National Institute of Environmental Health Sciences

Environmental Factor

Your Online Source for NIEHS News

September 2015

NIEHS Spotlight

Low-dose mixtures and cancer highlighted at NIEHS symposium

The Halifax Project Low Dose Theory Symposium considered how exposures to low doses of chemical mixtures may contribute to cancer.

Global collaboration to combat e-waste Video

NIEHS and international collaborators focused on strategies to combat e-waste at a conference and workshop in Indonesia.

Environmental justice featured in new NIEHS report

A new NIEHS report analyzes the role of the institute's grant funding in reducing environmental disparities and promoting environmental justice.

Summer interns share research at poster session Video

At the July 30 poster session, NIEHS interns shared the results of research they conducted over the summer.

Phil Brown receives environmental sociology award for outstanding work

The American Sociological Association recognized the work of NIEHS Council member Phil Brown, Ph.D., with the Practice and Outreach Award.

Clinical Feature

Genes strongly associated with myositis risk identified

NIEHS clinical researchers and colleagues reported identifying genetic risk factors associated with myositis, in the journal Genes and Immunity.

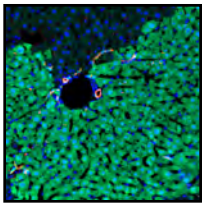
Science Notebook

NIEHS sheds light on main cause of mutations in certain cancers Video

A team led by Dmitry Gordenin, Ph.D., of NIEHS, reported in Nature Genetics that APOBEC3A is likely the main cause of mutations in certain cancers.

Kidney toxicity screening tool developed by grantee and NTP team

Researchers including NIEHS grantees and NTP scientists developed the first method to test for kidney toxicity using high throughput screening.



Newly discovered cells repair liver without cancer risk

Researchers funded by NIEHS have discovered a type of cell, present in healthy livers, that can regenerate damaged tissue without giving rise to cancer.

NIEHS Spotlight

EHP welcomes new editor in chief

NIEHS welcomed Sally Perreault Darney, Ph.D., as the new editor in chief of Environmental Health Perspectives, on Aug. 24.

Two SRP grantees selected as prestigious AAAS Fellows

Two SRP researchers began prestigious appointments as American Association for the Advancement of Science and Technology policy fellows.

NIEHS fellow begins career as assistant professor

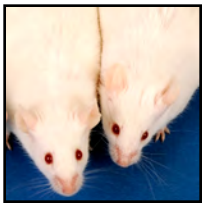
Wipawee (Joy) Winuthayanon, Ph.D., has begun her new career as an assistant professor at Washington State University.

Endocrine disruption pioneer Lou Guillette remembered

Video

Louis Guillette, Ph.D., a renowned researcher in environmental health and reproductive endocrinology, died Aug. 6.

Science Notebook

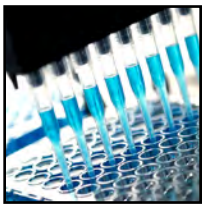


Fetal low-level arsenic exposure leads to early puberty and obesity in mice

NIEHS scientists reported that mice exposed prenatally to low levels of arsenic displayed signs of early puberty and became obese as adults.

NIEHS researchers identify key protein at work in breast cancer

The protein LIN28A plays a role in many types of breast cancer, say NIEHS scientists in a study published this month in the journal Molecular and Cellular Biology.



DREAM challenge results published in Nature Biotechnology

An innovative crowdsourcing challenge launched by NIEHS and partners in 2013 has come full circle with publication in Nature Biotechnology.

Fracking in Pennsylvania linked with increased hospitalizations

NIEHS-funded scientists have linked increases in hydraulic fracturing activity and hospitalization rates in Pennsylvania.

Interindividual variability highlighted in upcoming workshop

The National Research Council workshop Sept. 30-Oct. 1 will explore sources of individual variation in responses to environmental stressors.

This month in EHP

The September issue of Environmental Health Perspectives (EHP) examines seabed mining and its potential opportunities and risks.

Inside the Institute

NIEHS employees stock local food banks through Feds Feed Families

The Feds Feed Families campaign concluded Aug. 24, beating its goal and sending 3,830 pounds of food to local food banks.

Bee-cause - NIEHS pitches in for pollinator health

NIEHS has joined the national effort to protect the health of pollinating species by nurturing their habitats, including installation of bee boxes.

Extramural Research

Extramural papers of the month

- Epigenomic mapping of human tissues
- DEHP replacements may also cause health risks
- Living close to hydraulic fracturing associated with more hospitalizations
- Researchers identify pathway that can halt fibrosis progression

Intramural Research

Intramural papers of the month

- NTP team identifies aromatase inhibitors in Tox21 library
- RGS2 protein required for proper fertilization in mice
- Cholesterol trafficking protein could provide therapeutic target for inflammatory diseases
- BPA and phthalate exposure was not associated with subfertility
- MicroRNAs and chromatin modifiers steer the fate of human ES cells

Calendar of Upcoming Events

- **Sept. 2**, Rodbell Auditorium, 8:30 a.m. – 5:00 p.m. — Scientific Advisory Committee on Alternative Toxicological Methods meeting, register to attend in person or via webcast
- **Sept. 9**, Rodbell Auditorium, 8:30 a.m. – 5:15 p.m. — National Advisory Environmental Health Sciences Council meeting
- **Sept. 15**, Rodbell Auditorium, 11:00 a.m. – noon — Distinguished Lecture Seminar Series talk by mitochondrial geneticist Doug Wallace, Ph.D., of the Children's Hospital of Philadelphia Research Institute, speaking on "Mitochondrial-Cellular Interactions and Pathophysiology of Disease," hosted by Bill Copeland, Ph.D.
- **Sept. 16–18 (off-site event)**, NIH in Bethesda, Maryland — NIH Research Festival
- **Sept. 18**, Keystone 1003, 1:00 – 3:00 p.m. — NIEHS Worker Training Program Ebola Biosafety and Infectious Disease Response Training — Funding Opportunity Announcement 2015 Briefing Information Meeting, register to attend in person or via webcast
- **Sept. 18 (off-site event)**, Environmental Hall Field Auditorium, Duke University, noon – 1:30 p.m. — Integrated Toxicology and Environmental Health Program (ITEHP) Fall 2015 Seminar Series talk, featuring Carolyn Mattingly, Ph.D., from North Carolina State University, discussing "Casting a Wide Net to Uncover Pathways Between Environmental Exposures and Disease"
- **Sept. 24**, Keystone 1003, 10:00 – 11:00 a.m. — Keystone Science Lecture Seminar Series talk by James Dearing, Ph.D., of Michigan State University, and lead researcher with the National Cancer Institute Center of Excellence in Cancer Communication Research
- **Sept. 25 (off-site event)**, Environmental Hall Field Auditorium, Duke University, noon – 1:30 p.m. — ITEHP Fall 2015 Seminar Series talk, featuring Lilah Glazer, Ph.D., from Woods Hole Oceanographic Institute, highlighting "Environmental Toxicity of PCBs: Lessons From Fish as Environmental and Human Health Models"
- **Sept. 24–25 (off-site event)**, National Institutes of Health, Bethesda, Maryland — NTP Interagency Center for the Evaluation of Alternative Toxicological Methods workshop "Alternative Approaches for Identifying Acute Systemic Toxicity: Moving from Research to Regulatory Testing," register by Sept. 11
- **Sept. 28**, Rodbell Auditorium, 1:00 – 5:30 p.m. — NIEHS Worker Training Program (WTP) 2015 Fall Awardee Meeting, register to attend
- **Sept. 29–30**, Rodbell Auditorium, Sept. 29, 9:00 a.m. – 5:00 p.m.; Sept. 30, 9:00 a.m. – 1:00 p.m. — WTP Awardee Workshop, register to attend
- **Sept. 30–Oct. 1 (off-site event)** National Academy of Sciences (NAS), Washington, D.C. — NAS Workshop on Interindividual Variability, register to attend in person or via webcast
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Low-dose mixtures and cancer highlighted at NIEHS symposium

By Virginia Guidry

Scientists gathered at NIEHS Aug. 25 to consider how exposures to low doses of chemical mixtures may contribute to the development of cancer. The Halifax Project: Low Dose Theory Symposium was organized to discuss next steps, following publication of a special issue of the journal Carcinogenesis, which was written by a group of scientists known as the Halifax Project Task Force.

The name Halifax Project refers to a 2013 meeting in Halifax, Nova Scotia, that was supported by the NIEHS Superfund Research Program. At the meeting, 170 researchers from a variety of scientific disciplines discussed the potential of low doses of chemical mixtures to cause changes that lead to cancer.

"We are happy to have NIEHS eyes on the project," said Leroy Lowe, co-founder and president of Getting to Know Cancer, the organization that coordinated the Halifax Project, "because we are quite interested to hear from so many cancer biologists about how they think biology might inform risk assessment and toxicology."

"There are several questions about how to define low dose, determine the most relevant windows of susceptibility, and investigate exposures to mixtures," said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program (NTP). "One thing we know is that the toxicology of the 21st century should not be that of the 20th century."

Low-dose theory applied to cancer

As Lowe and other speakers emphasized, much of the research on the contribution of environmental exposures to cancer has emphasized carcinogens, which are single chemicals that are shown to lead to cancer. However, because cancer development is often a long, involved process, there may be opportunities for multiple chemicals to play independent roles, each contributing to the final disease state. Chemicals may either promote cancer or interfere with mechanisms in the body that correct abnormalities in cells (see sidebar).

"When we start talking about the ways mixtures may have synergistic effects, take a lesson from cancer therapy — clinicians don't expect to be able to act on the same mechanism with one chemical," said Lowe. "From an environmental health standpoint, we should be thinking about how we can enable these different hallmarks with different chemicals." (Photo courtesy of Steve McCaw)

Hallmarks of cancer

The Halifax Project was organized around the hallmarks of cancer. Cells that acquire these hallmarks, especially combinations of them, are more likely to be able to form malignant tumors.

- Evasion of growth suppressors
- Sustained signaling to promote proliferation
- Resistance to cell death
- Inducing blood vessel growth
- Enabling unlimited replication
- Activation of tissue invasion and metastasis
- Deregulated cell metabolism
- Genetic instability of tumor cells
- Immune system evasion
- Tumor microenvironment
- Inflammation

For the Halifax Project, scientists reviewed literature for evidence that chemicals might be able to act together to promote cancer, even though the chemicals may be considered noncancer-causing and the public may be exposed at low levels.

In the papers they wrote for the Carcinogenesis issue, the researchers presented 85 environmental chemicals that may act on key pathways, to result in one of 11 hallmarks, or phenotypes, of cancer. Over half of those chemicals exerted effects at levels similar to levels the general population is commonly exposed to. The scientists proposed that by acting on different pathways, these chemicals may produce a cumulative effect that leads to cancer.

During a question and answer period, Birnbaum, left, suggested that toxicologists, epidemiologists, and other scientists collaborate on the study of epigenetic factors contributing to cancer. Mark Miller, Ph.D., right, is Birnbaum's chief of staff and was the lead organizer of the event. (Photo courtesy of Steve McCaw)

Next steps for testing the hypothesis

The NIEHS symposium served as the next step toward developing a hypothesis. Researchers from government, academia, industry, and nongovernmental organizations, as well as the Halifax Project attended the meeting. Lowe and William Goodson III, M.D., who served as first author of the lead paper in Carcinogenesis, provided background on the Halifax Project and the implications of the findings. Attendees then broke into three roundtable discussions on emerging research needs.

According to Goodson, researchers face several challenges, including the need for more relevant epidemiology studies, improved understanding of biology and physiology, focusing on chemicals beyond those that imitate estrogen, finding reliable cell models, understanding exposure mixtures, and mapping the epigenome. (Photo courtesy of Steve McCaw)

- Information gaps regarding the theory of how low-dose mixtures contribute to carcinogenesis.
- Key research methodologies that would enable the testing of this hypothesis.
- Potential implications of low-dose mixture theory on policy and decision-making, as well as the potential for influence on disease endpoints besides cancer.

"The next stages of this project concern whether we can translate what we see as a problem into science that demonstrates that it is an issue," said Lowe.

Margaret Kripke, Ph.D., chief scientific officer for the Cancer Prevention and Research Institute of Texas, described increasing evidence of the influence of environmental chemicals in the development of cancer. (Photo courtesy of Steve McCaw)

Transdisciplinary cooperation is key

Participants agreed that an important next step is to generate data to test the low-dose mixtures theory. "You've got a theory saying that low doses to environmental chemicals somehow are working together to increase cancer," said Richard Peffer, Ph.D., senior toxicologist at Syngenta. "If that was the case, there should be some experimental data pointing to that."

Participants emphasized that transdisciplinary conversations are essential to future research. “The epidemiologists, toxicologists, biologists, and oncologists all need to be talking to industry, and there needs to be a back and forth,” said Goodson. “The stakeholders here are not the doctors and industry. The stakeholders are our children, our grandchildren, and our great-grandchildren, and whatever we do now is going to change their lives. It behooves us to try to do it right.”

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

Kim Lyerly, M.D., from Duke University, commended the successful collaboration of nearly 200 scientists on the Halifax Project. “We may not address all the questions today, but certainly the capacity to bring people together to work on a common theme in a way that is productive is remarkable,” he said. (Photo courtesy of Steve McCaw)

Nicole Kleinstreuer, Ph.D., a contract scientist supporting NTP, reported from the roundtable group that addressed how the application of low-dose mixture theory might inform risk assessment and policy decision-making. (Photo courtesy of Steve McCaw)

William Bisson, Ph.D., from Oregon State University, gave the report from the roundtable that discussed key research methodologies for testing the low-dose mixture hypothesis. (Photo courtesy of Steve McCaw)

Nigel Walker, Ph.D., left, and Warren Casey, Ph.D., brought the NTP perspective to the discussion on needs for novel research methodologies. (Photo courtesy of Steve McCaw)

Masoud Manjili, D.V.M., Ph.D., from the Virginia Commonwealth University Massey Cancer Center, summarized the findings from the roundtable group that assessed data needed to better inform the low-dose mixture theory. (Photo courtesy of Steve McCaw)

Return to Table of Contents

Global collaboration to combat e-waste

By Paula Whitacre

As computers, appliances, and other electronics grow more numerous and their usable life shortens, a worldwide surplus of electronic waste, or e-waste, has developed, creating a market for the valuable components, such as copper, that can be extracted from the discarded devices. NIEHS has taken a leadership role in developing strategies to understand, prevent, and treat the adverse health effects caused by dismantling or burning the e-waste to recover the marketable components.

In August, NIEHS and the World Health Organization (WHO) convened a workshop in Indonesia, focused on strategies to reduce exposure to e-waste. Collaborators included the Chulabhorn Research Institute in Thailand; Children's Health and Environment Program at the University of Queensland, Australia; and U.S.-based nonprofit Pure Earth.

Fobil discussed lessons learned from an intervention at the Agbogbloshie e-waste site in Accra, Ghana, recently identified by Green Cross of Switzerland and Pure Earth as one of the 10 most polluted places in the world. (Photo courtesy of Michelle Heacock)

Heacock, left, with Marie-Noel Brune from WHO. NIEHS and WHO collaborated on the e-waste project that led to the daylong event. (Photo courtesy of Michelle Heacock)

The e-waste workshop included small group discussions on reducing exposures, monitoring, and communication. (Photo courtesy of Michelle Heacock)

Providing practical recommendations

"NIEHS is a WHO Collaborating Centre for Environmental Health Sciences, and e-waste is one of our center's five focus areas of concern," explained Michelle Heacock, Ph.D., health scientist administrator for the NIEHS Superfund Research Program (SRP), who helped organize the event. Members of the WHO Collaborating Centres Network for Children's Environmental Health were also involved.

The workshop featured experts in health, engineering, and other fields. Presenters discussed case studies from Ghana, Uruguay, China, and the Philippines, highlighting successes and lessons learned. Building on the case studies, breakout groups addressed reducing exposures, monitoring, and communications.

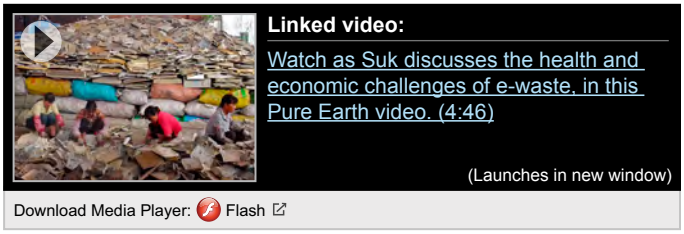
"We organized the workshop with the goal of providing practical recommendations," Heacock said. "And we incorporated engineering techniques and discussions on strategies, such as how to communicate risk and increase use of personal protective equipment."

For example, Julius Fobil, Dr.P.H., from the University of Ghana in Accra, and Bret Ericson of Pure Earth, discussed the introduction of a wire stripping machine to more safely extract copper at one of the most polluting e-waste sites in Africa, which operates in central Accra. They emphasized the importance of building community trust, as workers worry about the immediate economic toll of new policies and practices.

A complex health and economic challenge

The workshop opened with a short video (linked below) in which William Suk, Ph.D., SRP director, explained how burning or dismantling e-waste results in contaminants, such as polychlorinated biphenyls and other chlorinated organics, entering the water and air. Research supported by NIEHS and others has shown the harmful effects of direct and indirect exposures, including effects on a growing fetus.

Yet many low-income communities depend on e-waste for their livelihood, making the solutions extremely complex. "It's a real conundrum," he said. "You want to protect people's health. At the same time, you want to ensure they can support themselves."



Conference crosses geographic, institutional, and discipline borders

The International Conference of the Pacific Basin Consortium on Environment and Health rotates meeting locations and includes topics of concern to the host country, as well as research from throughout the region.

The Superfund Research Program (SRP) at NIEHS and the National Cancer Institute (NCI) Center for Global Health were among the co-sponsors of the 2015 conference. Ann Chao, Ph.D., from NCI, co-chaired a panel on environmental contributions to cancer in Southeast Asia.

In addition to an e-waste panel, SRP staff and grantees were involved throughout the conference. "The PBC [conference] parallels the goals of the SRP — environmental science and engineering, human health, and community engagement — but on a global scale," Heacock said.

Conference planners include trainees, especially those from the host country, to help them expand their knowledge of the connections between environment and health.

Presentations of research supported by NIEHS included:

- Bernhard Hennig, Ph.D., University of Kentucky, on nutrition interventions against environmental insults.
- Celia Chen, Ph.D., Dartmouth College, on connecting mercury science to policy.
- Keith Pezzoli, Ph.D., University of California, San Diego, on creating just and healthy bioregions.

Jeffrey Crosby, Ph.D., chief technical officer of Picoyune, spoke about a mercury sensor and monitor that is more robust and less expensive than current methods. SRP supported the initial development, as part of the University of California, Berkeley program. That program is an example of how SRP research can lead to a small business innovation, Heacock said.

Broadening the discussion

The workshop followed the 16th International Conference of the Pacific Basin Consortium for Environment and Health (PBC), held Aug. 10-13 at the University of Indonesia in West Java. At the conference, NIEHS and WHO co-chaired a panel on the topic (see text box).

NIEHS and WHO launched their joint e-waste program at the previous PBC conference in 2013. According to Heacock, the network of people working on e-waste issues is growing and more collaborations are planned. She underscored the value of presenting the topic at the PBC conference as well as holding the workshop, to reach a wider audience with information on e-waste and its impacts.

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

Return to Table of Contents

Environmental justice featured in new NIEHS report

By John Yewell

For the first time, a new report from the NIEHS Division of Extramural Research and Training (DERT) highlights the institute's contributions to reducing environmental health disparities and supporting environmental justice.

The 80-page report, "Advancing Environmental Justice," presents the results of an analysis of projects funded by NIEHS from 1998 to 2012. It also includes a brief history of the environmental justice movement, an evaluation of the role of NIEHS funding, and suggested next steps.

The report is available as a free PDF download from the NIEHS Environmental Health Disparities and Environmental Justice Web page. (Photo courtesy of NIEHS)

Spreading the word and moving forward

The analysis revealed 155 projects that concentrated on some aspect of environmental justice, many of which used community-engaged research to address a range of environmental hazards. "The report gives a nice snapshot of results from a lot of incredible work across the country," said Liam O'Fallon, a program analyst with DERT and coordinator of the NIEHS Partnerships for Environmental Public Health (PEPH) program, which produced the report.

The project began in 2012 to fill an information gap. "We knew that NIEHS had a long history of supporting environmental justice work through several programs, but we had never taken a look at the totality of our grants," O'Fallon said. "We wanted to be able to understand and communicate the outcomes all our efforts."

What is PEPH?

Partnerships for Environmental Public Health is a network of scientists, community members, educators, healthcare providers, public health officials, and policymakers who share the goal of increasing the impact of environmental public health research at the local, regional, and national levels.

O'Fallon acknowledged that methodological limitations may have caused some projects to be missed. Regardless, he said, the number and variety of grant projects focused on environmental justice was wide ranging. In fact, 23 different grant mechanisms were represented among the projects examined.

The effort supports Goal 6 of the NIEHS strategic plan — to understand the disproportionate risks of disease in vulnerable populations, and to define and support public health and prevention solutions in affected populations.

"The report tells an important story about the valuable contributions our grantees have made to environmental justice issues," said O'Fallon. (Photo courtesy of Steve McCaw)

Emphasis on community involvement

O'Fallon noted that one of the most noteworthy findings was the value of community-engaged research and the importance of developing the skills of community groups and researchers to work effectively together.

"These projects highlight the importance of working in partnership with community residents," he said. "Community members have local knowledge and skills that help environmental health research succeed, and they help to inform policy, which can have a lasting public health impact."

For example, the report highlights a Texas project, Communities Organized Against Asthma and Lead, through which several organizations collaborated to identify and characterize the risks of lead poisoning and asthma in children. The report states, "As the project evolved, close collaboration with the City of Houston Health and Human Services Childhood Lead Poisoning Prevention Program ensured that project findings and recommendations informed public policy. Their results also helped researchers understand the need to consider alternate methods to measure asthma prevalence within the Hispanic population." An appendix to the report provides more detail.

Along with the report, PEPH produced an annotated bibliography of 2,146 peer-reviewed studies generated by grantees. The bibliography is designed to make environmental justice information more accessible to researchers, communities, and stakeholders.

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

Return to Table of Contents

Summer interns share research at poster session

By Geoffrey Feld

This summer, more than two dozen high school, college, and graduate students participated in the NIH Summer Internship Research Program (SIP). On July 30, they shared the results of their training, at the annual poster session in Rodbell Auditorium.

Over the course of the summer, the students immersed themselves in biomedical research at NIEHS. Aided by scientists and staff, as well as the Office of Fellows' Career Development (OFCD), the students took on challenging research projects, attended seminars, participated in career development workshops, and ended the internship with the highly anticipated poster session.

"I always get glowing feedback from the lead scientists and other poster session attendees saying how impressed they are with the quality of work done over the summer," said Debbie Wilson, summer intern coordinator for the NIEHS Division of Intramural Research. "This summer was no exception."

Sridhar, right, began her internship after finishing her sophomore year. She received the High School Research Poster Award from NIEHS Deputy Scientific Director Bill Schrader, Ph.D., left. Sridhar was mentored by Pandiri, who heads the Molecular Pathology Group. (Photo courtesy of Steve McCaw)

Motivation is key to success

Like other interns, Nikhil Milind, a high school junior at the North Carolina School of Science and Mathematics in nearby Durham, sustained his motivation from the moment he began the application process. While volunteering locally, Milind reached out to his eventual NIEHS collaborator, Kyathanahalli Janardhan, Ph.D., a contractor in the Cellular and Molecular Pathology Branch. Milind hopes to continue his research classifying rat uterine sarcomas next summer.

Richard Gilliam, from St. Augustine's University, worked with Tammy Collins, Ph.D., director of OFCD, and Shyamal Peddada, Ph.D., of the Biostatistics and Computational Biology Branch, to analyze career outcomes of recent NIEHS postdocs. "Mr. Gilliam's drive and dedication were critical to the project's success," said Collins. "He gained skills in advanced data analysis, which will translate to any research field he chooses to enter."

Building career momentum

Some SIP participants come to NIEHS with specific career goals in mind. Craig McGowan will apply his summer research on the human toxicological effects of the 2010 Deepwater Horizon oil spill toward completion of his masters' degree in biostatistics at the University of North Carolina-Chapel Hill (UNC).

Summer intern poster award winners

High School — Shivpriya Sridhar, a senior at Enloe High School in Raleigh, North Carolina, worked in the Cellular and Molecular Pathology Branch of the National Toxicology Program, with Arun Pandiri, Ph.D., as mentor. Sridhar's poster was titled, "Immunohistochemical Characterization of Islets of Langerhans in F344/N Rats Exposed to Cobalt by Inhalation Exposure."

Undergraduate — Ying Chen Bailey Lien, a junior at the University of Pittsburgh, worked with Patricia Jensen, Ph.D., in the Neurobiology Laboratory, and presented "A New Mouse Line for Chemogenetic Activation of Locus Coeruleus Noradrenergic Neurons."

Graduate — Craig McGowan, a masters student at UNC, studied "Respiratory Symptoms and Eye Irritation Related to Corexit 9500A and 9527A Exposure in the GuLF STUDY," with Dale Sandler, Ph.D., of the Epidemiology Branch.

McGowan said his project, which won the Graduate Student Poster Award, reinforced his desire to do research. He plans to volunteer at NIEHS as he finishes his thesis.

Other interns arrive with research backgrounds and gain new insights. Caroline Vilas, a UNC senior majoring in biochemistry, was uncertain about pursuing a career in research. Ultimately, encouragement from SIP alumni friends and members of her undergraduate lab led her to seek the internship opportunity.

"Meeting and working with scientists at NIEHS who enjoy what they do has really encouraged me to pursue research," she said. Vilas studied interactions of the enzyme Tdp2 with topoisomerase, a target of certain cancer drugs. "Our hypothesis-driven research style helped me learn a lot about problem-solving in the lab," she added.

Heeding the call to help

Many NIEHS scientists and staff, both first-time participants and returning veterans, shared in the interaction with enthusiastic young scientists, from direct research mentors and lead scientists, to judges for the poster session.

Vilas's mentor, first-timer Matthew Schellenberg, Ph.D., a visiting fellow in the Genome Stability Structural Biology Group, said the program benefits both students and mentors. From coaching Vilas in ways to communicate her research to nonexperts, to contemplating how her results fit into the overall goals of his own research, Schellenberg used the opportunity to train and learn.

"What really makes the program outstanding is the amazing students that apply, combined with the resources and facilities available here," says Schellenberg. He hopes to mentor another SIP participant next year.

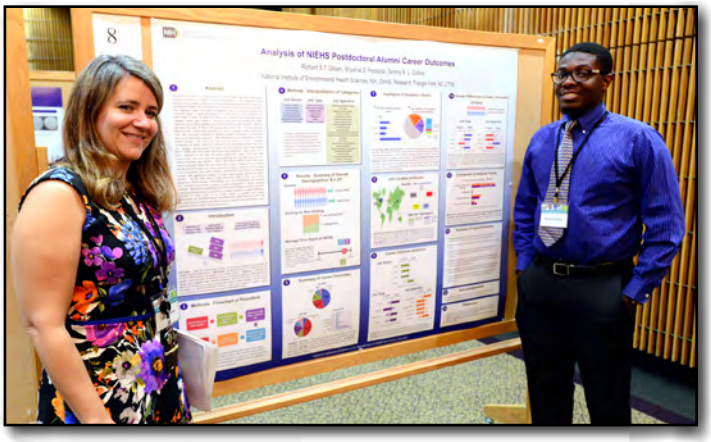
Palmyra Romeo, a former Intramural Research Training Award (IRTA) postbaccalaureate fellow in the Synaptic and Developmental Plasticity Group, helped train interns in her lab and has taken leadership roles in educational events. This was her third year volunteering to serve as a poster session judge.

"I always leave the poster sessions encouraged about the bright young minds learning about science," says Romeo. Regardless of whether SIP participants ultimately choose careers in science, she said, "I think it is crucial that our future generations develop a solid understanding of how basic research works."

(Geoffrey Feld, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Genome Stability Structural Biology Group.)

Lien, right, with Schrader, left, was the undergraduate award winner for her poster and presentation on her summer research in the Laboratory of Neurobiology. Lien helped create a new mouse line to allow researchers to study the response of certain neurons in the brainstem to environmental exposures. (Photo courtesy of Steve McCaw)

Schrader, left, presented McGowan, right, with the Graduate Research Poster Award. McGowan said that his interest in studying the effects of the Deepwater Horizon oil spill came naturally, because of the easily relevant link to human health. (Photo courtesy of Steve McCaw)



Many poster session visitors were curious about the findings of Gilliam, right, shown with Collins, left. He found that approximately 45 percent of NIEHS fellows entered the academic sector, with about half of those entering tenure track positions. His findings corresponded with those of postdocs across the National Institutes of Health, he said. (Photo courtesy of Steve McCaw)

Jourdan Bouldin, now a senior at North Carolina State University, studied the molecular mechanisms of the Glis1 protein, to shed light on its transcriptional activity. She worked in the Cell Biology Group with group lead Anton Jetten, Ph.D., and IRTA fellow Rob Brown, Ph.D. (Photo courtesy of Steve McCaw)

Milind explained his research into cell staining techniques to classify specific sarcoma phenotypes. "Working for two months at NIEHS alongside researchers and experts alike helped me understand that biology is the right field for me," said the rising high school junior. (Photo courtesy of Steve McCaw)

The interns' summer research experience was enhanced by workshops, such as the one shown above, a communication challenge, and a journal club, which provided insight into the elements of a successful scientific publication. (Photo courtesy of Steve McCaw)

Accepting the challenge to communicate research in plain language

Recognizing the importance of being able to clearly communicate scientific research, the popular NIEHS Big Picture, Small Talk series offered the summer interns a science communication challenge. At the July 23 event, organizers gave each intern three minutes to share their research in a nontechnical presentation. Ten interns accepted the challenge, and administrative staff judged them on how well they expressed their main message.

The judges selected Yue Jiang, a graduate student at UNC, who worked with mentor Shanshan Zhao, Ph.D., in the Biostatistics and Computational Biology Branch. Jiang summarized his work on a new approach to predicting breast cancer risk, based on an individual's family history.

Interns Sam Arbes, Richard Gilliam, Nicole Gonzalez, Shiyi Li, Craig McGowan, Brinkley Raynor, Sarah Sugarman, George Truong, and Ben Whitfield also participated. Wilson hosted the event, and Peggy Mooring, Abee Boyles, Ph.D., and Collins organized it.

Phil Brown receives environmental sociology award for outstanding work

By Sara Mishamandani

Phil Brown, Ph.D., an NIEHS grantee and member of the NIEHS Advisory Environmental Health Sciences Council, is the 2015 recipient of the American Sociological Association Environment and Technology Section Practice and Outreach Award. It is given in recognition of outstanding contributions to furthering environmental causes in society. Brown received the prestigious award Aug. 23 at the association's annual meeting in Chicago.

Brown will serve on the NIEHS National Advisory Environmental Health Sciences Council through 2018. As a council member, he helps advise the NIEHS director, assists in evaluating existing and new NIEHS programs, and participates in the implementation of the strategic plan. (Photo courtesy of Phil Brown)

Brown, who is the University Distinguished Professor of Sociology and Health Sciences at Northeastern University, has a long history of community-engaged participatory research. Working at the forefront of environmental health and justice research for the past 25 years, he has fostered productive collaborations with community groups, governmental organizations, and a wide range of academic researchers, to reduce exposures and improve public health.

Strengthening SRP community partnerships

Since 2009, Brown has directed Community Engagement Cores at NIEHS Superfund Research Program (SRP) centers — first at Brown University, and now at Northeastern. Brown currently directs the Northeastern Social Science Environmental Health Research Institute and co-leads the SRP center's Community Engagement Core and Research Translation Core.

Through the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) SRP center, Northeastern and partnering institutions study the effects of environmental contaminants on preterm birth in Puerto Rico. Brown works with the center to report data back to post-partum and expectant mothers involved in the PROTECT study and explain the findings. He is one of the pioneers of the report-back process, developed in a decadelong partnership with Silent Spring Institute, to empower individuals and improve communication between researchers and communities.

Along with Silent Spring, Brown co-directs a new NIEHS-funded program, the Transdisciplinary Training at the Intersection of Environmental Health and Social Science, to train graduate students and postdoctoral fellows in the kind of collaborative work he does.

"Dr. Brown provides invaluable guidance to the education and engagement work at community clinics across Puerto Rico," said Akram Alshawabkeh, Ph.D., Northeastern SRP center director. "These efforts have marshalled public and private resources to eliminate the disparity in preterm birth and promote access to health promotion and early intervention services for families with preterm babies."

A key ally

At the Brown University SRP center, Brown worked to better understand and clean up environmental contamination, promote efforts to inform community members and students of environmental justice issues, and help build a local environmental justice and environmental health network. He was also instrumental in establishing the Environmental Justice League of Rhode Island.

"Phil has been a key ally for our work," said Sylvia Broude, executive director of the Toxics Action Center. "From serving on our advisory board, to being a trainer for our staff on the history of the toxics movement and on environmental justice, Phil's commitment to environmental justice and toxics organizing is unmatched, and we are grateful for his support of our work. I can't imagine a more worthy choice for this award."

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

Return to Table of Contents

EHP welcomes new editor in chief

By Kelly Lenox

Sally Perreault Darney, Ph.D., was welcomed Aug. 24 as the new editor in chief of the NIEHS journal Environmental Health Perspectives (EHP). She previously served in the U.S. Environmental Protection Agency (EPA) Office of Research and Development.

Darney brings extensive experience in both research and program management. She has published over 100 research papers and review articles in the fields of reproductive toxicology, environmental epidemiology, and children's health. As a program director at EPA, she influenced research priority strategic planning in chemical safety, sustainable communities, children's health, and health disparities.

At EPA, Darney most recently co-led a large research project focused on assessing health disparities in vulnerable groups and providing healthy environments for children. (Photo courtesy of Sally Perreault Darney)

Leadership and vision

"Sally will provide leadership and scientific vision to EHP and help shape the future direction of the journal," said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program.

In an editorial for the September issue of EHP, Darney described her vision for the journal. "The challenge, as I see it, is for EHP to make new knowledge accessible in forms that are fit for purpose for the scientific community, for regulatory application at national and local scales, and for the public, to inform personal and community-based decisions," she wrote. "Fit for purpose means not only understandable by diverse audiences, but also globally accessible. We can do this by marrying new data sharing and contemporary social networking tools in today's digital age with traditional scholarly publishing."

Darney brings experience in scholarly publishing and peer review, having served as co-editor in chief of the Journal of Andrology, associate editor for the journal Biology of Reproduction, and on editorial boards and peer review panels in the reproductive and environmental sciences.

A leading journal in the environmental health sciences, EHP is published monthly and is available free online.

Return to Table of Contents

Past EHP editors

Darney follows a talented list of scientists at the helm of EHP.

Jane Schroeder, D.V.M., Ph.D., interim, 2014-2015
Hugh Tilson, Ph.D., 2008-2014
Kenneth Korach, Ph.D., interim, 2007
James Burkhart, Ph.D., interim, 2006
Tom Goehl, Ph.D., 2001-2005
George Lucier, Ph.D., and **Gary Hook, Ph.D.**, 1974-2001
Robert Goyer, M.D., and **Hans Falk, Ph.D.**, 1974
Falk and **Douglas Lee, M.D., Ph.D.**, 1972-1973

Two SRP grantees selected as prestigious AAAS Fellows

By Sara Mishamandani

This month, NIEHS Superfund Research Program (SRP) researchers Wendy Heiger-Bernays, Ph.D., and Bradley Newsome, Ph.D., join an elite group of scientists and engineers as American Association for the Advancement of Science (AAAS) Science and Technology Policy Fellows to help connect good science to government decision-making.

The highly competitive AAAS Science and Technology Fellowship provides scientists and engineers from a spectrum of career stages with opportunities to learn firsthand about policymaking. At the same time, they contribute their knowledge and analytical skills to federal policy efforts. Heiger-Bernays and Newsome will begin their one-year fellowships on Sept. 1, both in Washington, D.C.

Newsome, second from right, at the SRP Annual Meeting in Nov. 2014 with, from left, Suk, Hennig, and Collman. (Photo courtesy of Heather Henry)

Bradley Newsome

Newsome, who was a graduate student and postdoctoral fellow at the University of Kentucky (UK) SRP Center, will work in the Chief Office of Scientific Workforce Diversity, led by Hannah Valantine, M.D., within the office team of NIH Director Francis Collins, M.D., Ph.D.

"This is a tremendous opportunity for Brad. Dr. Valantine's office is doing some very creative things and it's fabulous to have an environmental health scientist working there," said Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training. "Brad can bring the unique challenges and opportunities in environmental health sciences to activities coming from NIH leadership."

Newsome received his doctoral degree in May 2014 and was a postdoctoral scholar under the guidance of Bernhard Hennig, Ph.D., a professor of nutrition and toxicology and UK SRP Center director. At the UK SRP Center, Newsome studied molecular techniques to understand how polychlorinated biphenyl toxicity is associated with the early phases of atherosclerosis.

He also served as the graduate and postdoctoral training coordinator in the Center's Training Core. As part of his AAAS fellowship, Newsome will address the changing needs of scientific training and the vital role of a diverse workforce in driving needs-based innovation.

Newsome was selected to receive the annual SRP Karen Wetterhahn Memorial Award in 2014, for outstanding contributions to research and educational needs.

Heiger-Bernays is an associate professor in the Department of Environmental Health at the Boston University School of Public Health. (Photo courtesy of Cyndey Scott)

Wendy Heiger-Bernays

Heiger-Bernays, associate professor at the Boston University (BU) School of Public Health, will work in the Office of Chemical Safety and Pollution Prevention at the U.S. Environmental Protection Agency. Her project uses computational toxicological data to identify chemicals that disrupt hormones before they are brought to market (see related story).

Heiger-Bernays researches migration of contaminants in urban gardens and their associated risks, the effects of contaminants on fish and their potential human health effects, and the risks posed by exposure to flame retardants. With training in molecular toxicology and risk assessment methods, her work incorporates elements from both the laboratory and field. As the leader of the BU SRP Center's Research Translation Core, she also helps researchers and regulatory groups use science to inform policy and practice.

"Heiger-Bernays is an excellent addition to the team tasked with incorporating an alternative scientific approach to screen chemicals for their ability to interact with the endocrine system," said Bill Suk, Ph.D., director of the NIEHS SRP. "She will have the opportunity to improve how we evaluate chemicals to inform decision-making in a way that decreases costs and reduces animal testing."

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

Return to Table of Contents

NIEHS fellow begins career as assistant professor

By Shannon Whirledge

In July, former NIEHS trainee Wipawee "Joy" Winuthayanon, Ph.D., began her new career as an assistant professor in the School of Molecular Biosciences at Washington State University, where she will continue her research on estrogen action in the uterus and oviduct during pregnancy.

Preparing for the job search

Winuthayanon joined the NIEHS Receptor Biology Group, headed by Ken Korach, Ph.D., in 2007 as a predoctoral fellow, and she stayed on as a postdoctoral fellow, using her time at NIEHS to beef up her resume. Winuthayanon authored several papers, four of which were featured as Intramural Papers of the Month. One of them, a 2011 publication in the Proceedings of the National Academy of Sciences, was highlighted by the Faculty of 1000 as a must read.

She also volunteered to teach students as part of the NIEHS Scholars Connect and Citizen Schools programs. She said that these experiences confirmed her desire to teach and strengthened her abilities.

Teaching was just one of the many opportunities that prepared her for the job search, Winuthayanon said. She also took part in professional career development classes through the National Institutes of Health (NIH) Office of Intramural Training and Education and attended the NIEHS annual career fairs, where she received help with learning how to network.

"No one likes networking, I think, but I talk to people when I am at a professional society meeting," she said. In fact, Winuthayanon learned of the job posting for her current position while networking at a recent Gordon Research Conference.

"NIEHS allows postdocs to focus on the science, and provides great resources and opportunities to trainees for career development," said Winuthayanon. (Photo courtesy of Steve McCaw)

Lab support for success

Winuthayanon credits Korach and senior biologist Sylvia Hewitt, as well as her co-mentor Carmen Williams, M.D., Ph.D., for helping her meet people in her field and achieve her goal of landing an independent research position at an academic institution. "I wasn't sure that I could do it, but they encouraged me," she said.

Williams, who leads the NIEHS Reproductive Medicine Group, cited Winuthayanon's focus on research as a key strength. "Joy was unafraid to dive in and learn new techniques needed, so she could follow the path her research was taking," Williams said. "She wasn't intimidated by the unknown. Rather, she reveled in it as an opportunity to explore."

Williams highlighted Winuthayanon's proposal for a National Institutes of Health (NIH) Pathway to Independence Award as another important aspect of her training. Even though the proposal wasn't funded, it received a very positive review and contributed to her success as a job candidate. "Going through this process gave her the beginnings of a research plan for her job seminars, and, of course, the framework for a future NIH grant proposal in her new position," Williams said.

Recognition for work well done

Winuthayanon received awards as an NIEHS trainee that reflected her commitment to both teaching and research, including the following:

- 2013 — NIEHS Group Merit Award for development of the first NIEHS Scholars Connect Program boot camp
- 2012 — NIH Fellows Award for Research Excellence

Big goals reached in small steps

Now that Winuthayanon has achieved her goal, she is able to reflect on the skills that helped her along the way. "The most important part is to have great time management skills," she said. "Set a big goal, break it apart into smaller tasks, and achieve those tasks one by one."

These skills will serve her well, as she moves forward in her long-term career plans. "[My goals include] pushing the science forward, publishing, winning grants, helping people in my lab to succeed, and gaining tenure," said Winuthayanon.

(Shannon Whirledge, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction.)

Return to Table of Contents

Endocrine disruption pioneer Lou Guillette remembered

By Eddy Ball

The death of Louis "Lou" Guillette, Ph.D., Aug. 6 shocked and saddened colleagues worldwide in the environmental health and reproductive endocrinology communities.

Guillette was a professor of obstetrics and gynecology, and director of the Marine Biomedicine and Environmental Sciences center at the Medical University of South Carolina (MUSC). His long list of honors included a Heinz Award, and his appointments as a Howard Hughes Medical Institute professor, and endowed chair of marine genomics at the South Carolina Centers of Economic Excellence.

"If the environment isn't healthy for a baby alligator or a baby dolphin, it probably isn't healthy for us as well," Guillette said. (Photo courtesy of the Heinz Foundation)

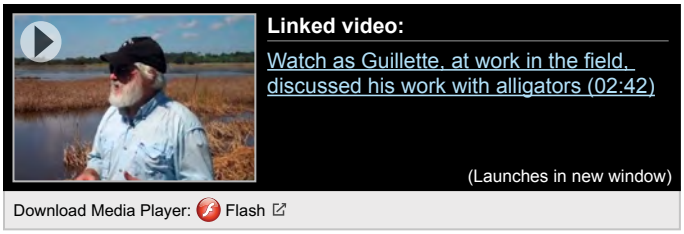
Health scientist administrator Jerry Heindel, Ph.D., who oversees the NIEHS endocrine disruption grants portfolio, summed up what a number of colleagues, whose lives Guillette touched, had to say about his life and work.

"I can't believe it," Heindel said when he received the news. "What a sad day, but what an incredible career and huge impact he had on us all."

A longtime NIEHS grantee, Guillette's cause of death was a bacterial lung infection, worsened by a weakened immune system from an eight-year course of treatment for non-Hodgkin lymphoma.

Health effects of chemical exposures — from alligators to humans

The hallmarks of Guillette's career included his ability to translate findings about endocrine disruption from species such as alligators to the harmful effects in humans. He was also known for his focus on the effects of chronic low-dose chemical exposures, and his tireless advocacy for prevention.



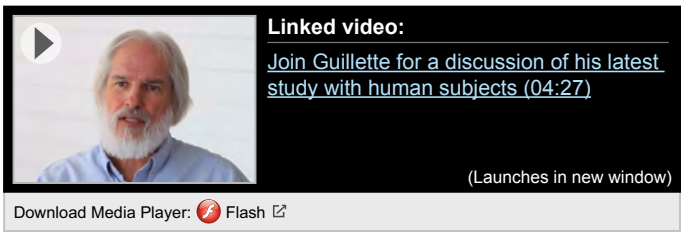
Guillette was among the members of the expert panel that issued a consensus statement on the chemical bisphenol A (BPA) in 2006 (see story) that helped spark controversy over its potentially harmful health effects. The panel's conclusions led to a surge of research on BPA in products ranging from water bottles to medical tubing.

At the time of his death, Guillette was leading a prospective clinical study of expectant mothers, as well as patients at a fertility clinic, to determine what effects environmental contaminants may be having on their reproductive health.

Guillette posted a collection of photos online of wildlife and his research in the field. Several show him and his crew braving the snapping jaws of large alligators in the course of their studies. (Photo courtesy of Louis Guillette)

An outstanding and beloved scientist, teacher, and individual

Tributes published in the Gainesville Sun, Orlando Sentinel, and Charleston Post and Courier featured a number of testimonials from his family, as well as colleagues and students at MUSC and the University of Florida, where he taught from 1985 to 2010 and was named Teacher of the Year in 2008.



In this photo of his study group in 2014 at the Lake Woodruff National Wildlife Refuge in Florida, Guillette, crouching, is right at home in the wild with students and colleagues. (Photo courtesy of Louis Guillette)

“He had a wonderful way of taking difficult and important scientific concepts and making them accessible to reporters, advocates, and the public,” added Gwen Collman, director of the NIEHS Division of Extramural Research and Training.

Guillette’s outstanding scientific achievements, mentoring, and communication skills, as well as his sense of humor, were highlighted by his personal and extensive scientific families at a celebration of Lou’s life. The celebration was hosted by his widow, Elizabeth (Buzzy), a retired anthropologist, at the family’s home on Johns Island, South Carolina, near the estuaries where he conducted recent wildlife studies.

He is also survived by his two sons, John Vittands and Matt Guillette, and two daughters, Kaiya Hefle and Tammy Mandell. Not surprisingly, three of his children are pursuing careers in science.

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

Return to Table of Contents

Clinical Feature

Genes strongly associated with myositis risk identified

By Tara Ann Cartwright and Kelly Lenox

NIEHS scientists are among the authors of a paper that identified the primary genetic risk factors associated with myositis and its main forms in the Caucasian population in Europe and the U.S. The paper, published Aug. 20 in the journal Genes and Immunity, is the largest study conducted to date on this rare disease spectrum (see sidebar).

Fostering collaboration

NIEHS clinical researchers Frederick Miller, M.D., Ph.D., and Lisa Rider, M.D., and biologist Terrence O'Hanlon, Ph.D., are part of an international collaboration called the Myositis Genetics Consortium (MYOGEN), a group Miller established six years ago. The goal of the research group is to identify genetic factors associated with myositis.

Two years ago, MYOGEN published its first genome-wide association study. The authors identified a genetic region known as the major histocompatibility complex (MHC) as the primary region associated with adult and juvenile dermatomyositis. More importantly, the researchers demonstrated that dermatomyositis shares non-MHC genetic features with other autoimmune diseases.

In the new study, the consortium focused on the most common myositis forms — dermatomyositis and polymyositis. The researchers wanted to understand more about the specific risk factors in the MHC, particularly in a region on chromosome 6 called the human leukocyte antigen (HLA) region. This region has shown a strong genetic association with human autoimmune diseases. A particular group of these genes, called the 8.1 ancestral haplotype (AH8.1), is found in a significant number of Caucasians and is linked with myositis syndromes.

Potential cause of myositis

The researchers analyzed and compared 1,710 cases of either adult- or juvenile-onset myositis, with 4,724 control subjects. They found that multiple genes that make up AH8.1 define the genetic risk for all types of myositis.

"The highly conserved HLA 8.1 ancestral haplotype is unique in that it defies the normal process of genetic mutations and chromosomal switching, therefore suggesting that it has provided a survival benefit in Caucasian populations," said Miller.

Miller is deputy chief of the NIEHS Clinical Research Branch and head of the Environmental Autoimmunity Group. He is based at the National Institutes of Health Clinical Center in Bethesda. (Photo courtesy of Steve McCaw)

What is myositis?

Myositis syndromes, or idiopathic inflammatory myopathies (IIM), are a diverse group of complex muscle diseases. They are characterized by muscle weakness, general fatigue, difficulty swallowing or breathing, and skin rashes.

There are three different subsets of IIM:

- Dermatomyositis
- Polymyositis
- Inclusion body myositis

As a group, they are quite rare, with only 5 to 10 new cases per million people each year.

Link to other autoimmune diseases

Rider said that AH8.1 also has a role in many immune functions that could contribute to the development of other autoimmune diseases. For instance, people with AH8.1 tend to have higher levels of autoantibodies and more death of white blood cells. In addition, intestinal bacteria that make up the microbiome have been shown to be influenced by certain HLA variants that are also risk factors for several autoimmune diseases.

Miller said MYOGEN will use the findings as the basis for future work. "We should be able to use these data to develop the molecular profiles that could allow for novel diagnostics and therapeutics for myositis and other autoimmune diseases," he said.

Rider is deputy chief of Miller's group. (Photo courtesy of Steve McCaw)

Citations:

Miller FW, Chen W, O'Hanlon TP, Cooper RG, Vencovsky J, Rider LG, Danko K, Wedderburn LR, Lundberg IE, Pachman LM, Reed AM, Ytterberg SR, Padyukov L, Selva-O'Callaghan A, Radstake TR, Isenberg DA, Chinoy H, Ollier WE, Scheet P, Peng B, Lee A, Byun J, Lamb JA, Gregersen PK, Amos CI. 2015. Genome-wide association study identifies HLA 8.1 ancestral haplotype alleles as major genetic risk factors for myositis phenotypes. Genes Immun; doi:10.1038/gene.2015.28 [Online 20 August 2015].

Miller FW, Cooper RG, Vencovsky J, Rider LG, Danko K, Wedderburn LR, Lundberg IE, Pachman LM, Reed AM, Ytterberg SR, Padyukov L, Selva-O'Callaghan A, Radstake TR, Isenberg DA, Chinoy H, Ollier WE, O'Hanlon TP, Peng B, Lee A, Lamb JA, Chen W, Amos CI, Gregersen PK; Myositis Genetics Consortium. 2013. Genome-wide association study of dermatomyositis reveals genetic overlap with other autoimmune disorders. Arthritis Rheum 65(12):3239–3247.

(Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group.)

Myositis clinical research at NIEHS

In addition to genetic factors, Miller's group is studying environmental risk factors for myositis. They are especially interested in individuals with myositis who have served in the military, because of the high incidence rate of this disease. Healthy individuals are also needed. Men and women may enroll at the National Institutes of Health Clinical Center in Bethesda, Maryland, the NIEHS Clinical Research Unit in Research Triangle Park, North Carolina, or through their physician's office.

The study has the following eligibility requirements:

- Healthy individuals or those diagnosed with myositis during military service
- Active, reserve, and inactive duty personnel
- Able to give consent, complete questionnaires, and donate blood

Individuals that meet the criteria should contact Komal Patel at (301) 443-6053 or komal.patel@nih.gov. Please refer to the study using the ClinicalTrials.gov identifying number: NCT01734369.

Science Notebook

NIEHS sheds light on main cause of mutations in certain cancers

By Robin Arnette

New research published Aug. 10 in the journal Nature Genetics found that a mutation-causing enzyme, known as APOBEC3A (A3A), is most likely the main cause of mutations in certain cancers. Previous work implicated another APOBEC enzyme, known as APOBEC3B (A3B).

Dmitry Gordenin, Ph.D., head of the NIEHS Mechanisms of Genome Dynamics Group and co-author, led the team of scientists from several institutions that made the discovery. Gordenin said the results not only have far-reaching implications for diagnosis and personalized treatment of cancer, but also help scientists better understand the genome instability of the disease.

"Until our work, this specific APOBEC enzyme had not been identified as a cause of the DNA mutations that cause cancer," Gordenin said. "We hope that the thousands of cancer researchers around the world will use the information to further the field."

"If cancer samples have a strong APOBEC mutagenesis signature, it's coming from APOBEC3A," Gordenin said. "If APOBEC mutagenesis is low in a particular cancer sample, it's being caused by APOBEC3B." (Photo courtesy of Steve McCaw)

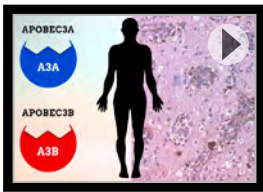
Searching for the source

Gordenin explained that APOBEC proteins perform an important function in the immune system by restricting the spread of viruses within the body. A few years ago, he and his group were surprised when they found these same proteins could generate clusters of mutations in some cancers. He published those results in a 2012 issue of the journal Molecular Cell. A year later, he determined that APOBEC enzymes were responsible for a large number of mutations in 80-90 percent of bladder and cervical cancers, and 20-30 percent of head and neck, breast, and lung cancers.

Other researchers also saw APOBEC-induced damage in cancer, but many of them reported A3B was responsible, rather than A3A. To determine which protein was the culprit, team members engineered two varieties of yeast. One strain produced A3A and the other produced A3B. Once Gordenin and colleagues identified the DNA sequences that each APOBEC protein preferentially mutated in yeast, they used the findings to mine data from The Cancer Genome Atlas, a cancer database funded and managed by the National Cancer Institute and the National Human Genome Research Institute.

Interview with the scientists

Nature Genetics also published an interview with Gordenin and Chan, APOBEC3A takes the lead.



Linked video:

This video, produced by Research Square in collaboration with Nature Publishing Group, displays the mechanisms at work in APOBEC-induced cancer. (3:35)

(Launches in new window)

Download Media Player: Flash

Their study concluded that A3A caused 10 times more DNA sequence changes than A3B in cancer samples with a high number of APOBEC-induced mutations. In samples with small numbers of APOBEC mutations, A3B was responsible.

Bioinformatics makes sense of the data

The discoveries were made, in part, using an analytical package developed by the NIEHS Integrative Bioinformatics Support Group led by David Fargo, Ph.D. Gordenin said the software was key in determining which APOBEC protein was causing the most damage. It was so important that collaborators at the Broad Institute of the Massachusetts Institute of Technology and Harvard incorporated the software into its Firehose analytical package. Fargo noted one of the best things about the software, designed by a contractor working in his group, is its versatility.

"Flexible analytical tools, primarily developed by Dr. Les Klimczak, can be configured to highlight and evaluate mutation patterns, presenting exciting translational science opportunities," Fargo said.

According to Gordenin, the success of the study was also dependent on the dedication, creativity, and talent of Kin, Chan, Ph.D., lead author and research fellow in the Gordenin group. Chan was a recipient of a prestigious National Institutes of Health Pathway to Independence Award.

Gordenin summed up the importance of the paper by saying it combined results from basic science studies with the statistical exploration of big data cancer genomics.

Citation: Chan K, Roberts SA, Klimczak LJ, Sterling JF, Saini N, Malc EP, Kim J, Kwiatkowski DJ, Fargo DC, Mieczkowski PA, Getz G, Gordenin DA. 2015. An APOBEC3A hypermutation signature is distinguishable from the signature of background mutagenesis by APOBEC3B in human cancers. Nat Genet; doi:10.1038/ng.3378 [Online 10 August 2015].

Return to Table of Contents

"Our work reaffirms that basic science knowledge can explain what's observed in human cancers, which in turn can be used to inform decision-making for personalized medicine," Chan noted. (Photo courtesy of Steve McCaw)

Fargo's group promotes and develops bioinformatics tools and resources that support in-house research endeavors at NIEHS. (Photo courtesy of Steve McCaw)

Kidney toxicity screening tool developed by grantee and NTP team

By Kelly Lenox

A team of researchers, including NIEHS grantees and National Toxicology Program (NTP) scientists, developed the first method to test for kidney toxicity using high throughput screening (HTS). Because drugs and environmental chemicals can cause injury to kidneys, the new test could help reduce a significant health burden for patients and decrease the financial risk for pharmaceutical and chemical companies.

The team, led by Vishal Vaidya, Ph.D., of Harvard Medical School, and including molecular toxicologist Scott Auerbach, Ph.D., from NTP, published their approach Aug. 10 in the Journal of the American Society of Nephrology. "This high-throughput assay allows, for the first time, rapid and robust screening of kidney toxic compounds, to support chemical risk assessment and facilitate elimination of drug candidates early in the process before they reach humans," Vaidya said.

Vaidya received the 2015 Achievement Award from the Society of Toxicology, for his significant early career contributions to the field of toxicology. In 2011, he received an NIEHS Outstanding New Environmental Scientist award. (Photo courtesy of Vishal Vaidya)

High throughput screens were lacking

HTS, which has been advanced by the Tox21 collaboration, is rapidly becoming the standard tool for predictive toxicology, which aims for early detection of adverse health effects from chemical compounds, including medicines.

"The lack of adequate models to accurately predict human toxicity contributes to an underestimation of the kidney toxic potential of new therapeutic candidates," the scientists wrote, "which also explains why nephrotoxic effects in patients are often only detected during late phase clinical trials, or in some cases, after regulatory approval."

Using the right cells

The authors reported three important advances. First, they confirmed that the cells they used were suitable for the job. A particular type of kidney cell, called human proximal tubular epithelial cells (HPTECs), is the predominant target of most substances that are toxic to the kidney.

The researchers characterized the structure and function of HPTECs. The cells were shown to possess characteristics of differentiated epithelial cells, which made them desirable for use in *in vitro* systems.

Auerbach is with the NTP Molecular Toxicology and Informatics Group, where he focuses on the analysis and interpretation of multivariate datasets and oversees the DrugMatrix database. (Photo courtesy of Steve McCaw)

Finding a biomarker

Next, the team identified a biomarker more sensitive than the currently used assays — cell viability and cell death — to indicate toxicity before changes occurred that might damage the cells.

"A few years ago at SOT [the Society of Toxicology annual meeting], Vishal stopped by the NIEHS booth, where we were demonstrating DrugMatrix," Auerbach said. DrugMatrix is a molecular toxicology database that contains toxicogenomic profiles for hundreds of compounds. "DrugMatrix enabled us to provide a list of prototype kidney toxicants for him to test," he said.

After exposing the HPTEC cells to nine kidney toxins and analyzing the expression of 1,000 genes, the researchers found that expression of one gene, HO-1, was significantly increased in the presence of the toxins.

The team validated the HO-1 biomarker in two ways. Edward Kelly, Ph.D., and Jonathan Himmelfarb, M.D., at the University of Washington, found that, following a kidney toxicant challenge, HO-1 was induced in a kidney-on-a-chip system that uses living tissue to accurately model organ function. Auerbach, collaborating with Dan Svoboda, Ph.D., of Sciome, LLC, examined two rat toxicogenomic databases and identified a significant association between HO-1 expression and kidney injury.

Additional analyses helped the team refine the assay. "Sensitivity and specificity can be improved even further by combining the readout for HO-1 concentration and the total cell number, measured in the same well," reported the authors.

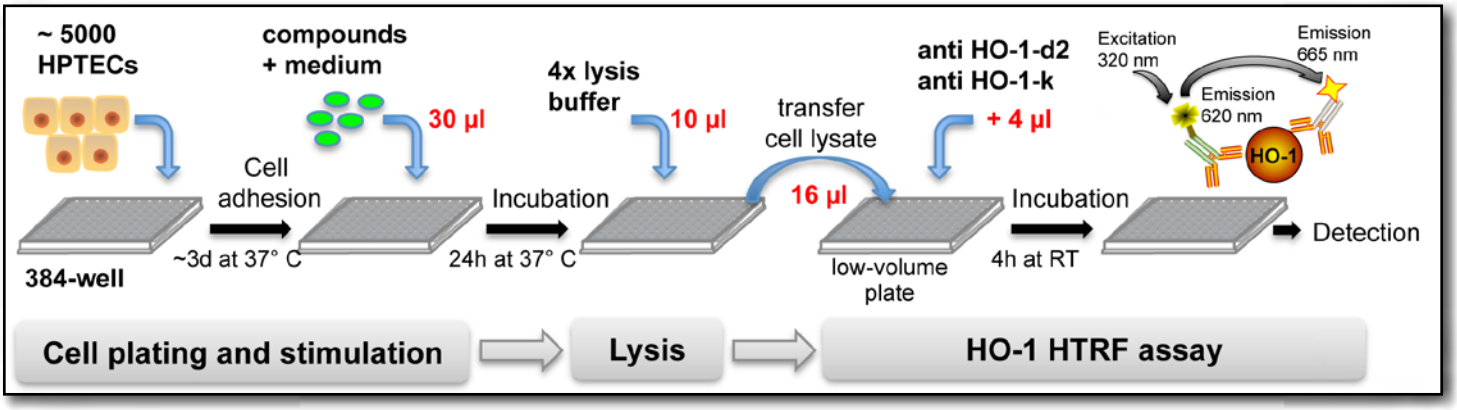
Developing and validating the test

Finally, the team developed a new assay to measure HO-1 in a rapid and cost-efficient manner. They used a test called a homogeneous time resolved fluorescence (HTRF) assay (see image below). "The HO-1 levels obtained in response to most of the [39 tested] compounds … correlated well with immunofluorescence," the authors wrote.

The authors noted some limitations to the method. For example, a chemical might undergo modification in the liver and produce a metabolite toxic to the kidney. This could be missed by the new tool.

However, the authors remarked that it is an important step forward, providing a test that is robust — it detects kidney toxicants from multiple classes of chemicals; it is sensitive, because it picks up toxicants at a high rate; and it is specific, which means it correctly identifies compounds that are not kidney toxicants.

Citation: Adler M, Ramm S, Hafner M, Muhlich JL, Gottwald EM, Weber E, Jaklic A, Ajay AK, Svoboda D, Auerbach S, Kelly EJ, Himmelfarb J, Vaidya VS. 2015. A Quantitative Approach to Screen for Nephrotoxic Compounds In Vitro. J Am Soc Nephrol; doi:10.1681/ASN.2015010060 [Online 10 Aug 2015].



Scheme of the HTRF assay performed in a 384-well plate. When the acceptor labeled antibody and the donor labeled antibody bind to HO-1, the two dyes are brought into close proximity with each other. Excitation of the donor with a light source triggers a fluorescence resonance energy transfer toward the acceptor. The emission fluorescence can be detected after incubation for four hours. This signal is proportional to the amount of human HO-1 present in the cell lysate. (Image courtesy of Vishal Vaidya)

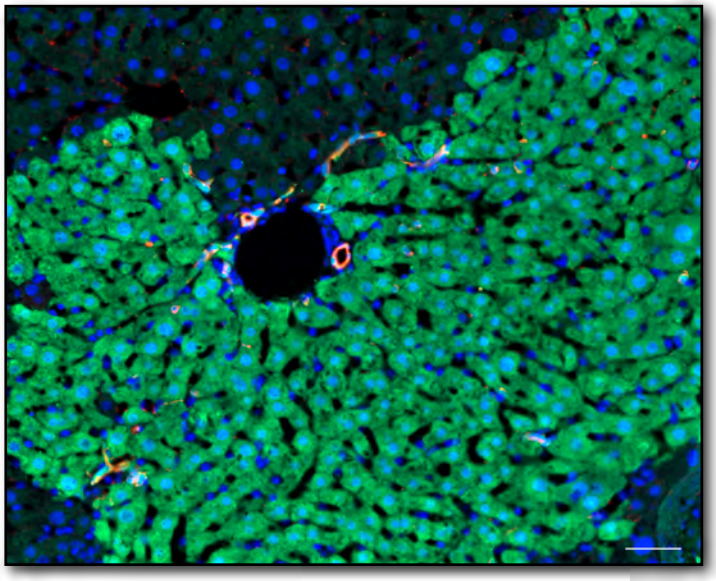
Return to Table of Contents

Newly discovered cells repair liver without cancer risk

By Virginia Guidry

The liver is unique among organs for its ability to regenerate after being damaged. The repair mechanism remained controversial until recently, when researchers funded by NIEHS discovered a type of cell responsible for the process.

The newly discovered cells, known as hybrid hepatocytes, are present in a healthy liver. When liver cells are depleted by chronic damage, such as long-term exposure to toxic chemicals, hybrid hepatocytes multiply rapidly. Importantly, they divide and grow without causing cancer, which is a risk with rapid cell division. The findings were published Aug. 13 in the journal Cell.



Hybrid hepatocytes, shown in green, have been shown to regenerate liver tissue following chronic damage. (Photo courtesy of UCSD)

"This is the first time anyone has shown how liver cells safely regenerate," said William Suk, Ph.D., director of the NIEHS Superfund Research Program (SRP).

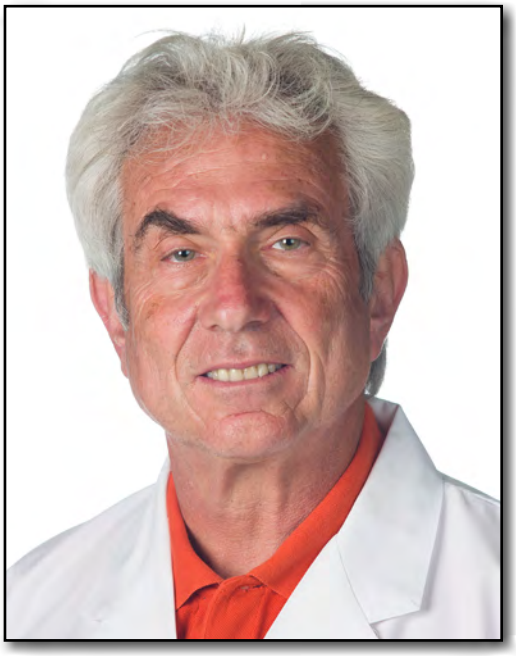
The wonder of hybrid hepatocytes

The research was conducted at the University of California, San Diego (UCSD) Superfund Research Center, under the leadership of Michael Karin, Ph.D., distinguished professor of pharmacology and pathology at the UCSD School of Medicine and a member of the prestigious National Academy of Sciences.

One of the goals of the Superfund Research Program is to better understand how toxic chemicals affect human health. The liver plays an essential role in this process by helping to remove toxicants from the body. "The entire [SRP] program at UCSD is focused on the effects of toxicants on liver metabolism and functionality," said Suk.

The team studied liver function in mice following chronic exposure to carbon tetrachloride, a chemical commonly associated with Superfund sites. The scientists were able to track the hybrid hepatocytes and observe how they contributed to the regeneration of tissue.

They then exposed healthy mice to three known cancer-inducing pathways and watched the hybrid hepatocytes closely. Liver cancer never originated from any of these cells. The researchers confirmed that there are similar cells in humans.



"Hybrid hepatocytes represent not only the most effective way to repair a diseased liver, but also the safest way to prevent fatal liver failure by cell transplantation," noted Karin. (Photo courtesy of UCSD)

Potential therapy from cell transplants

There may be therapeutic benefits from this discovery. Chronic liver disease is the main reason for liver transplants.

Hybrid hepatocytes may be an excellent candidate for future cell transplantation, due to their impressive capacity to regenerate tissue without initiating cancer. Moreover, hybrid hepatocytes were unmatched by any other cell in reversing liver damage when transplanted into diseased mice. Their potential depends on how easily the human cells can be isolated and further expanded in culture.

Citation: Font-Burgada J, Shalapour S, Ramaswamy S, Hsueh B, Rossell D, Umemura A, Taniguchi K, Nakagawa H, Valasek MA, Ye L, Kopp JL, Sander M, Carter H, Deisseroth K, Verma IM, Karin M. 2015. Hybrid periportal pepatocytes regenerate the injured liver without giving rise to cancer. Cell 162(4):766-779.

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

Return to Table of Contents

Fetal low-level arsenic exposure leads to early puberty and obesity in mice

By Robin Arnette

Female mice exposed *in utero*, or in the womb, to low levels of arsenic through drinking water displayed signs of early puberty and became obese as adults, according to NIEHS scientists.

The finding is significant because the exposure level of 10 parts per billion used in the study is the current U.S. Environmental Protection Agency standard, or maximum allowable amount, for arsenic in drinking water. The study, which appeared online Aug. 21 in the journal Environmental Health Perspectives, serves as a good starting point for examining whether low-dose arsenic exposure could have similar health outcomes in humans.

Yao leads the NIEHS Reproductive Developmental Biology Group. (Photo courtesy of Steve McCaw)

Profound effects from prenatal exposure

The researchers divided pregnant mice into three groups. The control group received no arsenic in its drinking water, while the two experimental groups received either the EPA standard of 10 parts per billion of arsenic or 42.5 parts per million of arsenic, a level known to have detrimental effects in mice. One part per billion is a thousand times smaller than one part per million. The mice were exposed during gestation, between 10 days after fertilization and birth, which corresponds to the middle of the first trimester and birth in humans.

"We unexpectedly found that exposure to arsenic before birth had a profound effect on onset of puberty and incidence of obesity later in life," said NIEHS reproductive biologist and co-author Humphrey Yao, Ph.D. "Although these mice were exposed to arsenic only during fetal life, the impacts lingered through adulthood."

Health repercussions later in life

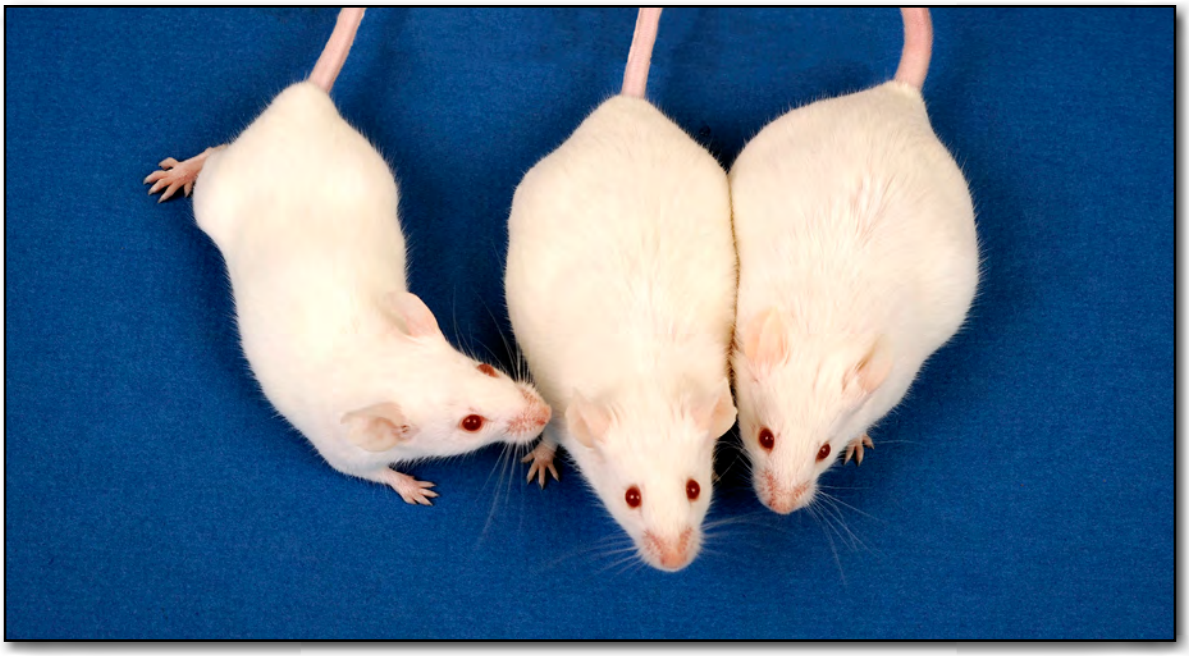
The impacts Yao is referring to are obesity and early onset puberty, particularly in female mice. The researchers did not examine in this study whether males also experienced early onset puberty, but they did confirm that male mice exposed to arsenic *in utero* also displayed weight gain as they aged. Both the low and high doses of arsenic resulted in weight gain.

According to lead author NIEHS biologist Karina Rodriguez, Ph.D., the research team performed the experiment in three separate batches of mice, each containing a control and two experimental groups, and achieved similar results. She said although the biological process responsible for these effects remains unknown, the study highlights the need to continue researching long-term impacts of what mothers eat, drink, and breathe during pregnancy on the health of the offspring.

"It's very important to study both high doses and low doses," said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program. "Although the health effects from low doses were not as great as with the extremely high doses, the low-dose effects may have been missed if only high doses were studied."

As one of the main researchers studying the mice, Rodriguez played a major role in the discovery. (Photo courtesy of Steve McCaw)

Citation: Rodriguez KF, Ungewitter EK, Crespo-Mejias Y, Liu C, Nicol B, Kissling GE, Yao HH-C. 2015. Effects of in utero exposure to arsenic during the second half of gestation on reproductive end points and metabolic parameters in female CD-1 mice. Environ Health Perspect; doi:10.1289/ehp.1509703 [Online 21 August 2015].



Mice exposed to low-level arsenic in utero become obese adults. *The control mouse, left, was not exposed to arsenic during embryonic development and is a normal weight. In comparison, mice exposed to arsenic at 10 parts per billion, center, and 42 parts per million, right, are visibly heavier. The study also determined that these exposed mice entered puberty earlier than controls. (Photo courtesy of Steve McCaw)*

Return to Table of Contents

NIEHS researchers identify key protein at work in breast cancer

By Ernie Hood

The RNA-binding protein LIN28A is an important regulator of processes that play a role in many types of breast cancer, including alternative splicing, a process in which a single gene may code for multiple proteins, and other gene expression programs. These are the key findings of a study published by NIEHS researchers in the September issue of the journal Molecular and Cellular Biology.

LIN28 has been previously known to have critical functions in the timing of events during embryonic development and in cancer. Scientists in the NIEHS Chromatin and Gene Expression Group discovered that LIN28 contributes to tumor progression through multiple mechanisms, including inhibition of tumor suppressors. They studied breast cancer cells using analytical methods called RNA-Seq and RIP-Seq, or RNA immunoprecipitation sequencing, to learn more about the function of LIN28 in breast cancer.

The LIN28 protein occurs in two forms in mammals. LIN28A, through its regulation of splicing and gene expression, appears to produce a diverse family of proteins. The type of protein produced can lead to different types of breast cancer. "For example, alternative splicing of the ENAH gene yields distinct transcripts that encode different proteins," explained Trevor Archer, Ph.D., the group's lead scientist.

"These proteins are expressed differently in the various subtypes of breast cancer," added staff scientist and co-author Harriet Kinyamu, Ph.D., who made the initial discovery of LIN28 expression in the lab.

Archer also serves as head of the NIEHS Epigenetics and Stem Cell Biology Laboratory. He said that while the signaling pathways or environmental cues that normally regulate LIN28A are not known, it will be interesting to search for compounds, such as endocrine disruptors, that may affect LIN28 expression in breast cancer cells. (Photo courtesy of Steve McCaw)

By analyzing data from The Cancer Genome Atlas, the team found what they called "striking and significant correlations between the expression of LIN28 and specific breast cancer subtypes." The protein was found to be particularly overexpressed in the HER2 breast cancer subtype, although the reason for that overexpression remains unknown.

Potential therapeutic target

The findings represent an important advance in basic science, by adding to the understanding of the mechanisms that lead to breast cancer, which is now recognized to be a disease composed of several different subtypes with varying causes.

LIN28 may be a factor in many of the subtypes. As the authors noted, "The suite of mRNAs whose expression is affected [by LIN28A] includes genes that function in cell metabolism, the immune response, cell proliferation, and cell-to-cell communication, processes that are classic hallmarks of breast cancer biology."

With LIN28A now identified as a master regulator, Kinyamu said that it is a potential therapeutic target. "Because it is a protein, drugs or small molecules that either alter LIN28 expression or inhibit its activity are the most likely possibilities," she said, noting that although LIN28A therapy might be most effective in HER2-positive breast cancers, it could also affect other types of the disease.

Editorial spotlight

The paper was singled out for recognition by the journal's editors for a Spotlight feature, for articles of significant interest.

"We were excited they recognized our groundbreaking work on LIN28 gene regulatory mechanisms in breast cancer cells," said Archer. "We hope the spotlight encourages more research toward understanding LIN28 function in breast cancer."

Citation: Yang J, Bennett BD, Luo S, Inoue K, Grimm SA, Schroth GP, Bushel PR, Kinyamu HK, Archer TK. 2015. LIN28A modulates splicing and gene expression programs in breast cancer cells. Mol Cell Biol 35(18):3225–3243.

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

Kinyamu led the project in the Archer lab. (Photo courtesy of Steve McCaw)

Jun Yang, a biologist in Archer's group, served as co-lead author of the paper. (Photo courtesy of Steve McCaw)

Brian Bennett, Ph.D., a contractor with the NIEHS Biostatistics and Computational Biology Branch, provided bioinformatics support and served as co-lead author of the paper. (Photo courtesy of Steve McCaw)

Return to Table of Contents

DREAM challenge results published in Nature Biotechnology

By Robin Mackar

An innovative international crowdsourcing challenge launched by NIEHS and partners in 2013 has come full circle with an Aug. 10 publication in Nature Biotechnology.

"Prediction of human population responses to toxic compounds by a collaborative competition" takes readers through the Dialogue for Reverse Engineering Assessments and Methods (DREAM) Challenge process and describes the development of computational models to predict potential adverse health effects in populations. "The challenge offered the unique opportunity to compare performance across a wide variety of state-of-the-art methods for the prediction of cytotoxic response to environmental compounds," the authors wrote. Allen Dearry, Ph.D., and Raymond Tice, Ph.D., from NIEHS were among the approximately 140 authors involved in developing the publication.

Meeting the challenge

Using data generated as part of the Toxicology in the 21st Century program (Tox21) effort, this community-based toxicogenomics challenge was organized by scientists from NIEHS, the National Center for Advancing Translational Sciences, the Carolina Center for Computational Toxicology at the University of North Carolina at Chapel Hill, DREAM, and Sage Bionetworks.

The organizers provided participants with cellular toxicity data generated by testing 156 different chemical compounds on 884 distinct lines of lymphoblastoid cells, a cell type scientists have found especially useful in molecular and functional studies. The cell lines represented individuals from nine subpopulations in Europe, Africa, Asia, and the Americas. Data on single nucleotide polymorphisms (SNP) were available from the 1000 Genomes Project for all the cell lines. Gene expression data were also available for a smaller number of lines.

The challenge included two subchallenges that allowed participants to take on either or both. The first challenge asked the investigators to use the biological data (SNPs, basal gene expression) provided on one group of cell lines to develop a model that accurately predicted responses of other cell lines to compound exposure. The other challenge involved using intrinsic chemical properties of a subset of chemicals to develop a model that accurately predicted how a particular population would respond to other chemicals.

"The winning computational models provide significant advances in our ability to predict toxicity risk for environmental chemicals and set the stage for future data-driven challenges and competitions in environmental health science," Dearry said. (Photo courtesy of Steve McCaw)

International effort

Representing more than 30 countries, 213 people participated in the challenge. Thirty-four teams responded with 99 submissions to the first subchallenge, and 24 teams responded with 85 submissions to the second. The Quantitative Biomedical Research Center at the University of Texas Southwestern Medical Center in Dallas, Texas won both challenges by providing the most accurate predictions.

"The ability of the top teams to predict population-level toxicity for unknown compounds — based on similarities in chemical structure to known compounds — far surpassed our anticipations," said Lara Mangravite, Ph.D., director of systems biology at Sage Bionetworks. "This was a true case where crowdsourcing the problem provided answers that would otherwise never have been found."

Before his retirement earlier this year, Tice headed the NTP Biomolecular Screening Branch and played a key role in establishing the Tox21 program. He continues to advise NTP on Tox21 and high-throughput screening efforts. (Photo courtesy of Steve McCaw)

Kudos to NIEHS partners

Much of the credit for bringing this challenge to fruition goes to Stephen Friend, M.D., Ph.D., president of Sage Bionetworks and Gustavo Stolovitzky, Ph.D., from the IBM Computational Biology Center.

"Steven, Gustavo, and their teams have a wonderful vision for tackling biomedical problems using innovative approaches," said Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program (NTP). "NIEHS and NTP are proud to have participated in this first-ever crowdsourced toxicological effort, which has not only brought us new computational models, but new collaborations as well."

Citation: Eduati F, Mangravite LM, Wang T, Tang H, Bare JC, Huang R, Norman T, Kellen M, Menden MP, Yang J, Zhan X, Zhong R, Xiao G, Xia M, Abdo N, Kosyk O; NIEHS-NCATS-UNC DREAM Toxicogenetics Collaboration. 2015. Prediction of human population responses to toxic compounds by a collaborative competition. Nat Biotechnol;doi:10.1038/nbt.3299 [Online 10 Aug. 2015].

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

Return to Table of Contents

Fracking in Pennsylvania linked with increased hospitalizations

By Ernie Hood

NIEHS-funded researchers have reported associations between increased hydraulic fracturing, or fracking, activity and increased hospitalization rates in three Pennsylvania counties. The study was published July 15 in the journal PLOS ONE.

The authors noted that although they did not show that fracking caused the increased hospitalizations, the strength of the associations during the five-year period studied suggests that health care costs should be considered in analyses of economic benefits from hydraulic fracturing.

The study was conducted by scientists from two NIEHS environmental health sciences research centers — the Center of Excellence in Environmental Toxicology (CEET) at the University of Pennsylvania, and the Center for Environmental Health in Northern Manhattan at Columbia University.

As deputy director of CEET, Panettieri directs the CEET Integrative Health Sciences Facility Core. He is also a professor of pulmonary medicine, and director of the Comprehensive Asthma Program, as well as the Airways Biology Initiative at the University of Pennsylvania. (Photo courtesy of the University of Pennsylvania)

Most comprehensive study to date

The researchers examined more than 95,000 hospital inpatient records from 2007 to 2011, in what they called the most comprehensive study of its kind on the health effects of unconventional gas and oil drilling, which includes fracking. They looked at 25 specific medical categories, as well as overall inpatient prevalence rates. Prevalence refers to the total number of cases in a given population at a given time.

The team also tracked the number of wells created during the fracking process and their density, or number of wells per square kilometer, in three counties that lie on the Marcellus Shale formation in northern Pennsylvania. Bradford and Susquehanna counties experienced dramatic increases in fracking during the five-year period. Wayne County, which was used as a control, had a similar population but no active wells. The number and density of wells was then compared with the prevalence rates for patients from the study area.

Cardiology and neurology admissions linked

The scientists found a statistically significant association between cardiology inpatient prevalence rates and both the number of wells and well density. Neurology inpatient prevalence rates showed a significant association with well density.

The researchers said their findings are remarkable, even though the cause for the increase in inpatient prevalence rates remains unknown, and their approach did not address demographic changes, such as population growth. "We are struck by the finding that these differences were observable within a short period of time from 2007-2011," the authors wrote. They pointed to a combination of possible factors, including exposure to diesel exhaust and fine particulate matter from truck traffic and well operations.

Insights to guide future studies

Claudia Thompson, Ph.D., NIEHS Population Health Branch lead, said the collaborators are providing new information in a sector where it is sorely needed. "This is environmental epidemiology at its best," she said, "and we are quite proud that our research centers are working diligently and creatively to characterize links between exposures and adverse human health effects."

The team was led by CEET Deputy Director Reynold Panettieri Jr., M.D. "Our findings provide important clues for designing epidemiological studies to associate specific toxicant exposures with health endpoints," he said.

Citation: Jemielita T, Gerton GL, Neidell M, Chillrud S, Yan, B, Stute M, Howarth M, Saberi P, Fausti N, Penning TM, Roy J, Propert KJ, Panettieri RA Jr. 2015. Unconventional gas and oil drilling is associated with increased hospital utilization rates. PLoS One 10(7):e0131093. (Summary)

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

Return to Table of Contents

Interindividual variability highlighted in upcoming workshop

NIEHS and the National Research Council (NRC) will hold a free workshop Sept. 30 – Oct. 1 to explore the factors that affect how an individual responds to environmental stress. Interindividual Variability: New Ways to Study and Implications for Decision Making will focus on recent scientific advances that could shed light on sources of variation in responses between different people.

(Image courtesy of NAS)

Within any population, factors such as inherited characteristics, stress, body weight, and genetics can influence the type and degree of response that people may have to environmental stressors. Accounting for this interindividual variability is a challenge for decision-makers tasked with setting chemical safety regulations.

The workshop will include presentations, panel discussions, and breakout sessions on topics such as:

- *In vitro* toxicology methods using highly diverse cell lines.
- *In vivo* methods using highly diverse animal populations.
- Epidemiologic analytical approaches that explore mediators within the causal pathway.

The event is part of the NRC Emerging Science for Environmental Health Decisions series and will be held at the National Academies of Sciences, Engineering, and Medicine Keck Center. The workshop will also be webcast.

Join researchers, professionals, and policy experts to explore new tools and how they may be used to advance the science behind risk-based decisions. Registration is required, whether attending in person or via webcast.

Return to Table of Contents

This month in EHP

http://twitter.com/ehponline

The September issue of Environmental Health Perspectives (EHP) examines seabed mining and its potential opportunities and risks.

Going Deep: Cautious Steps Toward Seabed Mining

With land-based mineral sources in decline, the ocean floor offers the mining industry a new and largely untapped frontier. Proponents of seabed mining say it will inflict less environmental damage than mining on land. But without appropriate safeguards, seabed mining could erode the capacity of oceans to provide essential ecological services and accelerate concerns about their overall health.

Research summaries featured this month include:

Air Pollution and Birth Weight: New Clues About a Potential Critical Window of Exposure — Researchers studying the effects of air pollution cleanup efforts for the 2008 Summer Olympics in Beijing report that babies whose eighth month of gestation occurred during the Olympics weighed more, on average, than babies born during the same period in 2007 and 2009 .

After the Fall: Gastrointestinal Illness Following Downpours — Scientists show that emergency room visits for gastrointestinal illnesses increased after heavy rainfalls in areas of Massachusetts served by combined sanitary and stormwater sewer systems, suggesting that combined sewer overflows may adversely affect human health.

Return to Table of Contents

Extramural papers of the month

By Nancy Lamontagne

- Epigenomic mapping of human tissues
- DEHP replacements may also cause health risks
- Living close to hydraulic fracturing associated with more hospitalizations
- Researchers identify pathway that can halt fibrosis progression

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

Epigenomic mapping of human tissues

As part of the National Institutes of Health Roadmap Epigenomics Program, an NIEHS grantee and colleagues produced a new atlas of human tissue epigenomes and found that DNA methylation varies greatly among the tissues.

Epigenetic changes influence gene expression without changing the genetic code. To understand the mechanisms involved in disease development, scientists must link genetic information, which is identical in most cells across the body, with epigenetic changes that can vary by tissue. As a starting point, the researchers created a baseline assessment of the epigenome, by conducting DNA sequencing of 18 tissue types from four people, and examining DNA methylation.

The researchers reported widespread differences in levels of methylation between tissues. Organs differed extensively in the degree of genome-wide methylation. For example, the pancreas had an unusually low level of methylation, while the thymus had high levels of methylation. As expected, methylation levels tended to be lower around areas of DNA that coded for genes expressed by the type of tissue analyzed. In other words, a cell from muscle tissue had less methylation near muscle-related genes. One surprising finding was that many tissues exhibited non-CG methylation, a type of methylation previously thought to be widespread only in the brain and stem cells.

Citation: Schultz MD, He Y, Whitaker JW, Hariharan M, Mukamel EA, Leung D, Rajagopal N, Nery JR, Urich MA, Chen H, Lin S, Lin Y, Jung I, Schmitt AD, Selvaraj S, Ren B, Sejnowski TJ, Wang W, Ecker JR. Human body epigenome maps reveal noncanonical DNA methylation variation. Nature 523(7559):212-216.

Return to Table of Contents

DEHP replacements may also cause health risks

Potential health risks related to di-2-ethylhexylphthalate (DEHP) is leading manufacturers to switch to chemically similar di-isononyl phthalate (DINP) and di-isodecyl phthalate (DIDP) in products such as furnishings, cookware, and plastic food packaging. However, these replacements may also pose health risks in children, according to new research from an NIEHS grantee and colleagues.

The researchers published two studies that examined the effects of DINP and DIDP on 2009-2012 participants in the National Health and Nutrition Examination Survey (NHANES), a program of studies designed to assess the health and nutritional status of adults and children in the United States.

One study examined participants ages 6 to 19 and found a significant association between high blood pressure and the presence of DINP and DIDP urinary metabolites. The other study examined participants 12 to 19 years old, and revealed a link between DINP and DIDP concentrations and increased insulin resistance. Specifically, 34.4 percent of the adolescents with the highest DINP metabolite urinary levels showed insulin resistance, compared to 23.4 percent of the adolescents with the lowest levels of DINP. Similarly, for DEHP, 37.7 percent of study participants with the highest levels had insulin resistance, compared to 20.5 percent with the lowest DEHP levels.

Citations:

Trasande L, Attina TM. 2015. Association of exposure to di-2-ethylhexylphthalate replacements with increased blood pressure in children and adolescents. Hypertension 66(2):301-308.

Attina TM, Trasande L. 2015. Association of exposure to di-2-ethylhexylphthalate replacements with increased insulin resistance in adolescents from NHANES 2009-2012. J Clin Endocrinol Metab 100(7):2640-2650.

Return to Table of Contents

Living close to hydraulic fracturing associated with more hospitalizations

Researchers from two NIEHS Environmental Health Science Core Centers found that hospitalizations for heart conditions, neurological illness, and other health problems were higher among people living near unconventional gas and oil drilling sites, also known as hydraulic fracturing or fracking sites, in Pennsylvania. The work points to a need for more research to determine the reason for the increased hospitalization rates.

From 2007 to 2011, the researchers examined the link between drilling well density, or the number of wells within a square kilometer, and health care use by zip code in three northeastern Pennsylvania counties. Bradford and Susquehanna Counties experienced a significant increase in drilling activity during this time period, while Wayne County acted as the control because of a ban on drilling. Examining 198,000 hospitalizations, including multiple hospitalizations for the same person, the researchers found an association between 25 specific medical categories and patients' proximity to active wells.

The analysis showed that the number of people hospitalized for cardiology and neurology health problems was significantly higher in areas closer to active wells. Specifically, the rates of cardiology hospitalizations were significantly associated with number of wells per zip code ($p<0.00096$) and wells per square kilometer ($p<0.00096$) while neurology inpatient hospitalizations were significantly associated with wells per square kilometer ($p<0.00096$). Hospitalizations for skin conditions, cancer, and urology problems were also associated with the proximity of dwellings to active wells. The authors say that more studies are necessary to compare toxicant exposure to number of wells.

Citation: Jemielita T, Gerton GL, Neidell M, Chillrud S, Yan B, Stute M, Howarth M, Saberi P, Fausti N, Penning TM, Roy J, Propert KJ, Panettieri RA Jr. 2015. Unconventional gas and oil drilling Is associated with increased hospital utilization rates. PLoS One. 10(7):e0131093. (Story)

Return to Table of Contents

Researchers identify pathway that can halt fibrosis progression

Research, funded in part by NIEHS, has identified a molecular pathway that can be targeted to stop pulmonary fibrosis, a progressive and fatal disease that causes damage and scarring in lung tissue. Understanding the molecular mechanisms involved in pulmonary fibrosis may help lead to treatments that prevent or halt the disease.

Although scientists don't fully understand the mechanisms involved in pulmonary fibrosis, they do know that reactive oxygen species play a critical role, and that pulmonary macrophages help regulate how the body responds to lung injury. Previous studies have found that the mitochondrial production of hydrogen peroxide by pulmonary macrophages is directly linked to pulmonary fibrosis, and that the small GTP-binding protein, Rac1,

directly mediates the hydrogen peroxide production. Since the protein modification process known as geranylgeranylation is required to activate Rac1, the researchers hypothesized that interrupting this protein modification might halt the production of oxidative stress and fibrosis.

Results from cell and mouse experiments showed that targeting the isoprenoid pathway by using digeranyl bisphosphonate to impair geranylgeranylation lessened mitochondrial import of Rac1, mitochondrial oxidative stress, and the progression of the fibrotic response to lung injury.

Citation: Osborn-Heaford HL, Murthy S, Gu L, Larson-Casey JL, Ryan AJ, Shi L, Glogauer M, Neighbors JD, Hohl R, Brent Carter A. 2015. Targeting the isoprenoid pathway to abrogate progression of pulmonary fibrosis. Free Radic Biol Med 86:47-56.

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

Return to Table of Contents

Intramural papers of the month

By Robert Brown, Greg Buchold, Tara Ann Cartwright, Simone Otto, and Qing Xu

NTP team identifies aromatase inhibitors in Tox21 library

Using a high-throughput screening system called the AroER tri-screen assay, a research team led by scientists from the National Toxicology Program (NTP) identified environmental chemicals in the Tox21 10K library that inhibit aromatase activity. Aromatase is found in a cellular structure known as the endoplasmic reticulum. It triggers the conversion of testosterone to estradiol, and androstenedione to estrone, in the final step of the steroid biosynthesis pathway. More importantly, aromatase plays a key role in maintaining balance between androgen and estrogen, which helps maintain human endocrine health.

The AroER tri-screen assay identified 113 possible compounds that selectively interact with aromatase. Mechanistic studies demonstrated that 10 of these, including both drugs and fungicides, had novel structures. A reversibility assay confirmed that four of the compounds — trovafloxacin, imazalil, erlotinib, and amlodipine besylate — irreversibly inhibit aromatase in a concentration-dependent manner. Enzyme kinetic analysis further revealed that erlotinib, imazalil sulfate, and trovafloxacin mesylate are noncompetitive inhibitors, whereas amlodipine besylate is a competitive inhibitor.

Taken together, this study suggests that exposure to a number of natural or synthetic environmental chemicals, through diet, medication, or fungicides used in agriculture, may significantly affect human endocrine health. **(TAC)**

Citation: Chen S, Hsieh JH, Huang R, Sakamuru S, Hsin LY, Xia M, Shockley KR, Auerbach S, Kanaya N, Lu H, Svoboda D, Witt KL, Merrick BA, Teng CT, Tice RR. 2015. Cell-based high-throughput screening for aromatase inhibitors in the Tox21 10K library. Toxicol Sci; doi:10.1093/toxsci/kfv141 [Online 3 July 2015].

Return to Table of Contents

RGS2 protein required for proper fertilization in mice

NIEHS scientists and collaborators found that a compound called regulator of G-protein signaling 2 (RGS2) blocks premature calcium signaling in a fertilizable egg, or oocyte. The release of calcium signals the egg to start developing, which can prevent a proper sperm-egg union if it is too early. Other research has suggested that RGS2 may be used as a therapeutic agent for cardiovascular disorders, but this study is the first to determine its role in reproduction.

Team members discovered that expression of RGS2 is particularly high in mature eggs. To determine its function, they depleted eggs of RGS2. They then used *in vitro* fertilization, calcium imaging, and immunoblots to investigate changes in the depleted oocytes. The fertility of the RGS2 knockout mice was also analyzed during the study.

When RGS2 expression was depleted, exposure to acidic pH or acetylcholine caused premature activation of the egg. In addition, the zona pellucida, a protein matrix that surrounds the egg, was cleaved prematurely in both RGS2-depleted eggs and eggs from RGS2 knockout mice. These effects are caused by calcium signaling and do not occur if calcium signaling is blocked by RGS2. The zona pellucida changes may explain why RGS2 knockout mice are subfertile. **(SO)**

Citation: Bernhardt ML, Lowther KM, Padilla-Banks E, McDonough CE, Lee KN, Evsikov AV, Uliasz TF, Chidiac P, Williams CJ, Mehlmann LM. 2015. Regulator of G-protein signaling 2 (RGS2) suppresses premature calcium release in mouse eggs. Development 142(15):2633-2640. (Story)

Return to Table of Contents

Cholesterol trafficking protein could provide therapeutic target for inflammatory diseases

NIEHS researchers determined that the cholesterol transporter ATP binding cassette A1 (ABCA1) controls the repertoire of proteins, known as the proteome, within macrophage rafts, which are membrane structures that serve as platforms for signal transduction. They also found that stomatin-like protein (SLP)-2 is an ABCA1-regulated raft protein that controls raft composition and raft signaling. How cells control which proteins localize to rafts has remained poorly understood. This study may help scientists understand the cell signaling mechanisms that underlie inflammatory diseases, including atherosclerosis and cardiovascular disease.

In macrophages, lipid rafts concentrate or organize cell surface signal transduction, and their specific collection of proteins dictates their level of responsiveness to inflammatory stimuli. In this study, scientists found that macrophages deleted for the gene that encodes ABCA1 had wide-ranging changes in the raft proteome. They also found that SLP-2, one of the proteins that increased in abundance in ABCA1-null macrophage rafts,

was itself an important determinant of lipid raft composition, organization, and inflammatory response. In light of these findings, the investigators suggest that SLP-2 is an important regulator of the innate immune response of macrophages and may represent a promising new therapeutic target for a number of illnesses. **(RB)**

Citation: Chowdhury SM, Zhu X, Aloor JJ, Azzam KM, Gabor KA, Ge W, Addo KA, Tomer KB, Parks JS, Fessler MB. 2015. Proteomic analysis of ABCA1-null macrophages reveals a role for stomatin-like protein-2 in raft composition and Toll-like receptor signaling. Mol Cell Proteomics 14(7):1859-1870.

Return to Table of Contents

BPA and phthalate exposure was not associated with subfertility

Certain phthalates and bisphenol A (BPA) have shown reproductive effects in past animal studies. However, in this study, NIEHS scientists and their collaborators found little evidence that BPA and phthalate metabolites reduce fertility. They measured these rapidly-metabolized and ubiquitous environmental contaminants in archived urine samples from 221 women enrolled in the Early Pregnancy Study (EPS).

The scientists then analyzed the association between the environmental exposures and follicular- and luteal-phase lengths, time to pregnancy, and early pregnancy loss. Higher concentrations of both urinary monocarboxyoctyl phthalate and BPA were associated with a shortening of the luteal phase by approximately half a day. However, more problematic reproductive problems, including lowered progesterone, longer time to pregnancy, and increased early fetal losses, were not observed. This research with naturally-conceiving women suggests that estimates of risk based only on subfertile women undergoing *in vitro* fertilization may overestimate the risks to the general population. **(GB)**

Citation: Jukic AM, Calafat AM, McConnaughey DR, Longnecker MP, Hoppin JA, Weinberg CR, Wilcox AJ, Baird DD. 2015. Urinary concentrations of phthalate metabolites and bisphenol A and associations with follicular-phase length, luteal-phase length, fecundability, and early pregnancy loss. Environ Health Perspect; doi:10.1289/ehp.1408164 [Online 10 July 2015].

Return to Table of Contents

MicroRNAs and chromatin modifiers steer the fate of human ES cells

NIEHS researchers have demonstrated that gene-silencing microRNAs regulate chromatin-remodeling proteins to direct the differentiation of human embryonic stem (ES) cells. The findings provide a novel epigenetic mechanism for ES cell programming that may also apply in human embryogenesis.

During human embryonic development, ES cells differentiate into three primary germ layers — endoderm, mesoderm, and ectoderm. These three layers eventually produce all of the specialized organs and tissues in the body. Both microRNAs and chromatin modifiers are essential parts of a network involved in controlling ES cell proliferation and differentiation, but the connection between the two players is unclear.

In this study, the researchers found that microRNA-302 (MiR-302), which is highly expressed in ES cells, repressed the expression of chromatin remodeling proteins BAF170 and BAF53a by binding with corresponding target sites. BAF170 suppression was required for changes in downstream genes and signaling pathways during

differentiation. When ES cells were differentiated into endoderm, BAF170 decreased along with an induction of MiR-302. Conversely, BAF170 overexpression drove the cells toward ectodermal differentiation and blocked the induction of mesodermal and endodermal markers during directed endodermal differentiation. These results suggest that MiR-302-mediated repression of BAF170 is required for effective endodermal differentiation in human ES cells. **(QX)**

Citation: Wade SL, Langer LF, Ward JM, Archer TK. 2015. MiRNA-mediated regulation of the SWI/SNF chromatin remodeling complex controls pluripotency and endodermal differentiation in human ESCs. Stem Cells; doi:10.1002/stem.2084 [Online 29 June 2015].

(Greg Buchold, Ph.D., is a former NIEHS postdoctoral fellow in the NIEHS Reproductive and Developmental Biology Laboratory. Robert Brown, Ph.D., is an Intramural Research and Training Award (IRTA) fellow in the NIEHS Cell Biology Group. Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group. Simone Otto, Ph.D., is an IRTA fellow in the NIEHS Ion Channel Physiology Group. Qing Xu is a biologist in the NIEHS Metabolism, Genes, and Environment Group.)

Return to Table of Contents

Inside the Institute

NIEHS employees stock local food banks through Feds Feed Families

By Ian Thomas

NIEHS employees closed out the 2015 Feds Feed Families campaign with a strong showing at the Aug. 26 final curbside collection. Employees and contractors donated 3,830 pounds of nonperishable food, cleaning supplies, and personal hygiene items over the course of the campaign, exceeding the goal by 330 pounds. The food and other items collected will stock the shelves of the Durham Rescue Mission and the Food Bank of Central and Eastern North Carolina.

"Knock Out Hunger" was this year's Feds Feed Families campaign theme. NIEHS exceeded its collection goal by 330 pounds. (Photo courtesy of Steve McCaw)

"One out of every five children in North Carolina is food insecure," said Monya Brace, a member of the NIEHS Office of Management and a co-coordinator of this year's effort. "Most of those kids rely on free breakfast and lunch during the school year. That means during the summer they often times go hungry."

Other co-coordinators this year included Pinkney Wilder, of the NIEHS Signal Transduction Laboratory, and Bill Jirles, program analyst in the Office of the Director and president of the American Federation of Government Employees Local 2923.

Robbie Majors, of the NIEHS Division of Extramural Resources, and Andrea Lynn, from the Office of Management, helped out at the Keystone collection site. (Photo courtesy of Steve McCaw)

Meeting family needs nationwide

Launched in 2009 as part of President Obama's United We Serve campaign, Feds Feed Families helps food banks and pantries remain stocked during summer months when they typically see a rise in need, but fall in donations. In the years since the program began, federal workers have donated 39 million pounds of food and hygiene items — 14.8 million pounds in 2014 alone — to support families across the nation.

Feds Feed Families accepts food items such as canned meats, meals, fruits, and vegetables, as well as cereal, peanut butter, juice, rice, pasta, and dried beans. Infant diapers, wipes, and hygiene products are also collected.

Because of staff efforts, NIEHS maintains its ranking as one of the most generous organizations in the area and a top performer nationwide.

Donations totaled 2,616 pounds on the final day, with the aid of curbside pick-up at the main entrance of NIEHS Building 101 and the Keystone building. Helping out, from left, were NIEHS Director Linda Birnbaum, Ph.D.; Leslie Lynch; Janet Hall, M.D.; Brace; William Boyd; and NIEHS Scientific Director Darryl Zeldin, M.D. (Photo courtesy of Linda Birnbaum)

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

Return to Table of Contents

Bee-cause - NIEHS pitches in for pollinator health

By Ian Thomas

NIEHS has joined a national effort to protect the health of pollinating species in the U.S., by nurturing the habitats in which they live. It is all part of the National Strategy to Promote the Health of Honeybees and Other Pollinators, an initiative unveiled earlier this summer by the Obama administration.

Developed through a collaborative executive branch effort, the strategy outlines a comprehensive approach to reducing the impact of pollinator stressors by conducting research to understand, prevent, and recover from pollinator losses; expanding public education programs and outreach; increasing and improving pollinator habitat; and developing public-private partnerships across all these activities.

"From a public awareness standpoint, any strategy that sheds light on this issue is a very good thing," said Bill Willis, NIEHS biologist. "This effort, when coupled with the White House's strategy to control invasive plant species, could prove extremely beneficial to numerous pollinating species, and the environment as a whole in the years to come."

NIEHS scientists unite for the bee-cause

Willis is one of several NIEHS employees promoting pollinator health around the institute's North Carolina campus. Projects include the control of invasive plant species that damage habitat, promotion of native wildflowers and other plants needed for pollinator nutrition, and the construction of artificial habitats such as bee boxes, which provide a home to mason bees. Several were installed Aug. 3 in the NIEHS Memorial Garden and elsewhere around the campus.

"The expectation is for facility managers to examine their buildings, grounds, and practices for opportunities to transition to more pollinator-friendly plant species," said NIEHS Environmental Compliance Officer Bill Steinmetz. "Our hope is to improve the sustainability of the NIEHS landscape and to serve as an exemplar for public-private partnerships and other outreach groups, by showing them that caring for our local bees is a very doable thing." Steinmetz, who chairs the joint EPA-NIEHS Site Ecology Team and the NIEHS Environmental Management System Workgroup, works year-round to improve habitats on campus.

Others taking part include Christine Flowers, director of the NIEHS Office of Communications and Public Liaison and caretaker to a private honeybee colony at her home, and Jack Bishop, Ph.D., a retired senior scientist and a member of the North Carolina Beekeeper's Association.

"Each hive is like an individual with its own resilient personality," said Bishop. "Unfortunately, bees today face a litany of challenges for their survival and they need all the protection we as beekeepers can give them."

A vital crop resource in decline

Agricultural experts agree that pollinators are critical to U.S. environmental health, as well as its economy and food security. According to the U.S. Department of Agriculture (USDA), honeybee pollination alone adds more than $15 billion in value to agricultural crops each year, thereby helping to ensure that diets are rich in fruits, nuts, and vegetables.

"Well over 30 percent of world food crops depend on bees," noted Willis. "And about 90 percent of wild plants require bees."

Bee boxes, like the one above, may help increase the overall abundance of cavity dwelling species and pollination success. (Photo courtesy of Steve McCaw)

What you can do to help bees survive

- Plant a pollinator garden
- Avoid pesticides or choose nonchemical solutions
- Provide a pesticide-free source of water and mud for nesting
- Plant native plants from your ecoregion
- Provide a variety of native flowering trees, shrubs, and wildflowers that bloom throughout the seasons
- Provide nesting habitats of bare soil, free of mulch or grass
- Build or buy your own bee houses

But the state of decline that many pollinating species are now experiencing is indisputable. USDA estimates that honeybee colonies dropped from 6 million in 1947 to just 2.5 million in 2014.

An alarming downturn

Scientists say the reasons for this decline are numerous. Colony death during the winter, for instance, is not uncommon. This is largely due to the elements and harsh temperatures. Other contributors, such as disease, parasites, pesticides, and habitat loss, also play a part in the decline.

What has beekeepers most worried is the growing rise in colony death during the summer months. This was recently reflected in an annual survey from the federally-funded Bee Informed Partnership, which showed a 40 percent drop in American honeybee colonies from 2014 to 2015.

The five most common bee families in North America:

- Apidae — honeybees, bumblebees, carpenter bees, squash bees, southeastern blueberry bees, cuckoo bees
- Halictidae — sweet bees
- Andrenidae — miner bees
- Megachilidae — mason bees and leafcutter bees
- Colletidae — yellow-masked bees

At present, there are more than 4,000 native bee species in the U.S.

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

Among Willis's major interests is the protection of the local mason bee. Mason bees are solitary insects that play an important role in early spring fruit tree and berry pollination, especially where local honeybee populations are in decline. (Photo courtesy of Amy Brix)

Flowers, left, and Willis installed several bee boxes in the NIEHS Memorial Garden, to attract mason bees. (Photo courtesy of Steve McCaw)

Return to Table of Contents

National Institute of
Environmental Health Sciences

Director of Communications: Christine Bruske Flowers
Editor-in-Chief: Kelly Lenox | Managing Editor: Eddy Ball | Science Editor: Robin Arnette