she called for a reinvention of ICCVAM.

In her editorial and during opening remarks at the public meeting, Birnbaum called for the ICCVAM agencies to take a more active role in setting the priorities of the committee.

“Rather than the NIEHS directing the activities of ICCVAM . . . , the interagency agenda will now be driven by the partner regulatory agencies — the agencies that will ultimately implement the ICCVAM-recommended methods,” said Birnbaum.

ICCVAM was established by [Congress in 2000](#), to reduce, replace, or refine the use of animals in toxicity testing.

### ICCVAM priority areas

Anna Lowit, Ph.D., from the U.S. Environmental Protection Agency (EPA), interim co-chair of ICCVAM, presented an overview of the committee’s



Casey discussed the need to take advantage of ongoing activities in the U.S. and internationally that are working on the development of alternative tests. (Photo courtesy of Steve McCaw)



Tice, far left, joined Christine Kelley, Ph.D., center; the NIH ICCVAM representative, and Pertti (Bert) Hakkinen, Ph.D., from the National Library of Medicine, at the SACATM meeting. Tice will now serve as the NIEHS principal representative to ICCVAM. (Photo courtesy of Steve McCaw)

draft “[A New Vision and Direction for ICCVAM](#),” which includes setting immediate priorities, improving communications with stakeholders and the public, and exploring new paradigms to validate and use alternative toxicological methods.

Lowit identified several projects that ICCVAM believes can be successful in the short term. These areas include biologics, or non-animal methods, for testing vaccines that protect pets and livestock against the disease leptospirosis; acute oral testing to identify substances that could be poisonous when ingested or absorbed through the skin; and skin sensitization, or testing, to identify substances that could cause allergic contact dermatitis.

SACATM members agreed with the priority areas, although some members, like Daniel Wilson Ph.D., from Dow Chemical Company, told the group to not forgo some of the other areas they were pursuing, such as skin and eye irritation methods.

### Separation of powers

NTP Interagency Center for the Evaluation of Alternative Toxicological Methods ([NICEATM](#)) acting director Warren Casey, Ph.D., led the discussion on what role NICEATM will play in ICCVAM with a dramatic, but encouraging, analogy. Referring to the spacecraft Voyager, he made the point that working on alternative test methods is like the challenge put forth in the 1960s to put a man on the moon.

“Replacing animals is our challenge, but it is possible,” Casey said. “We just need to work together and take advantage of the advances being made in science and technology.”

Casey noted that NICEATM will continue to provide administrative and scientific support for ICCVAM, but there will be more of a separation of powers, to ensure ICCVAM activities are driven by agency needs and approved by consensus.

To this end, Casey noted the appointment of Raymond Tice, Ph.D., chief of the NIEHS [Biomolecular Screening Branch](#), to serve as the Institute’s principal ICCVAM representative. Tice is also the NIEHS and NTP lead for Tox21, a multiagency effort that uses high throughput and other cutting-edge technologies to assess the safety of chemicals. Both ICCVAM and NICEATM are expanding their efforts to work more closely with Tox21, which represents a new paradigm shift for [toxicity testing](#).



*The interim co-chairs for ICCVAM, Anna Lowit, Ph.D., from EPA, and Abigail Jacobs, Ph.D., from FDA, represented the 15 member agencies that make up ICCVAM, at the meeting. (Photo courtesy of Steve McCaw)*



*Matheson presented the ICCVAM strategy for skin sensitization AOPs. (Photo courtesy of Steve McCaw)*

## Agency updates

Afternoon speakers included Joanna Matheson, Ph.D., of the U.S. Consumer Product Safety Commission, discussing adverse outcome pathways (AOPs). Tice provided an overview of Tox21 activities, and Richard McFarland, M.D., Ph.D., from the U.S. Food and Drug Administration (FDA), and Geetha Srinivas, D.V.M., Ph.D., of the U.S. Department of Agriculture, reported on international vaccine workshops.

Casey concluded by showing the declining number of test method submissions going to one of ICCVAM's international partners, the European Centre for the Validation of Alternative Methods (ECVAM). Unlike its U.S. counterpart, ECVAM was specifically set up with resources, staff, and labs to scientifically validate alternative methods that research laboratories have developed.

“There are not many new methods coming through the pipeline,” Casey added. “We have to turn to science to do something different.”

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



*Nicole Kleinstreuer, Ph.D., from ILS, a contractor for NICEATM, complemented Matheson's talk, with highlights from current activities by NICEATM on skin sensitization AOPs. (Photo courtesy of Steve McCaw)*



*Birnbaum with outgoing SACATM chair Steven Niemi, D.V.M. (Photo courtesy of Steve McCaw)*



*Ochoa, left, and Tracie Bunton, D.V.M., Ph.D., right, from EICARTE LLC, gave feedback to ICCVAM representatives. (Photo courtesy of Steve McCaw)*

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# Rutgers holds high school summer program

By Eddy Ball, Jamie Moscovitz, and Alessandro Venosa

Thanks, in part, to NIEHS-funded programs at Rutgers University, 46 high school students gained new insights into laboratory techniques and real-world applications of toxicology this summer.

The young people, rising sophomores, juniors, and seniors from 30 high schools in New Jersey and surrounding states, were participants in the first Toxicology, Health, and Environmental Disease (THED) High School Summer Program held at the Rutgers University Environmental and Occupational Health Sciences Institute (EOHSI) and Ernest Mario School of Pharmacy. The Rutgers Robert Wood Johnson Medical School and the School of Public Health, along with the NIEHS Center for Environmental Exposure and Disease, provided additional support for the program.

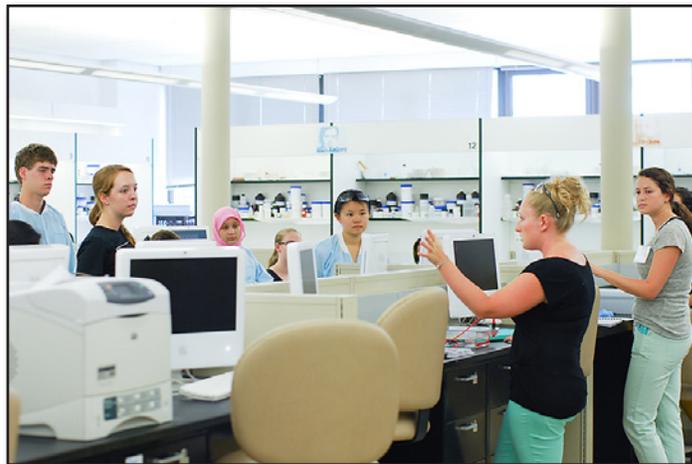
The instructors, who were graduate students and faculty of the Joint Graduate Program in Toxicology at Rutgers, included NIEHS-funded [Training in Environmental Toxicology](#) trainees Jamie Moscovitz, Kristin Bircsak, and Thea Golden, Pharm.D., and NIEHS Outstanding New Environmental Scientist awardee [Lauren Aleksunes, Pharm.D., Ph.D.](#) Participants met with undergraduates supported by the NIEHS Summer Research Training in Environmental Health Sciences grant and the Program Director Debra Laskin, Ph.D. The students also participated in tours of research facilities organized by the Community Outreach and Education Core of the NIEHS-supported Center for Environmental Exposures and Disease.

“The program gave us a chance to let these students in on a well-kept secret,” Aleksunes said. “Toxicology isn’t just an important part in the foundation of public health. It’s a lot of fun, too.”

## A fast-paced and effective curriculum

The two one-week-long instructional sessions in July had ambitious goals, with overall objectives for the program including:

- Introducing students to a variety of modern laboratory techniques used in the biomedical and environmental health sciences fields



As a small group of high school students gathered on the other side of the bench, graduate student instructors Allison Isola, center; and Moscovitz, right, explained background information for upcoming laboratory sessions. (Photo courtesy of Wilson Rodriguez)



Participants began the week with hands-on practice in the fundamentals of pipetting. (Photo courtesy of Wilson Rodriguez)

- Training students to analyze results and determine real-world applications of data collected
- Exposing students to different career opportunities within medicine, pharmacy, toxicology, environmental health science, and research, through presentations and discussions with professionals.

The curriculum revolved around three toxicology-related themes — cellular injury, cellular response, and genetic predisposition. Interestingly, three-quarters of the participants were female. Students said they enrolled in the program because of their interest in biomedical research.

Students spent 30 percent of the week participating in laboratory activities, and 70 percent in classroom activities, learning about critical concepts and applications of toxicology and public health to current events. Each activity had instructor to student ratios between 1-to-4 and 1-to-8, to ensure individual attention for participants. The week of learning culminated with group presentations to parents and instructors of the various activities completed.

### Evaluating specific outcomes

Students completed both preprogram and post-program surveys assessing research abilities and knowledge as outcomes. Following completion of the program, students scored themselves higher in their ability to perform laboratory techniques, including pipetting, DNA isolation, and cell culture.

Students also reported greater comfort with giving presentations and analyzing clinical findings. Using a 20 question true or false quiz on toxicology-related topics, students preprogram scored 67 percent correct, and post-program scored 81 percent correct. Furthermore, students ranked the genetics, histology, and pathology labs as their favorite activities.

Applications for the 2014 THED High School Summer Program will be available online at the [EOHSI Web page](#) in the spring.

(Jamie Moscovitz and Alessandro Venosa are Ph.D. candidates in the Joint Graduate Program in Toxicology at Rutgers University, and served as the primary course instructors for the 2013 program.)

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*During their week at Rutgers, most of the students gained their first experience in state-of-the-art histology and pathology. (Photo courtesy of Wilson Rodriguez)*



*After completing their safety training and donning protective gear, students fixed and stained cells during the dose-response laboratory session. (Photo courtesy of Wilson Rodriguez)*

# Public health group announces launch of Canadian Environmental Health Atlas

By Eddy Ball

Joanne Telfer, project officer at Simon Fraser University, announced Sept. 13 the official launch of the [Canadian Environmental Health Atlas \(CEHA\)](#), a project initiated in 2009 to advance knowledge about environmental health.

The ultimate aim of the atlas is to present a single comprehensive picture of environmental health in Canada that will bring together, in one document, traditional routes of exposure and the influence of human settlement on health. Spearheading the project was a [multidisciplinary team](#) made up of a geographer, a demographer, and epidemiologists, including veteran NIEHS [grantee](#) and Simon Fraser University professor [Bruce Lanphear, M.D.](#)

As Lanphear explained in a talk at NIEHS in December 2012 ([see story](#)), CEHA is the first effort to synthesize Canadian research across a range of environmental health topics and make information accessible to a general audience. “Not enough people know that the environment is key [to public health],” he said, pointing to the lack of user-friendly sources of information about environmental public health.



*Lanphear is a professor at the Child and Family Research Institute, and Simon Fraser University in Vancouver, British Columbia, who is an acknowledged authority on lead exposure and children's health. In 2012, he received the International Society for Environmental Epidemiology Research Integrity Award for his work promoting children's public health. (Photo courtesy of Steve McCaw)*

## An easily navigable source of information about environmental health

Originally envisioned as a conventional book format, the project quickly transitioned to an electronic resource that mixes short text passages with images linking to more detailed information. According to Lanphear, the team envisions the website working as a portal, or moderated wiki page, where new knowledge can be integrated into the atlas for easy access and translation for a general audience.

The project aims to promote disease prevention in three ways:

- Raising awareness of the many ways in which environmental influences affect human health.
- Highlighting the importance of environmental health in health promotion and disease prevention.
- Building a common vocabulary for interdisciplinary communication and collaboration in the broad domain of public health.

Users can easily access sections on major aspects of environmental health, ranging from air quality to social environments, specific diseases, disease categories, and toxicants. Additional links take users to key points about specific topics, as well as lists of resources and organizations, articles and publications, and news articles about environmental health. With its streamlined design and pull down menus, CEHA can appeal to audiences ranging from young students, who might feel intimidated by text-heavy pages, to people eager to learn as much as possible about a topic, and willing to read studies in scientific journals to get the information they want and need.

## Next steps

Looking ahead, the team members said they realize the atlas is only scratching the surface of environmental health. They envision the project as a continually evolving effort, and foresee adding one or two sections to it each month. In the future, they hope to expand CEHA to become a world atlas, as the team works with additional experts to highlight other aspects of environmental health, as well as those experts' own research.

According to Lanphear, another objective of CEHA is to raise appreciation and awareness of environmental health's pioneers and leading advocates. "I think we underestimate the importance of environmental health experts, and our team would like to help remedy that," he said. "Why shouldn't we celebrate [Harvard researcher] Doug Dockery or [NIEHS Director] Linda Birnbaum, the way we do sports celebrities or musicians?"

The screenshot shows the homepage of the Canadian Environmental Health Atlas (CEHA). At the top left is the CEHA logo and the title "CANADIAN ENVIRONMENTAL HEALTH ATLAS" with the tagline "Understanding Our Environment is Key to Promoting Health and Preventing Disease". To the right are links for "Email Sign Up" and "Feedback" and a search bar. Below this is a navigation bar with "Home", "Health Topics", "About", "Glossary", and "Credits". The main content area is titled "Our Health and the Environment" and features a large map of Canada with a cityscape overlay. To the left of the map is text explaining the link between health and the environment. Below the map are three buttons: "Our Health and the Environment", "Why a Canadian Environmental Health Atlas?", and "The Spatial Distribution of Health Hazards". Below this is a section titled "Exploring Today's Health Concerns" with three sub-sections: "Built Environments", "Environmental Contaminants", and "Drinking Water Quality". A sidebar on the left lists "Health Topics" with expandable options. A sidebar on the right offers search options for "Environmental Toxicants and Related Diseases" and lists resources like "Resources/Organizations", "Articles/Publications", "Downloadable Images", "In the News", and "Site Map". The footer contains logos for CIHR, IRSC, and the Social Sciences and Humanities Research Council of Canada.

The CEHA home page reflects the site's overall design — short bursts of text, vivid images, and a wealth of navigational opportunities. The project team wanted the atlas to welcome readers of virtually every level, but also offer opportunities for more in-depth exploration of environmental public health topics.

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# PEPH webinar highlights tribal efforts to address environmental justice and public health

By Audrey Pinto

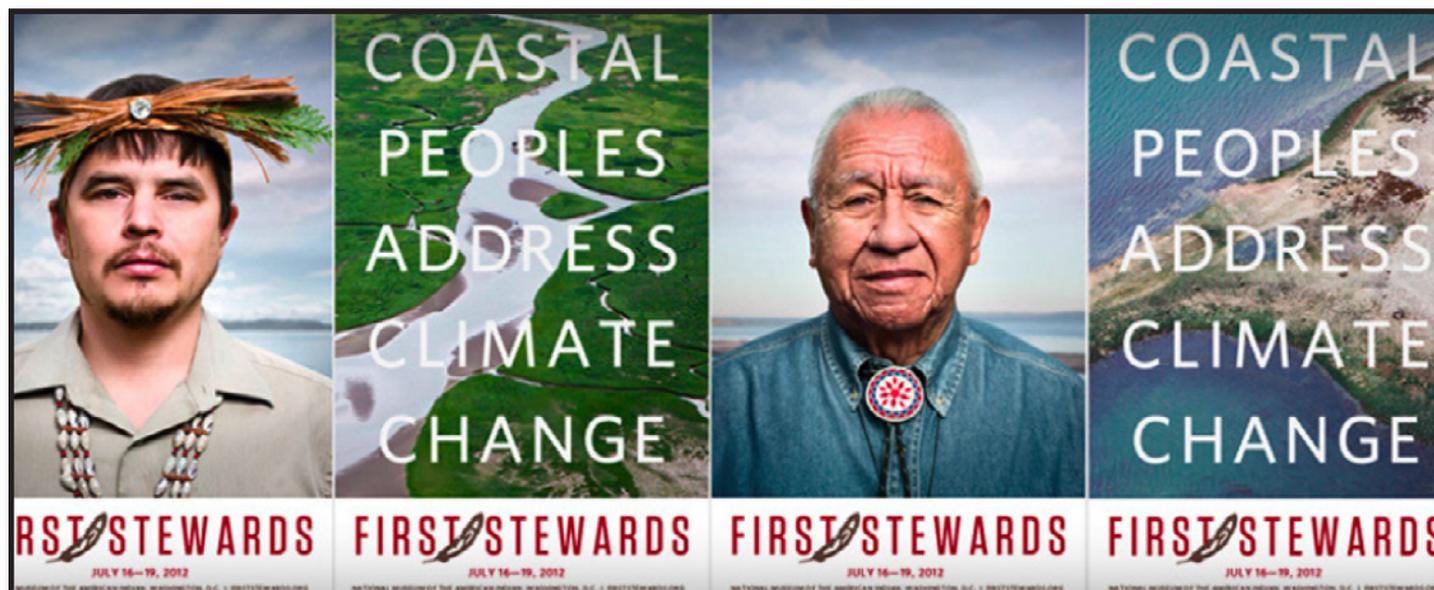
Three researchers, each of whom brought a unique perspective, came together to highlight environmental justice and health disparity issues, and their ongoing efforts to heal affected Native American communities. The NIEHS Partnerships for Environmental Public Health (PEPH) [webinar](#) Aug. 21 offered important insights into the tribal perspective on these important topics, and the research programs that may begin to address them.

Presenters included grantees [Johnnye Lewis, Ph.D.](#), research professor and director of the Community Environmental Health Program at the University of New Mexico; Assistant Professor [Annie Belcourt, Ph.D.](#), of the University of Montana, whose areas of emphasis include mental health and health disparities in American Indian communities; and [Clarita Lefthand-Begay](#), a Ph.D. candidate at the University of Washington, working in the areas of self-determination, environmental health stewardship, and water health disparities.



*Tribal members, such as the man shown, test the water on Navajo lands, to make sure it is safe for their cattle and themselves. (Photo courtesy of Johnnye Lewis)*

Building on the NIEHS commitment to support research initiatives to identify environmental components of health disparities, Lewis, Belcourt, and Lefthand-Begay presented informative case studies, showcasing their efforts to promote environmental and public health awareness. These narratives underscored the ongoing efforts by many tribal groups to mobilize collaborative community efforts to identify causes of environmental contaminants and their health-related effects; educate their local communities about the public health impact of these contaminants; and change patterns of exposure.



*Lefthand-Begay used photos of tribal members in this slide illustrating a Native American conference about climate change. (Photos courtesy of Clarita Lefthand-Begay)*

The talks also highlighted the importance of incorporating the traditional knowledge of tribal leaders and healers from different tribal groups, when considering how best to address environmental health disparities.

### **Water is sacred — it is the most essential element of life**

In her opening remarks, Lewis stressed that water is sacred to the very existence of Native tribes. Yet, many in the Navajo communities she works with do not have access to safe public water supplies, and routinely use unregulated water sources that are not regularly tested or treated.

Over the past decade, researchers from the [DiNEH Project](#) and government agencies, including the U.S. Environmental Protection Agency and the Centers for Disease Control and Prevention Agency for Toxic Substances and Disease Registry, have tested numerous water sources on tribal lands and found them contaminated with a mixture of toxic substances, including mercury, arsenic, uranium, selenium, thallium, and lead. Lewis pointed out that this legacy of exposure is associated with an increased risk of hypertension, autoimmune diseases, kidney disease, and lung cancer, but few tribal environmental programs have the expertise or funding to support broad-based research efforts to address this contamination.

### **The role of digital storytelling in public health education, promotion, and healing**

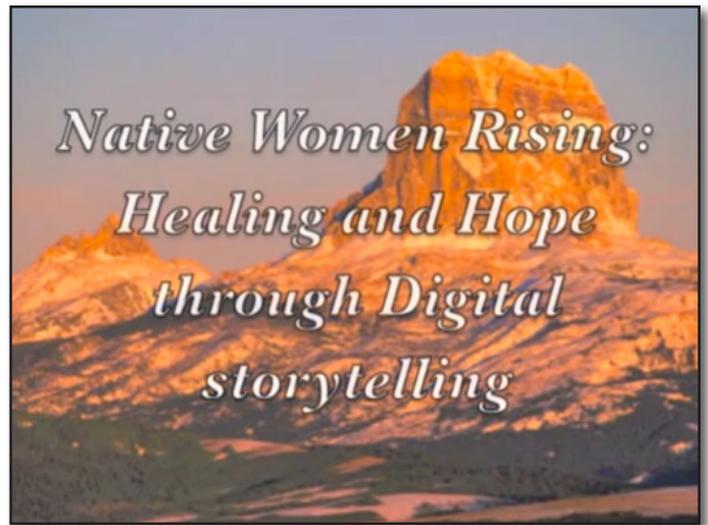
In her presentation, Belcourt noted that American Indians and Alaska Natives (AIANs) experience significant poverty and associated health disparities, including high rates of mortality due to poor air quality in homes from tobacco use, wood stoves, and mold; poor water quality, because many communities lack access to adequate water supply and waste disposal facilities; and a lack of public safety.

Belcourt discussed several ongoing collaborative projects designed for promoting healthy communities and protecting the local tribal lands for future generations, through education in culturally relevant formats. Through social media and the power of digital storytelling, AIANs are producing culturally sensitive health messaging that incorporates tribal ecological knowledge and a community-centered strategy to improve public health, prevent disease, and protect future generations. Recent examples of these projects include [Save Our Sacred Chief Mountain](#), [Fracking the Blackfeet Nation](#), and a [series of stories](#) created by Belcourt.

### **Self-determination and connection to land and water**

The final presentation, by Lefthand-Begay, discussed the importance of self-determination, and the need for structured decision-making regarding indigenous water values. To build trust among Native American populations, Lefthand-Begay proposed that the federal government should support and honor tribal self-determination and treaty-protected rights to access cultural resources within the boundaries of tribal lands. To strengthen ties between Native American tribes and federal agencies, Lefthand-Begay noted that the knowledge, skills, and values of indigenous communities should be reflected in decisions and policies that affect American Indian communities.

(Audrey Pinto, Ph.D., is technical editor for the journal *Environmental Health Perspectives*.)



*This photo and text from Belcourt's presentation expressed the role of Native American women and love of land in promoting environmental justice. (Photo courtesy of Annie Belcourt)*

# NIEHS hosts local middle school students

By Jacqueline de Marchena

Eighteen Lowes Grove Middle School students visited NIEHS Sept. 30, to begin learning about cell biology from Institute scientists. This class marked the debut of the newest [Citizen Schools](#) education outreach curriculum, “It’s a Small World: Cells and DNA,” developed through a collaboration between NIEHS trainee volunteers and the [Office of Science Education and Diversity \(OSED\)](#).

In this after-school program, students will learn how cells and DNA respond to environmental stressors. While NIEHS has collaborated with the Citizen Schools program at Lowes Grove Middle School in Durham, N.C., since 2012, with a program on respiratory health ([see story](#)), this semester’s program is the first time the students have been invited on campus and introduces a new curriculum. The nine remaining weekly classes in this fall’s program will be held at the school, led by postdocs, scientists, and other NIEHS volunteers.



Locklear, left, and Whiteside help Lowes Grove Middle School students inoculate blood agar plates with bacteria from their thumbs, during an exercise on the importance of hand washing. Shown in the background are OSED Director Ericka Reid, Ph.D., center, and Lao, right. (Photo courtesy of Steve McCaw)



**Linked video:**  
[Watch interviews and scenes from the debut NIEHS Citizen Schools program \(03:05\)](#)

(Launches in new window)

Download Media Player:  Flash [↗](#)

## Impressionable students learn about NIEHS

Coming to this class was the first time many of these students had visited a research facility. “I think some students were puzzled that we study things here [at NIEHS], even though we are not traditional students in a classroom,” said Huei-Chen Lao, the OSED K-12 Science Education and Outreach Coordinator leading the Citizen Schools outreach initiative.

Felicity Davis, Ph.D., an NIEHS visiting fellow who has participated in previous Citizen Schools outreach events, added, “It was good for the students to see where we work. Last time [in the spring semester program], we told the kids that we were scientists, all from diverse backgrounds, working together as a team, but I don’t think it really hit home. Having the students come to NIEHS allows them to contextualize our workplace and helps them understand where we are coming from.”



NIEHS industrial hygienist Sharon Beard gave an animated health and safety lecture for visiting students. (Photo courtesy of Steve McCaw)

## An opportunity to further develop teaching skills

A group of trainees developed the cell biology curriculum, being taught at Lowes Grove, through the efforts of several brainstorming sessions. “I can tell this was a good experience for the postdocs. It was more than just a curriculum development. We all learned how to work together as a team,” said Lao.

The course work incorporates a numerous hands-on activities, including making model cells, looking through microscopes, and observing a radiation cloud chamber developed by Bill Fitzgerald, NIEHS radiation safety officer. The outreach volunteers hope these activities will foster creativity and enthusiasm for the WOW! presentations, which will be led by students and conclude the 10-week course.

Lao said she is optimistic that the Citizen Schools outreach program will continue to attract talented and committed volunteers, and she is planning to facilitate the development of more science-based curricula. Coordinating more frequent field trips to the NIEHS campus, so that students can get more direct exposure to scientists, is also a priority.



*As part of Beard's exercise, students donned protective equipment for working in the lab. (Photo courtesy of Steve McCaw)*

## Volunteers for the fall Citizen Schools Apprenticeship

Floyd Adsit

Sara Andres, Ph.D.

Miranda Bernhardt, Ph.D.

Terry Blankenship-Paris, D.V.M.

Christopher Campos, Ph.D.

Felicity Davis, Ph.D.

Bill Fitzgerald

David Goulding

Sylvia Hewitt

Jacqueline Locklear, D.V.M.

Page Myers

Palmyra Romeo

Kirsten Verhein, Ph.D.

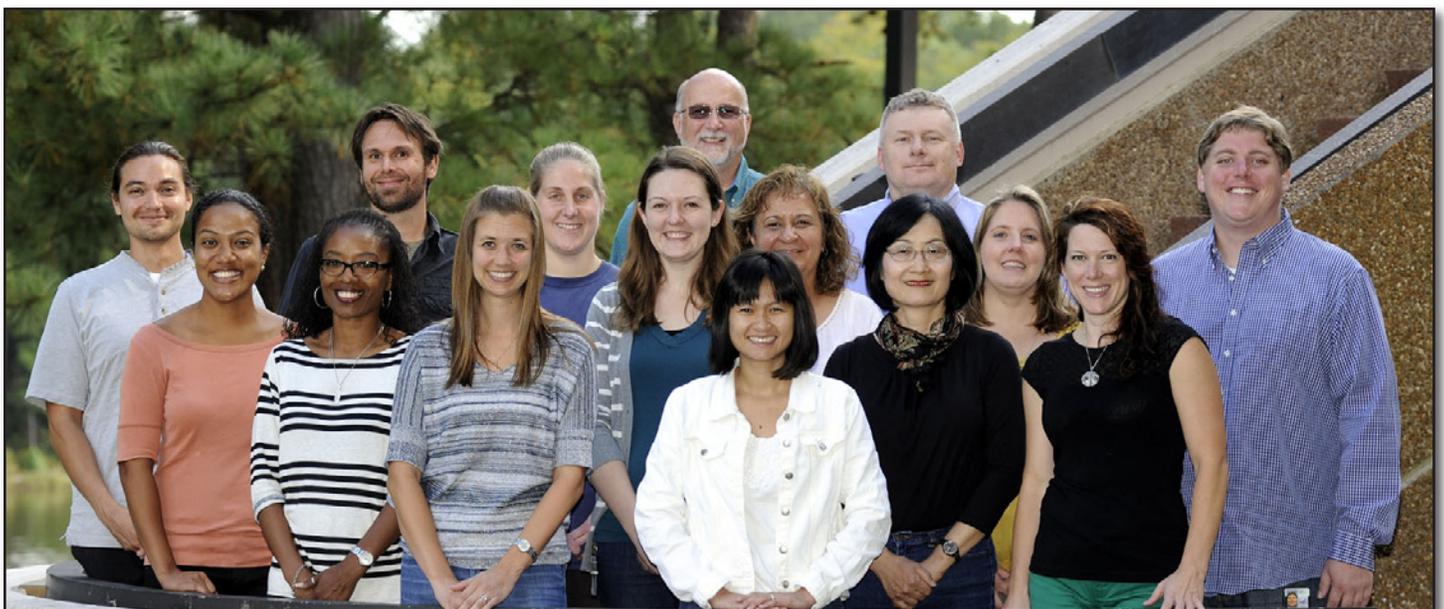
Shannon Whirlledge, Ph.D.

Tanya Whiteside

Kimberly Wiggins, Ph.D.

Wipawee (Joy) Winuthayanon, Ph.D.

Gary ZeRuth, Ph.D.



*This year's Citizen Schools group includes, from left, Campos, Wiggins, Reid, ZeRuth, Verhein, Andres, Bernhardt, Fitzgerald, Winuthayanon, Locklear, Lao, Adsit, Whiteside, Whirlledge, and Goulding. Not shown are Blankenship-Paris, Davis, Hewitt, Myers, and Romeo. (Photo courtesy of Steve McCaw)*

(Jacqueline de Marchena, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Developmental Neurobiology Group.)

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## SRP grantees gather in Baton Rouge for annual meeting

At the annual meeting of the NIEHS Superfund Research Program (SRP), more than 250 researchers, trainees, and administrators from across the nation gathered Oct. 15-17 in Baton Rouge, La.

The SRP supports multidisciplinary research to address human and environmental health challenges related to Superfund and other hazardous waste sites. Hosted by SRP grantees at Louisiana State University (LSU), the meeting provided a forum for discussing new research, technology, communication, and community engagement in critical areas related to the SRP mission.

The main meeting opened with remarks by Stephania Cormier, Ph.D., LSU SRP co-director. She discussed the state of the program and the wide range of SRP scientific disciplines featured in journal publications, grantee research highlights, and community engagement and research translation activities over the past year.

Following Cormier, LSU President and Chancellor F. King Alexander, Ph.D., related the mission of the SRP to his own background, describing how he grew up near a Superfund site and observed negative health effects firsthand. He spoke highly of the transdisciplinary group of researchers at the meeting and tasked them with continuing their substantial work to improve human health and the environment in the U.S. and around the world.

“This kind of university-wide research program is exactly the type of approach necessary for LSU to really make an impact in the health of its citizens,” Alexander said. “When you add that to the combined efforts of researchers at every Superfund site across the country, you get the kind of impact that truly affects a nation. I’m proud that LSU can play a part in that.”

### Sessions highlight science and other activities

Scientific session speakers shared research findings and implications of their work, with a focus on four main topics — halogenated pollutants; emerging contaminants and pollutant mixtures; developmental and other human health effects; and arsenic and heavy metals. Presentations ranged from research to better



*Cormier highlighted some SRP successes from the past year, from high impact publications to community success stories. (Photo courtesy of Kelli Palmer, LSU SRP)*



*Margaret Reams, Ph.D., LSU Community Engagement Core leader, left, introduced MacArthur Fellow Wilma Subra, who discussed her work after the Deepwater Horizon oil spill, during the research translation and community engagement session. (Photo courtesy of Kelli Palmer, LSU SRP)*

understand the health effects, mechanisms of actions, and variability in toxicity of legacy and emerging chemicals, to fieldwork and bench-scale projects to remediate these chemicals at hazardous waste sites and nearby communities.

For a full day prior to the beginning of the main meeting, grantees involved in research translation and community engagement gathered to hear speakers and participate in discussions related to communication strategies for forming stronger connections with communities, non-government organizations, and public agencies. They explored ways to engage communities facing environmental exposures, identify research gaps in understanding the societal effects of hazardous waste sites, and interact more effectively with each other and federal stakeholders.

### Celebrating research by trainees

Along with the traditional presentations and plenary sessions, the meeting set aside time for celebrating award-winning students.

SRP trainee Corin Hammond, a Ph.D. candidate at the University of Arizona, accepted the 2013 [Karen Wetterhahn Memorial Award](#). During her talk, she described her research on phytoremediation of mine wastes in semi-arid environments.

Six students also received prizes for their efforts in the annual student poster competition. In the non-biomedical poster session, the winners were Jing Sun of Columbia University; Leslie Knecht of the University of Miami; and Minghui Gui of the University of Kentucky. In the biomedical category, the winners were Daniel Gusenleitner of Boston University; Fabian Grimm of the University of Iowa; and Peter Wagner of Harvard University.



*Hammond, right, with LSU SRP Training Core leader Robin McCarley, Ph.D., who presented her with the Karen Wetterhahn Memorial Award. (Photo courtesy of Kelli Palmer, LSU SRP)*



*During a special lunch session, trainees were able to sit with principal investigators and learn about other SRP-funded research and the history of the program. (Photo courtesy of Kelli Palmer, LSU SRP)*



*Along with the main judged poster session for students, above, there was also a special job seekers' poster session to give potential employers the opportunity to meet trainees who are within one year of finishing their program. (Photo courtesy of Kelli Palmer, LSU SRP)*



Grantees involved with research translation and community engagement met over lunch to discuss specific topics of interest, including engaging with tribal communities, using mobile apps to promote environmental health engagement, and incorporating environmental health topics in K-12 education. (Photo courtesy of Kelli Palmer, LSU SRP)



Some of the 2013 KC Donnelly Externship awardees (see the SRP website for more information on the winners) and poster winners gathered for a photo at the meeting. From left, Gui, Sun, Leah Chibwe, Peter Wagner, Shohreh Farzan, Grimm, and James Rice. (Photo courtesy of Kelli Palmer, LSU SRP)

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## NIEHS welcomes new chief information officer

By Robin Arnette

Since Information Technology (IT), or the use of computers and software to manage information, continues to grow in importance in the modern world, the person in charge of IT within an organization plays a vital role in the success of the enterprise. NIEHS leadership recognized the need for a Chief Information Officer (CIO), and found the right fit in Bernard Brown II. He started at the Institute Sept. 9.

Brown comes to NIEHS after having spent the past two years at the White House. He served as Director of Operations and Engineering in the Executive Office of the President, and was responsible for ensuring that all unclassified technology — including computers, networks, and mobile devices — were continuously available in support of the President of the United States.

Several reasons prompted his move to North Carolina, including living in the Triangle, the excitement of a CIO position, and the willingness to take on new challenges, but Brown admitted one of his main motivations was being part of the NIEHS mission.



Brown is a native of Rochester, N.Y., and is the proud father of two adult children. (Photo courtesy of Steve McCaw)

“I’ve been looking to do a CIO position for a while, but when I looked into what NIEHS does, I realized it was something that I was really interested in,” Brown said. “I want to know how the environment affects us, our health, and everything we do.”

### **Bringing a wealth of experience**

Before Brown went to Washington to work for President Obama, he had already amassed a considerable amount of IT experience in the private sector, as well as serving as an officer in the United States Air Force. One of his professional achievements occurred when he led a team that built a satellite-based tactical weapons system for Air Force Space Command.

Brown’s computer skills weren’t his only attribute in service to his country. He was stationed at Aviano Air Base in northeastern Italy during the 1998-1999 Kosovo War. All of the bombing missions the North Atlantic Treaty Organization (NATO) flew in the conflict originated at Aviano, and Brown was in the middle of all the activity. He was also one of the leaders providing command and control for all communications and IT issues during that military operation.

Brown said his goals are to modernize the computing networks at NIEHS, as much as possible, which will help Institute employees do their jobs better. He’s only been in the position for a few weeks, but he’s accomplished several tasks.

“Already, in the short time since his arrival, he has been involved in tackling some IT and management challenges, such as the mandate to limit our IT contractor to essential services for the duration of the contract protest,” said Joellen Austin, NIEHS associate director for management.

Brown’s background has prepared him for the work ahead, and he’s moving forward with his IT vision for the Institute.

“I’m really excited about the job,” Brown added. “I’m dedicated to being successful and making everyone [at NIEHS] successful.”

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# Science Notebook

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## Council science talk focuses on asthma

By Ernie Hood

At every NIEHS National Advisory Environmental Health Sciences council meeting, members get a break from their weighty considerations of budgets and grant applications to enjoy an update on a specific research program. At the Sept. 10-11 session, **newly tenured** scientist Donald Cook, Ph.D., who leads the Immunogenetics Group in the NIEHS Laboratory of Respiratory Biology, relayed his group's discoveries in characterizing the molecular links between house dust and asthma.

### Asthma is not all the same

To appreciate the significance of Cook's work, it is first important to understand that asthma and its underlying allergic reactions are heterogeneous, or diverse. Thus, not all asthmatics respond to the standard treatment of inhaled corticosteroids. Allergic responses to specific environmental stimuli in the lung involve many different types of immune cells, including dendritic cells, airway epithelial cells, and various types of T cells, as well as inflammatory cells called neutrophils and eosinophils. An improved understanding of these cells, and the signaling pathways they comprise, offers the potential to develop improved therapeutic strategies that target specific types of asthma, including steroid-resistant asthma.

Cook explained that two different arms of the adaptive immune response — T helper (Th)2 cells and Th17 cells — contribute to allergic asthma.

“These two arms of the immune response, which respond differently to factors in the environment, can now explain some of the heterogeneity that we see in asthma. This knowledge offers potential opportunities to deliberately disrupt specific pathways that are associated with one or the other of these types of asthma,” explained Cook.

Allergic sensitization, which is the biological basis for allergic asthma, is caused by allergens found in plants, insects, and animals, but also by adjuvants, or ingredients that increase the immune response, such as those found in air pollution and microbial products.

### Dust in the wind

House dust contains several adjuvants, including dead bacteria and their products, which are particularly efficient adjuvants.

“The question we had was, which of these bacterial products are particularly potent at promoting the types of inflammation and immune responses that are seen in asthma?” said Cook.



*Cook explained that house dust is an excellent model to help characterize the allergic sensitization involved in asthma, because it is a complex environmental product to which we are all exposed on a daily basis. (Photo courtesy of Steve McCaw)*

The research homed in on one particular bacterial product called flagellin, which turned out to be especially potent at inducing allergic responses that bring eosinophils to the airways. Cook found that asthmatics had considerably higher titers of anti-flagellin antibodies than did control subjects with healthy airways. The finding was consistent with the hypothesis that exposure to environmental flagellin predisposes one to develop allergic asthma.

### Cellular cross-talk

Further exploring the cellular and molecular mechanisms that give rise to flagellin signaling, and hence to allergic sensitization, the team identified a signaling molecule called Myd88 that appears to play a key role in the process. However, the specific role of Myd88 depends on whether it is expressed in lung epithelial cells or lung dendritic cells. Furthermore, there appears to be cross-talk between these two cell types, although the specific molecules used for this communication remain unidentified.

### More dust data to come

Cook said that future experiments will be aimed at going into homes and measuring not only the flagellin, but also titers of antibodies against flagellin, and the kinds of asthma symptoms that the inhabitants have. Through this approach, he and his team hope to develop an improved understanding regarding associations between flagellin, antibodies to flagellin, and different types of allergic asthma. Eventually, this research may lead to new therapeutic strategies that could prevent or reverse the molecular course of events that give rise to asthma.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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## Study links tanning gene to increased risk of testicular cancer

By Robin Mackar

A gene important in skin tanning has been linked to higher risk for testicular cancer in white men, according to a study led by scientists from NIEHS and the University of Oxford in England. Nearly 80 percent of white men carry a variant form of this gene, which increased risk of testicular cancer up to threefold in the study.

The [research](#) appeared online Oct. 10 in the journal *Cell*, and is the result of an integrated analysis of big data supported by laboratory research. The team suspected that variations in a gene pathway controlled by the tumor suppressor gene p53 could have both positive and negative effects on human health.

### Protective variant permits unnatural stem cell growth

“Gene variations occur naturally, and may become common in a population if they convey a health benefit,” said [Douglas Bell, Ph.D.](#), author on the paper and lead researcher in the NIEHS Environmental Genomics



*Ex officio council member and U.S. Food and Drug Administration scientist Jesse Goodman, M.D., suggested that Cook might consider collaborating with researchers exploring the microbiome, to potentially identify other sources of flagellins. (Photo courtesy of Steve McCaw)*

Group. “It appears that this particular variant could help protect light-skinned individuals from UV skin damage, like burning or cancer, by promoting the tanning process, but it permits testicular stem cells to grow in the presence of DNA damage, when they are supposed to stop growing.”

Bell explained that p53 stimulates skin tanning when ultraviolet light activates it in the skin. It then must bind a specific sequence of DNA located in a gene called the KIT ligand oncogene (KITLG), which stimulates melanocyte production, causing the skin to tan.

To conduct the analysis, NIEHS staff scientist [Xuting Wang, Ph.D.](#), co-author and lead bioinformatics scientist on the paper, led a data mining expedition to sieve through many different data sets. The team selected possible leads from the intersection of more than 20,000 p53 binding sites in the human genome, 10 million inherited genetic variations genotyped in the 1000 Genomes Project, and 62,000 genetic variations associated with human cancers identified in genome-wide association studies (GWAS). These data sets were gathered through joint efforts of thousands of researchers from around the world.

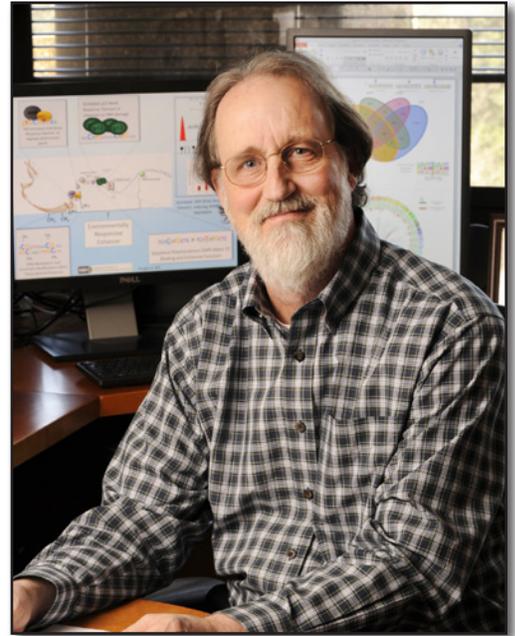
“In the end, one variant in the p53 pathway was strongly associated with testicular cancer, but also, surprisingly, displayed a positive benefit, which is probably related to tanning that has occurred as humans evolved,” Wang noted.

### **A significant marker of cancer risk, especially for Caucasian males**

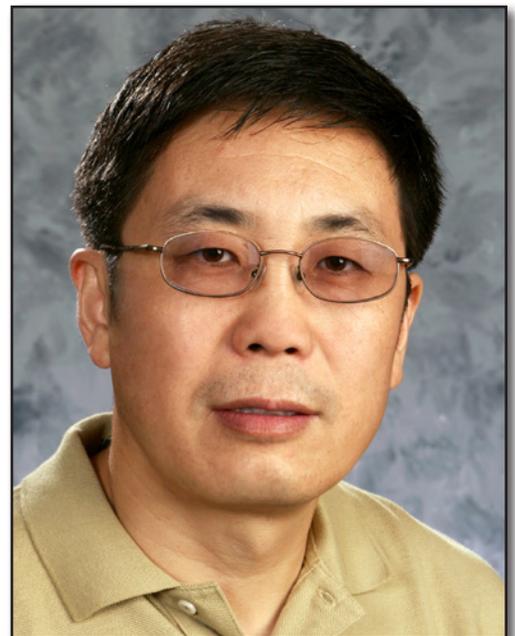
The group at the Ludwig Institute for Cancer Research at the University of Oxford, led by [Gareth Bond, Ph.D.](#), performed complex experiments to confirm the molecular mechanism that linked the variant with cancer and tanning.

“White males with a single nucleotide variation in KITLG, called the G allele, have the highest odds of having testicular cancer. In fact, the twofold to threefold increased risk is one of the highest and most significant among all cancer GWAS conducted within the past few years,” said Bond. “The high frequency of this allele in light skin individuals may explain why testicular cancer is so much more frequent in people of European descent than those of African descent.”

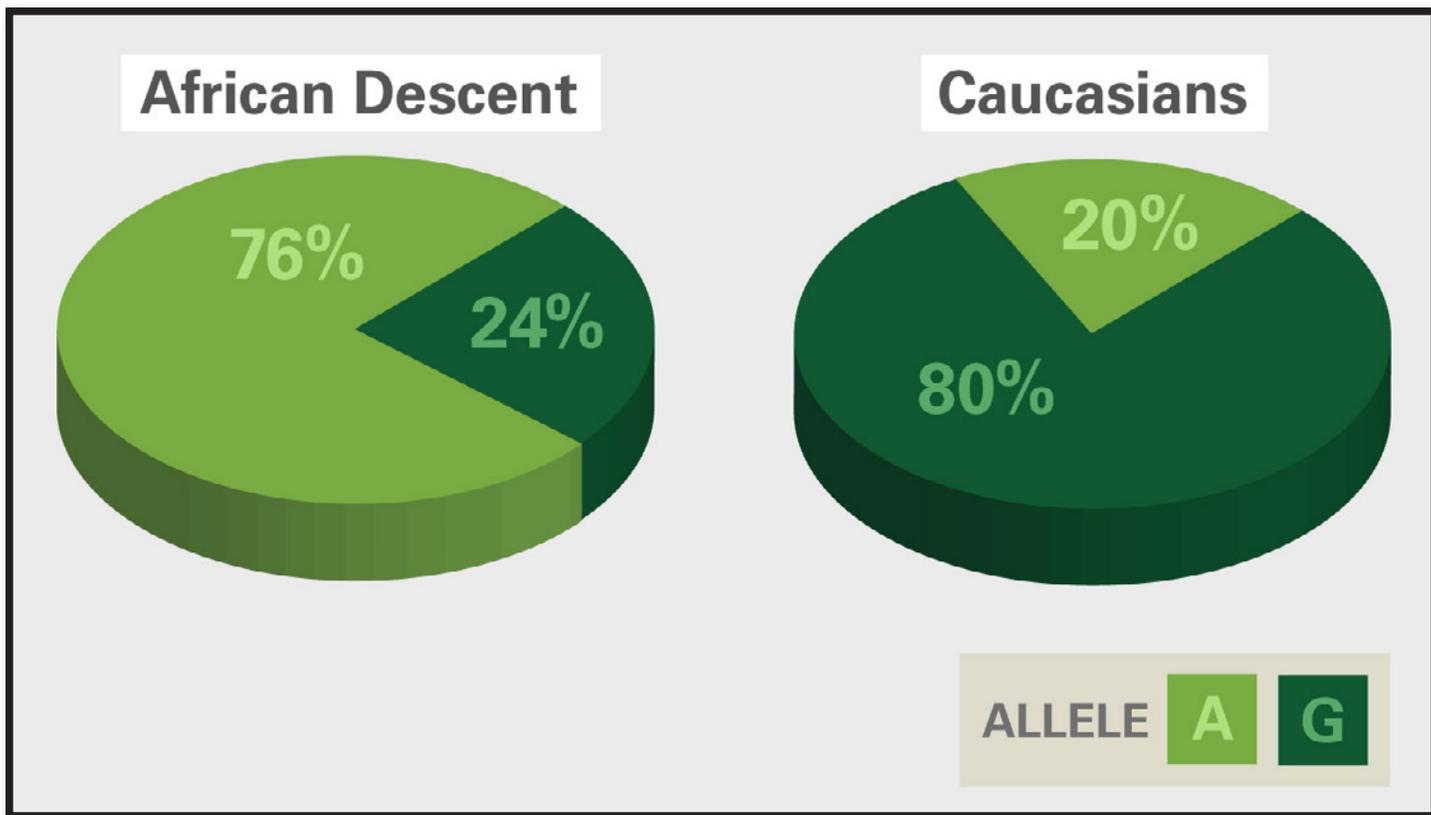
Bond said although the G allele increases testicular cancer risk, it might explain why testicular tumors are often easily cured with chemotherapy. “Most other tumors have a mutant p53, but in these testicular cell tumors, the p53 is functioning properly, and the drugs used for testicular cancer appear to work in concert with p53’s tumor suppression function to kill the cancer cells.”



*Lead researchers Bell and Bond are corresponding authors on the study. (Photo courtesy of Steve McCaw)*



*Wang shared first authorship on the study with a Ph.D. student at Oxford University, Jorge Zeron-Medina, M.D. Coauthors from Bell’s group included biologist Michelle Campbell and postdoctoral fellow Dan Su, Ph.D. (Photo courtesy of Steve McCaw)*



This pie chart illustrates the allele frequencies of the KITLG p53 response element single nucleotide variations in people of African and European descent. (Graphic courtesy of Douglas Bell)

Citation: Zeron-Medina J, Wang X, Repapi E, Campbell MR, Su D, Castro-Giner F, Davies B, Peterse EF, Sacilotto N, Walker GJ, Terzian T, Tomlinson IP, Box NF, Meinshausen N, De Val S, Bell DA, Bond GL. 2013. A Polymorphic p53 Response Element in KIT Ligand Influences Cancer Risk and Has Undergone Natural Selection. *Cell* 155(2):410-422.

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

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## NIEHS holds high throughput toxicogenomics platforms workshop

By Kristen Ryan

Leaders in the field of toxicogenomics met at NIEHS Sept. 16-17 to discuss the best methods for prioritizing approximately 1,000 genes for use in high-throughput toxicogenomics platforms.

The genes will be used for determining the effects of environmental toxins on cells or tissues from humans, rats, mice, zebrafish, and *Caenorhabditis elegans*. The High Throughput Transcriptomics Workshop — Gene Prioritization Criteria gave presenters an opportunity to summarize their respective gene sets, and discuss how these sets have been used to screen disease or toxic agent-related responses in cells from humans or rodents.

## Advancing predictive toxicology with gene expression profiles

NIEHS Deputy Director [Richard Woychik, Ph.D.](#), welcomed the group. NTP Biomolecular Screening Branch Chief [Raymond Tice, Ph.D.](#), then addressed the workshop goals and how the gene list would be used to advance [Tox21](#), a collaboration between several federal agencies to research and test chemicals using high throughput screening methods.

“In our next phase of Tox21, we plan to focus on high content screens and high throughput gene expression platforms, which is where this workshop comes in,” Tice said. “We want to identify a set of genes that could be applied to virtually any cell type, whether it is *in vitro* or *in vivo*, and would allow us to screen large numbers of cell samples in a short time at low cost.”

Joel Dudley, Ph.D., of the Icahn School of Medicine at Mount Sinai, discussed how large scale data integration could be used to select genes of interest. Justin Lamb, Ph.D., of Genometry Inc., described the development of the Broad Institute L1000 assay, and performance of the platform for detecting toxic responses in cultured human cells.

NTP molecular toxicologist [Scott Auerbach, Ph.D.](#), gave his presentation remotely, and asked the audience, “How does one balance data-driven versus knowledge-driven gene selection?” He argued that it is important to include chemical genomics data when selecting genes — a practice he uses to weight his gene selections.

The remainder of the first day included talks from Richard Judson, Ph.D., of the U.S. Environmental Protection Agency (EPA); David Gerhold, Ph.D., of the National Center for Advancing Translational Sciences (NCATS); Henghong Li, M.D., Ph.D., of Georgetown University; and Lena Smirnova, Ph.D., of the Johns Hopkins Bloomberg School of Public Health.

## Setting the stage for the project’s future directions

[Daniel Shaughnessy, Ph.D.](#), a health scientist administrator in the NIEHS Division of Extramural Research and Training, outlined the workshop’s focus for the second day, and set the stage for the morning’s scheduled speakers. These included Ruili Huang, Ph.D., of NCATS; Avrum Spira, M.D., of the Boston University School of Medicine; Julia Gohlke, Ph.D., of the University of Alabama; Carolyn Mattingly, Ph.D., of North Carolina State University; and Christopher Willis, Ph.D., of Thomson Reuters.

The afternoon was reserved for discussion, which was led by NTP Deputy Division Director for Science [Nigel Walker, Ph.D.](#) Walker moderated several discussions ranging from the goals of the workshop, biological systems, technologies to be utilized, and the types of approaches best suited to select and prioritize genes.



*“Hopefully, by the end of this workshop, we will have identified the kinds of criteria we think are optimal for this gene prioritization process,” Tice said. (Photo courtesy of Steve McCaw)*



*Lamb said large-scale gene expression profiling, using the L1000, yielded results that were similar to those produced using microarray studies. (Photo courtesy of Steve McCaw)*

One audience member wondered whether the central goal was to predict toxicity or disease. The majority of the group believed that predicting toxicity from a gene set was best suited for the proposed screening program. However, [John Bucher, Ph.D.](#), NTP associate director, said the aim was to determine overlap of chemically induced toxicity and disease pathways, to increase the probability of finding chemicals of interest to human health.

Tice concluded the workshop by providing a sequential set of future directions for the project, including the development of gene prioritization criteria based on responses to a request for information, publications, workshop presentations, and discussions.

(Kristen Ryan, Ph.D., is an Intramural Research Training Award fellow in the NTP Toxicology Branch.)



*Richard Paules, Ph.D., of the NIEHS Laboratory of Toxicology and Pharmacology, was particularly interested in using some of the gene sets to study the molecular mechanisms of response to environmental stresses. (Photo courtesy of Steve McCaw)*



*Judson summarized the EPA1000, a group of genes chosen because they are altered by chemicals and because of the pathways they affect. (Photo courtesy of Steve McCaw)*



*Gerhold laid out the pros and cons for an optimal method of picking genes for screening. He said, using an unsupervised, unbiased, mathematical approach is valid, but advocated that a supervised approach, using data from the literature and personal experience with genes, may be more useful. (Photo courtesy of Steve McCaw)*

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# Scientists document arsenic spread to previously unpolluted aquifer in Vietnam

By Nancy Lamontagne

NIEHS Superfund Research Program (SRP) researchers from Columbia University report clear evidence that human activity can increase the extent of naturally occurring arsenic in water. Their [study](#), published in *Nature*, shows that the dramatic increase in pumping of groundwater from an uncontaminated aquifer near Hanoi, Vietnam, is slowly drawing arsenic-contaminated water into the aquifer.

Under specific conditions, arsenic that naturally occurs in rocks can pollute wells used for drinking water. Arsenic contamination is widespread in South Asia, where an estimated 100 million people are exposed to levels high enough to cause heart, liver, and kidney problems, diabetes, and various cancers. Understanding the chemical processes involved in arsenic pollution could lead to the development of methods to remediate the problem.

“This is the first time we have been able to show that a previously clean aquifer has been contaminated,” said lead author and SRP grantee [Alexander van Geen, Ph.D.](#) “The amount of water being pumped really dominates the system. Arsenic is moving.”

The good news is that the arsenic is not moving as fast as the scientists feared it might, which leaves time, maybe even decades, for water managers to try to deal with the problem.

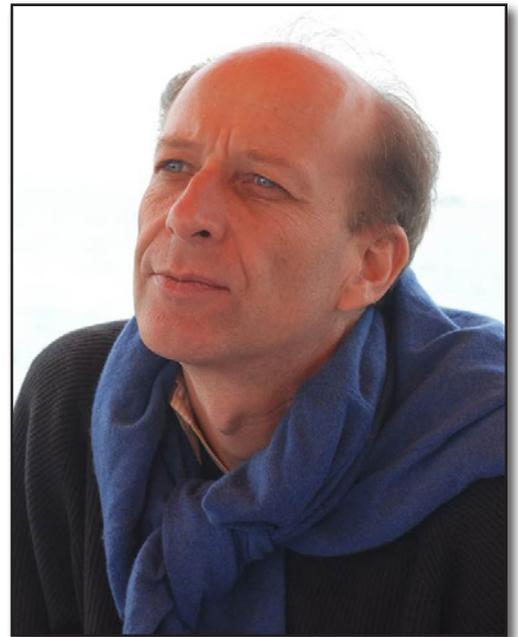
“While our findings stress the importance of periodic monitoring, they also point to the fact that increases in groundwater arsenic, if any, will be relatively slow,” said van Geen, a geochemist at Lamont-Doherty Earth Observatory at Columbia University.

## The carbon link

The researchers studied 31 wells around Van Phuc, a village about 5 1/2 miles southeast of Hanoi and bordered by a river. In this and other areas, the amount of arsenic in aquifers is associated with levels of dissolved organic carbon.

Water in an unpolluted aquifer in the village has little organic carbon, but water flowing into it, through the riverbed and from organic-rich soil and clay on top of the aquifer, contains high levels of organic carbon. As water enters the unpolluted aquifer, the carbon reacts with abundant iron rust stuck to sand grains, which appear orange. Arsenic in the sediment tends to stick to this rust, but the carbon causes the rust and arsenic to dissolve, leaving arsenic in the water. As the reactions proceed, the orange sands fade to grey.

The researchers found that in areas of Van Phuc closer to Hanoi, shallow wells draw from the safe orange sediments. However, wells closer to the river reach into the polluted grey sediments. Although high water levels in the safe aquifer should drain the polluted water toward the river, the increased water pumping in Hanoi is causing the safe aquifer to pull water from the contaminated one, as well as from the river.



*A study led by Alexander van Geen found that, although arsenic moved into a clean aquifer near Hanoi, the contamination is moving relatively slowly. “There is no reason to reject the use of low-arsenic aquifers without treatment, until alternatives become available,” he said. (Photo courtesy of Paolo Casella)*

Using helium and hydrogen isotope dating techniques, the investigators showed that over the last 40 to 60 years, water from the contaminated aquifer has migrated inland more than a mile. During the same period, high levels of arsenic contamination only moved about 370 feet.

### Enhanced carbon supply?

More research is needed to identify where the reactive carbon in the contaminated aquifers originates. “It could be organic clays capping the deposit of the river bank, in which case the change in groundwater flow, caused by Hanoi pumping, may have not only released arsenic, but also enhanced the reactive carbon supply,” van Geen said.

The research findings could have applications in other parts of the world. Similar situations may be occurring in the Indian state of West Bengal, but it is hard for researchers to study what is happening there, because of the large number of wells. In addition, landfills in the United States can sometimes release considerable levels of reactive carbon, which triggers the release of arsenic from uncontaminated aquifers downstream.



SRP researchers van Geen, seated, and co-author Benjamin Bostick, Ph.D., also of Columbia University, examined gray and orange drill cuttings from Van Phuc. Pumping for Hanoi’s municipal water supply nearly doubled from 2000 to 2010, and is causing the safe aquifer in Van Phuc to pull water from the contaminated one. (Photo courtesy of Michael Berg, Eawag: Swiss Federal Institute of Aquatic Science and Technology)

*Citation:* van Geen A, Bostick BC, Pham TK, Vi ML, Nguyen-Ngoc M, Phu DM, Pham HV, Radloff, Aziz Z, Mey JL, Stahl MO, Harvey CF, Oates P, Weinman B, Stengel C, Frei F, Kipfer R, Berg M. 2013. Retardation of arsenic transport through a Pleistocene aquifer. *Nature* 501(7466):204-207.

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



Bostick, center, collected a sediment core in Van Phuc. The arsenic contamination moves about 10 to 20 times slower than water travels — a benchmark rate that can be used to better understand how quickly arsenic will migrate at contaminated sites in the United States. “Furthermore, the study helps us to understand the sustainability of groundwater resources and the effects of groundwater use on water quality,” Bostick said. (Photo courtesy of Charles Harvey, Massachusetts Institute of Technology)

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# Reducing lead contamination in urban soils

By Marisa Naujokas

Most people are aware of the hazards of lead paint, but environmental health experts are now looking at lead contamination in urban soils, with increasing concern. Superfund Research Program (SRP) Health Science Administrator Heather Henry, Ph.D., organized a session at the American Chemical Society (ACS) Meeting Sept. 8-12 in Indianapolis, where scientists and U.S. Environmental Protection Agency (EPA) experts discussed challenges in cleaning up these soils.

## Stricter standards increase need for urban soil remediation

Ingestion of lead from soil and surface dust is a major exposure pathway in children. Lead is a neurotoxin, and studies have shown that exposure to high levels results in reduced IQ. Due to these findings, in 2012, the U.S. Centers for Disease Control and Prevention (CDC) recommended lowering the definition of elevated blood lead in children from 10 micrograms per deciliter to 5 micrograms per deciliter. According to EPA toxicologist Mark Maddaloni, Dr.P.H., the more stringent standard increases pressure on cities to find ways to remove lead in soils.

“We may not be able to dig our way down to these new ambitious CDC recommendations,” Maddaloni noted. He added, digging up backyards and hauling away contaminated soil is not feasible in many urban settings, so alternative cleanup approaches are needed.

## No one-size-fits-all answer

There is no one-size-fits-all approach, because soil characteristics determine effectiveness of different soil amendments. Amending soil involves mixing chemicals or other products into the soil to change the chemical composition and immobilize, or bind, the lead. A variety of phosphate amendments, such as compost, fish bone meal, and phosphate fertilizers are under investigation. Fish bone meal garnered publicity as a fix-all approach, but the presenters agreed that it does not work under all circumstances.

Ganga Hettiarachchi, Ph.D., from Kansas State University, showed that plant uptake of lead can be minimized, and soil quality can influence amendment effectiveness. Zhongqi (Joshua) Cheng, Ph.D., from Brooklyn College noted that the presence of other contaminants, such as arsenic, can also complicate cleanup efforts. For example, phosphate can mobilize arsenic, creating other problems. Christopher Schadt, Ph.D., of Oak Ridge National Laboratory, observed that microbial communities, including fungi, present in the soil, can be players in mobilizing soil lead.

## Lead bioavailability as a key parameter

Presenters also emphasized that lead bioavailability is a key measurement of soil lead risk. If soil lead is stabilized, so that it can no longer be absorbed into the body, exposure risks are greatly reduced. But, measuring bioavailability itself is a challenge, according to Kirk Scheckel, Ph.D., from the EPA, and Nick Basta, Ph.D., of Ohio State University. Their research suggests that the current laboratory *in vitro* method to predict lead bioavailability — known as the relative bioavailable leaching procedure, developed by John Drexler, Ph.D.,



Henry oversees the NIEHS SRP grants.  
(Photo courtesy of Steve McCaw)

of the University of Colorado Boulder and William Brattin of the Syracuse Research Corporation, Denver, Colo. — is not accurate for amended urban soils.

According to Basta, “Research is needed to evaluate other *in vitro* lab methods, and develop a new laboratory method to accurately evaluate the ability of soil amendments to reduce bioavailable lead.”

### Research to Risk Assessment

Henry and co-chairs Maddaloni and Scheckel organized this ACS session, as part of the SRP Research to Risk Assessment Initiative. The initiative brings together risk assessment experts and researchers, to exchange information and define research needs.

Henry said, “As a result of this ACS session, we are better positioned to communicate the state of science and potential shortcomings of using phosphate for lead soil remediation.”

(Marisa Naujokas, Ph.D., is a senior communication specialist with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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*Scheckel presented “Challenges of lead immobilization and risk assessment” at the ACS session on biogeochemistry interactions that affect bioavailability and remediation of lead in soils. (Photo courtesy of Heather Henry)*

## Bishop honored by Environmental Mutagenesis and Genomics Society

*By Robin Arnette*

When former National Toxicology Program (NTP) geneticist Jack Bishop, Ph.D., retired in 2012, after 40 years of federal service, he had amassed an impressive record of scientific accomplishments, including more than 100 peer-reviewed journals articles, presentations at dozens of national and international conferences, and decades of experience in germ cell mutagenesis and environmental toxicology. Now, he has one more accolade to add to the list.

The [Environmental Mutagenesis and Genomics Society \(EMGS\)](#) named Bishop as its 2013 Alexander Hollaender Award winner. The EMGS is dedicated to promoting research that examines the causes and consequences of damage to the genome and epigenome. According to its website, the award is given each year in recognition of outstanding contributions in the application of the principles and techniques of environmental mutagenesis to the protection of human health.

Bishop received the award during the society’s annual meeting Sep. 24 in Monterey, Calif., and joins two other NIEHS award recipients. Former NTP toxicologist Mike Shelby, Ph.D., won in 1988, and Biomolecular Screening Branch chief Raymond Tice, Ph.D., received the honor in 2009.

“I am very humbled and honored to receive this award and to be included in such a prestigious list of Alexander Hollaender Award winners,” Bishop said upon hearing the news.

Bishop came to NTP in 1985 from the U.S. Food and Drug Administration National Center for Toxicological Research in Jefferson, Ark., where he spent 10 years investigating chemically-induced mutagenesis in rodent germ cells. Prior to that, he was a research geneticist at the U.S. Department of Agriculture Bee Breeding and Stock Center Laboratory in Baton Rouge, La.

While at the NTP, he served in the [Toxicology Branch](#) as project officer for research that evaluated the reproductive and developmental toxicity of chemicals, and conducted his own studies in reproductive, developmental, and genetic toxicity. Bishop was also instrumental in the effort to develop biomarker assays for detecting genetic damage in rodent sperm, using fluorescence in situ hybridization.

Two examples of his work represent ground-breaking research in the field of environmental mutagenesis. His 2003 report found that the chemical agent N-hydroxymethylacrylamide had detrimental effects in mouse germ cells, or the cells involved in reproduction, rather than somatic cells, which comprise all of the other cells in an organism. Bishop also determined that pregnant women who took azidothymidine, a medication used to treat patients with HIV-AIDS, gave birth to children who sustained some genetic damage, as a result of the drug's ability to cross the placental barrier.

John Bucher, Ph.D., NTP associate director, said Bishop's commitment to research, organizing international workshops, and mentoring young scientists made him an outstanding candidate for the award.

"Jack has been instrumental in helping the NTP have a prominent and forward thinking role in the field of environmental mutagenesis," Bucher said. "NTP is fortunate to have had several NTP staff recognized by EMGS over the years."

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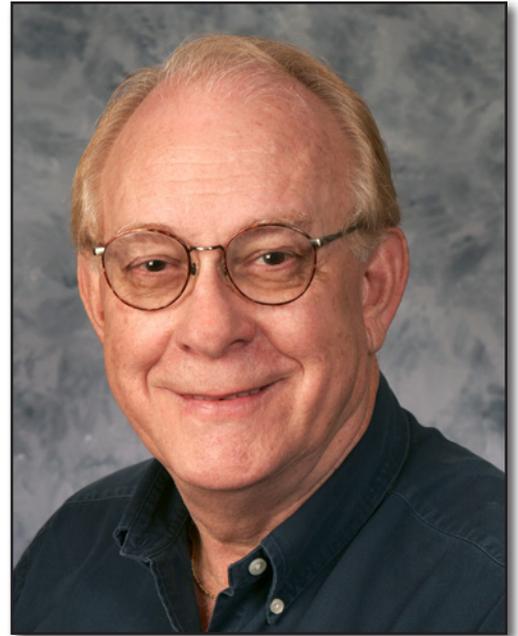
## **NIEHS celebrates National Postdoc Appreciation Week**

*By Heather Franco*

NIEHS celebrated its postdoctoral fellows Sept. 20 with a day full of events, including a general assembly meeting, a trivia contest, and a picnic. Fellows also had a chance to pick up career and professional development books, provided by the Burroughs Wellcome Fund, throughout the week.

Tammy Collins, Ph.D., director of the NIEHS [Office of Fellows' Career Development \(OFCD\)](#), explained, "This celebration is our way of saying thank you for the excellent scientific research carried out by the fellows and for their contributions to the NIEHS community."

The celebration was part of [National Postdoc Appreciation Week](#) Sept. 16- 20 sponsored by the National Postdoctoral Association (NPA). NIEHS is a sustaining member of NPA.



*During his long association with EMGS, Bishop served as treasurer, executive board member, and past president of one of its regional groups. (Photo courtesy of Steve McCaw)*

## Birnbaum fields postdoc questions

NIEHS and NTP Director Linda Birnbaum, Ph.D., opened the meeting by extending her open door policy and answering the fellows' questions. She covered topics ranging from IT contracts to the [NIEHS strategic plan](#).

According to Birnbaum, the strategic plan lays out some key areas for the future of environmental research. It contains 8 overarching themes, 11 goals, and 8 NIEHS cross-divisional implementation groups.

“These areas have lots of parts, and lots of people at the Institute are already interested in them,” explained Birnbaum.

She also highlighted the effects of early life exposures on long-term health, the concept of multiple exposures, and the science of the microbiome, as hot areas in environmental health research.

## New career development opportunities

The meeting continued with Collins and Tracy Clement, Ph.D., of the NIEHS [Gamete Biology Group](#), outlining new career development programs for NIEHS fellows. The OFCD provides fellows with the necessary skills and career development opportunities for future careers. It hosts a number of events ranging from workshops, to courses, to networking events. This year, Collins is beginning a program called Scientific Career Tracks.

“The objective of the program is to raise awareness of what the available careers are, and to provide real knowledge of what getting into those careers entails,” Collins said.

Collins plans to form a committee of volunteers that will work on the program, to provide a framework for career planning and create a central hub of career resources.

Complementing this program, Clement has developed a program called Enhancing Local Industry Transitions Through Exploration (ELITE), which is modeled in part from the Postdoc Industry Exploration Program founded at the University of California, Berkeley.

“The goal of the program is to help NIEHS fellows explore industry careers through on-site visits,” said Clement. “On these visits, fellows can learn about careers in industry, and network with industry scientists.”

## Ways for NIEHS postdocs to get involved

Rachel Goldsmith, Ph.D., the new [NIEHS Trainees Assembly \(NTA\)](#) president, ended the meeting by describing the activities of the assembly. The NTA, led by a steering committee of volunteers, represents the trainees to the NIEHS administration, as well as national and state committees; works with the OFCD to plan career development activities; and plans social events, such as the Fellows' Coffee Hour.



*Birnbaum answered questions about events happening at NIEHS, and the future of environmental research. (Photo courtesy of Steve McCaw)*



*Before Collins took over as director of the OFCD, she was a postdoc in the NIEHS Laboratory of Molecular Genetics, working with William Copeland, Ph.D., head of the Mitochondrial DNA Replication Group. (Photo courtesy of Steve McCaw)*

The OFCD and NTA also arranged a trivia competition following the general assembly meeting. Ten teams participated in a lively competition that has become a tradition among NIEHS fellows.

After trivia, postdocs and their families enjoyed a picnic sponsored by NIEHS lead researchers. It was a great way to end the day's celebration.



*Goldsmith is an Intramural Research Training Award fellow in the NIEHS Biomolecular Screening Branch. (Photo courtesy of Steve McCaw)*



*Raja Jothi, Ph.D., of the NIEHS Laboratory of Molecular Carcinogenesis, right, and his postdocs Senthilkumar Cinghu, Ph.D., left, and Andrew Oldfield, Ph.D., work together to answer a question during the trivia contest. (Photo courtesy of Steve McCaw)*



*The Institute celebrated all of its postdoctoral fellows as part of National Postdoc Appreciation Week. (Photo courtesy of Steve McCaw)*

(Heather Franco, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Reproductive and Developmental Toxicology.)

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# Annual LSB retreat caps another successful year

By Raj Gosavi

The NIEHS Laboratory of Structural Biology (LSB) held its annual retreat Sept. 12-13 at the North Carolina Botanical Garden, part of the University of North Carolina at Chapel Hill (UNC-CH). More than 50 attended the event.

This year's event featured talks by academic speakers, and was structured to facilitate an exchange of ideas between the new and established investigators, and LSB trainees aspiring to become young investigators.

The speakers were selected to represent universities, rather than government organizations, which allowed them to share valuable insights into the role of lead researchers at academic institutions. The major contribution to the success of the retreat was that the speakers were some of the most outstanding structural biologists in the field of DNA repair and crystallography ([see text box](#)).

The structural biologists speaking at the retreat discussed a wide range of techniques of interest to NIEHS scientists, including X-ray crystallography, nuclear magnetic resonance, mass spectrometry, and small-angle X-ray scattering (SAXS). Additionally, several of the talks went beyond these techniques and highlighted exciting new findings in structural biology.

## From single molecule studies to ultra-rapid nanocrystallography

With the breathtaking pace of technological advances in the field, the possibility of looking at single molecules was bound to happen in a matter of time. Stephen Kowalczykowski, Ph.D., from the University of California, Davis (UCD), presented his work on the single molecular visualization studies of RecBCD, a processive DNA helicase that unwinds and degrades DNA. Kowalczykowski's team engineered a system that allows them to track the movement and activity of a single molecule of RecBCD on a single DNA molecule.

"I didn't think that, in my lifetime, not only would it be possible to watch a single DNA, but also to watch a single enzyme on DNA," Kowalczykowski said.

In the discussion of another single molecule study, Dorothy Erie, Ph.D., from UNC-CH, described the use of atomic force microscopy, as well as single molecule fluorescence studies, to show the interaction between DNA and the mismatch repair protein MutS.



*NIEHS senior researcher Samuel Wilson, M.D., who headed up the retreat organizing committee, was generous in thanking the entire committee for the retreat's success. "LSB retreats provide an intense scientific experience for all the attendees every year," he said. (Photo courtesy of Steve McCaw)*



*Eichman's talk discussed his study on "Structural studies of replication fork regression by DNA damage response protein SMARCAL1," which utilized a combination of X-ray crystallography and SAXS to obtain important insights into the process. (Photo courtesy of Steve McCaw)*

New work that has the potential to change the way people think about X-ray crystallography was presented by Petra Fromme, Ph.D., from Arizona State University (ASU). Fromme talked about recent developments in the new area of femtosecond, or one-quadrillionth of a second, X-ray diffraction nanocrystallography, to obtain structures of challenging proteins, such as membrane proteins. With 12 times more intense X-rays, as compared to standard X-ray crystallography, she explained, there is no longer a need to grow large protein crystals, which had been a bottleneck in structural studies.

### Poster flashes and ask the experts

LSB retreat organizers used certain activities to vary the pace of the meeting. One of them, the poster flash slide exercise, was introduced at last year's LSB retreat. The exercise involves talking for one minute on a single slide, in a way that captures the essence of the poster and stimulates some playful banter among participants. This activity not only encourages creativity on the part of the presenter, but also provides a perfect platform for interaction at the poster.

Something new in the retreat was the Ask the Experts session. This activity took advantage of the speakers' background experiences and involved them in discussions with the retreat attendees on topics ranging from how to formulate a good research project to getting the work published and the role of collaborators — topics that aren't usually a part of a research presentation.



*Both Erie, left, and Ellenberger stressed the importance of communication in collaborative projects, and shared their thoughts on how to initiate and complete research projects. (Photo courtesy of Steve McCaw)*



*Fromme, who had proteins crystallized in a space shuttle, said she thinks this is an exciting time for structural biology. She remarked that, with future advances in instrumentation, femtosecond nanocrystallography can even eradicate the phase problem, which often slows crystallographers. (Photo courtesy of Steve McCaw)*



*Beese's talk on "Conformational changes that drive the human DNA mismatch repair machinery" highlighted the application of structural biology to her challenging projects. (Photo courtesy of Steve McCaw)*

Emphasizing the importance of keeping an open mind on the use of a variety of techniques and collaboration, Brandt Eichman, Ph.D., from Vanderbilt University, said, “It is important to utilize whatever technique is possible to get the required answer, and use a combination of structural biology techniques, as required.”

Similarly, Lorena Beese, Ph.D., from Duke University, encouraged better cross-communication between structural biologists and other disciplines, to formulate stronger and more meaningful collaborations.



*Ramsden provided a great example of efficient collaborative research from his several successful collaborations at the NIEHS. (Photo courtesy of Steve McCaw)*

(Raj Gosavi, Ph.D., is a research fellow in the NIEHS Structure and Function Research Group.)

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## Speakers at the LSB retreat

**Dale Ramsden, Ph.D.** — Professor of biochemistry and biophysics at UNC-CH. Research interests: V(D)J recombination and double strand break repair.

**Stephen Kowalczykowski, Ph.D.** — Distinguished professor of microbiology and molecular genetics, and of molecular and cellular biology at UCD. Research interests: Molecular mechanism of genetic recombination and biochemistry of DNA helicases.

**Brandt Eichman, Ph.D.** — Associate professor of biological sciences, and of biochemistry in the Department of Biological Sciences at Vanderbilt. Research interests: Structural biology of DNA repair and replication machinery.

**Lorena Beese, Ph.D.** — James B. Duke Professor of Biochemistry in the Duke University School of Medicine. Research interests: Structural biology of DNA replication and mismatch repair systems, as well as signal transduction proteins.

**Tom Ellenberger, Ph.D.** — Professor of biochemistry and molecular biophysics at the Washington University School of Medicine. Research interests: Investigating the molecular structures and cellular functions of proteins that replicate DNA, repair chemical damage, and regulate chromatin structure.

**Petra Fromme, Ph.D.** — Professor in the Department of Chemistry and Biochemistry at ASU. Research interests: Structural biochemistry and biophysics of membrane proteins.

**Dorothy Erie, Ph.D.** — Professor in the Department of Chemistry at UNC-CH. Research interests: Atomic force microscopy and fluorescence studies of protein-protein and protein-nucleic acid interactions in DNA mismatch repair.

# Superfund research grantee honored by American Chemical Society

By Sara Mishamandani

Louisiana State University (LSU) chemist and Superfund Research Program (SRP) Center Director Barry Dellinger, Ph.D., has been awarded the 2014 American Chemical Society (ACS) [Award](#) for Creative Advances in Environmental Science and Technology, sponsored by the ACS Division of Environmental Chemistry and the ACS Publications journal Environmental Science and Technology. [Dellinger](#) will receive the honor for his pioneering research on the sources, origin, and environmental chemistry of combustion-generated polychlorinated dibenzo-p-dioxins (PCDD) and polychlorinated dibenzofurans (PCDF).

The award is based on nominations of fellow scientists and further vote from the ACS Nomination Committee, and is meant to encourage creativity in research and technology, to provide a scientific basis for informed environmental decision-making or to provide practical technologies that will reduce health risk factors. Dellinger will receive the award at a ceremony March 18, 2014, in conjunction with the 247th ACS National Meeting and Exposition in Dallas.



*Dellinger is also the Patrick F. Taylor Chair of Environmental Chemistry at LSU. (Photo courtesy of Barry Dellinger and LSU)*

## Understanding the mechanisms of toxic combustion byproducts

Dellinger's research focuses on the environmental aspects of combustion. Although combustion and industrial thermal processes are essential to everyday life, they can produce a myriad of harmful pollutants. PCDD and PCDF are particularly toxic combustion byproducts, inducing tumors and birth defects in human populations.

“While the biomedical research community is hard at work understanding the health impacts of pollution, and the engineering community is developing methods for pollution control, surprisingly little is known about the mechanisms of formation of combustion-generated pollutants,” said Dellinger. “Our research places pollution prevention on a sound scientific basis, and provides a critical interface between engineering and biomedical research.”

Dellinger's team is determining how chemicals adsorb on various surfaces and form dioxins, and is studying the role of transition metals in the formation of dioxins. As an outgrowth of this research, Dellinger is also actively engaged in the development of innovative catalysts for destruction of toxic chlorinated hydrocarbons formed in combustion processes when chlorine is present.

## SRP work on environmentally persistent free radicals

The LSU SRP center focuses on newly identified pollutant-particle systems and environmentally persistent free radicals (EPFRs), which may form from the combination of pollutants and particulate matter.

EPFRs form in combustion and thermal processes, including hazardous waste incineration and diesel combustion. These processes create particulate matter (PM), tiny air pollution particles only detectable with an electron microscope. PM<sub>2.5</sub>, classified as fine PM, is 2.5-0.1 micrometers in diameter, which provides the perfect binding surface for EPFR formation. EPFR attachment to PM allows the EPFR to persist much longer than a typical free radical.

“In collaboration with the biomedical and engineering communities, we are working to determine the actual mechanism of biological activity, the source of these radicals, and their atmospheric chemistry,” said Dellinger.

Particles in the PM2.5 range can reach deep into the respiratory tract. Dellinger and his research group demonstrated that, when inhaled, EPFR on the PM2.5 scale generates reactive oxygen species (ROS) that result in DNA strand breakage. These breaks can result in development of various cancers and cardiovascular disease.

Dellinger’s team recently revealed the various ways EPFRs decay in the environment. In a [study](#) published in the journal *Environmental Science and Technology*, Dellinger also associated the amount of radical measured in PM2.5 to cigarette smoke, suggesting that inhaling air polluted by PM2.5 may equate to smoking 0.3-0.9 cigarettes a day in the United States, depending on residence. The cumulative effect of breathing this type of air pollution may negatively impact human health.

(Sara Mishamandani is a research and communication specialist for MDB Inc., a contractor for the NIEHS Superfund Research Program and Division of Extramural Research and Training.)

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## Former NIEHS postdoctoral fellows obtain NIH funding

*By Aleksandra Adomas*

Former NIEHS trainees Archana Dhasarathy, Ph.D., and Sergei Nechaev, Ph.D., along with collaborators from the University of North Dakota (UND), secured a \$10.5 million NIH grant to advance their research programs. Over the next five years, the award will fund the UND Institutional Development Award (IDeA) [Center of Biomedical Research Excellence \(COBRE\)](#) in the Epigenomics of Development and Disease. IDeA COBREs are thematic, multidisciplinary programs that augment and strengthen an institution’s biomedical research capacity.

### Grant writing skills

Dhasarathy and Nechaev left NIEHS in December 2011 to start their tenure-track careers as independent investigators at the UND School of Medicine and Health Sciences ([see story](#)). They were appointed in January 2012, and were able to finalize the writing of the grant proposal by the February 2012 deadline.

Dhasarathy found her experience with competing for an NIH Pathway to Independence Award, also known as K99, invaluable, while writing the COBRE proposal. She recalled the support and help she received from William Schrader, Ph.D., NIEHS Deputy Scientific Director, and her mentor, Paul Wade, Ph.D., head of the NIEHS Eukaryotic Transcriptional Regulation Group, while working on the K99.

“Bill [Schrader] was as disappointed as I was, when the grant wasn’t funded,” Dhasarathy said, “but, I was able to resubmit it with few edits, and it got great reviews.”



*“We have an exciting couple of years ahead,” Dhasarathy said, as she looks forward to future work at the UND center. (Photo courtesy of Wanda Weber, UND)*

The COBRE grant proposal that Dhasarathy and Nechaev wrote with three other junior faculty members at UND, received enthusiastic reviews and an outstanding score. However, federal budget sequestration delayed NIH funding decisions, and the grant was not approved until this past August, a year later than expected.

## Road to independence

Epigenetics/epigenomics is a fairly new research area at UND, and the COBRE grant will help the epigenetics research working group, established in 2010, create infrastructure. The funding will support generation, analysis, and management of next-generation sequencing data; acquisition of a sequencing instrument; and hiring of bioinformatic personnel. It will also create room for a few new investigators that UND hopes to bring on board in the coming years.

Dhasarathy and Nechaev's objective will be to generate results and publications that lead to their own independent funding (see text box). Dhasarathy is a chromatin expert, and will continue the line of research she initiated with Wade. She is interested in two transcription factors, Snail and Slug, and deciphering their role in cancer metastasis.

Nechaev focuses on answering the broad question of how alternative gene expression programs can be encoded in a genome that is shared by almost every cell in an organism. His hypothesis originates from his time in the NIEHS Transcriptional Responses to the Environment Group and work done with lead researcher Karen Adelman, Ph.D. Nechaev believes that the transcriptional enzyme, RNA polymerase II, plays a major role in this cell-type specific gene activation, through a phenomenon called pausing.

Nechaev loves his new life at UND, and thinks that the camaraderie among the staff will help propel the university's image as a place for good science.

"I have been pleasantly surprised by the cordial atmosphere at UND, and the interest in collaborations," Nechaev said. "Despite us being a relatively small-sized university, we have a very broad range of experts who are willing and eager to help."

During the past year and a half, Dhasarathy and Nechaev have woven themselves into the fabric of academic life at UND. In one example, Dhasarathy co-organized the first and second [UND Epigenetics and Epigenomics Symposia](#). She said organizing the meeting was the best way to stay abreast of cutting-edge research in human development and disease, and to promote interactions with national epigenetic experts.

(Aleksandra Adomas, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Carcinogenesis.)



*Nechaev said of his professional ambition, "My personal goal is to answer scientific questions that I have been asking, while moving the field forward to the best of my ability." (Photo courtesy of Wanda Weber, UND)*

## Challenges faced by new independent investigators

Dhasarathy and Nechaev agree that the first year as a tenure-track professor can be challenging, with setting up the laboratory space, starting experiments, and selecting people to work in their groups.

"The schedule of an assistant professor is full, with multiple little tasks, which may or may not have to do with science, but still need your attention," Nechaev pointed out. "It is becoming harder to dedicate time to research, but this is compensated by students in my lab that can plan and do experiments independently."

Dhasarathy agreed and said, "I've been very fortunate, so far, to work with four extremely talented undergraduates, and now the grant funding will help bring in good graduate and postdoctoral students."

# New insight into how neonatal exposure to DES affects uterus function in mice

By Robin Mackar

NIEHS in-house researchers are well known for their work on diethylstilbestrol (DES). Continuing in that tradition, a new [study](#) finds that mice exposed briefly to DES, a synthetic form of the female hormone estrogen, immediately after birth, had abnormal expression of the sine oculis homeobox 1 (Six1) gene in the uterus when they became adults.

The study, published in the October issue of *Molecular Endocrinology*, is the result of collaborative work between the Laboratory of Reproductive and Developmental Toxicology (LRDT) and the Laboratory of Molecular Carcinogenesis (LMC).

“DES exposure, just after birth, caused changes in specific epigenetic marks that regulate how genes are expressed in the uterus,” said Carmen Williams, M.D., Ph.D., head of the LRDT [Reproductive Medicine Group](#) and lead researcher on the study. “Some of these epigenetic changes persisted long after exposure,” Williams noted.

## Epigenetic changes

Epigenetic changes mean that the underlying DNA sequence remains normal, but gene expression has been modified.

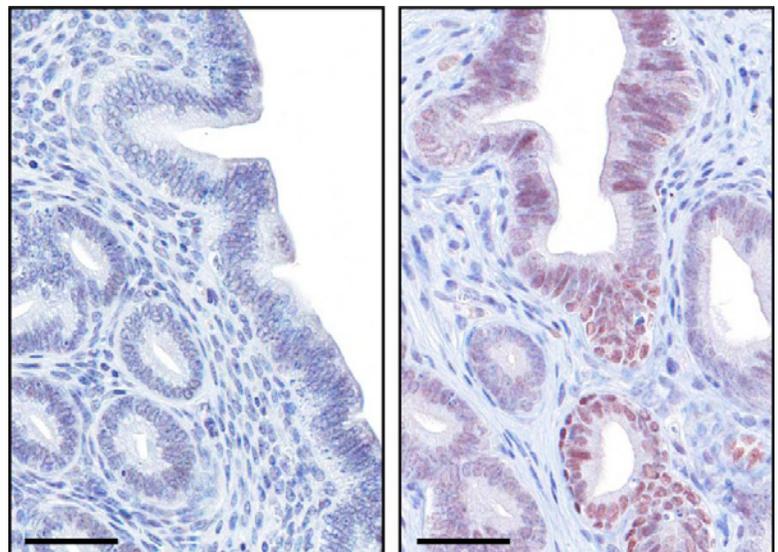
In this case, the epigenetic changes were observed in a gene called Six1. Very little is known about how Six1 is regulated. “In humans the Six1 gene is associated with several types of cancers, including breast and cervix cancers,” said Wendy Jefferson, Ph.D., a biologist in the Reproductive Medicine Group and first author on the paper.

DES was found to change the specific histone modifications that are associated with Six1 gene-regulatory regions functioning in the adult uterus. The particular histone modification changes found are typical of genes that are actively generating proteins. Persistence of the epigenetic changes probably explains why the Six1 protein is abnormally expressed in the uterus of older adult mice, when it normally is not there.

“These findings suggest that epigenetic changes, induced by early life exposures to estrogenic compounds, may explain the long-term effects of this exposure on fertility and the later development of cancer,” Williams said.



Jefferson has been working with Retha Newbold, formerly with NIEHS, and others, to understand the effects of DES. She has authored many papers on the topic. (Photo courtesy of Steve McCaw)



**Control**

**DES**

This image from the journal clearly shows the expression of Six1 (brown staining) in the uterine epithelial cells of adult mice that were treated for 5 days, after birth, with DES.

As a follow up to these animal studies, the researchers are collaborating with [Victoria Bae-Jump, M.D., Ph.D.](#), and her colleagues at the University of North Carolina at Chapel Hill Lineberger Comprehensive Cancer Center, to determine if Six1 expression is abnormal in the uterus of women with endometrial cancer.

DES was prescribed to millions of pregnant women between 1940 and 1971 to prevent miscarriage, premature deliveries, and other complications. Clinical studies found DES to be ineffective for these purposes and it is no longer prescribed. However, ongoing research by NIH and others continues to investigate the long-term health consequences associated with exposure to DES.

*Citation:* [Jefferson WN, Chevalier DM, Phelps JY, Cantor AM, Padilla-Banks E, Newbold RR, Archer TK, Kinyamu HK, Williams CJ.](#) 2013. Persistently altered epigenetic marks in the mouse uterus after neonatal estrogen exposure. *Mol Endocrinol* 27(10):1666-1677.

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

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*Williams, who heads the Reproductive Medicine Group, uses her skill set as a physician-scientist to better understand the link between environmental exposures and reproductive health problems. Members of her group collaborated with scientists in the LMC [Chromatin, Epigenetics, and Expression Group](#) headed by lead researcher and LMC Chief Trevor Archer, Ph.D. (Photo courtesy of Steve McCaw)*

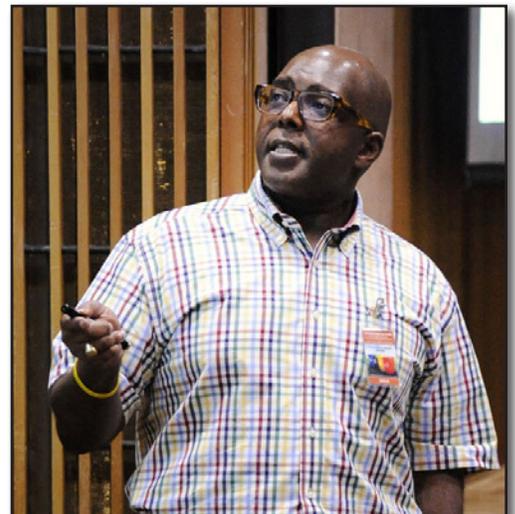
## Penn State professor explores consequences of non-regulated mitochondrial transcription

*By Deepa Singh*

Pennsylvania State University Professor [Craig Cameron, Ph.D.](#), spoke Sept. 23 at NIEHS on “Human Mitochondrial Transcription.” Hosted by Matthew Young, Ph.D., the talk was the final seminar in the 2013 Laboratory of Molecular Genetics Fellows Invited Guest Lecture Series.

The talk focused on the importance and function of the highly variable noncoding sequences of mitochondrial DNA in transcription regulation. “There might be a link between the changes in the noncoding sequences variability, which is seen in human populations, and diseases caused due to mitochondrial dysfunction,” said Cameron, who holds a number of patents, and has served as a consultant for several pharmaceutical companies in the development of vaccines for viral diseases.

Mitochondria, also known as the powerhouse of the cell, are important for a wide range of cellular processes. Therefore, mitochondrial dysfunction can cause various metabolic, degenerative, and age-related



*Cameron has received several awards from the Penn State Eberly College of Science, including his appointment earlier this year as the Eberly Chair in Biochemistry and Molecular Biology. He has also received the American Heart Association Established Investigator Award. (Photo courtesy of Steve McCaw)*

diseases. According to Cameron, better understanding mitochondrial transcription and how to influence it might lead to the discovery of more effective drugs for treating these diseases.

### **Inhibiting mitochondrial RNA polymerase**

The research in Cameron's lab focuses on the development of strategies to treat and prevent infections by RNA viruses. Currently, viral infections are treated with the use of antiviral ribonucleosides, with a synthetic base replacing the normal base. The idea behind this strategy is that the viral RNA polymerase promiscuously incorporates these synthetic compounds into nascent RNA, terminating viral RNA synthesis.

Cameron's lab contributed to this idea by showing that these antiviral ribonucleosides are RNA virus mutagens and were, in fact, increasing the number of mutations per genome, thus causing a genetic meltdown of the virus population. However, because of their adverse toxic effects on patients, none of these compounds survived all three phases of clinical trials.

Cameron's group later discovered that the human mitochondrial RNA polymerase (POLRMT) was an off-target for these antiviral ribonucleosides, and they were unknowingly inhibiting mitochondrial transcription as well. "These studies are beneficial for the antiviral drug discovery industry, since it demands ribonucleoside analogs that are substrates for the viral RNA polymerase and not for the POLRMT, as the safest and most efficient way of treating RNA virus infections," he said.



*Matthew Young, Ph.D., visiting fellow in the Mitochondrial DNA Replication Group, was host of the talk and shared Cameron's interest in the field of mechanisms of mitochondrial dysfunction that could lead to various diseases. (Photo courtesy of Steve McCaw)*

### **Misregulation implicated in a range of human diseases, including cancer**

Cameron also discussed his lab's contribution to the existing knowledge of the mitochondrial transcription machinery. It is known that the human mitochondrial genome encodes 13 proteins involved in the electron transport chain, on two different intensity strands — the heavy strand and the light strand. It was previously believed that transcription starts from two sites, known as the light strand promoter (LSP) and heavy strand promoter (HSP).

However, Cameron presented compelling evidence to show that transcription can be initiated from three sites in human mitochondrial DNA, consistent with the presence of three promoters (LSP, HSP1 and HSP2). Initiation from each promoter exhibits unique factor requirements implying the existence of regulated transcription in the cell. He explained, "The majority of the noncoding region between the light and the heavy strand promoter contributes to the transcription regulation, perhaps providing a link between misregulated transcription and disease."



*William Copeland, Ph.D., front, chief of the Laboratory of Molecular Genetics and head of the Mitochondrial DNA Replication group, led the discussion following Cameron's talk. (Photo courtesy of Steve McCaw)*

Despite insights from new investigations by his group, Cameron recognizes how much remains to be understood about mitochondrial transcription. “These are really the early days of this [research]. ... There really is a lot of regulation yet to be discovered.” Cameron closed his talk with an appeal to the NIH intramural community to expand its research efforts in this area.

(Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Mechanisms of Mutation Group.)

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## NTP postdoc takes top prize at NCSOT meeting

*By Eddy Ball*

The [North Carolina Chapter of the Society of Toxicology \(NCSOT\)](#) held its annual fall meeting and awards ceremony for postdoctoral fellows Oct. 24 at NIEHS. The event featured presentations on the meeting theme, “From the Mountains to the Coast: Environmental Toxicology Research in North Carolina,” by specialists from universities across the state.

Chaired by East Carolina University (ECU) toxicologist Jamie DeWitt, Ph.D., the meeting opened with presentation of the group’s President’s Award for Research Competition (PARC) to three area postdoctoral fellows, with first-place going [Yuanyuan \(Laura\) Xu, Ph.D.](#), a visiting fellow in the NTP Laboratories Inorganic Toxicology Group, headed by lead researcher Michael Waalkes, Ph.D.

In her winning abstract, Xu reported findings from a study on the contribution of inorganic arsenic exposure to the development of an important subset of breast cancers ([see text box](#)). Xu’s award, her second PARC first place, included a monetary award and a place on the program.

Two postdoctoral fellows at the U.S. Environmental Protection Agency tied for second place. Samantha Snow, Ph.D., and Yong Ho Kim, Ph.D., also received cash prizes.

The main program, organized by chapter vice-president Christie Sayes, Ph.D., consisted of three talks on environmental health and ecological issues with specific relevance for the state of North Carolina. “We’re branching a little away from the lab,” DeWitt said of the program. “We went from the mountains with trees, to the coast with hurricanes, and finally to the piedmont and bees.”

### Environmental sustainability in Western Carolina

Western Carolina University forest ecology professor and Associate Dean of the Graduate School [Brian Kloepfel, Ph.D.](#), gave the first presentation, which focused on watershed science. Kloepfel described natural and manmade changes to watersheds that impact the quantity and quality of the groundwater that makes up 96 percent of drinking water in the southeastern U.S.



*Unfortunately, Xu was unable to attend the meeting and make the oral presentation that was part of her first prize win. Her colleague, NTP biologist Erik Tokar, Ph.D., accepted the award plaque on her behalf. (Photo courtesy of Steve McCaw)*

According to Kloeppe, the combination of the upward temperature trend over the past 36 years and the devastation of the hemlock forest canopy over streams in western North Carolina through infestation by the woolly adelgid have resulted in higher water temperatures. Warmer water temperature in turn changes evaporation rates and makes water more hospitable to bacteria, with a potential impact on human health.

### Coastal preservation in Eastern Carolina

Turning to the other end of the state, ECU organic geochemist [Siddhartha Mitra, Ph.D.](#), presented findings from his research on air and water quality. Mitra opened with a discussion of hurricanes and tropical storms and the transport of dissolved black and organic carbons in rainwater.

In one of his especially telling experiments, Mitra and colleagues measured the dramatic spike in carbon and oil-derived hydrocarbons in the wake of Tropical Storm Bonnie in 2010, which swept across the Gulf of Mexico following the Deepwater Horizon oil spill and dumped polluted rainwater on interior Louisiana. He said post-Bonnie air quality was comparable to conditions in the inner city.

### Carolina insect colony collapse

Although air and water quality can make headlines, the focus of studies by North Carolina State University professor [David Tarp, Ph.D.](#), has even made it into the tabloids and onto talk radio. The mysterious honeybee colony collapse disorder (CCD) became news in 2006 and inspired a media hysteria that has highlighted speculation about the causes.

After joking about some of the wilder notions — blaming CCD on divine rapture, terrorism, or a Russian plot — Tarp suggested it's far more likely that a combination of factors is behind the sudden depopulation of hives. He said current studies are looking at how such factors as nutritional stress from transport; parasites and pathogens; and the complex chemical environment of beehives might work in synergy to alter bee behavior so suddenly and inexplicably that entire colonies disappear without a trace.



During her report on chapter activities since the spring meeting and upcoming plans, DeWitt described NCSOT as one of the Society's most active chapters and one of its largest. Of its 428 members, 61 are postdocs and 82 are students. "I think that's phenomenal," DeWitt said. (Photo courtesy of Steve McCaw)



PARC winners Snow, left, and Kim listened as DeWitt described the rigorous competition and the vote that resulted in a rare tie this year for second place. (Photo courtesy of Steve McCaw)



Tokar, right, was a coauthor on Xu's paper and a first-place PARC winner as a postdoctoral fellow in 2008 and 2009. (Photo courtesy of Steve McCaw)



*Kloepfel argued that an adequate supply of clean water is essential to sustainability. The best way to achieve that goal, he said, is through preventive maintenance of the distant forest and valleys that constitute the watershed. (Photo courtesy of Steve McCaw)*



*Mitra also presented findings from a study of onsite waste treatment systems as a potential source of pharmaceutical and personal care product pollution in water in eastern N.C. An estimated 85 percent of houses there are on septic systems and use wells for their water supply. (Photo courtesy of Steve McCaw)*



*“The ratio of chatter to data here is about a billion to one,” Tarpy said of the rampant — and sometimes off the wall — speculation about what is causing CCD. (Photo courtesy of Steve McCaw)*



*As this reaction to one of Tarpy’s quips by EPA biophysicist Carl Blackman, Ph.D., made clear, people in the audience were both edified and entertained by the dynamic speakers and the distinctive program. (Photo courtesy of Steve McCaw)*

## Making the connection between arsenic and breast cancer

For her prize-winning research Xu built upon previous data suggesting that arsenic may be an endocrine disruptor and the association some studies have found between arsenic exposure and breast cancer.

Through a series of experiments using the normal, estrogen receptor (ER)-negative breast epithelial cell line, MCF-10A, she and her colleagues built a convincing argument that arsenic induces an oncogenic phenotype and pinpointed a novel mechanism to explain the outcome through activation of aromatase.

The team subjected MCF-10A cells to continuous low level exposure to sodium arsenite over a 24-week period, producing what the researchers described as arsenic-transformed breast epithelial (ATBE) cells. They then compared ATBE to untreated control cells.

Xu reported significant to dramatic differences between ATBE and control cells for indices of oncogenicity and expression of critical genes relevant to breast cancer cells. ATBE cells showed increases over controls in colony formation (190 percent), secreted metalloproteinase (400 percent for MMP-9 and 290 percent for MMP-2), and proliferation rate (120 percent).

Expression of the tumor suppression genes p53 and PTEN was lowered by as much as 50 percent in ATBE cells. Other molecular markers and gene expression patterns for cancer cells were significantly abnormal compared to controls.

The researchers also observed widespread aromatase overexpression and marked increase in 17beta-estradiol, and established that the aromatase inhibitor letrozole was able to abolish 17beta estradiol increases and reverse the arsenic-induced oncogenic phenotype. The experiments provided evidence of transformation of breast epithelia through a process independent of ER, a process, they said, not previously considered.

*Citation:* Xu Y, Tokar EJ, Waalkes MP. 2013. Arsenic induces an oncogenic phenotype in human breast epithelia through an estrogen-receptor independent pathway by aromatase activation. NCSOT PARC abstract.

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## Upcoming GEMS meeting on cancer prevention and cure

*By Eddy Ball*

The Genetics and Environmental Mutagenesis Society (GEMS), based near NIEHS in Research Triangle Park, N.C., will hold its annual fall meeting Nov. 14 at the Sheraton Imperial Hotel in Durham. The group has posted its [agenda](#) and is currently accepting [registrations](#), with discount fees for GEMS members and students.

The theme of the meeting is “Exploiting the DNA Damage Response to Prevent and Cure Cancer.” Along with its three invited speakers, the meeting will feature posters and talks by lab scientists, and student competitions for best posters and best talk.

The featured speakers are distinguished faculty from major biomedical research centers in North Carolina.

- “Control of DNA Repair and Cancer by the Circadian Clock,” by [Aziz Sancar, M.D., Ph.D.](#), of the University of North Carolina at Chapel Hill (UNC) School of Medicine
- “Potentiating Top1 Poisons by Modulating the DNA Damage: New Strategies for AML Treatment,” by [William Gmeiner, Ph.D.](#), of the Wake Forest University School of Medicine
- “DNA Damage Responses: Bedside to Bench to Bedside,” by [Michael Kastan, M.D., Ph.D.](#), of the Duke University Cancer Institute

GEMS is celebrating its 31st anniversary this year, with an integrated pair of workshops on the mechanisms of cancer ([see story](#)), organized and hosted by President-elect William Kaufmann, Ph.D., of UNC. President Tom Hughes, of the U.S. Environmental Protection Agency, will lead a business meeting that will conclude the day’s proceedings.

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## This month in EHP

The current issue of [Environmental Health Perspectives \(EHP\)](#), published Oct. 1, highlights the transgenerational impacts of chemical exposure and the Minamata Convention on Mercury. Because of the interruption in government operations last month, EHP will publish its combined November-December issue Dec. 2.



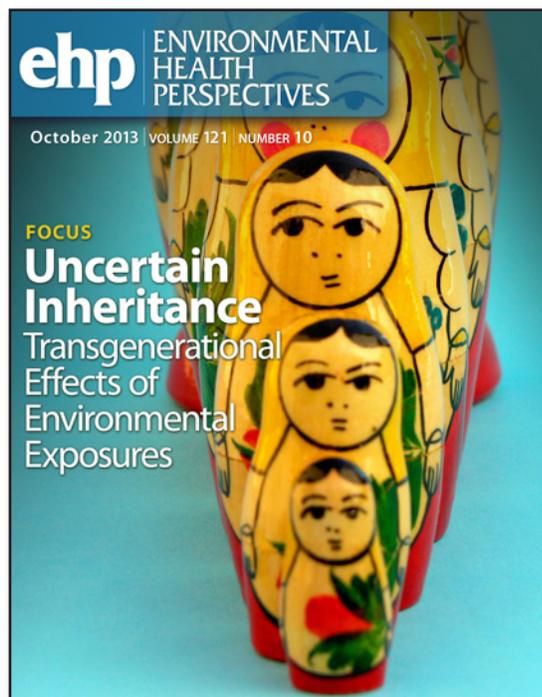
<http://twitter.com/ehponline>

### Uncertain Inheritance: Transgenerational Effects of Environmental Exposures

Several researchers have reported transgenerational effects in animals exposed to a number of chemicals, including permethrin, DEET, bisphenol A, several phthalates, dioxin, jet fuel mixtures, nicotine, and tributyltin, among others. Although no data yet exist for adverse effects in the great-grandchildren of exposed humans, several studies have documented multigenerational chemical impacts. The new findings are spurring a reevaluation of how scientists perceive environmental health threats, but how environmental exposures cause multigenerational and transgenerational effects remain unclear.

### The Minamata Convention on Mercury: A First Step Toward Protecting Future Generations

The Minamata disaster, the first large-scale incident of methylmercury poisoning, drew the world’s attention to the devastating effects of this powerful neurotoxicant, now known to be particularly dangerous to fetuses, infants, and young children. In October 2013, a new legally-binding instrument for the global



control of mercury pollution will be opened for signature at a diplomatic conference in Japan. Named the Minamata Convention on Mercury, the agreement is a response to the realization that mercury pollution is a global problem that no one country can solve alone.

### Featured research and related news articles this month include:

**Projected Impacts of Climate Change on Environmental Suitability for Malaria Transmission in West Africa** — A New Breed of Model: Estimating the Impact of Climate Change on Malaria Transmission

**Bulky DNA Adducts in Cord Blood, Maternal Fruit-and-Vegetable Consumption, and Birth Weight in a European Mother-Child Study (NewGeneris)** — Prenatal Protection? Maternal Diet and Bulky DNA Adducts

**Early Life Arsenic Exposure and Acute and Long-term Responses to Influenza A Infection in Mice** — Arsenic Handicap? Prenatal Exposure Worsens Influenza Infections in Young Mice

**Mimicking of Estradiol Binding by Flame Retardants and Their Metabolites: A Crystallographic Analysis** — Mechanism for Mimicry: Study Demonstrates How Flame Retardants Bind Key Protein

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## Extramural papers of the month

*By Nancy Lamontagne*

- [DNA methylation in the human genome](#)
- [Genome-wide sequencing links aristolochic acid to cancer](#)
- [A better understanding of tissue growth and repair](#)
- [BPA linked with obesity in children](#)
- [Prenatal nitrate exposure and birth defects](#)
- [Mechanism for amyloid-beta accumulation in Alzheimer's disease](#)
- [PBDE levels decrease in pregnant women after ban](#)
- [DNA methylation in children](#)

Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

## DNA methylation in the human genome

DNA methylation regulates the expression of genes that guide development and define cell types. In mammals, 70 to 80 percent of all cytidine-phosphate-guanosine (CpG) dinucleotides are methylated, but NIEHS-supported researchers report evidence that only a fraction of these CpGs likely participate in genome regulation in a developmental context. The DNA methylation signatures, called differentially methylated regions, that the researchers identified, can be used to guide new, more effective approaches that examine only the most informative portion of CpGs.

The researchers systematically investigated the DNA methylation of 42 whole-genome bisulphite sequencing data sets across 30 diverse human cell and tissue types. For cells and tissue undergoing normal development, they observed dynamic regulation for only 21.8 percent of autosomal CpGs. Genome-wide association studies showed that differentially methylated regions often contained single nucleotide polymorphisms associated with cancer and Alzheimer's disease. The investigators used their set of differentially methylated regions to correctly identify an unknown tissue sample and to classify the types of cells present in a heterogeneous sample.

*Citation:* Ziller MJ, Gu H, Müller F, Donaghey J, Tsai LT, Kohlbacher O, De Jager PL, Rosen ED, Bennett DA, Bernstein BE, Gnirke A, Meissner A. 2013. Charting a dynamic DNA methylation landscape of the human genome. *Nature* 500(7463):477-481.

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## Genome-wide sequencing links aristolochic acid to cancer

NIEHS grantees used genome-wide sequencing to identify a mutational signature of aristolochic acid that can link a person's cancer with exposure to the environmental mutagen. The research shows that genome-wide sequencing can be used to detect whether a person was exposed to carcinogens.

Aristolochic acid is found in *Aristolochia* plants, which have been used for medicinal purposes for more than 2,000 years. Recently, scientists discovered that consumption of the plants is associated with urothelial carcinoma of the upper urinary tract (UTUC). To determine the molecular signature of aristolochic acid in UTUC DNA, the researchers conducted exome sequencing of tumors from 19 individuals with documented exposure to aristolochic acid, and seven patients with no known exposure.

The analysis revealed an average of 753 mutations in each tumor in the aristolochic acid group, with 72 percent of the mutations being A:T-to-T:A transversions. For comparison, they found 91 mutations in tumors from the non-exposed group. The A:T-to-T:A mutational signature showed up frequently in oncogenes and tumor suppressor genes in UTUC tumors associated with aristolochic acid. The investigators also detected the aristolochic acid mutational signature in one patient's tumor from a UTUC cohort, without previous indication of aristolochic acid.

*Citation:* Hoang ML, Chen CH, Sidorenko VS, He J, Dickman KG, Yun BH, Moriya M, Niknafs N, Douville C, Karchin R, Turesky RJ, Pu YS, Vogelstein B, Papadopoulos N, Grollman AP, Kinzler KW, Rosenquist TA. 2013. Mutational signature of aristolochic acid exposure as revealed by whole-exome sequencing. *Sci Transl Med* 5(197):197ra102.

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## A better understanding of tissue growth and repair

NIEHS-supported work found that endothelial-derived epoxyeicosatrienoic acids (EETs) are critical in accelerating *in vivo* tissue growth. The findings could lead to new therapies for improving tissue repair and wound healing in the liver, lungs, and kidneys.

EETs are lipid mediators that regulate pain, inflammation, angiogenesis, and vascular tone. To better understand the role of these lipid mediators in tissue regeneration, the researchers used genetic and pharmacological tools to control endogenous EET levels in seven animal models — liver regeneration, kidney compensatory growth, lung compensatory growth, angiogenesis Matrigel plug assay, corneal micropocket assay, wound healing, and neonatal retinal vessel formation.

The investigators found that EETs accelerated tissue growth and organ regeneration during liver regeneration, kidney compensatory growth, lung compensatory growth, wound healing, corneal neovascularization, and retinal vascularization. They observed the same outcomes when they administered synthetic EETs and saw delayed tissue regeneration when EET levels were genetically or pharmacologically lowered. Soluble epoxide hydrolase inhibitors, which elevate endogenous EET levels, promoted liver and lung regeneration.

*Citation:* Panigrahy D, Kalish BT, Huang S, Bielenberg DR, Le HD, Yang J, Edin ML, Lee CR, Benny O, Mudge DK, Butterfield CE, Mammoto A, Mammoto T, Inceoglu B, Jenkins RL, Simpson MA, Akino T, Lih FB, Tomer KB, Ingber DE, Hammock BD, Falck JR, Manthati VL, Kaipainen A, D'Amore PA, Puder M, Zeldin DC, Kieran MW. 2013. Epoxyeicosanoids promote organ and tissue regeneration. *Proc Natl Acad Sci U S A* 110(33):13528-13533.

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## **BPA linked with obesity in children**

NIEHS-funded research found that higher levels of urinary bisphenol A (BPA) were associated with an increased risk for obesity in children participating in the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2010. The investigators did not find significant associations of BPA with any other chronic disease risk factors.

Children were classified into quartiles based on their urinary BPA levels (quartiles 1 to 4 = <1.3, 1.3-2.6, 2.6-4.9, and >4.9 nanograms/milliliter). The children with higher levels of BPA showed increased odds for obesity. Specifically, for quartiles 2 vs. 1, the odds ratio (OR) was 1.74, 95 percent confidence interval (CI) 1.17-2.60, P = .008; for quartiles 3 vs. 1, OR was 1.64, 95 percent and CI 1.09-2.47, P = .02; and for quartiles 4 vs. 1, OR was 2.01, 95 percent CI 1.36-2.98, P = .001. The same was true for having an abnormal waist circumference-to-height ratio: quartiles 2 vs. 1, OR 1.37, 95 percent CI 0.98-1.93, P = .07; quartiles 3 vs. 1, OR 1.41, 95 percent CI 1.07-1.87, P = .02; and quartiles 4 vs. 1, OR 1.55, 95 percent CI 1.12-2.15, P = .01. The researchers say that longitudinal analyses are needed to better understand the temporal relationships between BPA exposure and the development of obesity and chronic disease risk factors in children.

*Citation:* Eng DS, Lee JM, Gebremariam A, Meeker JD, Peterson K, Padmanabhan V. 2013. Bisphenol A and chronic disease risk factors in US children. *Pediatrics* 132(3):e637-e645.

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## **Prenatal nitrate exposure and birth defects**

With support from NIEHS, a large population-based, case-control study found that prenatal exposure to nitrate from drinking water was associated with certain birth defects. However, higher nitrate intake did not increase

associations between prenatal nitrosatable drug use and birth defects, suggesting that endogenous formation of nitrosatable compounds might not be the underlying mechanism for the birth defects.

Researchers used data from the National Birth Defects Prevention Study to link addresses of 3,300 case mothers and 1,121 control mothers in Iowa and Texas to public water supplies and nitrate measurements. Mothers of babies with spina bifida were twice as likely [95 percent confidence interval (CI): 1.3, 3.2] to ingest 5 milligrams (mg) or more of nitrate daily from drinking water versus control mothers, who consumed less than 0.91 mg of nitrate daily. From one month before conception through the first trimester, mothers of babies with limb deficiency were 1.8 times more likely than control mothers to ingest 5.42 mg. or more of nitrate daily (95 percent CI: 1.1, 3.1). The results for cleft palate and cleft lip for this time period were similar, with mothers 1.9 (95 percent CI: 1.2, 3.1) and 1.8 (95 percent CI: 1.1, 3.1) times more likely to ingest the high levels of nitrate, respectively.

The researchers concluded that future studies of birth defects could focus on prenatal exposure to mixtures of contaminants in drinking water, since nitrate contamination occurs with other water contaminants.

*Citation:* [Brender JD, Weyer PJ, Romitti PA, Mohanty BP, Shinde MU, Vuong AM, Sharkey JR, Dwivedi D, Horel SA, Kantamneni J, Huber JC, Zheng Q, Werler MM, Kelley KE, Griesenbeck JS, Zhan FB, Langlois PH, Suarez L, Canfield MA. 2013. Prenatal nitrate intake from drinking water and selected birth defects in offspring of participants in the National Birth Defects Prevention Study. Environ Health Perspect 121\(9\):1083-1089.](#)

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## Mechanism for amyloid-beta accumulation in Alzheimer's disease

An NIEHS grantee and colleagues report that low levels of copper can accumulate in the brain, leading to amyloid-beta plaques that are the hallmark of Alzheimer's disease. Researchers determined the molecular mechanisms by which copper accelerates Alzheimer's disease — information that could be useful for developing preventive and therapeutic approaches to control neurotoxic amyloid-beta levels in the aging brain.

Normal mice, a mouse model of Alzheimer's disease, and human cells were used to study copper-induced amyloid-beta accumulation in the brain. In normal aging mice, they found that copper accumulated in brain capillaries, and the accumulation was associated with a decrease in the amyloid-beta transporter known as low-density lipoprotein receptor-related protein 1 (LRP1), which normally removes amyloid-beta from the brain. The copper accumulation was also linked to higher brain amyloid-beta levels. In human brain endothelial cells, normal levels of copper caused LRP1 down-regulation. In the mouse model of Alzheimer's disease, copper accumulated in brain capillaries and, unlike in control mice, in the parenchyma. In these mice, copper not only down-regulated LRP1 in brain capillaries but also increased amyloid-beta production and neuroinflammation.

Overall, this work demonstrated that copper's effect on amyloid-beta homeostasis in the brain depends on whether it accumulates in capillaries or in the parenchyma.

*Citation:* [Singh I, Sagare AP, Coma M, Perlmutter D, Gelein R, Bell RD, Deane RJ, Zhong E, Parisi M, Ciszewski J, Kasper RT, Deane R. 2013. Low levels of copper disrupt brain amyloid-beta homeostasis by altering its production and clearance. Proc Natl Acad Sci U S A 110\(36\):14771-14776.](#)

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## PBDE levels decrease in pregnant women after ban

A new study, supported in part by NIEHS, found that levels of polybrominated diphenyl ether (PBDE) flame retardants in pregnant women have dropped since being banned in California and phased out of U.S. production in 2003-2004. The PBDE levels fell more quickly than expected, given the environmental persistence of these compounds.

The researchers previously studied pregnant women seen at San Francisco General Hospital in 2008-2009, finding that these women had PBDE concentrations that were among the highest in pregnant women, worldwide. For the new study, the researchers recruited 36 demographically similar women from the same clinic in 2011-2012. The scientists found that PBDE serum levels in the pregnant women had dropped by two-thirds since the 2008-2009 measurements. Specifically, adjusted least-squares geometric mean concentrations of PBDEs decreased 65 percent (95 percent CI: 18, 130) from 90.0 nanograms per gram (ng/g) lipid (95 percent CI: 64.7, 125.2) to 54.6 ng/g lipid (95 percent CI: 39.2, 76.2) ( $p = 0.004$ ). Also, PBDE metabolites, OH-PBDEs, decreased 6-fold ( $p < 0.0001$ ), and BDE-47, -99, and -100 declined more than BDE-153.

The researchers said that PBDE exposures likely declined because of regulatory action, and that their findings can be used to evaluate public policies and inform future public health interventions.

*Citation:* Zota AR, Linderholm L, Park JS, Petreas M, Guo T, Privalsky ML, Zoeller RT, Woodruff TJ. 2013. Temporal comparison of PBDEs, OH-PBDEs, PCBs, and OH-PCBs in the serum of second trimester pregnant women recruited from San Francisco General Hospital, California. *Environ Sci Technol* 47(20):11776-11784.

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## DNA methylation in children

In one of the first studies to look at DNA methylation changes in children, NIEHS grantees report that DNA methylation changes detected at birth persist through early childhood. Epigenetic changes such as DNA methylation can occur because of environmental and age-related factors, and are thought to be involved in the development of disease.

The researchers used an immunoassay to measure global DNA methylation in 165 children at birth (cord blood) and again at age 3. On average, DNA methylation was significantly higher in the 3-year-old children than at birth ( $p = 0.01$ ). However, for any individual child, the difference in methylation was less than would be expected by chance. They also found that the mother's BMI before pregnancy was negatively predictive of DNA methylation at birth and at age 3, even after the researchers accounted for the correlation between DNA methylation at the two time points.

Although the health impacts of small changes in DNA methylation aren't known, the researchers say their results imply that factors influencing DNA methylation during early childhood may have long-term effects. The findings also point to a need for more research on how factors, such as high BMI before pregnancy, could influence the trajectory of a child's health.

*Citation:* Herbstman JB, Wang S, Perera FP, Lederman SA, Vishnevetsky J, Rundle AG, Hoepner LA, Qu L, Tang D. 2013. Predictors and consequences of global DNA methylation in cord blood and at three years. *PLoS One* 8(9):e72824.

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

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## Intramural papers of the month

*By Aleksandra Adomas, Heather Franco, Mallikarjuna Metukuri, Bailey Schug, Deepa Singh, and Sheila Yong*

- [Assessing cockroach allergen exposure via its structure](#)
- [Study finds pregnancy length varies by up to five weeks](#)
- [Role of arginine in polymerase beta-catalyzed nucleotidyl transfer reactions](#)
- [Redundancy in DNA repair mechanisms protects cells from UV-induced DNA damage](#)
- [Crystal structures reveal how flame retardants may disrupt estrogen metabolism](#)
- [Probiotics use during pregnancy may reduce diseases in children](#)
- [Dermatomyositis shares genetic background with other autoimmune diseases](#)
- [Identification of novel immune regulatory elements and epigenetic plasticity in memory lymphocytes](#)

### Assessing cockroach allergen exposure via its structure

NIEHS scientists and their collaborators have obtained the crystal structure of the cockroach allergen Bla g 1. It is the first structure to be solved for this group of insect proteins. Determining the structure of Bla g 1 allows for the standardization of assays that measure it in absolute units.

The research team used recombinant protein rather than native Bla g 1, but comparisons using ELISA dose-response curves and antibody binding properties found that the Bla g 1 made by bacteria and the natural allergen were similar. Team members then solved the structure of Bla g 1 using X-ray crystallography, which revealed a novel fold with the capacity to bind various lipids.

Further analysis using mass spectrometry and nuclear magnetic resonance indicated that Bla g 1 could accommodate a variety of hydrophobic ligands that could be important for a variety of physiological purposes, including sensitizing humans. This finding correlated well with a digestive function in the cockroach, where Bla g 1 is associated with nutrient uptake.

Overall, the authors believe that this work would allow a better assessment of Bla g 1 exposure, which is important in evaluating new intervention strategies. Additionally, the structure may be useful in designing new immunotherapies. **(DS)**

*Citation:* [Mueller GA, Pedersen LC, Lih FB, Glesner J, Moon AF, Chapman MD, Tomer KB, London RE, Pomes A. 2013. The novel structure of the cockroach allergen Bla g 1 has implications for allergenicity and exposure assessment. J Allergy Clin Immunol; doi:10.1016/j.jaci.2013.06.014 \[Online 31 July 2013\].](#)

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## Study finds pregnancy length varies by up to five weeks

A recent study published by researchers in the NIEHS Epidemiology Branch found that the length of a normal human pregnancy can vary naturally by as much as five weeks. The researchers gathered information from the North Carolina Early Pregnancy Study, which took place 1982-1985, and followed the pregnancies of 125 women from conception through birth.

Using urinary hormone measures, the researchers were able to identify the precise point at which a woman ovulates and an embryo implants in the womb. They found that the median time for ovulation to live birth was 268 days, or 38 weeks and 2 days, but most surprising was the 37-day range of gestational length among healthy pregnancies.

The researchers took information from daily urine samples and analyzed the samples for three hormones connected with the onset of pregnancy: estrone-3-glucuronide, pregnanediol-3-glucuronide, and human chorionic gonadotropin (hCG). Implantation was determined as the first day of a sustained rise in hCG levels.

Women are normally given a due date that is calculated as 280 days after the onset of their last menstrual period, but these findings indicate that a range of dates may better communicate to women when they are likely to deliver. Also, biologic variability may be greater than previously thought. **(BS)**

*Citation:* [Jukic AM, Baird DD, Weinberg CR, McConnaughey DR, Wilcox AJ](#). 2013. Length of human pregnancy and contributors to its natural variation. *Hum Reprod* 28(10):2848-2855.

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## Role of arginine in polymerase beta-catalyzed nucleotidyl transfer reactions

NIEHS scientists showed that arginine in position 254 (Arg254) has a crucial role for stabilizing the active site of mammalian polymerase beta and enabling proton transfer during gap-filling DNA synthesis. Proton transfer from the primer O3' group to a nearby carboxylate group of aspartate in position 256 (Asp256) in the enzyme active site is a key step of the nucleotidyl transfer reaction catalyzed by polymerase beta. Knowing how the catalytic action of polymerases works is important for understanding factors controlling efficiency of correct nucleotide insertion and fidelity in DNA repair and replication.

The researchers mutated the Asp256 residue to glutamate and observed that the mutant was more than 1000 times less active than the wild-type enzyme and that the crystal structures were subtly different in the active site. Computational analyses determined that the O3' proton in the mutated polymerase still transferred to the nearby carboxylate in position 256, but it happened late in the reaction path. Since this late transfer was due to repositioning of Arg254 side chain, Arg254 was not able to stabilize the proton transfer from O3'. Also, the glutamate-containing enzyme did not undergo charge reorganization associated with the proton transfer, which is mediated by the catalytic magnesium ion in the active site. **(AA)**

*Citation:* [Batra VK, Perera L, Lin P, Shock DD, Beard WA, Pedersen LC, Pedersen LG, Wilson SH](#). 2013. Amino acid substitution in the active site of DNA polymerase beta explains the energy barrier of the nucleotidyl transfer reaction. *J Am Chem Soc* 135(21):8078-8088.

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## Redundancy in DNA repair mechanisms protects cells from UV-induced DNA damage

Using G2-arrested budding yeast, NIEHS scientists have identified redundancy in the mechanisms that repair UV-induced DNA damage. Given the conservation of repair pathways and links with various human pathologies including cancer, the finding may lead to new therapies for treating these diseases.

The researchers found that mutations in either translesion DNA synthesis (TLS) or homologous recombination (HR) reduced the repair efficiency of UV lesions, as surmised from formation and disappearance of repair intermediates. However, inactivation of both pathways led to accumulation of long-lived intermediates and loss of survival. Based on a physical assay they previously developed to detect recombination between sister chromatids, UV-induced recombination was not due to formation of DNA double-strand breaks. They concluded that TLS and HR are functionally redundant in protecting G2 cells from UV-induced DNA damage.

The authors proposed that repair of UV damage normally begins with formation of a small single-stranded DNA gap produced by nucleotide-excision repair. The TLS pathway can fill the gap, but in its absence, the HR pathway is initiated by the gaps and completes the repair. Identification of this pathway provides new insights into understanding genome instability and other environmental health risks associated with lesions such as those due to UV exposure. **(HF)**

*Citation:* [Ma W, Westmoreland JW, Resnick MA](#). 2013. Homologous recombination rescues ssDNA gaps generated by nucleotide excision repair and reduced translesion DNA synthesis in yeast G2 cells. *Proc Natl Acad Sci U. S. A.* 110(31):E2895-E2904.

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## Crystal structures reveal how flame retardants may disrupt estrogen metabolism

In a recent study, NIEHS and National Cancer Institute researchers revealed how brominated flame retardants (BFRs), chemicals widely used in consumer products to reduce the spread of fire, may disrupt estrogen metabolism. The research impacts public health since these compounds are released into the environment from existing and discarded products, and can be detected in various living organisms.

The authors used tetrabromobisphenol A (TBBPA), the most widely used BFR, and BFR metabolite 3-OH-BDE-47, to demonstrate how BFRs bind human estrogen sulfotransferase (SULT1E1). SULT1E1 normally binds to estrogen to regulate its concentration and excretion from the body. Interestingly, TBBPA and 3-OH-BDE-47 share a similar phenolic ring structure with estrogen that allows them to bind to SULT1E1.

The scientists unveiled three-dimensional crystal structures of SULT1E1 as a complex with estrogen, TBBPA, and 3-OH-BDE-47, respectively. They showed that both TBBPA and 3-OH-BDE-47 can bind to the same substrate-binding site in SULT1E1 as estrogen. Moreover, TBBPA and 3-OH-BDE-47 are structurally more flexible, and the bromine atoms on their phenolic ring enhance their binding affinity to SULT1E1. These findings show that SULT1E1 can accommodate structurally diverse halogenated compounds, suggesting that SULT1E1 can be inhibited by a wide range of BFRs at low doses. **(SY)**

*Citation:* [Gosavi RA](#), [Knudsen GA](#), [Birnbaum LS](#), [Pedersen LC](#). 2013. Mimicking of estradiol binding by flame retardants and their metabolites: a crystallographic analysis. *Environ Health Perspect* 121(10):1194-1199.

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## **Probiotics use during pregnancy many reduce diseases in children**

Based on data from the Norwegian Mother and Child Cohort Study (MoBa), a research team led by NIEHS scientists have determined that, for the general population, probiotics consumed during pregnancy and infancy may help prevent atopic eczema and rhinoconjunctivitis in early childhood.

The researchers used data from more than 40,000 mother and children pairs participating in the MoBa study, which recruited Norwegian women between 1999 and 2008. The authors assessed the consumption of Tine SA Biola and Cultura., two types of probiotic-enriched milk and yogurt, in pregnancy and infancy, using a pregnancy food frequency questionnaire and a postnatal questionnaire. These products contain lactobacilli and bifidobacteria species that are safe, and were the only probiotic foods widely available on the market during the time of the study.

Thirty-seven percent of pregnant mothers in the study consumed these probiotic milk and yogurt products, and 18 percent of them also gave their child probiotic milk products after 6 months of age. The researchers found that maternal probiotic milk consumption in pregnancy, as well as consumption during early childhood, was associated with a slightly reduced relative risk of atopic eczema at 6 months, and rhinoconjunctivitis symptoms between 18-36 months.

The findings indicate that probiotic intake might be beneficial for the prevention of atopic eczema and rhinoconjunctivitis in the general population of children. Previous studies focused on high risk children. The fact that only two probiotic products were available during the study period likely facilitated identification of potential health effects. **(BS)**

*Citation:* [Bertelsen RJ](#), [Brantsaeter AL](#), [Magnus MC](#), [Haugen M](#), [Myhre R](#), [Jacobsson B](#), [Longnecker MP](#), [Meltzer HM](#), [London SJ](#). 2013. Probiotic milk consumption in pregnancy and infancy and subsequent childhood allergic diseases. *J Allergy Clin Immunol*; doi:10.1016/j.jaci.2013.07.032 [Online 10 September 2013].

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## **Dermatomyositis shares genetic background with other autoimmune diseases**

NIEHS researchers, together with American and European collaborators, conducted the first genome-wide association study of any form of myositis, and found that dermatomyositis shares common genetic features with other autoimmune disorders. Pathogenesis of dermatomyositis, which is characterized by muscle and skin inflammation, is largely unknown, and identification of disease genetic predispositions could lead to novel diagnostic and therapeutic advances.

The scientists performed a genome-wide association study and examined genetic variants, or single nucleotide polymorphisms (SNPs), to determine if any of these variants were associated with the disease. Genotyping of more than 1,000 adult and juvenile patients of European ancestry, and 4,000 healthy control individuals,

confirmed a strong association of dermatomyositis with major histocompatibility complex (MHC). MHC molecules mediate recognition of body cells by lymphocytes, and are involved in autoimmune diseases.

The researchers then focused on SNPs outside of the MHC region that are specifically associated with autoimmune diseases. They were able to identify three genes — phospholipase C like 1 (PLCL1), B lymphoid tyrosine kinase (BLK), and chemokine ligand 21 (CCL21) — that could be linked with dermatomyositis. **(AA)**

*Citation:* Miller FW, Cooper RG, Vencovsky J, Rider LG, Danko K, Wedderburn LR, Lundberg IE, Pachman LM, Reed AM, Ytterberg SR, Padyukov L, Selva-O'Callaghan A, Radstake T, Isenberg DA, Chinoy H, Ollier WE, O'Hanlon TP, Peng B, Lee A, Lamb JA, Chen W, Amos CI, Gregersen PK; Myositis Genetics Consortium. 2013. Genome-wide association study of dermatomyositis reveals genetic overlap with other autoimmune disorders. *Arthritis Rheum*; doi:10.1002/art.38137 [Online 27 August 2013].

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## Identification of novel immune regulatory elements and epigenetic plasticity in memory lymphocytes

A collaborative team led by NIEHS investigators determined that the global reprogramming of the epigenome, or the epigenetic modifications of DNA, permits adult somatic cells to differentiate into diverse cell types. This reprogramming occurs when naive B cells enter the germinal-center (GC) reaction in secondary lymphoid organs and contributes to the cells' ability to rapidly differentiate into plasma cells when the body is rechallenged by antigens during a secondary immune response.

The authors purified four different B cell populations — naive, GC, memory, and plasma cells (PC) — from inflamed tonsils of eight individuals and performed global DNA methylation analysis using the methylated CpG island recovery assay (MIRA).

To investigate the function of DNA methylation changes associated with immune activation, the authors determined whether activation-induced differentially methylated regions were enriched for regulatory elements and also found that Alu elements display differential methylation patterns, correlated with decreased expression of the *de novo* methyltransferase DNMT3A in GC B cells.

The authors propose that the loss of DNA methylation during the naive to GC B cell transition permits these cells to differentiate toward memory or PC fates, and to generate the differential response to antigenic challenge. **(MM)**

*Citation:* Lai AY, Mav D, Shah R, Grimm SA, Phadke D, Hatzi K, Melnick A, Geigerman C, Sobol SE, Jaye DL, Wade PA. 2013. DNA methylation profiling in human B cells reveals immune regulatory elements and epigenetic plasticity at Alu elements during B-cell activation. *Genome Res*; doi:10.1101/gr.155473.113 [Online 6 September 2013].

(Aleksandra Adomas, Ph.D., is a research fellow in the NIEHS Laboratory of Molecular Carcinogenesis. Heather Franco, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Laboratory of Reproductive and Developmental Toxicology. Mallikarjuna Metukuri, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction. Bailey Schug studies health promotion and nutrition at Appalachian State University and is an intern in the NIEHS Office of Communications and Public Liaison. Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Laboratory of Molecular Genetics. Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)

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# Inside the Institute

## NIEHS celebrates Years of Service with 2013 honorees

By Ian Thomas

Staff from across NIEHS gathered Sept. 4 in Rodbell Auditorium for the Institute's annual Years of Service Awards ceremony. Hosted by NIEHS and NTP Director Linda Birnbaum, Ph.D., the event recognized a total of 48 Institute employees, commemorating career milestones of 10, 20, 30, and 40 years, as well as 18 retirees.

"As federal employees, we work directly for the American people," explained Birnbaum. "Here at NIEHS, that means maintaining a strong commitment to funding and supporting powerful research into the causes of disease. This requires a lot of hard work and dedication. But, beyond the hours, it also requires a very unique type of person to choose this as a career."

Aided by NIEHS Deputy Director Richard Woychik, Ph.D., Birnbaum presented each honoree with a framed certificate celebrating their milestone, as well

as a congratulatory handshake of appreciation. At the conclusion of the ceremony, awardees were then joined by colleagues, peers, and various members of NIEHS leadership for a reception in the building 101 lobby.



Birnbaum recognized NIEHS staff scientist Cho for her 10 years of service. (Photo courtesy Steve McCaw)

### Employees and their milestones

#### 10 years:

- Joel Abramowitz
- Christopher Fisher
- Stephanie Holmgren
- Floyd Adsit
- Katina Johnson
- Nicole Reeves
- Elizabeth Ruben
- Sukhdev Brar
- David Kinnamont
- Barbara Ruffin
- Marcus Bell
- Grace Kissling
- Erica Scappini
- Michelle Campbell
- Huiling Li
- William Schrader
- Lysandra Castro Marquez
- David Malarkey
- Beverly Sellers-Robinson
- Hye-Youn Cho
- Tiwanda Masinde
- Michael Spencer
- Laura DeGraff
- Robert Petrovich
- Kristine Witt
- Vivian Young

#### 20 years:

- Elizabeth Banks
- William Jirles
- Elizabeth McMillan
- Hamilton Brown
- Jerrel Yakel

**30 years:**

- Charles Alden
- Bonnie Allen
- Martha Barnes
- John Bucher
- Dorothy Duke
- Edward Eddy
- Donald Ellis
- Deborah Jones
- Frederick Miller
- Rickie Moore
- Daniel Morgan
- Ellen Moul
- Kathleen Ochoa
- Victor Sutton
- Christina Tang
- Michael Waalkes
- Clarice Weinberg

**40 years:**

- Teretha Lewis
- Ronald Mason
- Carol Shreffler

**Retirees:**

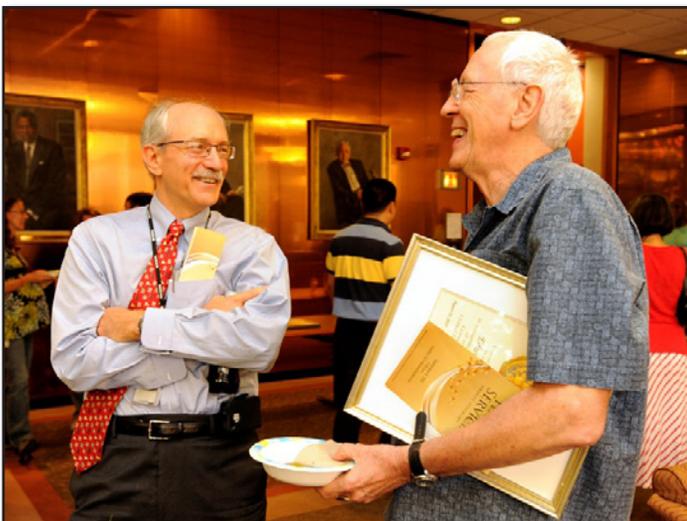
- Eddy Ball
- Alma Britton
- Rajendra Chhabra
- James Clark
- Harold Davis
- John French
- Raymond Grissom
- James Huff
- Robert Langenbach
- Lawrence Lazarus
- Michael Litton
- Dona McNeil
- Connie Riley
- Walter Rogan
- Cynthia Smith
- Emily Starnes
- Charles Tate
- Sally Tinkle



*Birnbaum congratulated NIEHS Management Analyst Bell, who also reached his 10 year milestone. (Photo courtesy Steve McCaw)*



*Alden, left, and Kissling celebrated years of service with their colleagues. (Photo courtesy Steve McCaw)*



*Woychik, left, congratulated Eddy on 30 years of federal service. (Photo courtesy Steve McCaw)*



*Following the ceremony, everyone in attendance enjoyed an opportunity for fellowship over cake and punch. (Photo courtesy Steve McCaw)*

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

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