

August 2015

NIEHS Spotlight



[Virtual forum on near-roadway air pollution highlights health effects](#)

NIEHS helped broaden public understanding of the impacts of air pollution from roadways, in a July 10 virtual forum.



[NIEHS opens doors for area teachers](#)

Nine North Carolina teachers spent two weeks immersed in the NIEHS Science, Teachers, and Research Summer Institute (STaRS) program.



[Groundbreaking EPA testing plan builds on NTP work to replace animal use](#)

The U.S. Environmental Protection Agency proposed replacing certain animal tests with methods developed in part by NTP scientists.



[NIEHS fellows stand out in 2016 FARE competition](#) 🏆

This summer, 16 NIEHS trainees were winners of the National Institutes of Health Fellows Award for Research Excellence (FARE).



[Environmental health community mourns loss of Paul Lioy](#) 🎧 Audio

Environmental health scientists mourn the loss of Paul Lioy, M.D., a champion of exposure science, who passed away July 8.

Clinical Feature



[Gibbons calls for reimagining clinical research](#) ▶ Video

Gary Gibbons, M.D., director of the National Heart, Lung, and Blood Institute, outlined his vision for the future of precision medicine in a July 20 talk.

Science Notebook



[Researchers rise to the challenge of studying mixtures](#)

Scientists from across the country participated in an NIEHS workshop evaluating statistical methods for studying exposures to chemical mixtures.



[Environmental influences on breast cancer risk — the evidence mounts](#)

NTP researcher Sue Fenton, Ph.D., focused a special issue of Reproductive Toxicology on environmental impacts on breast development and disease.



[NTP panel agrees flame retardant mixture exhibits carcinogenic activity](#)

The peer reviewers accepted NTP draft conclusions that a PBDE mixture showed clear evidence of carcinogenic activity in rats and mice.

NIEHS Spotlight



[Tibbetts Award recognizes NIEHS grantee innovation in rodent control](#)

SenesTech received a Small Business Administration Tibbetts Award for its safe, innovative approach to reducing rodent populations.



[Evaluating worker training from the mid-management perspective](#)

A new study gives worker health and safety training high marks and takes a rare look at how midlevel managers value NIEHS-funded programs.



[Wilson's mentoring award celebrated](#)

NIEHS staff celebrated lead researcher Samuel Wilson, M.D., who won the prestigious Ruth L. Kirschstein Mentoring Award from NIH.



[A scientist gives back — Rahman on women's environmental health](#)

Qamar Rahman, Ph.D., discussed the challenges Indian women face in the workplace, and her motivations to help improve women's health.



[Help document NIEHS history](#)

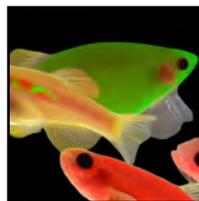
In preparation for its 50th anniversary next year, the institute requests nominations of notable accomplishments and the people behind them.



[NIEHS small business innovation shines at biotech convention](#)

NIEHS grantees, including Microvi Biotech Inc., were selected to exhibit in a special innovation zone at the BIO International Convention.

Science Notebook



[New method improves bone marrow transplants](#)

New research with zebrafish allows scientists to track which transplanted cells replenish bone marrow and which chemicals may aid the process.



[Society for Free Radical Biology and Medicine honors Mason](#)

NIEHS researcher Ronald Mason, Ph.D., received the 2015 Discovery Award from SFRBM, for significant advancements in redox research.



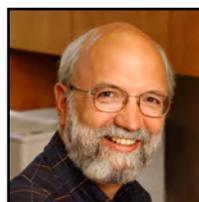
[Researchers identify protein that helps prepare healthy egg-sperm union](#)

NIEHS researchers have discovered that the protein RGS2 plays a vital role in a healthy egg-sperm union.



[Parma consensus statement on metabolic disruptors supported by NIEHS scientists](#)

NIEHS scientists and grantees are co-authors of a call for research on ways environmental exposures may disrupt metabolic pathways.



[Wilcox named Mentor of the Year by pediatric epidemiology society](#)

NIEHS epidemiologist Allen Wilcox, M.D., Ph.D., was named 2015 Mentor of the Year by the Society for Pediatric and Perinatal Epidemiologic Research.



[NIEHS environmental genetics leader speaks at Texas research center](#)

Steven Kleeberger, Ph.D., presented a June 17 mentoring seminar at Texas A&M University's Center for Translational Environmental Health Research.

Calendar of Upcoming Events

- **Aug. 4**, webinar, 11:00 a.m.–12:30 p.m. — NIEHS Exposure Science and the Exposome Webinar Series with Santosh Kumar, Ph.D., from the University of Memphis, discussing “Incorporating Mobile Exposure in Mobile Health Precision Medicine,” [register](#) to attend
- **Aug. 4**, in Building 101, Executive Conference Room, noon–1:00 p.m. — Receptor Mechanisms Discussion Group seminar with Brian Strahl, Ph.D., from the University of North Carolina at Chapel Hill School of Medicine, speaking on “Chromatin Mechanisms That Underlie Transcription and DNA Methylation Control”
- **Aug. 7**, in Building 101, F193, 1:00–2:00 p.m. — Signal Transduction Laboratory Special Seminar featuring Carlo Riccardi, M.D., Ph.D., from the University of Perugia School of Medicine, Italy, presenting “Anti-inflammatory Action of Glucocorticoids: Role of GILZ”
- **Aug. 10**, in Keystone 2164, 9:30–11:00 a.m. — NICEATM Skin Sensitization Modeling Seminar on “Probabilistic Hazard Assessment for Skin Sensitization Potency by Dose-Response Modeling Using Feature Elimination Instead of Quantitative Structure-Activity Relationships,” by Thomas Luechtefeld from Johns Hopkins University
- **Aug. 10-11 (off-site event)**, at the New York University Kimmel Center for University Life, New York City, 8:00 a.m.–5:00 p.m. — “ASPR/CDC/NIEHS Hurricane Sandy Conference: Translating Research Into Practice,” [register](#) to attend
- **Aug 12**, webinar, 1:00–2:30 p.m. — EPA/NIEHS Children’s Centers 2015 Webinar Series highlighting brain health, with Brenda Eskenazi, Ph.D., from the University of California, Berkeley; Susan Murphy, Ph.D., from Duke University; Heather Volk, Ph.D., from the Children’s Hospital Los Angeles; moderated by I. Leslie Rubin, M.D., from Emory University, [register](#) to attend
- **Aug. 19**, in Keystone 1003, 2:00–3:00 p.m. — Data Science Seminar Series with David Reif, Ph.D., from the North Carolina State University (NCSU) Bioinformatics Research Center and the NCSU Center for Human Health and the Environment
- **Aug. 25**, in Rodbell Auditorium, 9:30 a.m.–3:30 p.m. — NIEHS presents “Halifax Project: Low Dose Theory Symposium,” [register](#) to attend in person or via webcast.
- View More Events: [NIEHS Public Calendar](#)

NIEHS Spotlight

Virtual forum on near-roadway air pollution highlights health effects

By John Yewell

Air pollution has long been a public health concern, and the spike in pollutants often detected near roadways is receiving closer attention from researchers and policymakers. NIEHS helped broaden public understanding of these impacts in the July 10 virtual forum, “Near-Roadway Pollution and Health,” moderated by Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training (DERT). “Our presenters today come from the evolving robust network of air pollution researchers supported by NIEHS,” she said.

NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., welcomed the more than 300 participants. “Today, we are focusing on air pollution near roadways and what effects that exposure may have on human health,” she said. The virtual forum allowed panelists to address questions sent in from across the country via email and Twitter.

Before the event, the four invited experts discussed their own research at a mini-symposium (see [text box](#)) sponsored by DERT:

- [Joel Kaufman, M.D.](#), from the University of Washington
- [Toby Lewis, M.D.](#), from the University of Michigan
- [Rob McConnell, Ph.D.](#), from the University of Southern California
- [Veronica Vieira, Ph.D.](#), from the University of California, Irvine.

Disproportionate effects on kids and minorities

The first question many participants asked about near-roadway pollution was how far from a major roadway did they have to live for the air to be relatively healthy. “As a rule of thumb, about 500 to 1,000 feet is a reasonably safe distance,” said McConnell.

According to a 2010 [study](#) by the Centers for Disease Control and Prevention, more than 11 million people live within 500 feet of a major U.S. highway. These residents may be more likely to be affected by the pollution,



This Brooklyn neighborhood is an example of a densely populated area located close to roadway air pollution. (Photo courtesy of John Schelp)



From left, Birnbaum, McConnell, Lewis, Vieira, Kaufman, and Collman all participated in discussions during the one-hour event. (Photo courtesy of Steve McCaw)

which is sometimes called traffic-related air pollution, or TRAP. The speakers noted that minorities tend to be disproportionately affected, and children are also at higher risk.

“Kids who live near the highways seem to have more respiratory issues than the kids who live further away,” Lewis said. A viewer with an asthmatic child asked how to choose a location for a new home. Besides living at a distance from major roadways, Lewis recommended using a HEPA air filter, because outdoor air enters the home, especially those without air conditioning. “You can create an environment that has less particulate matter,” she said.

Lungs as gateway organs

Kaufman pointed out risks to organs other than lungs. “A large part of the burden of near-roadway air pollutants is actually on the cardiovascular system,” he said. McConnell referred to a [July 7 paper](#) in which he and collaborators estimated that the burden of cardiovascular disease attributable to particulate matter from traffic could be lessened by adoption of greenhouse gas reduction strategies.

McConnell pointed to other consequences. “There’s emerging evidence that it also has effects on the brain,” he said. “Evidence also shows correlations between near-roadway pollution during gestation and childhood obesity.”

Gauging and managing risk

Vieira discussed the complexities researchers face and advocated for use of personal monitors in studies. “A lot of times our exposure assessment methods [use] birth records or home address,” she said, pointing out that researchers do not always have information on travel, exercise, work, and other locations where study participants may spend time.

Measuring the risks is also no simple matter. Distance from traffic is important, but so are traffic volume, the types of vehicles, and the type of road, as well as meteorological conditions, such as wind, rain, humidity, and sunlight.

As for managing risk, “Good news!” said Birnbaum. “There are changes in policy and behaviors that are leading to cleaner air.” These include land use plans that reduce exposure to these pollutants, using filters in homes, schools, and workplaces, and increased use of fuel-efficient vehicles, carpooling, and biking.

The virtual forum was a collaboration among several NIEHS offices. “Pulling together this forum was joyful work,” said John Schelp, OSED special assistant for community engagement and outreach. “It takes a village to do a live broadcast, and collaborating with folks from DERT, OCPL [Office of Communications and Public Liaison], OD [Office of the Director], and contractors was great fun.”



Collman, right, shared questions sent via Twitter or email for Kaufman, center; Vieira, and the others. (Photo courtesy of Steve McCaw)



“We should be celebrating the overall improvement in outdoor air pollution levels,” said Birnbaum, left. “But we still have opportunities for improvement.” With her are McConnell, center, and Lewis. (Photo courtesy of Steve McCaw)

Citations:

Boehmer TK, Foster SL, Henry JR, Woghiren-Akinnifesi EL, Yip FY; Centers for Disease Control and Prevention (CDC). 2013. Residential proximity to major highways - United States, 2010. MMWR Surveill Summ. 62(Suppl 3):46-50.

Ghosh R, Lurmann F, Perez L, Penfold B, Brandt S, Wilson J, Milet M, Kunzli N, McConnell R. 2015. Near-Roadway Air Pollution and Coronary Heart Disease: Burden of Disease and Potential Impact of a Greenhouse Gas Reduction Strategy in Southern California. Environ Health Perspect [Online July 7, 2015; doi:10.1289/ehp.1408865].

(John Yewell is a contract writer for the NIEHS Office of Communications and Public Liaison)

Experts discuss their research on near roadway air pollution

By Kelly Lenox

At the mini-symposium, the invited experts shared insights from their research, including some preliminary findings. A look at the different studies they are doing shows the complexity of the task scientists face.

Kaufman and his colleagues are studying individuals in several cities, building upon the Multi-Ethnic Study of Atherosclerosis ([MESA](#)). They are researching links between exposures to near-roadway pollution and changes in cardiovascular health over time. Kaufman reported that exposures vary greatly from one part of a city to another, and that as distance from traffic increases, concentrations of some pollutants, such as nitrous oxides, decrease more quickly than others, including fine particulate matter.

Lewis described a community-based participatory research project in Detroit studying the effects of education, air filters, and air conditioners on asthma severity among residents living near traffic sources. Lewis said that Michigan has a high rate of adult asthma, with higher rates of asthma-related hospitalization and mortality in low-income areas. Currently, they are seeing effective reduction in particulate counts and variations in how much the machines are used. The involvement of community groups is proving crucial to understanding usage patterns and collecting detailed data.

McConnell and his team are looking into how near-roadway air pollution affects rates of asthma and obesity in southern California. McConnell said that evidence is emerging that near-roadway pollution may cause asthma, especially in genetically susceptible children. Similarly, there is growing evidence of an association between such exposures and increases in body mass index, a common measure of obesity.

Vieira discussed her team's use of satellite imagery to tease out links between fine particulate air pollution (PM2.5) and cardiac birth defects. By integrating data on PM2.5 levels and early gestation dates for babies born with such defects, they found that several conditions showed no association, and one, hypoplastic left heart syndrome, did show a possible link, prompting her call for further research. Vieira's team is also looking at the incidence of infant bronchiolitis, a lower respiratory infection that may be affected by short-term exposures.

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NIEHS opens doors for area teachers

By Kelly Lenox

On the morning of July 6, an energetic group of North Carolina public school teachers arrived at NIEHS for the two-week Science, Teachers, and Research Summer (STaRS) Institute.

Building on last year's expansion (see [story](#)), the nine teachers took part in hands-on laboratory research, science talks, facility tours, and discussion sessions. Hwei-Chen Lao, K-12 science education and outreach coordinator for the NIEHS Office of Scientific Education and Diversity (OSD), coordinated the program.

Calling on all corners of the institute

The number of staff who volunteered to work with the participants demonstrates the widespread support STaRS has across the institute. "This year, we had 36 volunteers," Lao said, "from postdocs and contractors, on up to lead researchers and the director. And some are already signing up for next year."

That breadth was on display during the "Ask a Scientist" panel discussion, where five scientists representing a variety of the jobs performed at NIEHS explained their work and answered questions.

"Our target population is first-generation college students," said John Eaton, who teaches at Wake Early College of Health and Sciences. "[Now] I can demonstrate that careers in the health sciences extend beyond the walls of the hospital."

The panel was also attended by another group of teachers, who spent the day at the institute as part of the SummerSTEM workshop organized by WakeEd Partnership (see [text box](#)).

Understanding the whole pipeline

This year, Lao added a visit to nearby Biogen to the schedule. Visiting the pharmaceutical company gave participants another perspective on biomedical research.

"We are able to take all of the pieces of the biotech product pipeline and put them together, from basic research to what happens in a major pharmaceutical company," said Mariel Barker Sellers, from East Columbus High School in Columbus County. "We will be able to present it to our students much more effectively."



At the closing session, participants were unanimous in their accolades for the hard work and high spirits Lao displayed throughout the program. (Photo courtesy of Steve McCaw)



Sellers was coached on DNA extraction by Molly Cook, left, of the Protein Expression Core Laboratory. (Photo courtesy of Steve McCaw)

“It was the ideal classroom for any teacher. The set up they have there is fantastic,” said Anna Densmore, a teacher at Washington High School in Beaufort County. Referring to their lab work at Biogen, she added, “It will be the perfect introduction to bacterial transformation.”

From labs to classrooms to careers

Presented in cooperation with [North Carolina New Schools \(NCNS\)](#), the professional development opportunity aims to enhance high school science teachers’ understanding of basic biomedical research. The teachers created lesson plans and classroom projects based on what they learned and presented them on the last day, demonstrating how they will translate their experiences into practice.

“The real world exposure to different types of issues, equipment, processes — all the things they bring back to the classroom will enhance their students’ understanding,” said Jason Kessler, community development coordinator for NCNS.

Broadening students’ understanding is one outcome that Ericka Reid, Ph.D., director of OSED, had hoped for. “Science education is built into our [strategic plan](#),” she said while welcoming the teachers on their first day. “Enhancing the teaching of environmental health sciences — goal eight — is why you are here.”

Reid also referred to goal nine, which focuses on diversity and developing a well-trained cadre of scientists. “Diversity is not just racial and ethnic,” she said, “but also [includes] a diversity of sciences, so that we can ask more of the right questions [in our research].”



Eaton expressed his appreciation for the personnel involved in the program. “The enthusiasm and passion that everyone here [at NIEHS] has for their job is top-notch,” he said. (Photo courtesy of Steve McCaw)



Jacob Daeffler, from South Creek High School in Martin County, expressed the enjoyment felt by participants for the laboratory experiences — from learning how to use a pipette to better understanding the processes that lead to scientific advances. (Photo courtesy of Steve McCaw)



Ariel Darden, from Weldon High School in Halifax County, and Jennifer Hulsey, from Overhills High School in Harnett County, worked together on protein quantification. Practical lessons were complemented by time spent with scientists. Thanking Ron Cannon, Ph.D., of the Intracellular Regulation Group, Hulsey said, “I can tell the passion that you have, when you hung out with us and just gave us time to talk. That’s what it’s all about.” (Photo courtesy of Steve McCaw)



Like last year, Bob Petrovich, Ph.D., head of the Protein Expression Core Laboratory, played an integral part in the program, by teaching lab techniques, giving lectures, being on hand to discuss research, and answering questions about the institute. (Photo courtesy of Steve McCaw)



Casey Balio, who teaches at Hawthorne Academy of Health Sciences in Mecklenburg County, described the biotech project she and her group designed, based on their experiences in the STaRS program. (Photo courtesy of Steve McCaw)



Densmore, left, and Tom Tomison of Wake County's Vernon Malone College and Career Academy, quantified protein using a color-based analysis. A later pathology lab included slide preparation. "We order slides for our students, and we don't have the opportunity to see how those slides are actually made," Densmore said. "And we got to keep these slides, so I can use them with my students." (Photo courtesy of Steve McCaw)



Ken Schaffer, from Wilson Early College Academy in Wilson County, plans to use many of the materials he found on the NIEHS website, from lists of papers on environmental health topics to public awareness posters. "I will also use the PowerPoint on environmental justice," he said, because his students in Wilson would find that relevant. (Photo courtesy of Steve McCaw)



The teachers posed with some of those who helped make the program possible, including, from right, Kessler; Reid, Lao, Cannon, in blue shirt, and Petrovich, third from left. (Photo courtesy of Steve McCaw)

Partnership with Wake County

On July 15 and 16, NIEHS welcomed 24 teachers from Wake County, North Carolina, to the institute. The teachers were part of the [WakeEd Partnership](#) SummerSTEM (science, technology, engineering, and math) program, which coordinated immersion experiences for teachers. Six local STEM-related institutions were included year, including NIEHS, Red Hat, SAS, Biogen, LORD Corporation, and the North Carolina Department of Transportation.

Two groups of about a dozen teachers each came for a full day. They learned about mass spectrometry from Jason Williams, Ph.D., and visited the NIEHS Fluorescence Microscopy and Imaging Center, where Jeff Tucker explained the power of the tool for biological research. The groups toured other areas of the institute and heard talks, ranging from humane treatment of research animals to the Ask a Scientist session, which exposed them to the broad range of roles performed by institute scientists.

“SummerSTEM exists to enrich each educator’s understanding of the knowledge and skills necessary to succeed in careers involving science, technology, engineering, and math (STEM),” read the [WakeEd press release](#).

“By working with teachers, we can have a greater impact on more students,” Lao said. “We’re already looking forward to next year.”

Groundbreaking EPA testing plan builds on NTP work to replace animal use

By Catherine Sprankle

The U.S. Environmental Protection Agency (EPA) has proposed replacing certain animal tests in its Endocrine Disruptor Screening Program (EDSP) with high-throughput assays and computational methods. In a [June 18 press release](#), EPA said the new approach, which was developed and validated by scientists at EPA and the [National Toxicology Program \(NTP\) Interagency Center for the Evaluation of Alternative Toxicological Methods \(NICEATM\)](#), will increase the pace of screening and decrease costs and animal use.

“This is the first proposal for using high-throughput assay data to replace toxicology tests required by law,” noted NICEATM scientist Nicole Kleinstreuer, Ph.D., who helped develop the computational model. She is a co-author of an [article in the journal Environmental Science and Technology](#), which described the new approach in detail. “Using this kind of technology in the EDSP will allow for faster screening of thousands of chemicals,” she said. EPA published a [June 19 Federal Register notice](#) asking for comments on the new approach, which focuses on testing for estrogenic activity. Comments will be accepted through August 18.

Screening for estrogenic activity

The screening program is designed to identify chemicals in the environment that may interfere with the normal function of hormones and potentially cause health problems in humans and animals. Chemicals identified in the Tier 1 screening phase as having the potential to interfere with normal hormone function progress to the Tier 2 testing phase.

EPA recently released results for the first 52 chemicals to complete Tier 1 screening under the current protocols, which can take more than five years for any given set of chemicals. Because thousands of chemicals remain to be screened, there is great interest in developing faster and cheaper approaches.

New approach will replace animal tests

Five EDSP Tier 1 assays are used to identify chemicals with potential to interfere with estrogen hormones. The new approach will replace three of these assays, including two that require the use of animals.



“The application of these innovative tools ... represents the first step in a paradigm shift for chemical safety testing, a practical approach to rapidly screen thousands of environmental chemicals for potential endocrine bioactivity in humans and wildlife, and the first systematic application of ToxCast data in an EPA regulatory program,” wrote Kleinstreuer and her co-authors. (Photo courtesy of Steve McCaw)

Casey presents proposed approach to international colleagues

Casey cited the new approach as an example of validation strategies for high-throughput and computational methods, at the [ASIATOX meeting](#) June 23–26 in Jeju City, South Korea.

While in Jeju City, Casey also served as an expert panelist at the International Workshop on Validation Management for Alternative Test Methods. During discussions on practical aspects of test method validation, he highlighted NICEATM’s procedures for evaluating data quality, managing validation studies, and working with regulatory agencies. The expert panel also reviewed a Korean study of a new method for identifying skin sensitizers.

To develop the new screening approach, EPA and NICEATM scientists first turned to the EPA [ToxCast](#) program and identified 18 high-throughput assays that represented key events in estrogen hormone function. Data from these assays were used in a computational model of the estrogen receptor pathway to determine the probability that the chemical would interfere with estrogen hormone function.

The accuracy of the model was evaluated by comparing the model's prediction against existing data curated by NICEATM from both animal and nonanimal tests. "This evaluation was key to ensuring that the new approach will be useful in the EDSP," explained NICEATM Director Warren Casey, Ph.D., who was also a co-author on the paper. "We used data from well-studied estrogen-active chemicals and compared the model scores with results obtained from methods currently used for regulatory decision-making."

Casey presented this approach to an [EPA advisory panel meeting](#) in December, at which members of industry and animal welfare groups expressed their support.

Citation: [Browne P, Judson RS, Casey WM, Kleinstreuer NC, Thomas RS](#). 2015. Screening chemicals for estrogen receptor bioactivity using a computational model. *Environ Sci Technol*; doi:10.1021/acs.est.5b02641 [Online 12 June 2015].

(Catherine Sprankle is a communications specialist for ILS, the contractor supporting NICEATM.)

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NIEHS fellows stand out in 2016 FARE competition

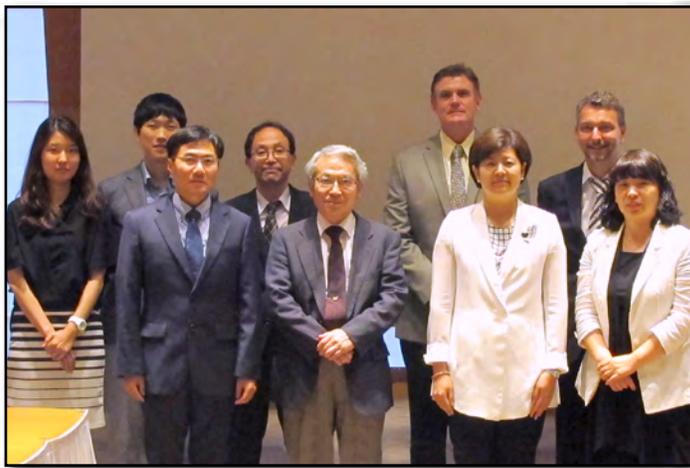
By Eddy Ball

This summer, 16 NIEHS trainees were winners of the National Institutes of Health (NIH) Fellows Award for Research Excellence (FARE) for fiscal year 2016. An awards ceremony will take place as part of the 2015 NIH Research Festival, Sept. 17-18 in Bethesda, Maryland.

"Winning the FARE is an honor for trainees and their mentors, signifying the high caliber of research being conducted at NIEHS" said Tammy Collins, Ph.D., director of the NIEHS Office of Fellows Career Development. "I congratulate the winners and each of the 59 fellows who put in the effort to submit abstracts in the competition."

Setting a high bar for junior researchers

Now in its 20th year, FARE entries are judged blind, and the top 25 percent of submitted abstracts are selected for recognition. The awards include a \$1,000 stipend to attend a scientific meeting, where the winners will present their abstract, either as a poster or an oral presentation.



During ASIATOX, Casey, fourth from right, met with members of the [International Cooperation on Alternative Test Methods](#). NICEATM coordinates test method validation activities with its international counterparts through the group, which also includes member organizations from the European Union, Canada, Japan, and South Korea. (Photo courtesy of Warren Casey)

To participate in the competition, trainees must report on recent first-author data collected while at NIEHS. Judges evaluate abstracts on the basis of scientific merit, originality, experimental design, and overall quality and presentation.

Notably, among this year's winners are four NIEHS trainees who previously won FARE awards — Julie Lowe, Ph.D.; Barbara Nicol, Ph.D.; Pengyi Yang, Ph.D.; and Xiaofeng Zheng, Ph.D. And two mentors, lead researchers Raja Jothi, Ph.D., and Michael Fessler, M.D., had two winners each from their respective groups.



Amanda Conway, Ph.D., a member of Jothi's Systems Biology Group, was recognized for her research project, "GABPa Positively Regulates Transcriptional Circuitry Controlling ESC Identity by Direct Hindrance of a Repressive Chromatin-modifying Complex." Conway was also a 2014 winner of the Postdoctoral Research Associate (PRAT) Program fellowship from the National Institute of General Medical Sciences. (Photo courtesy of Steve McCaw)



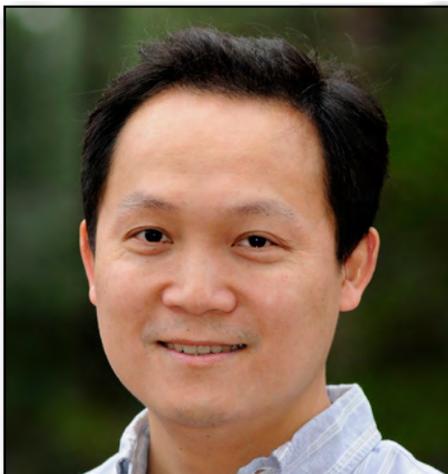
Shannon Farris, Ph.D., won a FARE for her work on "Plasticity in Hippocampal Area CA2: Lost in Translation?" She is a member of the Synaptic and Developmental Plasticity Group headed by Serena Dudek, Ph.D., and a 2014 Society for Neuroscience Early Career Policy Fellow. (Photo courtesy of Steve McCaw)



Ashutosh Kumar, Ph.D., completed his study, "Formation and Implications of Alpha-synuclein Radical Formed in Maneb- and Paraquat-induced Models of Parkinson's Disease," as part of the Free Radical Metabolism Group led by Ronald Mason, Ph.D. Kumar presented his work at the 2014 Society for Free Radical Biology and Medicine meeting, in Seattle, where he was honored with a Young Investigator Award. (Photo courtesy of Steve McCaw)



Kristin Gabor, Ph.D., is a member of Fessler's Clinical Investigation of Host Defense Group. Her award-winning study was titled "Smith-Lemli-Opitz Syndrome Reveals Requirement for Sterol Biosynthesis in the Innate Immune Response." (Photo courtesy of Steve McCaw)



Bo He, Ph.D., mentored by Molecular Endocrinology Group head John Cidlowski, Ph.D., reported that "Human Glucocorticoid Receptor Beta (hGRbeta) Has Unique Transcriptional Activity in Mouse Liver." (Photo courtesy of Steve McCaw)



Rui Liu, Ph.D., explored "Ambient Air Pollution Exposure and Risk of Parkinson Disease," a project mentored by Honglei Chen, M.D., Ph.D., head of the Aging and Neuroepidemiology Group. (Photo courtesy of Steve McCaw)



Lowe, the second FARE winner from Fessler's group, was recognized for her study, "The Novel p53 Target Tumor Necrosis Factor- α induced Protein 8 Variant 2 Is Increased in Human Cancers and Can Offset p53-dependent Tumor Suppression." (Photo courtesy of Steve McCaw)



Vijay More, Ph.D., won for his study, "A Lipid-sensing Transcription Factor, Peroxisome Proliferator Activated Receptor Alpha, Regulates Blood-brain Barrier Efflux Transporter Expression and Transport Activity," completed while he was a member of the Intracellular Regulation Group headed by David Miller, Ph.D. More is now on a postdoctoral fellowship at Merck in New Jersey. (Photo courtesy of Steve McCaw)



Nicol, working in the Reproductive Developmental Biology Group headed by Humphrey Yao, Ph.D., completed her second award-winning study, "New Insights into the Maintenance of Somatic Cell Identity in the Mouse Fetal Ovary." She was the winner of one of just three 2014 Women Scientist Advisors Committee Scholar Awards. (Photo courtesy of Steve McCaw)



Clinton Orebaugh, Ph.D., mentored by Thomas Kunkel, Ph.D., head of the DNA Replication Fidelity Group, won a FARE for his study, "Repair of Ribonucleotides Incorporated into the Nascent Lagging Strand." (Photo courtesy of Steve McCaw)



Matthew Schellenberg, Ph.D., completed his project, "Poly-ubiquitin Driven Activation of the DNA Repair Protein Tyrosyl-DNA Phosphodiesterase 2," as member of the Genome Stability Structural Biology Group headed by Scott Williams, Ph.D. In 2013, the Southeast Regional Collaborative Access Team honored Schellenberg with its Young Investigator Award. (Photo courtesy of Steve McCaw)



Alisa Suen was the only predoctoral fellow from NIEHS honored this year with a FARE. A member of the Reproductive Medicine Group led by Carmen Williams, M.D., Ph.D., she determined that "Aberrant Uterine SIX1 Expression May Promote Uterine Adenocarcinoma Following Neonatal Xenoestrogen Exposure." Suen won best oral presentation at this year's meeting of the Triangle Consortium for Reproductive Biology. (Photo courtesy of Steve McCaw)



Sonika Patial, D.V.M., Ph.D., demonstrated that “Genetic Deletion of an Instability Motif in the 3’-untranslated Region of Tristetraprolin (TTP) mRNA Increases TTP mRNA Stability and Protein Expression and Protects Against Immune-mediated Inflammatory Diseases.” Patial was also recognized by the American Society for Biochemistry and Molecular Biology in January 2015, when she was the winner of a Postdoctoral Travel Award. Her mentor, Perry Blackshear, M.D., D.Phil., is head of the Post-Transcriptional Gene Expression Group. (Photo courtesy of Steve McCaw)



Seddon Thomas, Ph.D., received a FARE for her work, “Dendritic and Epithelial Cell Crosstalk in the Lung: The Impact of Cell-specific Myd88 Expression on Chromatin Accessibility in Dendritic Cells and Consequent Immune Responses to Allergens.” She is a member of the Immunogenetics Group headed by Don Cook, Ph.D. Thomas also won a best poster award at the 2012 NIEHS Science Day competition. (Photo courtesy of Steve McCaw)



Yang, the second winner from Jothi’s group, was recognized for his study, “Reconstruction of Signaling Networks From Time-series Phosphoproteomics Data.” (Photo courtesy of Steve McCaw)



Zheng received his second FARE for the study, “Cnot3 Maintains the Pluripotent State in Early Embryos and Embryonic Stem Cells.” He was mentored by Guang Hu, Ph.D., head of the Stem Cell Biology Group. (Photo courtesy of Steve McCaw)

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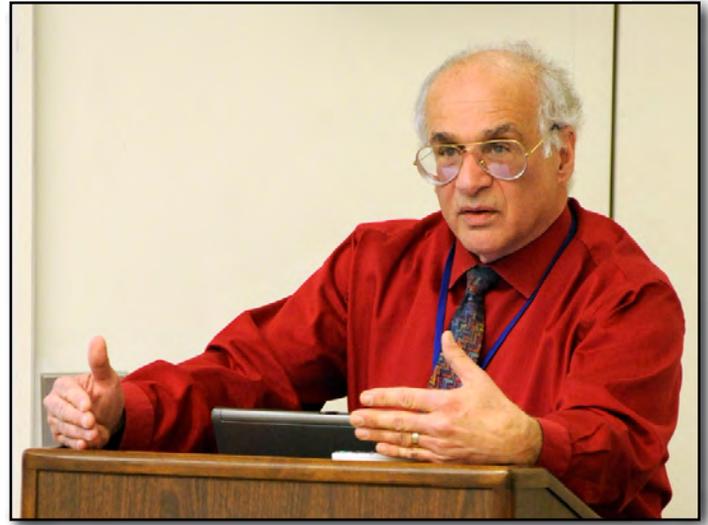
Environmental health community mourns loss of Paul Lioy

By Kelly Lenox

Many in the environmental health community are mourning the July 8 passing of Paul Lioy, M.D., an internationally respected exposure scientist. Lioy was director of exposure science and deputy director of government relations at the Rutgers University Environmental and Occupational Health Sciences Institute, which is funded in part by NIEHS.

Champion for exposure science

As the field of exposure science developed, Lioy became a champion of the study of the exposome, which is the total lifetime exposure to substances both from the environment and from within the body. He served as vice chair of the National Research Council Committee on Human and Environmental Exposure Science in the 21st Century and was instrumental in developing its 2012 report, "[Exposure Science in the 21st Century: A Vision and a Strategy](#)."



In April 2014, Lioy discussed the future of exposure science in a lecture co-hosted by NIEHS and the U.S. Environmental Protection Agency in Research Triangle Park, North Carolina (see [story](#)). (Photo courtesy of Steve McCaw)

"He understood the future, and his work on that report was important to moving the field forward," said Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training.

Working on the cutting edge characterized much of Lioy's career. He was one of the founders of the International Society for Exposure Analysis, now the [International Society for Exposure Science](#), and served as its president from 1993 to 1994. He also helped start the society's journal, now called *Journal of Exposure Science and Environmental Epidemiology*. Lioy was deputy editor of the journal at the time of his death.

An especially notable achievement was his recognition of the risk posed by the dust from the September 11 World Trade Center attacks in New York. Lioy quickly undertook analysis of the dust, to understand the health risks faced by emergency workers and residents. He documented the experience in his critically acclaimed book, "Dust: The Inside Story of Its Role in the September 11th Aftermath" ([review](#)).



Linked Audio:
[Listen to Lioy discuss his personal and professional perspectives on the WTC dust in this interview with Leonard Lopate, produced by WYNC. \(16:00\)](#)
(Launches in new window)

Download Media Player:  Quicktime 

Long history with NIEHS

Over the course of his career, Lioy's involvement with NIEHS took many forms, from grantee researcher and lecturer to associate editor for the NIEHS journal *Environmental Health Perspectives* (EHP), beginning in 2003. He published 35 papers in EHP, including four on his World Trade Center dust exposure research, as well as a landmark [editorial advocating a comprehensive approach to studying the exposome](#), co-authored with Stephen Rappaport, Ph.D.

His impact was recognized by David Balshaw, Ph.D., head of the NIEHS Exposure, Response and Technology Branch. “Paul had a unique gift for getting past the exposome as buzzword science,” Balshaw said. “He understood the importance of how we integrate information on exposures across a range of variables, from external contact to internal dose and biological response.”

Bill Suk, Ph.D., director of the Superfund Research Program at NIEHS, expressed the shock felt by many upon hearing the news of Lioy’s death. Suk said he first got to know Lioy in 1990, when they worked together to plan a workshop on exposure assessment.

“Since then, we continued to interact as colleagues and broke bread at various meetings, but especially at the Collegium Ramazzini.” The [Collegium Ramazzini](#) is an international academy of experts in occupational and environmental health. Suk also spoke at a 2008 symposium held in Lioy’s honor when he received the Fifth Annual Distinguished Alumni Award from the Rutgers University Graduate School (see [story](#)).

Friends and family have posted a website, [paullioy.com](#), for sharing memories and information about Lioy’s life and work.

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Tibbetts Award recognizes NIEHS grantee innovation in rodent control

By Kirsten Mease

SenesTech co-founders Loretta Mayer, Ph.D., and Cheryl Dyer, Ph.D., were recognized June 15 with one of the highest honors from the U.S. Small Business Administration (SBA), a Tibbetts Award (see [sidebar](#)). [SenesTech](#), their Flagstaff, Arizona biotechnology company, developed a novel technology for pest management that uses a humane, sustainable strategy to get to the root of the problem — reproduction. This approach may reduce the reliance on traditional rodenticides, which can adversely affect ecological and human health.

The patented bait technology developed by SenesTech delivers a liquid that disrupts fertility in both male and female rodents, causing significant reductions in urban rodent populations. The bait uses a combination of 4-vinylcyclohexene diepoxide (VCD) and triptolide, a natural product isolated from plants.

Mayer and Dyer received their grants, known as Phase I and Phase II small business innovation research (SBIR) grants, from NIEHS in 2011. These SBIR-funded projects enabled the company to prove its product was effective in an urban environment, through a pilot project using population modeling studies in the New York subway system. “This approach has great potential as a safer and more effective means for reducing rodent populations in urban and agricultural settings,” said [Daniel Shaughnessy, Ph.D.](#), NIEHS program manager for the SBIR grants.

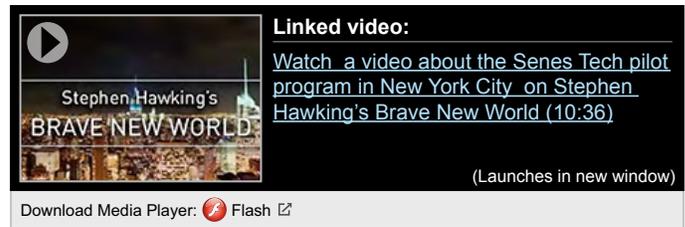


Maria Contreras Sweet, SBA administrator, left, presents a Tibbetts Award to Mayer, right, at the 2015 Tibbetts Award ceremony, held at the White House in the historic Indian Treaty room. Mease was in attendance. (Photo courtesy of Risdon Photography)

Innovative and effective approach to rodent population management

Reducing the ability to reproduce allows maintenance of rodent populations at a low level, which is critical to avoid the population rebound effect commonly seen after poisoning, when surviving rats can reproduce even faster and neighboring rats can move in. SenesTech's compound, when used as directed, is safe for handlers and nontarget species, such as pets, livestock, and wildlife. The bait stations were designed to avoid exposure to the fertility control agents by other wildlife and domestic animals.

Population modeling studies conducted by SenesTech scientists in several real-world settings, including the New York City subway system, demonstrated a 50 percent reduction in rat populations in a six-month period. A recent independent study conducted by the United States Department of Agriculture (USDA) found that SenesTech's product was 100 percent effective in rendering wild-caught rats infertile after consuming the bait. In addition to USDA, SenesTech is working closely with the U.S. Environmental Protection Agency (EPA) and expects to have EPA registration of their technology in the coming year.



Tibbetts Awards

Named after Roland Tibbetts, who was instrumental in developing the SBIR program, the annual [Tibbetts Awards](#) recognize promising scientists and their models of excellence in high technology.

Winners are selected based on the economic impact of their technological innovation, and the extent to which that innovation served federal research and development needs, encouraged diverse participation, and increased the commercialization of federal research.

The cost of major urban and agricultural pest challenges

According to SenesTech, annual economic losses caused by rodent populations in the U.S. exceed \$27 billion a year. Rodents reduce the quality of life in cities, damage urban infrastructures, destroy crops, contaminate animal feed, and transmit disease.

The Center for Infection and Immunity at Columbia University's Mailman School of Public Health confirmed in a [study published in October 2014](#) that rats in New York City carry more than 15 pathogens that can cause serious and sometimes life-threatening illnesses in humans, including the Seoul Hantavirus, salmonella, and *Escherichia coli*. Senestech is collaborating with and licensing their technology to companies like Orkin, Neogen, and other commercial partners, to bring their technology to market to address these public health threats.

NIEHS small business funds also enabled SenesTech to participate in two small business technical assistance programs through the National Institutes of Health — [Niche Assessment](#) and [Commercialization Assistance Program](#). “[This] allowed us to step out of the lab to build the business,” said Mayer.

(Kirsten Mease is a program analyst for Kelly Government Solutions, a contractor supporting the innovative small business grant programs at NIEHS.)

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Evaluating worker training from the mid-management perspective

By Eddy Ball

A new study gives high marks to worker health and safety training and takes a rare look at how mid-level managers value NIEHS-funded [programs](#).

The research focused on the perceptions of managers involved in meeting the Occupational Safety and Health Administration (OSHA) standards for Hazardous Waste Operations and Emergency Response (HAZWOPER) activities. As the researchers noted in their paper, “Few studies to date have considered this training from a management point of view.” The study was led by University of California, Los Angeles researchers Kevin Riley, Ph.D., and Linda Delp, Ph.D.

“This is an important part of our quality control — to obtain feedback from managers, to understand their perceptions on the value of training, and to develop strategies to improve workers’ access to training,” said Sharon Beard, industrial hygienist in the NIEHS Worker Training Program. “Our goals are to empower workers with knowledge to make positive change in the workplace, and to engage with management about the importance of health and safety in potentially hazardous work environments and measuring program effectiveness as objectively as possible.”

Published in the July issue of the American Journal of Industrial Medicine, the [study](#) is an analysis of responses from 109 operations and safety managers across the country regarding what motivates them to send their employees to the training, and what they value most about the programs.

Changes in attitudes

Survey responses indicated that changes in health and safety were well underway in their workplaces as a result of participation in training programs. As the most important factors in a manager’s decision to provide employees with HAZWOPER training, protecting employees from hazards rated highest at 33.3 percent, and regulatory compliance came in second at 31.5 percent. Although 81.6 percent ranked the OSHA requirement as highly important in their decision, 44 percent responded that they would provide the same level of training if there were no requirement in place.



Beard has administered NIEHS-funded minority and HAZWOPER training programs for more than 20 years. In 2013, the American Public Health Association honored her work with the Lorin Kerr Award for leadership in public policy advocacy. (Photo courtesy of Steve McCaw)

HAZWOPER training

There are three levels of NIEHS-funded [HAZWOPER](#) training offered on-site and usually at no cost to participants or employers.

- General site hazardous waste cleanup.
- Hazardous waste management.
- Emergency response to hazardous materials incidents.

The study surveyed programs offered by the following four organizations:

- Midwest Consortium for Hazardous Waste Worker Training.
- New England Consortium-Civil Service Employees Association.
- New Jersey-New York Hazardous Materials Worker Training Center.
- Western Region Universities Consortium.

On the down side, while more than three-quarters of respondents anticipated safer workplace practices as a result of training, only about one-third envisioned active involvement of workers in health and safety policymaking as an outcome. Without a standard in place, at least one-third of managers predicted their organizations would likely provide less frequent training or shift to online formats to save time and money.

According to the leads of worker health and safety training programs, even with mandates and training offered on-site at no cost to employers, managers are often reluctant to give workers release time to participate.

“We [at NIEHS] feel strongly that worker involvement is key to improving occupational health and safety,” Beard said. “Although training designed to meet or exceed NIEHS [minimum guidelines](#) clearly has an impact, changing management attitudes remains a challenge.”

Citation: [Riley K, Slatin C, Rice C, Rosen M, Weidner BL, Fleishman J, Alerding L, Delp L](#). 2015. Managers’ perceptions of the value and impact of HAZWOPER worker health and safety training. *Am J Ind Med* 58(7):780-787.

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Wilson’s mentoring award celebrated

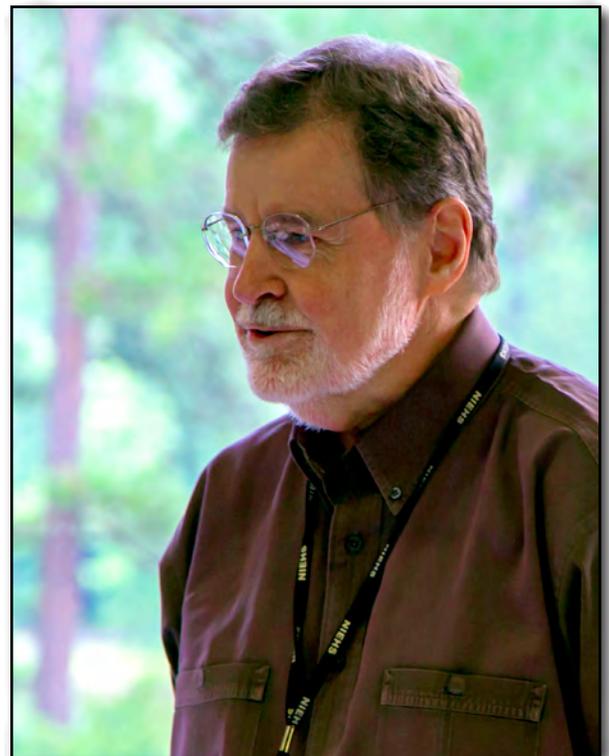
By Eddy Ball

More than 100 colleagues and trainees turned out July 22 to show their appreciation for NIEHS lead researcher [Samuel Wilson, M.D.](#), and celebrate his National Institutes of Health (NIH) mentoring award, the latest in a long list of honors for his work at NIEHS.

Wilson is one of this year’s recipients of the prestigious [Ruth L. Kirschstein Mentoring Award](#), the highest recognition at NIH for exemplary performance while demonstrating significant leadership, skill, and ability in serving as a mentor. Every year, each institute and center can nominate one candidate to receive the award.

Noting that the award will be officially made in September, NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., said, “I think it’s great that we went ahead to say, ‘Thank you, thank you’ [for your leadership, science, and mentoring].”

Wilson responded, “It’s a huge honor... for me and for the NTA [NIEHS Trainee Assembly] and the outstanding training program we have here.” Characteristically, he was quick point out his debt to others, naming several of his colleagues. “It [the award] really is for all of us.”



The award was especially meaningful, Wilson said, because he had worked closely with Kirschstein during her leadership of NIH. He also noted that the award helps NIEHS stand out among the institutes and centers at NIH. (Photo courtesy of Michael Garske)

Following the footsteps of a great mentor

The award is named for pathologist and polio vaccine developer [Ruth Kirschstein, M.D.](#), who served as director of the National Institute of General Medical Sciences and was the first woman to serve as a director of an institute. She was also deputy director of NIH in the 1990s and acting director of NIH in 1993 and 2000-2002. She died in 2009, and NIH published [Kirschstein's biography](#), "Always There," in 2011.

Kirschstein's strong commitment to high-quality training is also reflected in other awards named for her, including the NIH Ruth L. Kirschstein National Research Service Award and the American Society for Biochemistry and Molecular Biology Ruth Kirschstein Diversity in Science Award.

Wilson heads the DNA Repair and Nucleic Acid Enzymology Group at NIEHS. He also served as deputy director of NIEHS 1996-2007 and acting NIEHS and NTP director 2007-2009.

He was founding director of the Sealy Center for Molecular Science and director of the Center for Environmental Toxicology at the University of Texas Medical Branch 1991-1996, following service as a lead researcher with the National Cancer Institute.

(Eddy Ball, Ph.D., is a contract writer with the NIEHS Office of Communications and Public Liaison.)



Linked Audio:
[Listen to an NIH audio about the remarkable life of Ruth Kirschstein \(11:48\)](#)
(Launches in new window)

Download Media Player: [Quicktime](#)



Biologist Denise Appel, of the NIEHS Genome Stability Structural Biology Group, made a unique cake, formed to resemble the three-dimensional structure of polymerase beta, an enzyme-DNA complex, with the playful addition of workers to depict its key role in DNA repair. (Photo courtesy of Michael Garske)



Tammy Collins, Ph.D., in blue and white shirt, was part of the crowd of trainees and colleagues who showed their appreciation for Wilson's contributions to training at NIEHS. Collins, who was previously a postdoc at the institute, now heads the NIEHS Office of Fellows' Career Development. (Photo courtesy of Michael Garske)



Birnbaum and Wilson kept their comments brief, so attendees could have time to enjoy refreshments and socialize. (Photo courtesy of Michael Garske)



NIEHS Scientific Director Darryl Zeldin, M.D., left, enjoyed mingling with the crowd and talking with lead researcher Perry Blackshear, M.D., D.Phil., center, and Joel Abramowitz, Ph.D., special assistant to the deputy scientific director. (Photo courtesy of Michael Garske)



Lead researcher Robert Petrovich, Ph.D., left, head of the NIEHS Protein Expression Core, paused to admire the cake before serving refreshments. He co-organized the event with William Copeland, Ph.D., head of the Genome Integrity and Structural Biology Laboratory. (Photo courtesy of Michael Garske)



Wilson enjoyed the fellowship of colleagues during the event, including Mechanisms of Mutation Group head Roel Schaaper, Ph.D., right, and visiting fellow Mark Itsko, Ph.D. (Photo courtesy of Michael Garske)

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A scientist gives back — Rahman on women’s environmental health

By Simone Otto

NIEHS welcomed Qamar Rahman, Ph.D., for a July 8 talk on the challenges faced by Indian women in the workplace, titled “Women! A Vulnerable Population in Occupational Settings.” Rahman highlighted her motivation to give back to her community by working to improve the occupational and environmental health of Indian women.

Dean of research science and technology at Amity University in Lucknow, India, Rahman is also the former deputy director of the [Indian Institute of Toxicology Research](#) in Lucknow. She is an expert in inhalation toxicology, especially of nanoparticles and asbestos.

“Dr. Rahman is tremendously accomplished as a scientist and a dedicated champion for women,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program. “Her outstanding work earned her an honorary degree from Rostock University in Germany. In 600 years of the university’s history, she is the only Indian to receive such a degree. That’s quite an achievement.”

Environmental and occupational hazards

Rahman’s talk focused on occupational threats to the lung health of women, addressing three broad areas. The first was the lack of ventilation for indoor cooking. She explained that Indian women rely on the smoke to drive off mosquitos and heat the room, but breathing that smoke, from fuels such as kerosene, wood, and cow dung cakes, often leads to respiratory disease.

Next, Rahman turned to women employed in the manufacture of asbestos, a process recently banned in certain business sectors, but still occurring illegally. She said that many women develop asbestosis within 5 to 7 years of beginning such work.

Finally, Rahman discussed silicosis, a disease caused by the inhalation of silica from sand, rock, and mineral ores. She told of asking one worker, “Don’t you know this dust is toxic?” Rahman said the worker replied, “Yes, I know it well. But I do not want to die of hunger.”



Rahman shared how she has combined scientific innovation and scientific research with action to solve social issues, especially woman’s issues. (Photo courtesy of Steve McCaw)



Birnbaum, right, the first woman director of NIEHS, and Rahman share both a history as trailblazers for women and life-long passions for toxicology. (Photo courtesy of Steve McCaw)

Working to make a difference

Rahman's empathy for these women made her determined to help. "I thought, I've done so much in my life, now I can give it back," she said. Rahman serves as chair of the Foundation for Education and Economic Development. The foundation works to address issues that prevent social equality and development, through education and empowerment.

According to Rahman, Indian Prime Minister Indira Gandhi, quoting Bhim Rhao Ambedkar, Ph.D., D.Sc., said, "I measure the progress of a community by the degree of progress which women have achieved." Rahman discussed health issues of women worldwide, providing examples of nutritional, neonatal, and maternal health concerns. "Gender equality is very important," she said.

Active in the World Health Organization and the Indian government, Rahman forged a path for other women to follow, then turned back to help bring progress to the lives of local disadvantaged women.

During a [previous visit to NIEHS](#), Rahman spoke on the health effects of nanoparticles.

(Simone Otto, Ph.D., is an Intramural Research and Training Award fellow in the Ion Channel Physiology Group at NIEHS.)

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Help document NIEHS history

By Eddy Ball

In preparation for its 50th anniversary next year, NIEHS is calling on stakeholders to submit nominations for notable accomplishments and the people behind them.



NIEHS and the National Toxicology Program Director Linda Birnbaum, Ph.D., is urging all current and former employees, and those with knowledge of NIEHS' past, to join in documenting the institute's history, research highlights, public health impacts, milestones, and people who have shaped the institute over the past half century.

To this end, the NIEHS Office of Communications and Public Liaison created a special Web page at www.niehs.nih.gov/about/50years where nominations can be submitted. All submissions are due by Sept. 15, 2015.

Birnbaum also invites employees and others to send names and email addresses of people who may be interested in participating in the Nov. 1, 2016 anniversary event to [Kathryn Lawrence](#) or [Devlin Sawyer](#), support personnel for the 50th anniversary planning committee.

NIEHS already has some historical information, including a list of scientific accomplishments published in the January 1996 issue of the Environmental Factor newsletter (see [text box](#) below). However, Birnbaum and the planning committee now want to hear from others, in order to integrate a variety of perspectives for a more broad and inclusive range of the institute's basic research, community engagement, and public health initiatives.

If you have information you'd like to share towards this cause, please submit your nomination through the Web page above.



Nestled in a forest of pines, the original NIEHS North Campus and its signage were a far cry from the gated security and grand signs of today's campus. (Archive photo courtesy of Steve McCaw)



Seen from the air, the North Campus looked more like a high school than the place where NIEHS conducted research and other business for several decades before completion of its new, higher-tech facility. (Archive photo courtesy of Steve McCaw)



The advent of specialized human resources functions was not yet at hand, so it was still just plain personnel. (Archive photo courtesy of Steve McCaw)



Unlike working with today's collection of electronic resources, the original NIEHS library research experience involved turning pages and making handwritten notes. (Archive photo courtesy of Steve McCaw)



With fewer employees, NIEHS staff more easily participated in division-wide and institute-wide activities, such as picnics. (Archive photo courtesy of Steve McCaw)



One of the institute's early work-life accomplishments was a quality employer-sponsored day care facility on campus. (Archive photo courtesy of Steve McCaw)

The 50th anniversary list of scientific accomplishments will build upon this list from the January 1996 Environmental Factor.

NIEHS Scientific Accomplishments



The following list provides some scientific highlights of the Institute. More than half of the accomplishments listed here were achieved after 1990, a tribute to the maturation of the Institute into a first-class scientific research institution. NIEHS is still building on the strength of the early 1990's, which points to a brilliant future.

- NIEHS epidemiologists report that intercourse during the six days leading up to a woman's ovulation is most likely to result in conception of a child. (1995)
- Institute scientists announce the production of two lines of genetically altered mice that will have a significant impact on the study of colon cancer and the development of aspirin-like drugs. (1995)
- NIEHS supports the current work of Dr. Mario Molina, the co-recipient of the 1995 Nobel Prize in chemistry for his pioneering work on the depletion of the earth's ozone shield.
- NIEHS researchers, in collaboration with scientists from Johns Hopkins University, identify and clone a gene that suppresses the spread of prostate cancer in experimental animals. (1995)
- A mathematical model developed by Institute scientists provides an unprecedented analysis of the biochemical effects of a form of dioxin, and opens the door to the use of similar approaches for assessing the risks of other chemicals. (1995)
- NIEHS scientists, in collaboration with researchers from Italy, synthesize a new class of opioid compounds that have potential clinical uses, including the treatment of chronic and acute pain, the control of narcotic addiction and alcohol abuse, and the suppression of the immune response during transplant surgery. (1995)
- NIEHS' Dr. Martin Rodbell is co-recipient of the Nobel Prize in medicine for discoveries about the communication system that regulates cellular activity. (1994)
- Institute scientists, along with the University of Utah Medical Center, isolate a tumor-suppressor gene, BRCA1, that is thought to play a critical role in the development of hereditary breast and ovarian cancer. (1994)
- Institute investigators develop a strain of mouse that lacks functional estrogen receptors. This helps evaluate the different pathways by which some pesticides and other estrogen-like compounds may produce biological effects. (1993)
- Working with the largest available data base on the health effects of outdoor and indoor air pollutants, Institute investigators find a strong association between exposure to fine particles, sulfur dioxide, and acid aerosols, and an increase in respiratory symptoms, reduced lung capacity, and risk of early death. (1993)
- Scientists from the Institute's National Toxicology Program find that certain mixtures of chemicals found in groundwater near chemical waste sites, when given at environmentally relevant doses, can produce a "toxic state" that reduces the animal's ability to withstand bacterial, viral, and other environmental challenges. (1993)
- Recent National Toxicology Program studies conclude that laboratory animals dosed with various byproducts of water purification show significant increases in colon and rectal tumors. This suggests that reducing the organic contaminants in chlorinated drinking water may enhance the benefits of this water treatment method. (1993)
- Institute grantees identify a key molecule called the Ah receptor that will enable researchers to develop a better understanding of how dioxin affects human cells. (1990)
- NIEHS-funded studies show that asbestos and other fibrous materials stimulate the release of a highly reactive form of oxygen that has been shown to damage lung tissue. (1989)
- Institute scientists isolate bradykinin, a peptide hormone involved in pain perception, from cow's milk. (1989)
- Institute epidemiologists report that 25 percent of all pregnancies are lost before they can be recognized by the mother or her doctor, and that when later miscarriages are included, one in three pregnancies fails to survive to birth. (1988)
- Working with cancer cells taken from human lung tissue, Institute investigators isolate several opioid compounds that have particular significance for the control of cancer growth. (1983)
- NIEHS researchers develop a design strategy for evaluating the carcinogenicity of environmental agents. It will improve their ability to identify hazards and estimate risks while at the same time reducing the need for laboratory animals. (1981)
- Data generated by Institute epidemiologists link asbestos exposure to an increased incidence of lung tumors and mesotheliomas, and establishes that cigarette smoking greatly increases the risk of cancer in asbestos-exposed workers.
- Experiments conducted by NIEHS-supported investigators find that exposure to very low levels of lead during early childhood can lead to significant delays in cognitive and behavioral development. (1979)
- A laboratory animal model developed by NIEHS scientists predicts and confirms that exposure to diethylstilbestrol (DES) during pregnancy can result in various reproductive abnormalities in both male and female offspring. (1975)
- After performing the most extensive evaluation ever done on the Ames assay, a test that is used to screen chemicals for their ability to cause cancer, Institute researchers conclude that while the test is successful in a high percentage of cases, there appear to be a significant number of carcinogens missed by this procedure.
- NIEHS-supported investigators determine that exposure to the industrial chemical bischloromethyl ether (BCME) is the likely cause of increased lung cancers among plant workers. (1974)
- Data collected by NTP scientists on the toxic and carcinogenic potential of such substances as benzene, butadiene, methylene chloride, various dyes, and a host of drugs and food additives indicates that exposures to these substances should be limited or avoided entirely. This has resulted in federal regulations regarding permissible exposure limits for each.
- Animal studies conducted by NIEHS researchers provide a reasonable degree of certainty that many of the chemicals that people are exposed to are not likely to be carcinogenic. Some examples: the antibiotics penicillin and erythromycin stearate, and the chemical solvent toluene.
- *Tell us what we missed. Contact John Peterson (OC), ext. 7860.*

[Click to enlarge](#)

NIEHS small business innovation shines at biotech convention

By Sara Mishamandani

At the BIO International Convention June 15-18 in Philadelphia, four NIEHS-funded small businesses were among the 35 National Institutes of Health (NIH) grantees selected to exhibit in the Biotechnology Industry Organization (BIO) Innovation Zone. Each year, the convention attracts about 15,000 biotech leaders from 65 countries, covering a wide spectrum of life science innovations.

The BIO Innovation Zone was an exhibit space dedicated to showcasing NIH and National Science Foundation Small Business Innovation Research grantees, with a primary focus on biomedical technologies. The four NIEHS small business grantees chosen for the innovation exhibit were [Microvi Biotechnologies](#), [Giner Inc.](#), [TF Health Corporation](#), and [Trevigen Inc.](#)

Giner specializes in the development of proton exchange membrane-based electrochemical technologies; Trevigen focuses on a high-throughput platform to measure DNA damage and repair; and TF Health is developing a monitor to measure volatile organic compounds.

A spotlight on Microvi

In a space filled primarily with biomedical and pharmaceutical-oriented organizations, Microvi, a Superfund Research Program (SRP) small business grantee, was one of the few companies to focus on environmental cleanup.

“SRP was pleased to learn Microvi was chosen to showcase an environmental remediation application,” said Heather Henry, Ph.D., NIEHS SRP Health Scientist Administrator. “Their approach shows great promise to remove 1,4-dioxane from drinking water.” A suspected carcinogen, 1,4-dioxane is difficult to remove with conventional water treatment technologies.

“It was encouraging to find many organization representatives with not just knowledge of, but also interest in, bioremediation,” said Ameen Razavi, director of Innovation Research at Microvi, who represented the company at the convention. “We highlighted our 1,4-dioxane technology and our cometabolic remediation technology, and also discussed how our overall approach to water treatment is unique and novel.”



Razavi represented Microvi at the event. (Photo courtesy of Ameen Razavi)



The Innovation Zone included a tremendous range of organizations and provided an excellent opportunity for networking and partnership discussions. (Photo courtesy of Ameen Razavi)

An innovative approach to remove 1,4 dioxane

As part of its NIEHS [SRP-funded small business project](#), Microvi is developing a first-of-its-kind biological approach for 1,4-dioxane degradation. The technology, called MB-DX, uses microbes that degrade 1,4-dioxane effectively and reliably. The approach also overcomes common challenges to bioreactor performance, such as system stability and clogging. The company has successfully developed a prototype, which is now being scaled-up and piloted at a contaminated site.

“An interesting fact that resonated in our discussions was how closely the research and development in biomedical sciences can be integrated for bioremediation technologies,” said Razavi. “Many of the novel assays, metagenomics tools, real-time metabolite analyzers, and more were directly applicable to our work in ways that could only come through in such detailed, in-person discussions.”

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

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NIH seeks planning input

The National Institutes of Health (NIH) is developing a 5-year [strategic plan](#) to outline a vision for biomedical research that will ultimately extend healthy life and reduce illness and disability.

Senior leadership has developed a framework for the plan (see [graphic](#) on next page) that identifies areas of opportunity and principles to guide NIH support of biomedical research. They are now seeking comments and suggestions from a broad range of individuals and organizations through a [Request for Information](#) Web page.

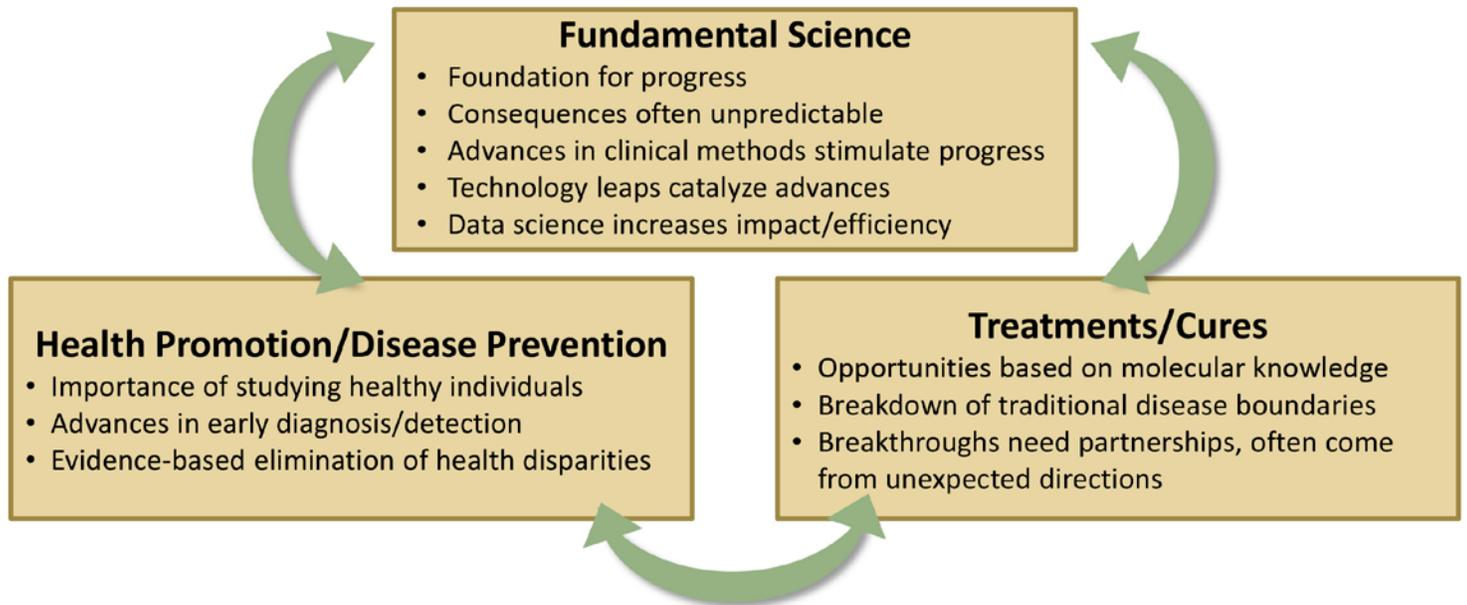


“Your input is vital to ensuring that the NIH Strategic Plan positions biomedical research on a promising and visionary path,” said NIH Principal Deputy Director Lawrence Tabak, D.D.S., Ph.D. He is also encouraging organizations, such as patient advocacy groups and professional societies, to submit a single response reflective of the views of the organization as a whole.

NIH will host webinars in early to mid-August, to gather additional input. They will be announced on the strategic plan [website](#) as they are scheduled.

Overview

- Mission of NIH
- Unique moment of opportunity in biomedical research
- Current NIH-supported research landscape
- Constraints confronting the community in the face of lost purchasing power



Setting Priorities

- Incorporate disease burden as important, but not sole factor
- Foster scientific opportunity; need for nimbleness
- Advance research opportunities presented by rare diseases
- Consider value of permanently eradicating a pandemic

Enhancing Stewardship

- Recruit/retain outstanding research workforce
- Enhance workforce diversity
- Encourage innovation
- Optimize approaches to inform funding decisions
- Enhance impact through partnerships
- Ensure rigor and reproducibility
- Reduce administrative burden
- Employ risk management strategies

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Clinical Feature

Gibbons calls for reimagining clinical research

By Eddy Ball

During a talk July 20 at NIEHS, Gary Gibbons, M.D., director of the National Heart, Lung, and Blood Institute (NHLBI), outlined his vision for the future of precision medicine.

Gibbons' presentation, "Charting Our Future Together: Setting an Agenda for the NHLBI," was hosted by NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D. The lecture attracted scientists from across the institute and, not surprisingly, a substantial number who are involved in [clinical research](#).

In her introduction, Birnbaum mentioned the full agenda of meetings planned for Gibbons, with both in-house researchers and grants program managers. "There's a lot of opportunity for cross talk and cross walk between our two institutes," she said.

Enduring principles

Gibbons began by describing the enduring principles of NHLBI. "Our institutes share a lot of common interests, and ongoing collaborations are something we can look forward to," he said.

Gibbons pointed to the shared respect for researcher-initiated discovery science, balanced grant portfolios, diversity in the biomedical workforce, implementation science, and elimination of health inequities.

Like Birnbaum, Gibbons could speak with pride about accomplishments — in the case of NHLBI, dramatic reductions of 70 percent in heart disease and 79 percent in stroke. Both are directly attributable to NHLBI public health interventions, metabolic pathway research, and large clinical trials. But he could also point to disappointments, such as poorly performing clinical trials and persistent health inequities related to racial segregation and poverty.

Precision medicine

Describing NHLBI and its goal for the next decade, Gibbons highlighted his institute's overarching goal — doing its part to realize President Obama's [vision](#) of a truly predictive precision medicine model.



"We've had a great deal of success," Gibbons told the audience as he introduced the topic of health inequities, an important theme of his presentation. "But we also recognize that what I showed you [to be] true in aggregate is not happening in every segment of our society." (Photo courtesy of Michael Garske)

Building upon the legacy of success

Gibbons described himself as a pragmatic optimist as he outlined the NHLBI vision of a world where the burden of cardiovascular, lung, and blood diseases can be prevented by capturing the promise of personalized precision medicine.

As he and his colleagues wrote in an *American Journal of Public Health* editorial, "This vision is not merely a collection of idle dreams; the boundless possibilities of this bold new world are well within our reach."

The model is based on an approach of integrating new tools and smart technology, analyzing large data sets, and networking. It would incorporate recognizable elements of personalized medicine with new research to redefine what Gibbons called clumped diseases, such as asthma and other lung diseases, to achieve more clearly targeted and effective interventions.



Gibbons provided a hypothetical scenario for a patient he called Carla, an African-American woman with no obvious disease, but a substantial risk for the future.

Carla, he said, has a family history that suggests she is at greater risk for chronic kidney disease (CKD). Genetic testing uncovered a gene variation linked to CKD and helped determine a plan to cut her risk. With new personal monitoring technology, Carla and her health care providers can continuously evaluate her vital signs, behavior, and diet.

This information stream can then empower her with the knowledge and encouragement to increase her compliance with the preventive program, and help reduce her inherited risk for developing a serious and potentially fatal disease.

Gibbons' message found a receptive audience among NIEHS clinical researchers, such as Shepherd Schurman, M.D., associate medical director of the institute's Clinical Research Unit and lead researcher for the Environmental Polymorphisms Registry (see sidebar).

“Dr. Gibbons outlined the challenges of precision medicine,” Schurman said. “We have exciting opportunities for integrating clinical and basic research, with new real-time monitoring technology emerging from sources such as our [exposure biology and the exposome](#) research.”

Citation: Mensah GA, Kiley J, Mockrin SC, Lauer M, Hoots WK, Patel Y, Cook NL, Patterson AP, Gibbons GH. 2015. National Heart, Lung, and Blood Institute Strategic Visioning: setting an agenda together for the NHLBI of 2025. *Am J Public Health* 105(5):e25-e28.

(Eddy Ball, Ph.D., is a contract writer with the NIEHS Office of Communications and Public Liaison.)



The audience included staff from the NIEHS Office of Human Research Compliance, among them Joan Packenhams, Ph.D., center, and protocol coordinator Craig Wladyka, left. (Photo courtesy of Michael Garske)

Environmental Polymorphisms Registry supports precision medicine

The NIEHS [Environmental Polymorphisms Registry](#) provides precision medicine researchers with the means to study how particular gene variations may interact with environmental exposures in ways that promote or protect against disease development.

Through the registry, the Office of Clinical Research maintains a biobank of DNA samples, which are available to approved researchers. Through the registry, scientists may ask the registrants to come back and participate in follow-up studies, based on their genetic and clinical profiles.



For Gibbons, a quote from former Surgeon General M. Joycelyn Elders, M.D., shown on the screen, spoke eloquently to the importance of health and education in the well-being of society. “You can’t educate a child who isn’t healthy, and you can’t keep a child healthy who isn’t educated.” (Photo courtesy of Michael Garske)



The Gibbons talk drew staff from across the institute, including lead researcher Donald Cook, Ph.D., left, and postdoctoral fellow Seddon Thomas, Ph.D., both of the Immunogenetics Group. Cook’s lab studies how environmental exposures influence allergic sensitization in the lung. (Photo courtesy of Michael Garske)



NIEHS grants program managers Thaddeus Schug, Ph.D., left, and Sri Naddadur, Ph.D., to his right, were also on hand to hear about the NHLBI strategic plan. (Photo courtesy of Michael Garske)



Gibbons and NHLBI Chief of Staff Nakela Cook, M.D., joined their NIEHS hosts following the talk. Shown, from left, are Cook, Birnbaum, Gibbons, and NIEHS Deputy Director Rick Woychik, Ph.D. (Photo courtesy of Michael Garske)

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Science Notebook

Researchers rise to the challenge of studying mixtures

By Virginia Guidry

Real-world chemical exposures occur in mixtures, yet researchers typically study exposures to single chemicals, due to analytical limitations. NIEHS invited scientists from across the country to a workshop July 13-14, to evaluate new statistical methods for studying exposures to mixtures of chemicals in the environment.

[Statistical Approaches for Assessing Health Effects for Environmental Chemical Mixtures in Epidemiology Studies](#) brought together epidemiologists, biostatisticians, toxicologists, and exposure scientists eager to tackle the topic.

The need to study mixtures

Studies of mixtures are tricky because of the need for complicated measurements, the difficulty of determining which components are of concern, and the lack of well-established statistical methods. “It is imperative that the study of environmental mixtures be driven by our research questions and not by the statistical tools at our disposal,” said [Joseph Braun, Ph.D.](#), of Brown University during his opening talk.

“Times have changed dramatically with our computing power and our understanding of the environment and the complexities of exposure,” said Gwen Collman, Ph.D., director of Extramural Research and Training at NIEHS. She added that scientists need to use emerging tools to better understand how the web of environmental exposures may contribute to a host of health endpoints.

Meeting the challenge

NIEHS organized the workshop around a challenge to researchers. Last year, a planning committee, led by [Danielle Carlin, Ph.D.](#), of NIEHS, invited scientists to analyze three epidemiological data sets and submit abstracts describing their approaches and results. More than 30 abstracts were submitted and displayed in the poster session. The committee selected 20 of them for workshop presentations.

Two of the data sets the committee provided contained simulated data, generated by meeting planners so that the analyses would be more straightforward and the results



“One of the greatest challenges is that there is really not a consensus yet on how we should approach these questions,” Braun said.

“This workshop will help us develop a framework for selecting and applying available [statistical] tools.” (Photo courtesy of Steve McCaw)

Collaborative planning team

The meeting was planned collaboratively by scientists at NIEHS and grantee institutions, including:

- Danielle Carlin, Ph.D., NIEHS, chair
- Joseph Braun, Ph.D., Brown University
- Caroline Dilworth, Ph.D., NIEHS
- Chris Gennings, Ph.D., Icahn School of Medicine at Mount Sinai
- Russ Hauser, M.D., Sc.D., Harvard University
- Bonnie Joubert, Ph.D., NIEHS
- Cynthia Rider, Ph.D., NIEHS
- Thomas Webster, D.Sc., Boston University

easier to compare. The third data set came from the [Health Outcomes and Measures of the Environment \(HOME\)](#) study, based at the Cincinnati Environmental Health Center and funded in large part by NIEHS.

Attendees shared solutions using a variety of statistical methods (see sidebar), and lively discussion characterized the event. [Veronica Vieira, D.Sc.](#), from the University of California, Irvine, echoed the enthusiasm many attendees expressed about the opportunity to compare approaches. “[It’s great] to see so many different methods applied to the same data sets, because replication is a big deal,” she said.

The organizers commended participants for the time they spent analyzing data for the challenge. “When you consider that the environmental health community was willing to put hundreds of person-hours into this, that response says something about the field,” said Braun, as he reflected with fellow planning team member [Russ Hauser, M.D., Sc.D.](#), of Harvard University. Organizers also celebrated the involvement of both junior and senior scientists in the workshop.

Continuing development of statistical methods

The meeting served as an important springboard for determining how to analyze chemical mixtures in epidemiological studies. “I strongly support the use of more challenges like this to move the field forward,” said [Gaurav Pandey, Ph.D.](#), from the Icahn School of Medicine at Mount Sinai. He has seen similar meetings fuel advances in genomics and computational biology.

According to Carlin, the event highlighted the need for more data sets to be made available, so researchers can conduct comparisons and refine their statistical methods.

Several participants recommended keeping focused on public health research questions as new statistical methods emerge. Others emphasized the need to match statistical methods with the research questions they are best suited to answer.

Hauser reminded scientists to generate results that are useful to policymakers, a goal that may be more complicated with analysis of mixtures. “We have to remember when we publish our results, whether on mixtures or individual chemicals, ultimately, they will be used by risk assessors to protect public health,” he said.

Carlin said the organizers will prepare a report and commentary on the workshop.



Danielle Carlin, Ph.D., left, and Cynthia Rider, Ph.D., both of NIEHS, led the planning for the workshop, which built on outcomes from a [2011 NIEHS mixtures workshop](#). (Photo courtesy of Steve McCaw)

Variety of Statistical Methods

Researchers used a variety of statistical methods to analyze data, including the following:

- Bayesian additive regression tree (BART)
- Bayesian estimation of weighted sum
- Bayesian kernel machine regression (BKMR)
- Exposure surface smoothing (ESS)
- Least-absolute shrinkage and selection operator (LASSO)
- Least-angle regression (LARS)
- Multivariate adaptive spline assessments
- Principal components analysis (PCA)
- Stepwise multiple linear regression
- Weighted quantile sum (WQS) regression

(Virginia Guidry, Ph.D., is a technical writer and public information specialist in the NIEHS Office of Communications and Public Liaison.)



Hauser said the goal of the workshop was to bring researchers together to systematically evaluate different statistical approaches and methods for studying exposures to chemical mixtures. (Photo courtesy of Steve McCaw)



Pam Factor-Litvak, Ph.D., center, of Columbia University, was among the 160 attendees in the Rodbell Auditorium, while 75 more joined via the webcast. (Photo courtesy of Steve McCaw)



Birgit Claus Henn, Sc.D., from Boston University, described her team's use of BKMR to study one of the simulated data sets. (Photo courtesy of Steve McCaw)



Webster, seated between Gennings, left, and Coull, contributed to several of the discussions that made the workshop so productive. (Photo courtesy of Steve McCaw)



Novel statistical methods were featured in oral presentations, panel discussions, and poster sessions, where Changchun Xie, Ph.D., of the University of Cincinnati, explained his technique of using LASSO. (Photo courtesy of Steve McCaw)



Sarah Kreidler, Ph.D., of Neptune Inc., spoke about the use of Bayesian networks for mixtures analysis. (Photo courtesy of Steve McCaw)



Coull, foreground, discusses the first simulated data set with panelists, from left, Katrina Waters, Ph.D., Pacific Northwest National Laboratory; Sung Kyun Park, Sc.D., University of Michigan-Ann Arbor; Gennings, not shown; Vieira; Shuo Chen, Ph.D., University of California, Irvine; and Ghassan Hamra, Ph.D., Drexel University. (Photo courtesy of Steve McCaw)



Park described shrinkage methods used to analyze the real-world data set, including LASSO, Elastic Net, and LARS. (Photo courtesy of Steve McCaw)



James Nguyen, right, of the U.S. Environmental Protection Agency explained his approach to Abhra Sarkar, Ph.D., from Duke University, left, and Susan Teitelbaum, Ph.D., of the Icahn School of Medicine at Mount Sinai. (Photo courtesy of Steve McCaw)

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Environmental influences on breast cancer risk – the evidence mounts

By John Yewell

As a kid growing up on a farm in Wisconsin, Sue Fenton was fascinated by dairy cows. “I always wondered how they could produce milk nearly year-round, for year after year,” she said.

Now a Ph.D. and a reproductive endocrinologist with the National Toxicology Program (NTP) at NIEHS, [Fenton](#) highlighted the cutting edge of mammary gland research, guest editing “Environmental Impact on Breast Development and Disease,” a July 2015 special issue of the journal *Reproductive Toxicology*.

The extent of the problem was spelled out in a [summary article](#) co-authored by Linda Birnbaum, Ph.D., director of NIEHS and NTP, and Gwen Collman, Ph.D., NIEHS Director of Division of Extramural Research and Training.

“Despite decades of research, the number of women diagnosed with breast cancer continues to rise,” they wrote. “In 2014, an estimated 233,000 women and 2400 men in the United States were diagnosed with breast cancer, and approximately 40,000 women died from it.”

It’s complicated

According to Fenton, the breast’s susceptibility to cancer is exceptional among the reproductive organs. “Other tissues such as the ovary, testis, and uterus are also critical for reproduction; yet, they do not display the high degree of carcinogenicity in humans as seen in the breast,” she wrote in her editorial.

The reason, she explained, is the complexity of the tissue, which makes it difficult to get a handle on the reasons for its carcinogenicity.

“There are many cell types in the mammary gland, plus its own fat, which means it has its own hormones from fat. And the breast actually receives signals from about ten different organs,” she said. “This is one of the reasons why more people don’t do this kind of work. You can’t just take the epithelial cells out of their tissue, use them in culture, and expect them to behave as they would in the body, as you can do with many other tissues.”



Fenton addressed the elusive link between breast cancer and chemical exposure. “We may never have enough evidence to prove that something caused a disease, because we’re exposed to so many things in mixtures,” she said. “We need to move from the idea of strict causation to one of increasing or decreasing risk.” (Photo courtesy of Steve McCaw)

Recommendations for further study

The paper co-authored by NIEHS Health Scientist Administrator [Leslie Reinlib, Ph.D.](#), shared an expert panel’s recommendations for research on EDCs and breast cancer. The panel included scientists with extensive experience in using rodent models and in leading population studies.

Recommendation highlights:

- Breast cancer environmental research can be facilitated by long-term animal studies.
- Rodent models show mammary tumors to 130 weeks, similar to 80 years in women.
- Whole Mount Mammary Methods should be used to improve prediction and insights in gene-environment studies.

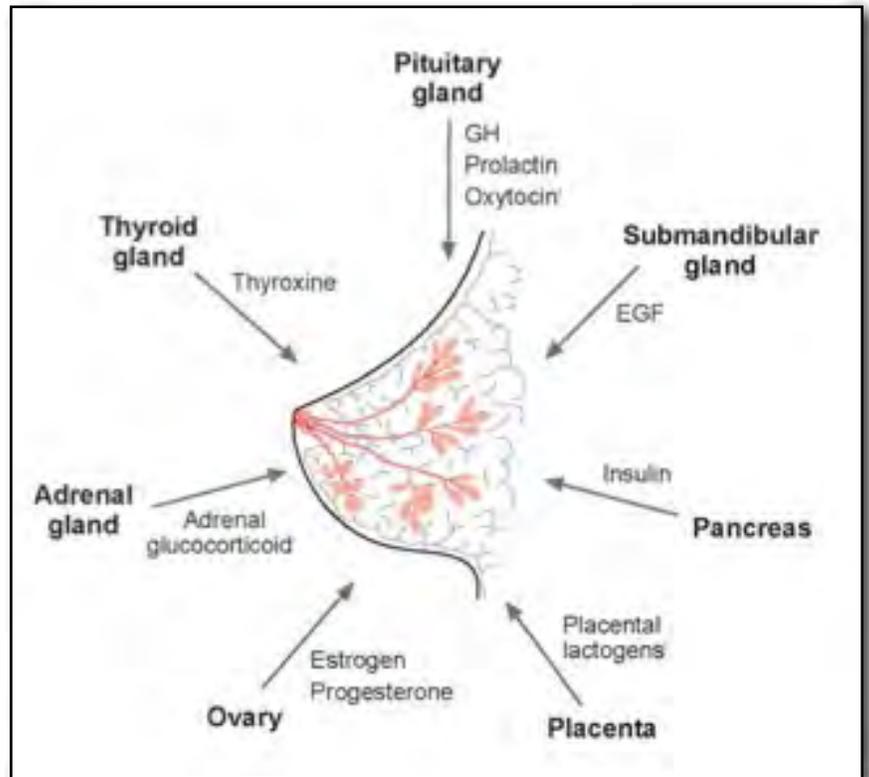
*Citation: [Teitelbaum SL, Belpoggi F, Reinlib L](#). 2015. Advancing research on endocrine disrupting chemicals in breast cancer: Expert panel recommendations. *Reprod Toxicol.* (54):141-147.*

Timing matters

To better understand how endocrine disrupting chemicals (EDCs) cause cancer, the scientists in the special issue relied on animal studies and on associations found in cohorts of children.

“We looked at early exposure to a chemical, as opposed to at the time of diagnosis, and we’re finding some strong risk factors associated with that,” Fenton said. “Fetal exposure, or *in utero* exposure, or prenatal — one of those words is used in almost every one of these studies. I didn’t ask for such papers. It’s just that people are recognizing the importance of it, and they are setting their experiments up that way.”

Birnbaum and her co-authors reinforced the importance of timing in their summary. “There are windows of susceptibility during the life course,” they wrote. “To understand the role of the environment in the etiology of breast cancer, we must understand life stages when the breast is most susceptible to environmental insults.”



The mammary gland is unusual in the number of organs it receives signals from and the number of hormones the tissue responds to. (Image courtesy of Sue Fenton)

A sense of urgency

The evidence for the role of chemical exposure shows up in outcomes such as early puberty and accelerated breast development, which Fenton said is rampant across the globe. “It’s happening much faster than gene change, it’s not genetic,” she said. “It’s definitely the environment playing a role.”

Over the years, with growing evidence for the environmental contributions to cancer, Fenton has acquired a sense of urgency. “It’s one of the most often diagnosed cancers in women, and we know so much less than we know about other cancers.”

Citations:

Fenton SE. 2015. A special issue dedicated to a complex tissue. *Reprod Toxicol.* (54):1-5.

Forman MR, Winn DM, Collman GW, Rizzo J, Birnbaum LS. 2015. Environmental exposures, breast development and cancer risk: Through the looking glass of breast cancer prevention. *Reprod Toxicol.* (54):6-10.

(John Yewell is a contract writer for the NIEHS Office of Communications and Public Liaison)

A wealth of strong research

The issue includes a wealth of studies among its 18 papers. “I knew most of these researchers professionally, so thought they would send high quality manuscripts,” Fenton said. “I was right.” She was happy to note that the scientific community seemed to concur. After only two weeks, one of the papers had already been downloaded 263 times. The following papers are among those in the special issue.

- [California breast cancer prevention initiatives: setting a research agenda for prevention](#), by P. Sutton, et al.
- [In utero preeclampsia exposure, milk intake and pubertal development](#), by Jeremy Michals Schraw, et al.
- [The mammary gland is a sensitive pubertal target in CD-1 and C57Bl/6 mice following perinatal perfluorooctanoic acid \(PFOA\) exposure](#), by Deirdre K. Tucker, et al.
- [Prenatal Bisphenol A exposure delays the development of the male rat mammary gland](#), by Laura Kass, et al.
- [Mixtures of environmentally relevant endocrine disrupting chemicals affect mammary gland development in female and male rats](#), by Karen Riiber Mandrup, et al.
- [Estrogens in the wrong place at the wrong time: Fetal BPA exposure and mammary cancer](#), by Tessie Paulose, et al.
- [Alteration of mammary gland development and gene expression by *in utero* exposure to arsenic](#), by Daniela A. Parodi, et al.
- [Segregated responses of mammary gland development and vaginal opening to prepubertal genistein exposure in Bcl2 ^{-/-} female mice with lipodystrophy](#), by Rong Li, et al.
- [Paradoxical zinc toxicity and oxidative stress in the mammary gland during marginal dietary zinc deficiency](#), by Zeynep Bostanci, et al.
- [Alcohol intake stimulates epithelial proliferation in an authentic model of the human breast](#), by Anke Schennink, et al.
- [Dietary exposure *in utero* and during lactation to a mixture of genistein and an anti-androgen fungicide in a rat mammary carcinogenesis model](#), by P. Phrakonkham, et al.
- [Effect of maternal exposure to endocrine disrupting chemicals on reproduction and mammary gland development in female Sprague-Dawley rats](#), by Fabiana Manservisi, et al.
- [Concentrations of environmental phenols and parabens in milk, urine and serum of lactating North Carolina women](#), by Erin P. Hines, et al.
- [Application of Sholl analysis to quantify changes in growth and development in rat mammary gland whole mounts](#), by Jason P. Stanko, et al.
- [Hypothesis: Activation of rapid signaling by environmental estrogens and epigenetic reprogramming in breast cancer](#), by Lindsey S. Trevino, et al.
- [Evaluating chemical effects on mammary gland development: A critical need in disease prevention](#), by Gwendolyne Osborne, et al.

NTP panel agrees flame retardant mixture exhibits carcinogenic activity

By Ernie Hood

The National Toxicology Program (NTP) convened a panel to peer review a [draft NTP technical report](#) on toxicology and carcinogenesis studies of a pentabromodiphenyl ether (PBDE) mixture, also known as technical grade DE-71.

The peer review panel voted to accept the draft NTP conclusions that described clear evidence of carcinogenic activity in male and female rats and mice, based on study data that documented increased incidences of various liver tumors. The panel met in a [June 25 virtual meeting](#), with the experts participating via videoconference.

PBDE persists in the environment

PBDEs were nominated for NTP study by the California Office of Environmental Health Hazard Assessment. PBDEs are known to have widespread human exposure through household dust and foods, with children often experiencing higher exposures. The Centers for Disease Control and Prevention has found that most people retain PBDEs in body tissues. They also persist in the environment, so they are considered bioaccumulative, persistent organic pollutants.

A mixture of six PBDE compounds, known as DE-71, was used in the past as an additive flame retardant, often in furniture. Because of the limited availability of individual PBDE compounds, NTP chose the DE-71 mixture for a study in rats and mice, to characterize the toxic and carcinogenic potential of PBDEs.

The 3-month toxicology studies were conducted in F344/N rats and B6C3F1/N mice. Wistar Han rats were used in the 2-year toxicology and carcinogenicity studies, reflecting a change in selected rat strain by NTP at that time.

According to the report, although production of PBDEs was voluntarily phased out in the U.S. in 2004, and the European Union also banned their sale and use, the chemicals remain in the environment from older products still in use and in products that are being discarded. PBDEs can be detected in water, wildlife, and humans, as well as in various food products, such as meat, poultry, and fish.



June Dunnick, Ph.D., was the NTP study scientist for the DE-71 project and presented the study design and outcomes to the peer review panel. (Photo courtesy of Steve McCaw)



Kenneth Portier, Ph.D., chaired the peer review meeting, managing the remote participation by his fellow panelists and the in-person contributions from NTP staff. Portier is managing director of the Statistics and Evaluation Center at the American Cancer Society in Atlanta. (Photo courtesy of Steve McCaw)

Clear evidence

The NTP technical report described the methods, results, and NTP conclusions on the levels of evidence for carcinogenic activity under the specific conditions of the study. Peer reviewers were asked to review and evaluate the scientific and technical elements of the study and its presentation in the draft report, and to determine whether the study's experimental design, conduct, and findings support the NTP's conclusions regarding the carcinogenicity and toxicity of the tested substance.

In the series of 3-month and 2-year studies, DE-71 was administered to male and female rats and mice. In the 2-year studies, exposure began during pregnancy and continued through birth into adulthood, so that the animals were exposed throughout their lifetime. NTP found that the mixture was a multispecies carcinogen. Liver tumors were the primary outcome.

The draft NTP technical report also described a variety of [nonneoplastic lesions](#), which are noncancerous or precancerous growths that develop due to abnormal cell or tissue growth. Such lesions were seen in both species and sexes of the test animals, particularly in the liver and the thyroid gland.

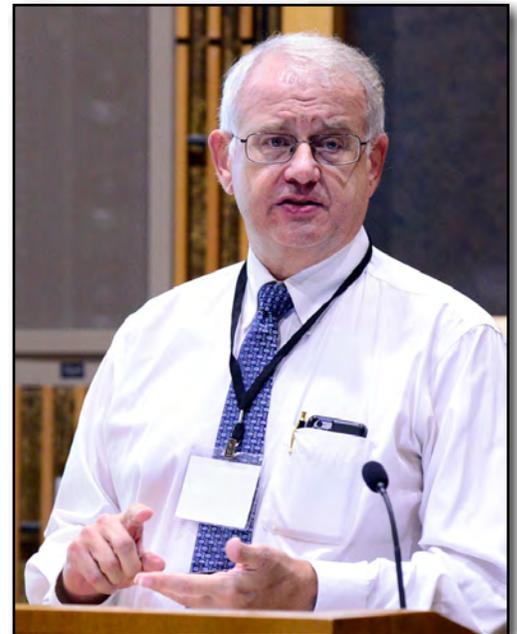
(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison)



On hand from NTP to provide technical expertise were, from left, toxicologist Chad Blystone, Ph.D., study pathologist Amy Brix, D.V.M., Ph.D., and pathologist David Malarkey, D.V.M., Ph.D. (Photo courtesy of Steve McCaw)



With the peer reviewers participating by videoconference, the central table was filled with NTP personnel. The virtual meeting ran smoothly and could serve as a model for future such events. (Photo courtesy of Steve McCaw)



Toxicologist Paul Foster, Ph.D., briefed the panel on the perinatal bioassays and the NTP statistical approach, which used mixed-effects models, analyzing data from each pup while accounting for within-litter correlations. (Photo courtesy of Steve McCaw)

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New method improves bone marrow transplants

By Robin Arnette

New research has developed a system used in zebrafish that allows scientists to track which cells replenish bone marrow during transplantation and which chemicals make the transplantation process more efficient.

In cases of leukemia and certain other cancers, physicians generally prescribe radiation therapy. Although radiation kills malignant cells, it also kills normal cells, such as those in the bone marrow. Without viable bone marrow, the body cannot produce the red blood cells that carry oxygen throughout the body nor the white blood cells that make up the immune system.

The new findings could lead to therapeutic agents that may help patients undergoing bone marrow transplants. NIEHS Scientific Director [Darryl Zeldin, M.D.](#), was part of the team, led by Leonard Zon, M.D., of Harvard University and Boston Children's Hospital, that made the discovery. The work appeared in the July 23 issue of the journal *Nature*.

Transplant model uses cellular competition

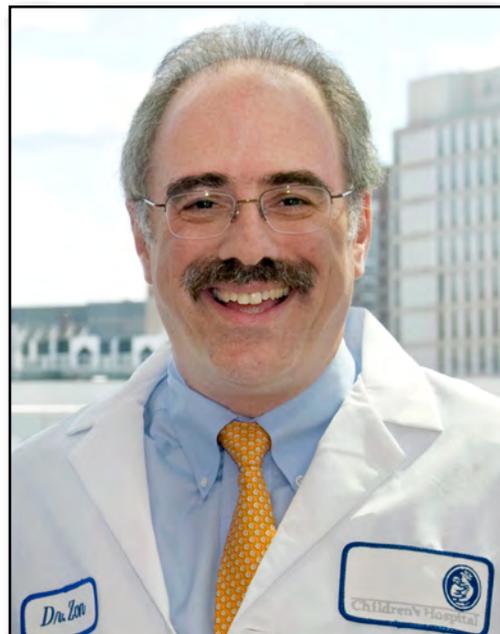
During bone marrow transplantation, new cells enter bone and begin multiplying in a process called engraftment. Because [Zon](#) and his colleagues wanted to track the cells, they labeled one set of marrow cells with a green fluorescent protein and treated them with a chemical known to increase engraftment. They labeled a second set of cells with a red fluorescent protein and left them untreated. Team members then injected both cell types into a strain of laboratory-created, see-through zebrafish and measured the green-to-red ratio.

Using this competitive transplant model, the researchers saw that the zebrafish had more green tissue than red tissue, indicating that the chemical applied to the green-treated cells was effective in increasing engraftment. If it had not been effective, the fish would have been equal parts green and red.

“With this novel system, scientists can now screen chemicals for their ability to affect engraftment,” Zeldin said.

Therapeutic applications to humans

The research team used the procedure to screen hundreds of chemicals, and found a handful of them that increased the ability of bone marrow cells to engraft. One of these chemicals was epoxyeicosatrienoic acid (EET), which is a lipid or fatlike molecule produced by the body. Treating green-colored cells with EETs also



Zon is the Grousbeck Professor of Pediatric Medicine at Harvard Medical School, an investigator with the Howard Hughes Medical Institute, and director of the Stem Cell Program at Boston Children's Hospital. (Photo courtesy of Boston Children's Hospital)

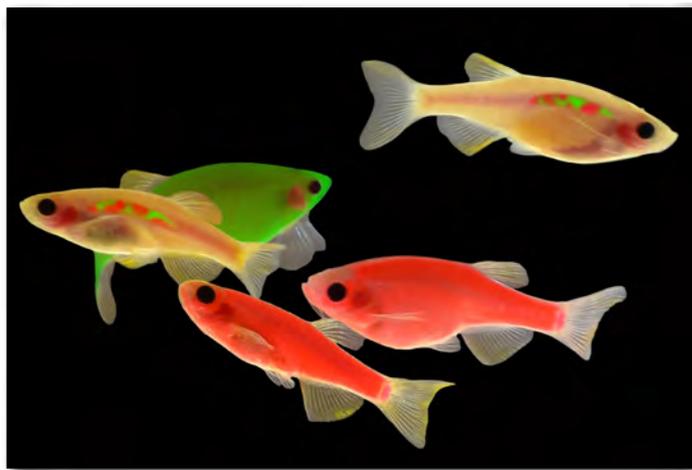


“The National Toxicology Program has a library of thousands of chemicals that could be screened using this method to see which ones increase or decrease engraftment,” Zeldin said. (Photo courtesy of Steve McCaw)

resulted in more green-colored cells being seen in the zebrafish model than red-colored cells. Before this study, scientists were unaware that EETs could promote engraftment.

“For years, people have thought that there are proteins and sugars that influence how stem cells migrate, but we’re finding that the lipids are really affecting the migration pathway,” Zon said.

Zon wondered if the method and positive EET affect would translate to mammals, so he used it to study engraftment of marrow cells in mice. EETs enhanced engraftment of the marrow. As a result of this work, patients undergoing bone marrow transplants in the future could receive EETs or compounds that affect EET levels to ensure a successful transplant.



The chemically treated green marrow cells and untreated red marrow cells are clearly visible in the zebrafish. (Photo courtesy of Ellen van Rooijen and Pulin Li)

Citation: [Li P, Lahvic JL, Binder V, Pugach EK, Riley EB, Tamplin OJ, Panigrahy D, Bowman TV, Barrett FG, Heffner GC, McKinney-Freeman S, Schlaeger TM, Daley GQ, Zeldin DC, Zon LI. 2015. Epoxyeicosatrienoic acids enhance embryonic haematopoiesis and adult marrow engraftment. Nature 523\(7561\):468-471.](#)

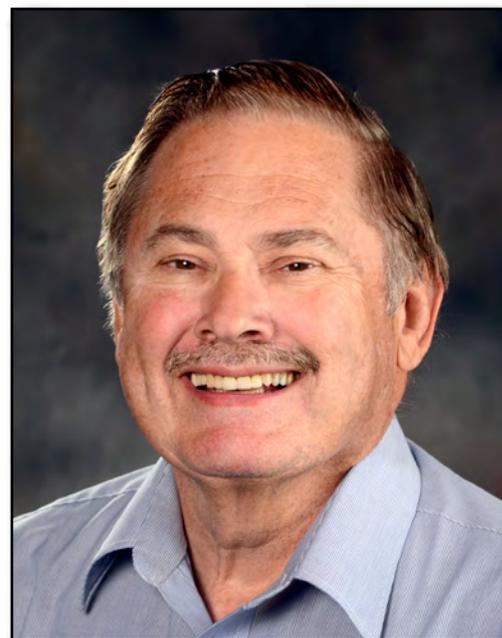
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Society for Free Radical Biology and Medicine honors Mason

By Robin Arnette

NIEHS researcher Ronald Mason, Ph.D., has received the 2015 Discovery Award from the Society for Free Radical Biology and Medicine. As part of the award, which recognizes recent significant advancements in the field of redox research, Mason will present a featured lecture, “We Detect Free Radicals Not Because It Is Easy, But Because It Is Hard,” at the [society’s 22nd annual meeting](#) Nov. 20 in Boston. He will also receive a medal and the opportunity to publish a review article in the society’s journal, *Free Radical Biology and Medicine*.

As head of the NIEHS Free Radical Metabolism Group, [Mason](#) studies molecules that have a single unpaired electron. Known as free radicals, these molecules are continually formed in the body during normal metabolism, and several mechanisms exist to control them when they reach high levels. However, an imbalance between the production of free radicals and the body’s ability to counteract or detoxify their harmful effects, referred to as oxidative stress, can cause tissue damage. This process is believed to both play a role in aging and lead to disease.



Mason and his group developed and validated the immuno-spin trapping technique, among other innovations. (Photo courtesy of Steve McCaw)

Innovations stem from interdisciplinary expertise

Immuno-spin trapping, a highly sensitive method for detecting free radicals, is one of Mason's best-known innovations, and it is applicable to both medicine and redox biology. Redox, or reduction-oxidation, chemical reactions that involve the gain or loss of electrons among molecules.

Immuno-spin trapping has proven particularly useful in detecting and identifying protein-derived and DNA-derived radicals, as well as the free radical metabolism of toxic chemicals and biochemicals. The method has been used *in vitro* and *in vivo*, revealing more details about the molecular mechanisms that lead to oxidative stress.

Mason said the approach was largely the result of his interest in many fields. "Because my training is in physical chemistry, but I publish in biochemistry, pharmacology, toxicology, and even medical journals, it would be difficult for me to thrive in an academic department, which is divided by discipline," Mason said. "I owe much of my scientific success to the intellectual environment at NIEHS, which supported my multidisciplinary approach to human disease."

During his more than 35 years of pioneering research at NIEHS, Mason has received several honors, including the Society for Free Radical Biology and Medicine Senior Investigator Lifetime Achievement Award in 2007. NIEHS Scientific Director Darryl Zeldin, M.D., said, "This [Discovery Award] is the latest in a long string of awards recognizing Ron's outstanding contributions to science in general and specifically to the field of free radical biology. I congratulate him on this highly deserved honor."

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Researchers identify protein that helps prepare healthy egg-sperm union

By Robin Mackar

Researchers in the NIEHS Reproductive Medicine Group have discovered a protein that plays a vital role in a healthy egg-sperm union. An embryo cannot survive without male chromosomes, and the protein RGS2 can delay an egg's development into an embryo, which allows time for sperm to arrive and merge with the egg in a healthy fertilization process.

"These findings show the critical role that the protein RGS2 plays in preserving the fertilizability of the ovulated egg," said Carmen Williams, M.D., Ph.D., a lead author on the paper, [published online](#) in the journal *Development*. "Other researchers have shown that RGS2 plays an important role in regulating heart function and blood pressure, but this is the first demonstration of the protein's significant role in fertilization."



Williams leads the NIEHS Reproductive Medicine Group, which focuses on basic reproductive biology of early mammalian embryo formation. The team focuses on specific questions that have direct relevance to human reproduction and how the environment influences these aspects of reproduction. (Photo courtesy of Steve McCaw)

The maturing egg

[Williams](#) explained that an immature egg found in the ovary is not very good at rallying the necessary calcium signaling that is needed to respond to sperm. However, during the maturation process, the egg stores calcium, preparing it for fertilization. At fertilization, the sperm causes calcium to be released in the egg, turning it into a developing embryo (see diagram below).

The mouse study shows that during maturation the egg synthesizes RGS2, which suppresses calcium signaling. This safety mechanism ensures that the egg does not begin releasing calcium and start developing before the sperm arrives. Beginning development too early prevents the egg from merging with the sperm.

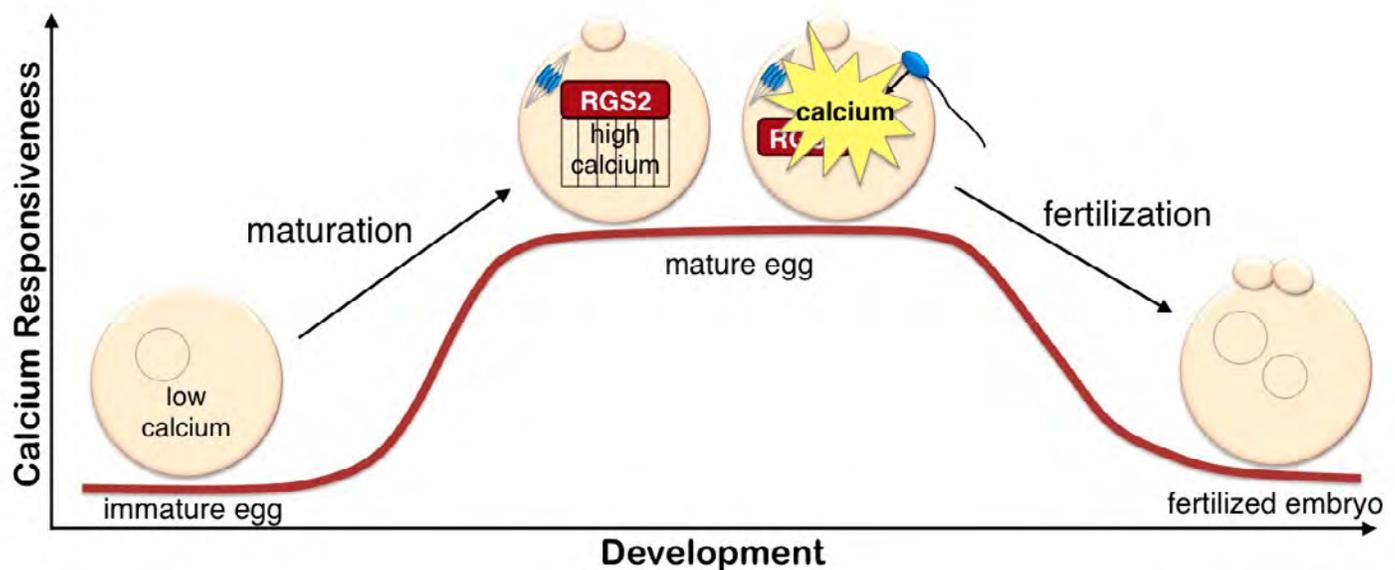
Therapeutic use

The RGS2 protein is also being studied as a therapeutic target for hypertension and other heart ailments.

“Understanding the role RGS2 plays in reproduction is important when considering the possible benefits and side effects of any new treatments, as well as understanding the impact that toxins might have on human fertility,” said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program.

Citation: [Bernhardt ML](#), [Lowther KM](#), [Padilla-Banks E](#), [McDonough CE](#), [Lee KN](#), [Evsikov AV](#), [Uliasz TF](#), [Chidiac P](#), [Williams CJ](#), [Mehlmann LM](#). Regulator of G-protein signaling 2 (RGS2) suppresses premature calcium release in mouse eggs. *Development*; doi: 10.1242/dev.121707 [Online 9 July 2015].

(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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Parma consensus statement on metabolic disruptors supported by NIEHS scientists

By Kelly Lenox

NIEHS scientists and grantees are among the authors of a paper calling for new research on the role that environmental exposures may play in disrupting metabolic pathways. The paper, published June 20 in the journal *Environmental Health*, also explains the concept of metabolic disruptors.

Known as the [Parma consensus statement](#), it is the product of a May 2014 meeting in Parma, Italy, where an international group of researchers grappled with how metabolic disrupting chemicals may be involved in the development of obesity and related metabolic disorders.

The authors said they hope the new consensus statement will achieve several goals:

- Aid in understanding the role of metabolic disruptors in the epidemics of obesity and metabolic disease.
- Move the field forward by assessing the current state of the science.
- Identify needed research on the role environmental chemical exposures may play in these diseases.

[Jerry Heindel, Ph.D.](#), health scientist administrator in the NIEHS Division of Extramural Research and Training (DERT), was the paper's lead author. "At the meeting, we wanted to assess what is known about metabolic disruptors and agree on the best way to move forward," he said. "This statement distills the discussions that took place among the wide range of researchers, from toxicologists and neurobiologists to risk assessors and clinicians."

Why environmental exposures are of concern

The statement explains why the scientists are concerned about metabolic disruptors, including saying that there is more to the environmental component of obesity, diabetes, and metabolic syndrome (see [sidebar](#)) than diet and exercise alone can explain. As the authors wrote, "There are no known classical genetic mechanisms that could explain the remarkable changes in body composition that have occurred over recent decades. Therefore, there has been a significant focus on identifying changes in gene expression and epigenetic marks caused by environmental factors."



Heindel develops and administers the NIEHS grants program in endocrine disruptors, developmental basis of diseases, reproductive toxicology, and obesity. (Photo courtesy of Steve McCaw)



Schug is a health scientist administrator in DERT, where he supports research on male and female reproduction, metabolism, development and disruption of endocrine systems, nanotechnology, and projects related to green chemistry. (Photo courtesy of Steve McCaw)

Furthermore, they wrote that susceptibility to metabolic disorders is, at least in part, programmed by *in utero* exposures. Such programming may alter centers in the brain that affect appetite and satisfaction, and impact numbers of fat cells and organ function, among other outcomes.

Focus of future research

The authors call for a multidisciplinary and integrated research strategy to further test the hypothesis that metabolic disruptors are involved in development of obesity, diabetes, and metabolic syndrome. Among the many suggested targets for future research are defining the role of metabolic disruptors in type 1 and type 2 diabetes, developing and validating screening tests to detect and prioritize metabolic disruptors, and developing an integrated conceptual approach linking animal studies with long-term human studies.

“There is a need for more research to test the hypothesis that metabolic disruptors do indeed alter the likelihood of developing obesity, diabetes, and metabolic syndrome,” said another co-author on the paper, [Thad Schug, Ph.D.](#) He oversees a portfolio of grants related to the development and disruption of endocrine systems, for the NIEHS Population Health Branch.

The statement closes with a call to research: “A coherent, enhanced research agenda will help identify strategies to prevent metabolic diseases through actions that can be taken by individuals as well as public health agencies. History shows that prevention is always the best strategy.”

Citation: Heindel JJ, Vom Saal FS, Blumberg B, Bovolín P, Calamandrei G, Ceresini G, Cohn BA, Fabbri E, Gioiosa L, Kassotis C, Legler J, La Merrill M, Rizzir L, Machtinger R, Mantovani A, Mendez MA, Montanini L, Molteni L, Nagel SC, Parmigiani S, Panzica G, Paterlini S, Pomatto V, Ruzzin J, Sartor G, Schug TT, Street ME, Suvorov A, Volpi R, Zoeller RT, Palanza P. 2015. Parma consensus statement on metabolic disruptors. *Environ Health.* 14(1):54.

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What is metabolic syndrome?

According to the authors, metabolic syndrome is characterized by a cluster of symptoms, including:

- Insulin resistance.
- Hyperglycemia.
- Abdominal obesity.
- Dyslipidemia, or abnormal amount of lipids in the blood, either high or low.
- Hypertension.

The collection of symptoms increases risk for:

- Type 2 diabetes.
- Cardiovascular disease.
- Liver diseases.
- Inflammatory and immune disorders.

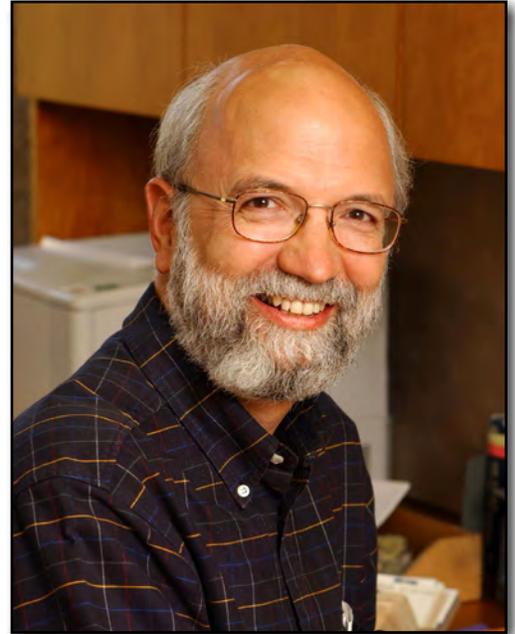
Wilcox named Mentor of the Year by pediatric epidemiology society

By Robin Arnette

NIEHS epidemiologist [Allen Wilcox, M.D., Ph.D.](#), was named 2015 Mentor of the Year by the [Society for Pediatric and Perinatal Epidemiologic Research](#) (SPER). Wilcox accepted the award during the organization's 28th annual meeting June 15-16 in Denver.

SPER was founded in 1988 with the objective of fostering epidemiologic research on pregnancy and children. Candidates for its Mentor of the Year serve as role models by demonstrating great communication skills, motivating their mentees to excel, and displaying high standards of scientific performance and integrity.

Wilcox has been a member of SPER since its founding and has been advising postdocs and students interested in the epidemiology of pregnancy, infancy, and childhood even longer. He said training young people to enter the field is nearly as important as the research itself, but he had to learn the nuances of mentoring on his own.



Wilcox heads the Reproductive Epidemiology Group within the NIEHS Epidemiology Branch. (Photo courtesy of Steve McCaw)



Linked video:
[Watch as Wilcox discusses how the environment affects fertility, pregnancy, and childhood development. \(4:54\)](#)

(Launches in new window)

Download Media Player:  Flash [↗](#)

“When I started as an epidemiologist, there were no postdoctoral fellowships — we were just thrown into the deep end,” Wilcox said. “It took me a while to figure out how to be a mentor, but the rewards are fantastic. I learn as much as I teach.”

One person who can attest to Wilcox's mentoring skills is Anne Marie Jukic, Ph.D., a postdoctoral fellow in his group. Jukic, who will join Yale University this year as an assistant professor, said she was well-positioned for a successful academic career as a result of his superb training. She and several other current and former postdocs nominated Wilcox for the award.

“Dr. Wilcox strikes a fine balance between encouraging independence and providing guidance,” Jukic said. “I sincerely hope I can become the mentor he has been to me.”

NIEHS Scientific Director Darryl Zeldin, M.D., echoed the SPER decision to choose Wilcox for this year's award. “Allen Wilcox has been an outstanding mentor to countless numbers of students, postdocs, and faculty at NIEHS for several decades,” Zeldin said. “This honor is long overdue and is a reflection of his firm commitment to supporting the careers of junior scientists.”

The News & Observer of Raleigh, North Carolina, highlighted the award when it featured Wilcox as [Tar Heel of the Week](#) in its August 2 edition.

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NIEHS environmental genetics leader speaks at Texas research center

By Greg Buchold

Steven Kleeberger, Ph.D., presented a June 17 mentoring seminar at the Texas A&M University [Center for Translational Environmental Health Research](#) (CTEHR). Headed by Cheryl Walker, Ph.D., CTEHR is one the newer [Environmental Health Sciences Core Centers](#) funded by the institute's Division of Extramural Research and Training (see sidebar).



Linked Audio:
[Listen Kleeberger discuss his studies of environmental and genetic factors that lead to lung disease, in this CTEHR Environmental Health Podcast. \(20:55\)](#)
(Launches in new window)

Download Media Player:  Quicktime [↗](#)



Environmental contributors to lung disease

[Kleeberger](#), head of the NIEHS Environmental Genetics Group, discussed "Susceptibility to Environmental Lung Disease: Contributions from the Nuclear and Mitochondrial Genomes."

He focused on three recent advances in his laboratory's multidisciplinary approach to understanding environmental lung disease.

The first advance involved a translational collaboration with the [Infant Foundation](#) in Argentina that identified a genetic variation, or single nucleotide polymorphism (SNP), in humans that enhances respiratory syncytial virus (RSV) disease in children. This SNP is comparable to one that Kleeberger and his team discovered in a similar gene in mice, which codes for an immune response. The human SNP enhances lung inflammation and disease, producing effects similar to those found when researchers disrupted the gene in mice.

Second, in a study of children in Buenos Aires, Argentina, Kleeberger and his collaborators examined loss-of-function mutations in a gene involved in immune function, known as toll-like receptor 4. These mutations dramatically worsened responses to a bacterial endotoxin in children from high socioeconomic status (SES) households, but they were surprisingly protective in lower SES populations (see [story](#)).

"No one responds the same way to the same stimulus, in terms of environmental exposures," Kleeberger said in the CTEHR podcast. "Understanding those factors that contribute to individual response is really key."
(Photo courtesy of Steve McCaw)

A Texas consortium to advance environmental health

CTEHR is a collaboration among Texas A&M University, Texas A&M Health Science Center, Baylor College of Medicine, and the University of Houston (see [story](#)). Researchers focus on five thematic areas that affect human environmental health — early life exposures, metabolism, the microbiome, chronic disease, and emerging technologies.

The center is also part of the Healthy Texas Initiative, launched in June and operated through the newly created [Texas A&M Institute for Public Health Improvement](#). The pilot program, Healthy South Texas 2025, aims to reduce preventable diseases by 25 percent in south Texas by 2025, through education on diabetes, asthma, and infectious diseases.

A third study used ultra-deep sequencing methods to detect genetic variations in the mitochondrial genome of inbred mouse strains. The researchers identified a variety of novel mitochondrial targets that appear to affect susceptibility to a disorder known as bronchopulmonary dysplasia, which occurs in premature infants receiving oxygen therapy for underdeveloped lungs and lung infections (see [summary](#)).

Kleeberger enjoyed interacting with students at the breakfast and seminar, hosted by the Career Development Program. “One of the high points of the visit was meeting with the students, fellows, and faculty members,” Kleeberger said. “What an enthusiastic and interesting group! It was great to talk with them about their science.”

Citations:

Caballero MT, Serra ME, Acosta PL, Marzec J, Gibbons L, Salim M, Rodriguez A, Reynaldi A, Garcia A, Bado D, Buchholz UJ, Hijano DR, Coviello S, Newcomb D, Bellabarba M, Ferolla FM, Libster R, Berenstein A, Siniawski S, Blumetti V, Echavarría M, Pinto L, Lawrence A, Ossorio MF, Grosman A, Mateu CG, Bayle C, Dericco A, Pellegrini M, Igarza I, Repetto HA, Grimaldi LA, Gudapati P, Polack NR, Althabe F, Shi M, Ferrero F, Bergel E, Stein RT, Peebles RS, Boothby M, Kleeberger SR, Polack FP. 2015. TLR4 genotype and environmental LPS mediate RSV bronchiolitis through Th2 polarization. *J Clin Invest* 125(2):571-582.

Nichols JL, Gladwell W, Verhein KC, Cho HY, Wess J, Suzuki O, Wiltshire T, Kleeberger SR. 2014. Genome-wide associated mapping of acute lung injury in neonatal inbred mice. *FASEB J* 28(6):2538-2550.

(Greg Buchold, Ph.D., is a former NIEHS postdoctoral fellow in the Reproductive and Developmental Biology Laboratory.)

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Big data presents big challenges, big opportunities in environmental health

By John Yewell

The challenges of processing today’s avalanche of information and the opportunities gained by making it available to scientists and the public were the subjects of a June 24 webinar, “[Integrating Data from Multidisciplinary Research](#).”

The program was the first in a series exploring how complex data sets are being used to solve environmental health problems. It was part of the National Institutes of Health (NIH) [Big Data to Knowledge](#) (BD2K) initiative, which aims to advance understanding of human health and disease by taking advantage of the wealth of information contained in biomedical big data.

Underscoring the NIEHS [strategic plan](#) goal of integrating data tools across disciplines, webinar speakers drew from both in-house and grantee research experience in their presentations.



“Increases in data volume, variety, and velocity have transformed ocean science,” said DiMarco. “We are just beginning to explore the new potential of this transformation.” (Photo courtesy of Texas A&M University)

From floppy disks to terabytes

How big has Big Data become? Consider this — one system alone, the Intergovernmental Oceanographic Commission’s Global Ocean Observing System collects a terabyte of data every day, according to [Stephen DiMarco, Ph.D.](#), from Texas A&M University. His presentation described how scientists use the data to address impacts on human health and society.

Tackling modern data challenges provides new opportunities to the NIEHS Superfund Research Program (SRP), said SRP Director [William Suk, Ph.D.](#), another presenter. “The next step is increased collaboration to enable sharing of data, which is essential for expedited translation of research results into knowledge to improve human health.”

Privacy and precision medicine

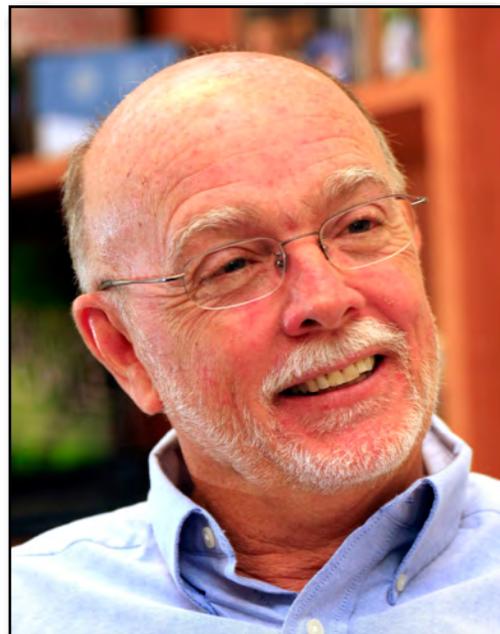
According to Allen Dearry, Ph.D., director of the NIEHS [Office of Scientific Information Management](#), the confluence of better data collection, greater computing power, and heightened public perception around environmental health has made the large-scale studies necessary to test medical interventions possible. These studies can be tailored to individuals and are known as the precision medicine initiative (see [story](#)).

“Seventy-four percent of the public are now willing to share their health information to improve prevention and treatment of disease,” Dearry said. “It’s really just now that we have the capacity to carry out this kind of effort.”

Technical capacity alone is not enough; issues of privacy and confidentiality must also be addressed. “NIH is trying to ensure that we are able to protect confidentiality, especially of electronic health records,” said Dearry, explaining how work to make data more widely available, by using cloud-based platforms, has been slowed by concerns over data security.

PROTECT — breaking the exposure-disease link

David Kaeli, Ph.D., from Northeastern University, described his work managing and integrating data from the [Puerto Rico Testsite for Exploring Contamination Threats](#) (PROTECT), which is supported by SRP. Researchers study the effects of environmental contaminants on preterm birth in Puerto Rico by following 1,800 expectant mothers and by gathering data about dozens of chemicals, trace metals, and pesticides from more than 1,000 wells, springs, and other sources.



“By integrating and sharing data across different research domains,” said Suk, “we hope to enhance environmental health solutions, reduce the burden of disease, and improve public health.” (Photo courtesy of Steve McCaw)

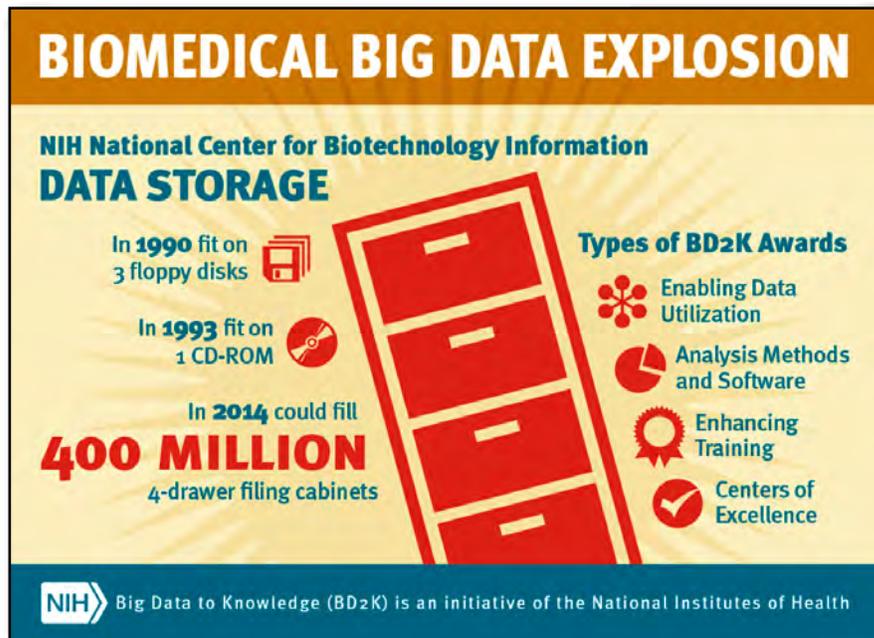


Dearry described an NIH approach to promote BD2K. Known as a commons, the collaborative computer environment would marry data and discoverability across computing platforms. (Photo courtesy of Steve McCaw)

Scientists hope to prevent exposure to environmental hazards through better detection, while minimizing the environmental impact of cleanup activities, which is known as green remediation. This contributes to the central goal of SRP, which is to understand and break the links between chemical exposure and disease.

Michelle Heacock, Ph.D., health scientist administrator for the NIEHS SRP, served as moderator for the webinar, which was hosted by SRP and the U.S. Environmental Protection Agency.

(John Yewell is a contract writer for the NIEHS Office of Communications and Public Liaison)



“Security and privacy have to be baked in from the beginning,” said Kaeli, who directs the Computer Architecture Research Laboratory at Northeastern University. (Photo courtesy of Northeastern University)

Data collection has exploded in recent years, creating new challenges for analysis, sharing, and privacy, which NIH is addressing with the BD2K program. (Photo courtesy of NIH)

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Scientific experts agree with NTP about cobalt and cancer

By Robin Mackar and Kira Bradford

A panel of scientific experts agreed with the National Toxicology Program (NTP) draft recommendation to list a class of [cobalt and cobalt compounds](#) as reasonably anticipated to be human carcinogens. The class includes cobalt and cobalt compounds that release cobalt ions *in vivo*.

Once the draft is finalized and approved, the listing will become part of the congressionally mandated [Report on Carcinogens](#) (RoC), explained Ruth Lunn Dr.P.H., director of the Office of the RoC, during her opening remarks at the [July 22 peer review panel meeting](#).

Cobalt is a naturally occurring metallic element that can be present in different forms. It is mixed with other metals to make alloys that can be used to make durable industrial products, such as military and industrial equipment. NTP representatives said cobalt is also used to make rechargeable batteries, pigments, and some medical devices.

Sources of exposures

People can be exposed to cobalt compounds through occupational or other sources. Individuals who work in hard metal production producing cobalt powder, working with diamond cutting wheels, or polishing diamonds are all at potentially high risk for exposure.

People may also be exposed to low levels of cobalt through food, cigarette smoke, and the environment.

Another major source of exposure is from hip implants. These medical devices often include metal components that contain cobalt. Patients with hip implants that failed due to excessive wear or corrosion by body fluids may have been exposed to higher levels of cobalt than the general public.

All panel members agreed that there was significant exposure to cobalt and cobalt compounds in the United States. Cobalt in the form of vitamin B12 is not subject to listing because it does not release cobalt ions in the body.

Human cancer studies

NTP walked the panel through the occupational health studies that were evaluated and included in the draft. Both NTP and the peer reviewers determined there was inadequate evidence in these studies to evaluate the relationship between human cancer and cobalt exposure.

Cancer and toxicity studies on hip replacements were not included in the RoC evaluation. “The complexity of the mixtures of chemicals and metals that may be used in some medical devices makes it difficult to home in on cobalt specific metals and how they may impact cancer,” said Lunn.

The panel suggested that NTP look at the available literature to be sure nothing was missed by excluding these studies. NTP Associate Director John Bucher, Ph.D., said the NTP would review the joint replacement patient literature.

Animal and mechanistic data support reasonably anticipated listing

The evidence to support this preliminary listing decision is based on sufficient evidence in animal studies, and on supporting data from studies of mechanisms, or biological changes, that contribute to the development of cobalt-related cancers.

After hearing the presentations and reading the materials, the 10-member panel, chaired by [Melissa McDiarmid, M.D.](#), from the University of Maryland, unanimously voted in favor of NTP listing these compounds as reasonably anticipated to be a human carcinogen.



Lunn, left, briefed the peer review panel on the preparation of the draft monograph. Sanford Garner, Ph.D., from ILS, a contractor supporting the Office of the RoC, presented information on the properties of, and human exposure to, cobalt compounds. (Photo courtesy of Michael Garske)



McDiarmid, in addition to her duties as chair, provided her perspective as a physician to the panel. (Photo courtesy of Michael Garske)

NTP will consider the panel’s comments, as well as [public comments](#) received, as it makes revisions to the draft. The updated monograph will be presented to the NTP Board of Scientific Counselors at an upcoming meeting.

(Robin Mackar is news director in the NIEHS Office of Communications and Public Liaison, and a frequent contributor to the Environmental Factor. Kira Bradford, a Ph.D. candidate at the University of North Carolina at Chapel Hill, contributed to the story as part of the Immersion Program to Advance Career Training, or ImpACT, internship program.)



Diane Spencer, a health scientist in Office of the RoC, presented cancer evaluation studies in experimental animals. (Photo courtesy of Michael Garske)



Panel members Anatoly Zhitkovich, Ph.D., right, from Brown University, and C. William Jameson, Ph.D., with CWJ Consulting LLC, provided many insights throughout the meeting. (Photo courtesy of Michael Garske)



Ruth Danzeisen, Ph.D., toxicologist from the Cobalt Development Institute, presented public comments at the meeting. These and other public comments will be considered by NTP when revising the monograph. (Photo courtesy of Michael Garske)



Stanley Atwood, Ph.D., left, of ILS, presented the mechanistic data on cobalt compounds. Gloria Jahnke, D.V.M., health scientist in the Office of the RoC, shared a few thoughts with him during one of the breaks. (Photo courtesy of Michael Garske)

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This month in EHP

The August issue of Environmental Health Perspectives (EHP) highlights threats posed by land subsidence in river delta regions, and the impact that reduced populations of pollinators may have on micronutrients in the human diet.

Delta Subsidence: An Imminent Threat to Coastal Populations

Sea-level rise threatens to inundate coastlines around the world. Some of the world's most vulnerable coasts are river delta regions, which are home to roughly half a billion people. These areas face the far more immediate threat of subsidence. With its associated risks of flooding, infectious diseases, saltwater intrusion, and infrastructure disruption, subsidence is a multifaceted problem that requires site-specific solutions — and soon.

Pollinator Power: Nutrition Security Benefits of an Ecosystem Service

Scientists have only recently calculated the extent to which food supplies depend on pollinators. Now several new studies suggest that reduced populations of bees and other pollinators may adversely affect not only the marketplace, but also the availability of essential micronutrients in the human diet, potentially increasing malnutrition in areas already struggling with this issue.

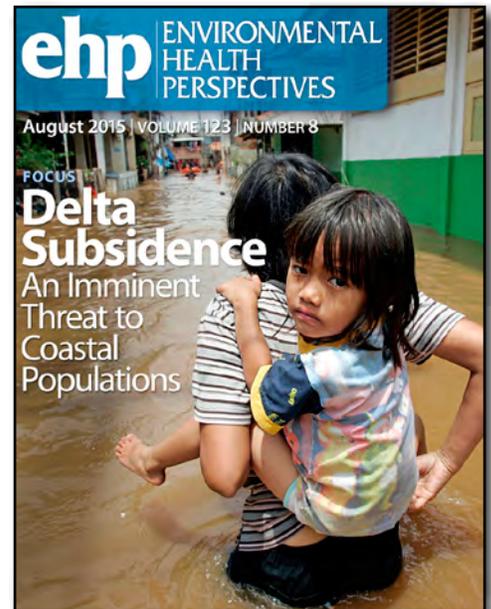
Featured research and related news articles this month include:

- **How Good Is Good Enough? Cookstove Replacement Scenarios to Reach Indoor Air Goals** — A new study examines how much compliance is required to realize the benefits of cleaner technologies.
- **Plumbing Pathogens: A Fixture in Hospitals and Homes** — Scientists review the epidemiology and ecology of microbes known as opportunistic premise plumbing pathogens, which can thrive in household and hospital plumbing systems.
- **Arsenic and Blood Pressure: A Long-Term Relationship** — Researchers provide new evidence of arsenic's ability to elevate blood pressure, potentially leading to hypertension and more serious clinical outcomes.
- **A Closer Look at Obesogens: Lipid Homeostasis Disruption in *Daphnia*** — According to a new report, reproductive problems in a tiny freshwater crustacean called *Daphnia magna* may be caused by an obesogen that alters lipid transport from the pregnant female to the egg.

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<http://twitter.com/ehponline>



Extramural papers of the month

By Nancy Lamontagne

- Prenatal DDT exposure linked with increased breast cancer risk
- Cinnamon-derived compound helps prevent colon cancer in mice
- Paper devices quantify metals in aerosols
- Lower leukemia risk associated with day care attendance or prolonged breastfeeding

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

Prenatal DDT exposure linked with increased breast cancer risk

A new study, funded in part by NIEHS, found that women exposed prenatally to higher levels of the pesticide dichlorodiphenyltrichloroethane (DDT) were nearly four times more likely to develop breast cancer as adults than women exposed to lower levels before birth. During the 1960s, DDT was used widely in the U.S., and women prenatally exposed during that time are now reaching the age of increased breast cancer risk.

The researchers conducted a follow-up of 9,300 daughters of women who participated in the Child Health and Development Studies, which tracked Kaiser Foundation Health Plan members who received obstetric care in Alameda County, California from 1959 to 1967. The researchers studied 103 women who were diagnosed with breast cancer by age 52, and 315 controls matched by birth year.

Independent of the mother's history of breast cancer, elevated levels of the DDT isomer o,p'-DDT in the mother's blood were associated with a nearly fourfold increase in the daughter's risk of breast cancer (odds ratio for fourth quartile vs. first = 3.7, 95 percent; confidence interval = 1.5–9.0). Levels of o,p'-DDT in fourth quartile participants were double or triple that of women in the first quartile. Among the women diagnosed with breast cancer, 83 percent had estrogen receptor positive breast cancer.

The authors point out that experimental studies are necessary to confirm these findings and to understand the mechanisms involved. If confirmed, this research could lead to biomarkers and interventions targeting DDT-associated breast cancer.

Citation: Cohn BA, La Merrill M, Krigbaum NY, Yeh G, Park JS, Zimmermann L, Cirillo PM. DDT exposure in utero and breast cancer. *J Clin Endocrinol Metab*; doi:10.1210/jc.2015-1841 [Online 16 June 2015].

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Cinnamon-derived compound helps prevent colon cancer in mice

Researchers, funded in part by NIEHS, showed that adding a compound found in cinnamon to the diet of mice protected against colorectal cancer. They also revealed new information about the role that nuclear factor-E2-related factor 2 (Nrf2) plays in the compound's protective effects.

The Nrf2 molecular pathway is a master regulator of the cellular antioxidant defense, and thus plays a key role in protecting cells against stressors, such as carcinogen exposure and environmental damage. Cinnamon is a rich dietary source of cinnamaldehyde, which brings about an Nrf2-regulated antioxidant response in human epithelial colon cells.

In the new study, the researchers first used human colon epithelial cells to better understand the molecular mechanisms involved in Nrf2 activation. They found that cinnamaldehyde-induced Nrf2 activation was largely dependent on the status of Kelch-like ECH-associated protein 1 (Keap1)-Cys151. Keap-1 is a stabilizer of Nrf2 that, together with other molecules, promotes antioxidant pathways. The scientists also compared the protective potential of the compound in a mouse colorectal cancer model with Nrf2 and without Nrf2. When the mice received cinnamaldehyde supplementation, only those expressing Nrf2 showed colorectal cancer suppression, providing evidence that cinnamaldehyde's protective effects depend on Nrf2.

Together, the new findings suggest that cinnamaldehyde, an FDA-approved food additive, may be a feasible way to suppress colorectal cancer. However, the researchers said that more studies are needed to determine the cinnamaldehyde dose needed for Nrf2 activation, and to test the feasibility of using cinnamon powder as a source of cinnamaldehyde for dietary cancer prevention.

Citation: Long M, Tao S, Rojo de la Vega M, Jiang T, Wen Q, Park SL, Zhang DD, Wondrak GT. 2015. Nrf2-dependent suppression of azoxymethane/dextran sulfate sodium-induced colon carcinogenesis by the cinnamon-derived dietary factor cinnamaldehyde. *Cancer Prev Res (Phila.)* 8(5):444-454.

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Paper devices quantify metals in aerosols

NIEHS grantees developed a simple technique that uses microfluidic paper-based devices to quantify concentrations of nickel, copper, and iron in airborne particulate matter. Commercial techniques typically cost more than \$100 per sample and require trained specialists for operation, so low-cost approaches that are applicable at the point-of-need would greatly improve exposure assessment for particulate metals.

The researchers used paper substrates to create devices that can determine the amount of a substance of interest in only a drop of sample. Unlike other colorimetric approaches, the new technology does not require an external optical device for analysis. Instead, it relies on distance-based detection, which can be visually read much like the temperature on a thermometer.

The researchers demonstrated that the paper analytical devices can achieve detection limits as low as 0.1 micrograms for individual measurements of nickel and copper, and 0.05 micrograms for iron. When analyzing all three metals simultaneously, the devices showed a detection limit of 1 microgram for nickel and iron, and 5 micrograms for copper. They further tested the method by measuring the three metals in samples of certified welding fumes and found that the levels measured with the paper devices matched known values determined with gravimetric analysis.

Citation: Cate DM, Noblitt SD, Volckens J, Henry CS. 2015. Multiplexed paper analytical device for quantification of metals using distance-based detection. *Lab Chip* 15(13):2808-2818.

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Lower leukemia risk associated with day care attendance or prolonged breastfeeding

Findings from a large pooled analysis reinforced the hypothesis that day-care center attendance in infancy and breastfeeding for at least six months are both associated with a decreased risk of acute lymphoblastic leukemia (ALL). ALL accounts for 80 percent of childhood acute leukemia, which is the most common cancer for children under 15 years old.

The researchers used data from 11 case-control studies participating in the Childhood Leukemia International Consortium to examine the association between ALL and early stimulation of the immune system. To do this, they looked at day care attendance, birth order, breastfeeding, and maternally reported common infections in infancy. The study included 7,399 ALL cases and 11,181 controls aged 2-14.

The researchers found that attending day care during the first year of life was associated with a reduced risk of ALL (odds ratio = 0.77, 95 percent confidence interval: 0.71, 0.84). The earlier a child began day care, the lower the risk of ALL ($P < 0.0001$). The researchers also observed a reduced risk associated with breastfeeding for 6 months or more (odds ratio = 0.86, 95 percent confidence interval: 0.79, 0.94).

Although early exposure to common infections may be responsible for the association with day care, there was no significant relationship between ALL and common infections in infancy. Understanding the potential mechanisms involved in this association requires assessing both the severity and the timing of infections.

Citation: Rudant J, Lightfoot T, Urayama KY, Petridou E, Dockerty JD, Magnani C, Milne E, Spector LG, Ashton LJ, Dessypris N, Kang AY, Miller M, Rondelli R, Simpson J, Stiakaki E, Orsi L, Roman E, Metayer C, Infante-Rivard C, Clavel J. 2015. Childhood acute lymphoblastic leukemia and indicators of early immune stimulation: a Childhood Leukemia International Consortium study. *Am J Epidemiol* 181(8):549-562.

(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 Robin Arnette, Tara Ann Cartwright, Deacquinta Diggs, Ernie Hood, and Qing Xu

- NTP finds that chronic cobalt metal exposure leads to lung tumors in rodents
- Bidirectional transcription facilitates gene responsiveness
- Nonmotor symptoms are sign of early Parkinson's disease
- NIEHS scientists decipher the conformational maturation of an HIV enzyme
- Preterm births are not strongly linked to seasons of the year

NTP finds that chronic cobalt metal exposure leads to lung tumors in rodents

Scientists in the National Toxicology Program (NTP) found a high incidence of Kras mutations and lower incidences of Egfr and Tp53 mutations in cobalt metal dust (CMD)-induced rodent lung tumors, compared to those arising spontaneously. Furthermore, the Ames assay, a test for bacterial mutagenicity, yielded positive results, indicating a carcinogenic potential for CMD. These findings are significant because the genetic alterations are similar to those seen in human lung cancer.

The majority of the Kras mutations in CMD-induced rodent lung tumors consisted of exon 1 codon 12 G to T transversions, while the lung tumors arising spontaneously usually harbor codon 12 G to A transitions. G to T transversions are commonly associated with oxidative damage to DNA and are one of the most common Kras mutations in human lung cancers. In addition, results of the Ames assay demonstrated the capacity of cobalt (II) ions to induce mutations at G:C base pairs. These results support the CMD-induced lung tumor mutation data.

This study suggests that differential mutation spectra may be used to potentially distinguish between lung tumors resulting from chemical exposures and those arising spontaneously. The data may also be used to compare mutations between rodent and human cancers. **(DD)**

Citation: [Hong HH, Hoenerhoff MJ, Ton TV, Herbert RA, Kissling GE, Hooth MJ, Behl M, Witt KL, Smith-Roe SL, Sills RC, Pandiri AR. 2015. Kras, Egfr, and Tp53 mutations in B6C3F1/N mouse and F344/NTac rat alveolar/bronchiolar carcinomas resulting from chronic inhalation exposure to cobalt metal. Toxicol Pathol; doi:10.1177/0192623315581192 \[Online 9 June 2015\].](#)

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Bidirectional transcription facilitates gene responsiveness

NIEHS researchers have shed new light on the regulatory landscape surrounding mammalian protein-coding genes, enhancing the understanding of the basic mechanisms of how cells respond to stresses from their environment. The scientists reported that bidirectional promoters contributed to an optimized environment for recruitment of transcription factors and the transcription machinery.

Using bone marrow-derived macrophages from C57BL/6 mice, high-throughput sequencing of transcription start site (TSS)-associated RNAs was performed to precisely annotate both sense and anti-sense TSSs near mouse mRNA genes. Bidirectional promoter architecture was found to be widespread, as anti-sense TSSs were observed at more than 75 percent of active promoters. The study revealed two previously unappreciated features of promoter architecture that affect both resting and stimulus-responsive transcription, as seen during immune challenge.

First, the distance between protein-coding sense and noncoding, upstream anti-sense (TSSs) is related to the size of the nucleosome-depleted region, the level of signal-dependent transcription factor binding, and gene activation. Second, a group of anti-sense TSSs with an enhancer-like chromatin signature was seen in the macrophages. The scientists propose that anti-sense promoters serve as platforms for transcription factor binding and establishment of active chromatin to further regulate or enhance sense-strand mRNA expression. **(EH)**

Citation: [Scruggs BS, Gilchrist DA, Nechaev S, Muse GW, Burkholder A, Fargo DC, Adelman K. 2015. Bidirectional transcription arises from two distinct hubs of transcription factor binding and active chromatin. Mol Cell 58\(6\):1101-1112.](#)

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Nonmotor symptoms are sign of early Parkinson's disease

Scientists from the NIEHS Epidemiology Branch and the Biostatistics and Computational Biology Branch have determined that the presence of several nonmotor symptoms of Parkinson's disease could effectively differentiate patients with early Parkinson's from healthy controls. They also found differences between men and women in the presentation of nonmotor symptoms. In one of the largest analyses to date, researchers examined five major areas of nonmotor symptoms — sleep, olfactory, neurobehavioral, autonomic, and neuropsychological domains.

Parkinson's is a progressive neurodegenerative disorder that is clinically diagnosed by the presence of cardinal motor dysfunction. However, patients with Parkinson's also suffer from a range of nonmotor symptoms, such as sense of smell loss, depression, sleep disorders, constipation, pain, and cognitive dysfunction.

In addition to finding that nonmotor symptoms differentiate Parkinson's patients from healthy volunteers, the study indicated potential sex differences among Parkinson's patients with nonmotor symptoms. For example, male patients with Parkinson's performed significantly worse than female patients with regard to odor identification. Female patients outperformed their male counterparts on global cognition and memory domain, but experienced higher trait anxiety, which is sustained worry or nervousness in response to a perceived threat.

Since many Parkinson's nonmotor symptoms may develop years before disease diagnosis, research on these symptoms may eventually help identify individuals at risk for the disease and help scientists understand the disease origin. **(TAC)**

Citation: Liu R, Umbach DM, Peddada SD, Xu Z, Troster AI, Huang X, Chen H. 2015. Potential sex differences in nonmotor symptoms in early drug-naive Parkinson disease. *Neurology* 84(21):2107-2115.

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NIEHS scientists decipher the conformational maturation of an HIV enzyme

NIEHS researchers have analyzed the molecular changes that occur during the maturing of human immunodeficiency virus (HIV) reverse transcriptase (RT), a key enzyme in the life cycle of the virus that causes acquired immunodeficiency syndrome (AIDS). The authors anticipate that their new understanding of the maturation pathway may lead to the development of alternate inhibition strategies that interfere with the process.

The mature form of RT, a target of pharmaceutical compounds used to treat AIDS, consists of a catalytic p66 subunit and a structural p51 subunit. Both subunits are derived from a single peptide chain that is present in the HIV virion, or the entire viral particle. Unfortunately, the high mutagenic rate of HIV allows it to develop mutated forms of RT that can escape drug inhibition.

Maturation of RT from the single polypeptide to form the active, two subunit enzyme is a complex process that until now has been largely uncharacterized. Using isotopic labeling in combination with nuclear magnetic resonance, the research team found that a key feature of the maturation is a metamorphic polymerase domain, which is similar to a puzzle that has two alternate solutions. **(QX)**

Citation: Zheng X, Perera L, Mueller GA, DeRose EF, London RE. 2015. Asymmetric conformational maturation of HIV-1 reverse transcriptase. *eLife*; doi:10.7554/eLife.06359.001.

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Preterm births are not strongly linked to seasons of the year

A research team led by scientists at NIEHS explored possible seasonal effects on risk of preterm birth in Norway. While earlier studies from other groups suggested huge effects of season on preterm birth, the more careful analysis by the NIEHS-led group showed that season has little effect on preterm birth in the country. Their findings cast doubt on previous studies that suggested that spring conception produces shorter pregnancies.

Preterm birth is a common pregnancy complication that endangers both the survival and the long-term health of the infant. Understanding seasonal effects on preterm birth could implicate environmental causes that could be modified to reduce risk. Norway experiences strong seasonal variation and has also maintained an excellent birth registry. Therefore, it provides an ideal source of population-level data for studying effects of season on reproductive health. Couples often plan their pregnancies with attention to season, meaning that the mix of planned and unplanned pregnancies and the gestational age distribution of the fetuses that are at risk of early birth also change through the seasons. Consequently, the statistical analysis must be done carefully to avoid confounding biases.

The authors offered that the remaining risk pattern observed, with somewhat increased risk for conceptions occurring during early January and early July, could be a behavior-mediated effect of seasonal holidays in Norway, and unintentional conceptions during those times. The peaks coincide with New Year's Day and the start of summer break in Norway. **(RA)**

Citation: [Weinberg CR, Shi M, DeRoo LA, Basso O, Skjaerven R](#). 2015. Season and preterm birth in Norway: a cautionary tale. *Int J Epidemiol*; doi:10.1093/ije/dyv100 [Online 4 June 2015].

(Robin Arnette, Ph.D., is a science writer and editor in the NIEHS Office of Communications and Public Liaison. Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group. Deacquinta Diggs, Ph.D., is a National Health and Environmental Effects Laboratory fellow in the U.S. Environmental Protection Agency Developmental Toxicity Branch. Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison. Qing Xu is a biologist in the NIEHS Metabolism, Genes, and Environment Group.)

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Inside the Institute

Colleen Anna honored in NIEHS memorial garden

By Kelly Lenox

After retired NIEHS biologist Colleen Anna passed away in February, her former coworkers and friends at the institute spearheaded a drive to mark her life in a special way.

Many of Anna's contributions to NIEHS were celebrated when she retired from 34 years of government service in 2010, including her tireless work for environmental awareness and stewardship, and her role as a biologist in the Eicosanoid Biochemistry Group (see [story](#)).

At the end of June, her life was celebrated with the planting of two trees in the NIEHS memorial garden, and the installation of a plaque in the wall overlooking the lake. "Colleen was a very valued colleague," said Rachel Frawley, a health scientist with the National Toxicology Program. "She was always reaching out to help others and leading work-life initiatives, in addition to anchoring the team in her lab."

Due to the generosity of her friends, not one, but two trees were planted in memory of Anna — a crape myrtle, which was in full bloom, and a magnolia, which bore many buds and one fragrant blossom at planting time. "Both trees are large and healthy, and in very peaceful locations — very fitting for an environmentalist and outdoor enthusiast," said Frawley.

Considering Anna's long list of endeavors — from charter member and chair of the NIEHS Environmental Awareness Advisory Committee, and Earth Day celebration coordinator, to employee mentor, and organic farming teacher for Bring Your Child to Work Day — the gift of the trees will enable staff at NIEHS to remember her warm and open spirit.



Anna's many gifts were assets in the laboratory and garden alike. (Photo courtesy of Steve McCaw)



Anna's plaque is displayed on the garden's memorial wall, which overlooks Discovery Lake. (Photo courtesy of Diane Spencer)



The pink crape myrtle, planted in Anna's honor, will brighten up the garden for years to come. (Photo courtesy of Diane Spencer)



The magnolia, planted near the entrance to the garden, displayed a single exuberant bloom on planting day. (Photo courtesy of Bill Willis)

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HHS celebrates LGBT Pride Month

By Eddy Ball

Representatives of federal agencies and community organizations participated June 24 in a commemoration of Lesbian, Gay, Bisexual, and Transgender (LGBT) Pride Month.

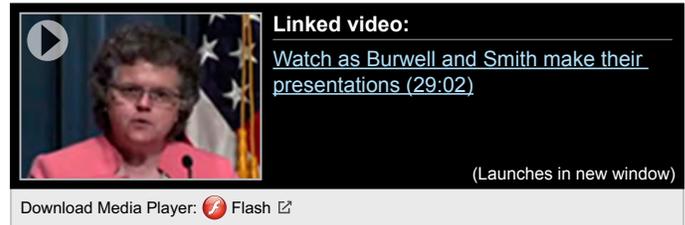
The event, “Supporting and Celebrating LGBT Families,” was webcast live from the Small Auditorium of the Hubert H. Humphrey Building in Washington, D.C. Speakers and panelists shared personal stories, and emotions ranged from enthusiastic self-affirmation and qualified optimism, to anger about ongoing discrimination and sadness over past misunderstandings.

U.S. Department of Health and Human Services (HHS) Secretary Sylvia Burwell delivered opening remarks that reinforced the leadership support for LGBT equality and acceptance that was articulated by [President Barack Obama](#) and National Institutes of Health (NIH) Director Francis Collins, M.D., Ph.D., in their proclamations of LGBT Pride Month.



Burwell made the connection between the Affordable Care Act and equal opportunity and inclusion for LGBT individuals. She has described LGBT inclusion as the civil rights issue of our time. (Photo courtesy of HHS)

“We celebrate our LGBT community,” Burwell told the audience. “Let’s embrace the diversity of faces and families that make this department great.”



One man’s journey to affirming his identity

Keynote speaker [Albert Smith Jr.](#), Sexual and Gender Minority (SGM) Portfolio Strategist in the [NIH Office of Equity, Inclusion, and Diversity](#), helped set the tone with a moving narrative of his coming of age. He spoke of his transition from a child blessed with an accepting family, through adolescent shame and discrimination because of his identification as a gay teen, to an epiphany during his studies at Oxford University.

“I needed to assess what I was becoming,” Smith said of his personal challenge when he entered the university. “I vowed to not return to the U.S. the same person.” He described an experience in his flat in England, after years of struggling with his identity. “I met myself anew that day, in front of a mirror that saved me.”

When birth gender and identity gender do not match

The panelists who followed Smith developed several of his themes regarding transgender children and their family experiences.

[Diego Sanchez](#), director of policy for Parents, Families, and Friends of Lesbians and Gays (PFLAG), described the unexpected support he received from his military family in the 1960s. Assigned female gender at birth, he said, “When I was 5, I told my parents I was born wrong.”

While Sanchez’ parents helped him make his transition from birth gender, the next speaker, the parent of a transgender female, said she had much more to learn. [Catherine Hyde](#), transgender coordinator with PFLAG, and her husband realized early on that something was very different about their child, who celebrated her 20th birthday this year.

The couple followed advice current in the 1990s and discouraged cross-gender play. “We shamed our child,” she said as she tearfully recalled her child’s suicidal thoughts and self-mutilation. “We had no idea how big that gender thing really was.”

The personal merged with the bigger picture in presentations by [Sharon Lettman-Hicks](#) of the National Black Justice Coalition, and [Rebecca Cokley](#) of the National Council on Disability. As Lettman-Hicks and Cokely explored the dimensions of compounded discrimination, they reflected, sometimes bitterly, on the social and familial stress experienced by people who may be LGBT, people of color, and individuals with one or more disabilities.

The emotionally charged discussion ran over its allotted 90 minutes, but at its conclusion there seemed to be unanimous agreement with the assessment by moderator [Kathy Greenlee, J.D.](#), administrator of the HHS Administration for Community Living, and Assistant Secretary for Aging.

Award-winning efforts to address SGM issues

Later this summer, Collins will present an NIH Director’s Award to the NIH SGM Research Coordinating Committee (RCC).

The NIEHS representative on the RCC, statistician Bill Quattlebaum, and representatives from other NIH institutes, centers, and offices will share the award for their efforts to promote research on the health issues and health disparities relevant to SGM communities.



“You’re probably the best panel in history,” she told the guests, as she invited the audience to talk individually with the panelists following the broadcast.

(Eddy Ball, Ph.D., is a contract writer for the NIEHS Office of Communications and Public Liaison.)



Smith reflected on his mother’s words of consolation as he was growing up hearing his peers make derogatory comments. “These words [from her] were not only life changing for me, but life saving for me.” (Photo courtesy of Damien Jackson)



Describing the social environment when LGBT individuals were coming out in the 1970s, Greenlee said there were no real models for young people. “There was nothing positive,” she said. “It was only negative.” (Photo courtesy of HHS)

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