NIEHS National Institute of Environmental Health Sciences

Environmental Factor

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September 2011

NIEHS Spotlight

Panel discusses multiple benefits of federally funded research

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NIEHS employees honored with NIH Director's Awards

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Trainees form backbone for EHP teacher workshops Audio

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Poster session marks high point for summer interns

The 2011 NIH Summer Internship Program at NIEHS marked the culmination of eight to twelve weeks of sustained effort in NIEHS labs with the annual poster session July 28.

NTA showcases private sector career building

The NIEHS Trainees Assembly hosted a Quintiles Open House event July 25, to help young scientists better understand what is available in the private sector.

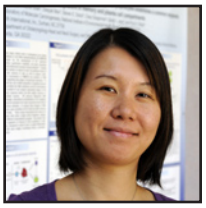
Science Notebook

Birnbaum speaks at Dioxin 2011 Video

NIEHS/NTP Director Linda Birnbaum, Ph.D., was a featured speaker at two sessions during the weeklong Dioxin 2011 in Brussels, Belgium.

Mardis discusses current genomic technologies and cancer models

Elaine Mardis, Ph.D., co-director of The Genome Institute at Washington University in St. Louis, presented a seminar on "Genomic studies of mouse models of human cancer."



Fellow wins WSA award for research excellence Video

Postdoctoral fellow Anne Lai, Ph.D., has been selected to receive one of two NIH Women Scientist Advisors Scholar Awards presented this year.

Fuchs discusses replication past DNA damage

Robert Fuchs, Ph.D., shared his research about mechanisms of replication past damaged DNA, during his talk Aug. 1 at NIEHS.

Study identifies role of mold in asthma development

University of Cincinnati scientists found mold exposure during a critical window of development was associated with a three-fold greater risk for asthma later in childhood.

NIEHS Spotlight

Olden leads school to accreditation Video

Thanks in great part to the leadership of Ken Olden, Ph.D., City University of New York will welcome its first class to the fully accredited School of Public Health this fall.

Postdoctoral fellow launches career as a scientific coordinator

Jana Stone, Ph.D., left NIEHS July 29 for the post of scientific coordinator at the Duke Institute for Genome Sciences and Policy Center for Systems Biology.

Arizona grantee honored for mentoring

NIEHS grantee Patricia Hoyer, Ph.D., was honored with the 2011 Society for the Study of Reproduction (SSR) Trainee-Mentoring Award.

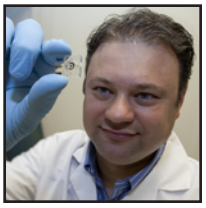
NIEHS ethics program nominated for excellence award

The NIEHS Ethics Program is being recognized by the U.S. Office of Government Ethics for its highly successful Ethics Day event May 25 in Rodbell Auditorium.

Researcher links economic recession with growing minority health disparities

Scientists and administrators from NIEHS were treated to an informal discussion of recent research with one of the field's foremost experts, Irene Dankwa-Mullan, M.D.

Science Notebook



UC grantees' lab-on-a-chip detects toxic heavy metals in humans

An ongoing NIEHS-funded study at the University of Cincinnati examining the health effects of manganese on children will soon have a new tool at its disposal.

Highest levels of flame retardant chemicals reported in California pregnant women

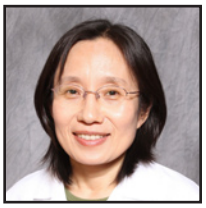
A team of scientists reported very high levels of polybrominated diphenyl ethers and their hydroxylated metabolites among California pregnant women.

Superfund webinar showcases trainees

The Superfund Research Program aired the final installment in its 2011 Trainee Webinar Series Aug. 16, featuring two of its outstanding young environmental engineers.

NIEHS investigator links UV exposure and aging to cataracts and macular degeneration

Joan Roberts, Ph.D., suggests that the aging process itself, in conjunction with excessive UV exposure, plays a major role in the onset of cataracts and macular degeneration.



Study suggests nutritional supplements could one day prevent skin cancer

A new study found that decreased levels of a known tumor suppressing protein led to an increased risk for ultraviolet-induced, non-melanoma skin cancer in mice.

NIEHS Spotlight

NIH seeks new ideas for Common Fund Programs

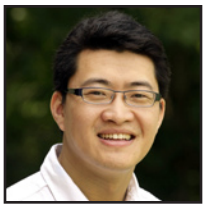
NIH leadership is reaching out to internal and external scientists and stakeholders for ideas about new research programs for 2013, to be supported by its Common Fund.

Superfund awards support early-career researchers

The KC Donnelly Externship Award Supplement supports SRP trainees pursuing translational and transdisciplinary opportunities.

SRP celebrates an important milestone

In August, the Superfund Research Program issued the 200th edition of the SRP Research Briefs, celebrating nearly 15 years of disseminating cutting-edge scientific findings.



Postdocs receive Gordon Conference travel awards

Three NIEHS/NTP postdocs received travel awards and the chance to present posters of their work at the Gordon Research Conference Aug. 7-12 in Andover, N.H.

NIEHS seeks director of clinical research

NIEHS is accepting applications through Sept. 30 from senior investigators qualified for a tenured appointment as director of its Clinical Research Program.

Science Notebook

Understanding how embryonic stem cells work

A new NIEHS-funded paper explains how two seemingly opposing mechanisms in embryonic stem cells actually work together in a unique cellular collaboration.

NTP researcher wins poster award at conference in Germany

NTP scientist Scott Auerbach, Ph.D., took home top poster honors at the OpenTox 2011 InterAction Meeting for his work on bioinformatics and disease-informing assays.

This month in EHP

An image of burning forestland serves as a fitting backdrop for the feature news story in this month's EHP, "Fields and Forests in Flames: Vegetation Smoke and Human Health."

2012 NIH Director's Award programs funding opportunities

In August, NIH announced that it is welcoming proposals for the 2012 NIH Director's Pioneer Award and New Innovator Award programs through early October.

Upcoming bioinformatics conference at Friday Center

The third Toxicogenomics Integrated with Environmental Sciences Conference will take place Sept. 15-16 at the UNC William and Ida Friday Center in Chapel Hill.

Inside the Institute

Goal exceeded, as NIEHS Feds Feed Families drive concludes

Volunteers at NIEHS collected a record volume of non-perishable food, infant products, and hygiene items, during the 2011 Feds Feed Families food drive.

NIEHS mentoring makes summer special for Hispanic intern

From her first contact with NIH up to her last day at NIEHS Aug. 12, summer intern Yasmin Crespo-Mejias enjoyed the support and encouragement of quality mentors.

Remembering Joe Wachsman

Friends and colleagues at NIEHS were saddened to hear of the death of Joe Wachsman, Ph.D., July 10 in Denver, following a brief illness.

Extramural Research

Extramural papers of the month

- Discovery of the seventh and eighth bases of DNA
- Autism and prenatal vitamins
- Microparticle delivery increases efficacy of doxorubicin in treatment of mesothelioma
- Genetic map of African-Americans will aid the study of diseases

Intramural Research

Intramural papers of the month

- Rodent model examines Parkinson's progression
- Cadmium induces transcription without calcium mobilization
- CAR mediates the activation of *Sult1e1* gene by the garlic extract diallyl sulfide
- A novel mechanism that may underlie learning and memory

Calendar of Upcoming Events

- **Sept. 1-2**, in Rodbell Auditorium, 8:30a.m. -5:00p.m. — National Advisory Environmental Health Sciences Council meeting
- **Sept. 7-8 (offsite event)**, Sheraton Iowa City Hotel, Iowa — Engaging Communities to Advance Environmental Health Policy PEPH Workshop: Engaging Policy and Decision Makers
- **Sept. 8-9**, in Rodbell Auditorium, 8:30a.m. -5:00p.m. — Workshop to examine the interactions between environmental exposures and infectious agents
- **Sept. 13**, in Executive Conference Room, 12:00-1:00 p.m. — Receptor Mechanisms Discussion Group, featuring Joyce Goldstein, Ph.D., topic TBA
- **Sept. 13-16 (offsite event)**, Doubletree Hotel in Portland, Ore. — 8th International Phytotechnology Society Conference, "Putting Plants to Work Where We Live, Labor, Breathe, and Play"
- **Sept. 15-16 (offsite event)**, at the William and Ida Friday Center for Continuing Education in Chapel Hill, N.C. — Third International Toxicogenomics Conference, "Toxicogenomics Integrated with Environmental Sciences (TIES)"
- **Sept. 22**, in Rodbell Auditorium, 11:00a.m.-5:00 p.m. — N.C. Society of Toxicology Fall Meeting
- **Sept. 23**, in Rodbell Auditorium, 1:00-2:00 p.m. — National Postdoc Appreciation Day
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Panel discusses multiple benefits of federally funded research

By Eddy Ball

Moderated by journalist Rose Hoban, a panel of area scientists joined U.S. Rep. David Price and NIEHS/NTP Director Linda Birnbaum, Ph.D., Aug. 28 for a discussion of federally funded science, outlining its scientific, social, and economic benefits. The event, which was also webcast, gave the panelists an opportunity to communicate why their scientific research is a valuable impetus for improving quality of life for people locally, nationally, and worldwide — as well as to explain their work to a wider community.

Hoban introduced the program, and, after each panelist delivered a brief presentation, she coordinated the question and answer session. (Photo courtesy of Steve McCaw)

Hoban who is the founder of N.C. Health News and a former health care reporter for North Carolina Public Radio, set the tone for the discussion with her welcome to the audience. "I think the people who started RTP [Research Triangle Park] would be pleased to see how it has developed, spurred on by federal funding," she said, pointing to the impact of job creation and new ideas in changing the face of North Carolina positively, as well as the effect of federally funded scientific research on people throughout the U.S. and even in developing countries.

Birnbaum echoed those themes in her opening remarks. "NIEHS is a really important part of the N.C. economy," she noted. "There are 1400 people who work at NIEHS, and we're responsible statewide for a half-billion dollars of economic impact each year." The work of researchers supported by NIEHS funding stimulates the economy, she added, as an important co-benefit of the Institute's mission of improving public health and quality of life.

As Birnbaum made opening remarks, her fellow scientists on the panel waited their turns to speak. Shown, left to right, are Hollingsworth, Rodes, Swenberg, and Patisaul. (Photo courtesy of Steve McCaw)

Impact on research and economy

Joining Birnbaum and Price on the panel were NIEHS grantees John Hollingsworth, M.D., an associate professor of medicine at Duke University; Heather Patisaul, Ph.D., an assistant professor of biology at North Carolina State University (NCSU); Charles Rodes, Ph.D., a senior fellow at RTI International; and James Swenberg, D.V.M., Ph.D., a Kenan Distinguished Professor of environmental sciences and engineering at the University of North Carolina at Chapel Hill (UNC).

The panelists took turns talking about the work they do to improve health and the collateral benefits of their research in terms of employment, training, technological development, and economic stimulus. Each pointed to direct economic benefits from improved health, the thousands of jobs supported by research, the hundreds of millions of dollars of economic impact, the hundreds of new researchers trained, and new technologies, which improve health and quality of life, while also stimulating income for small businesses.

Swenberg offered an impressive statistic about how federal funding can have a domino effect in terms of indirect economic impact. He described the way an investment of $1.5 million in a UNC pilot project funded by NIEHS resulted in 30 times that amount of economic activity through investments from other funding sources.

Although the business at hand was serious, there were lighter moments as well, such as the one Birnbaum, left, and Price so obviously enjoyed, above. (Photo courtesy of Steve McCaw)

An important story to tell

As the final speaker, Price congratulated the panel and urged the audience to carry the effort forward.

"We are in the midst of a national debate about our funding priorities," Price continued, emphasizing that the multiple benefits of federally funded research is an important story to tell again and again, to as many people as possible. "The core research enterprise in this country is central to the country's competitive position on the world stage," he added, and scientists need to make sure that message is heard.

Looking ahead

During the question and answer segment of the program, panelists considered ways to spread the message to educate the public. Price said, "We need to leave no doubt that we're good stewards of public dollars." Birnbaum added, "We need to be out there communicating with the public and promoting science literacy."

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NIEHS employees honored with NIH Director's Awards

Twenty-five NIEHS employees were among the 378 individuals recognized for exemplary service at the 2011 NIH Director's Award ceremony Aug. 2 in Bethesda, Md. The award, the highest given by NIH to its employees, recognizes superior performance or special efforts significantly beyond regular duty requirements, but directly related to fulfilling the NIH mission.

The NIH Director's Award honors leadership and superior performance for employees in four categories: scientific/medical, technical/clerical/support, administrative, and common fund leadership.

Birnbaum, right, joined Collins at front stage as she accepted a Director's Award on behalf of employees honored for their contributions to the Deepwater Horizon Gulf Oil Spill Response. (Photo courtesy of NIH)

Collins, left, joined representatives of the Gulf Long-term Followup (GuLF) STUDY team. Shown, left to right, Collins, Sandler, Birnbaum, and Miller. (Photo courtesy of NIH).

NIEHS and NTP employees were singled out for their contributions to the Deepwater Horizon Gulf Oil Spill Response, GuLF STUDY (Gulf Long-term Followup Study), and NIH PROMIS Working Group. NIEHS/NTP Director Linda Birnbaum, Ph.D., was one of the dignitaries on stage. She both represented the Institute and received an award as part of the Deepwater Horizon Gulf Oil Spill Response Team.

NIEHS scientists and staff honored for trans-NIH efforts

- **Deepwater Horizon Gulf Oil Spill Response Team:** For the 2010 Gulf Oil Spill response, implementing public health protection programs for cleanup workers, developing the GuLF STUDY, and assembling a research consortium.

  Kathy Ahlmark, Robin Arnette, Ph.D., Eddy Ball, Ph.D., Sharon Beard, Linda Birnbaum, Ph.D., John Bucher, Ph. D., Gwen Collman, Ph.D., Allen Dearry, Ph.D., Dorothy Duke, Christine Flowers, Chip Hughes, Paul Jung, M.D., Lora Kutkat, Richard Kwok, Ph.D., Robin Mackar, Scott Masten, Ph.D., Aubrey Miller, M.D., Ted Outwater, James Remington, Dale Sandler, Ph.D., Anne Thompson, Cheryl Thompson, Claudia Thompson, Ph.D., Leroy Worth, Ph.D.,

- **Gulf Long-term Followup (GuLF) STUDY:** For rapidly developing protocol for Gulf Long-term Followup (GuLF) STUDY, obtaining institutional review board clearance and Office of Management and Budget approval, completing administrative tasks associated with longitudinal federal research study.

  Lawrence Engel, Ph.D., Christine Flowers, Richard Kwok, Ph.D., Aubrey Miller, M.D., Dale Sandler, Ph.D.

- **NIH PROMIS Working Group** (National Institute of Arthritis and Musculoskeletal and Skin Diseases): For outstanding efforts in promoting the use of NIH Patient Reported Outcomes Measurement Information System (PROMIS) tools in clinical research.

  Martha Barnes

Emceed by Phil Lenowitz, NIH deputy director of Human Resources, the program opened with remarks by NIH Director Francis Collins, M.D., Ph.D. Referring to concern over raising the debt ceiling, Collins said, "It's perhaps particularly appropriate that we gather here this afternoon to celebrate the dedication of many giving themselves in such a thoughtful, creative way to try to serve the public."

As he pointed to specific efforts recognized by the awards, Collins added with pride, "This is NIH. This is who we are." He singled out for individual mention Randy Schools, who has served as president of the NIH Recreation and Welfare Association since 1977. Collins noted, "It's about time to say 'thank you' to Randy."

Continuing a tradition at ceremonies of this kind, Collins segued easily from talk to music, as he accompanied himself on guitar and sang a ballad he composed, "Dare to Dream." The audience joined him for the chorus, which included the song's title and the words, "Of the need to help the world/ We all agree/ This is NIH/ So let's make history."

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Trainees form backbone for EHP teacher workshops

By Eddy Ball

During the planning process for the most recent Environmental Health Perspectives (EHP) teacher workshops, Bono Sen, Ph.D., turned to an often-untapped source of teaching talent at the Institute—its 200-plus-member core of trainees. Sen, who is EHP's Science Education and Outreach Program manager, recruited eleven current and former postdoctoral fellows to teach most of the sessions during the two days of workshops, held Aug. 2-3 in Rodbell Auditorium .

Listen as Sen discusses the expanded Science Education Program with EHP Podcast Host Ashley Ahearn

Read Transcript

Michelle Heacock, Ph.D., right, presenting "Death by Particles," set the tone for the workshop, as she demonstrated how to help students envision lung capacity with the help of a simple prop. (Photo courtesy of Steve McCaw)

"Working with trainees," Sen said of the experience, "is a win-win situation for everyone involved." Trainees get valuable science communication and teaching experience, and the workshops benefit from the presenters' individual expertise as well as their contagious enthusiasm about environmental health science.

As their evaluations clearly indicated, the attendees agreed strongly that the workshop was a valuable use of their time, something they would readily recommend to others. Having access to scientists during the workshop was something the teachers said they considered valuable. One participant wrote of the experience, "Exceeded my expectations! This is my first in-person workshop, and I am incredibly thrilled and impressed with all of the wonderful teaching resources and classy packaging of materials."

For Sen, it was especially gratifying that teachers and science outreach specialists valued the workshop opportunity enough to spend the time and money necessary to come from as far away as the Outer Banks, the mountains of Western North Carolina, and even out of state.

Wide-ranging, fast-paced, and hands-on learning

Sen, a postdoc herself at the U.S. Environmental Protection Agency (EPA) prior to joining the staff at EHP in 2009, worked with postdoctoral fellow Julie Hall, Ph.D., to design and coordinate the workshops, "Air, Water, and You" Aug. 2 for environmental educators, and "The Environment — A Human Health Perspective" Aug. 3 for teachers. The trainees, often working outside their areas of expertise, prepared short presentations and led attendees in classroom activities for their students.

An exercise in Trivedi's presentation, "Cleaner Air and Water on the Fly," showed this participant the way adsorption cleans water passed through activated charcoal. However, as Trivedi observed, "You still have to dispose of the pollutants." (Photo courtesy of Steve McCaw)

Studies and news stories published in EHP formed the core of the workshop handbook, but most of the presenters took the curriculum to the next level with demonstrations of activities, instruction on making materials, video clips, and comprehensive lists of Web-based resources. With no shortage of questions from attendees, presenters sometimes found themselves talking more than they had planned about their own research.

Topics ranged from the expected, such as air and water pollution, and specific diseases of the lung and cardiovascular system, to the unexpected, such as the effects of the built environment on health, principles of green building design, and new technology for identifying sources of pollution in the oceans.

In her presentation on "Robolobsters," Rachel Goldsmith, Ph.D., took participants through an eye-opening exercise demonstrating a sensing device that mimics the superior smelling ability of lobsters. (Photo courtesy of Steve McCaw)

Building an experienced core of trainee instructors

Several of the trainees involved in the EHP workshops also contributed to the weeklong EHP student workshop held at the EPA in June (see story) and workshops for the Summer Internship Program in 2010 and 2011. EHP also goes offsite for presentations at area schools, such as Orange High School in Hillsborough, N.C. (see story), and Sen plans to expand trainee involvement in them during the upcoming year.

Faced with a more challenging job market than in previous years, trainees increasingly value opportunities to enhance their prospects on the bench and off. "I think it's important to learn how to effectively communicate science at several different levels," said postdoctoral fellow Erin Hopper, Ph.D. "And it's valuable for me to take something I don't know that much about, research it, and then train teachers how to get the lessons across to their students."

"It's fun and exciting," added postdoctoral fellow Darshini Trivedi, Ph.D. "I loved talking about my research on cardiovascular disease, answering questions, and renewing my own enthusiasm for my work."

Several trainees, such as Nisha Cavanaugh, Ph.D., have also discovered the benefits of participation in the workshops in terms of networking. “One of my presentations led to a proposal from an outreach specialist at UNC [University of North Carolina at Chapel Hill] to give a seminar for teachers on my work with DNA repair enzymes,” she said.

Kang, left, led an exercise with teachers that emphasized the importance of teamwork and communication in science learning and teaching. (Photo courtesy of Bono Sen)

It’s hard to imagine there’s much that’s funny about malaria, but intern Linh Pham, Ph.D., managed to keep the humor level up in her presentation on “Climate Change and Vector Borne Diseases.” (Photo courtesy of Steve McCaw)

During an exercise from her segment on “Unequal Housing, Unequal Health,” trainee Kathryn Haas, Ph.D., stopped to talk with teachers during an exercise on the effects of the built environment on health. (Photo courtesy of Steve McCaw)

Even at the podium, presenters were full of energy and enthusiasm. Trainee Chaitra Cheluvaraju, Ph.D., above, and Trivedi presented the health effects of smoking on the lungs and the heart, as part of “Bans, Bans, Good for the Heart!” (Photo courtesy of Steve McCaw)

Presenters honor roll

Guest speakers at the workshop included Public Affairs Specialist Ed Kang and biologist Huei-Chen Lao of NIEHS, and Laura Jackson, Ph.D., of EPA. NTP scientists Andrew Rooney, Ph.D., and Nigel Walker, Ph.D., participated in a panel discussion Aug. 3 about risk assessment.

Still the backbone of the workshops was its core of current and former postdocs:

Biologist Mercedes Arana, Ph.D.
Biologist Windy Boyd, Ph.D.
Postdoctoral fellow Nisha Cavanaugh, Ph.D.
Postdoctoral fellow Chaitra Cheluvaraju, Ph.D.
Postdoctoral fellow Rachel Goldsmith, Ph.D.
Postdoctoral fellow Kathryn Haas, Ph.D.
Postdoctoral fellow Julie Hall, Ph.D.
Postdoctoral fellow Michelle Heacock, Ph.D.
Postdoctoral fellow Erin Hopper, Ph.D.
Program Analysis Branch intern Linh Pham, Ph.D.
Postdoctoral fellow Darshini Trivedi, Ph.D.

Gretchen Santo, who teaches grades 9-12 at the Beaumont School in Cleveland Heights, Ohio, incurred the expense of airfare and two nights lodging, to attend both days of the workshop. She returned home convinced it was worth every cent of the cost. (Photo courtesy of Steve McCaw)

At the end of their busy two days teaching, the team took a break outside. Shown in front, left to right, are Haas, Arana, Trivedi, Cavanaugh, and Heacock. Seated in back, left to right, are Cheluvaraju, Sen, Goldsmith, Hopper, Hall, and Boyd. (Photo courtesy of Steve McCaw)

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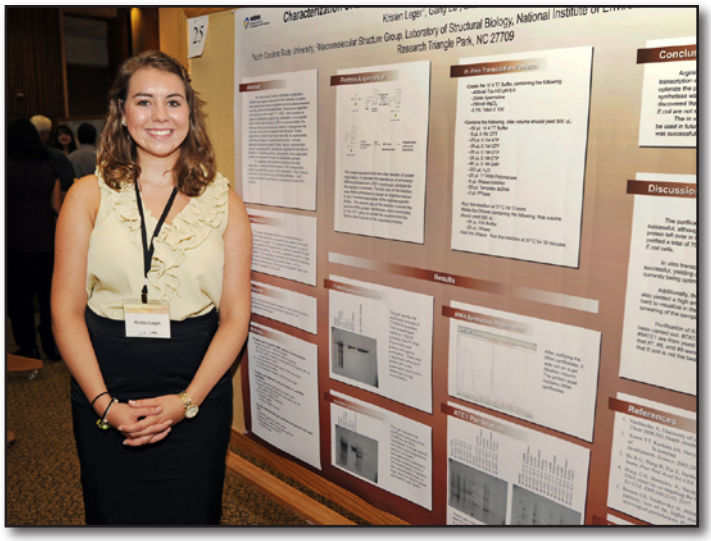
Poster session marks high point for summer interns

By Melissa Kerr

The 2011 NIH Summer Internship Program at NIEHS marked the culmination of eight to twelve weeks of sustained effort in NIEHS labs with the annual poster session July 28 in Rodbell Auditorium. The event gave the 45 interns an opportunity to talk about their accomplishments within the Institute's labs over the summer program and showcase their abstracts and posters.

The auditorium was filled with students presenting their findings, postdoctoral fellows judging the posters, and NIEHS scientists interested in the interns' scientific discoveries. The noise level was high and the aisles crowded as the interns spoke about their work, their mentors, and the experiences the summer program provided them.



Kristen Leger from North Carolina State University said she looks forward to continuing the research into protein arginylation modification through an internship during the fall. (Photo courtesy of Steve McCaw)

A summer of focused research and learning

At the beginning of the summer program, interns join a lab based on their individual interests and have the unique opportunity of truly being incorporated into a laboratory setting. During the summer, they work on a project from start to finish, designing and conducting experiments for their pilot studies, which have the potential of becoming part of peer-reviewed publications or presentations at scientific meetings.

William G. Enloe High School rising senior Diana Dayal, second from left, joined with her proud parents and her mentor, visiting fellow Ezequiel Marron, Ph.D., to her right, at Dayal's poster. (Photo courtesy of Steve McCaw)

During the poster session, the young scientists get valuable experience in thinking on their feet, as they articulate the contents of their posters and the research involved, as well as field questions and observations from senior scientists. The posters are judged by postdoctoral fellows on the quality of the science, the poster presentation, and the oral presentation.

Rahul Jaswaney, one of the winners in the undergraduate division, said he was grateful for the guidance he received. His experience in the lab of Robert Langenbach, Ph.D., has fed Jaswaney's interest in research. "Dr. [Darshini] Trivedi's emphasis on understanding the bigger picture of this project allowed me to keep each experiment in proper perspective," he explained. "I truly enjoyed working on this project."

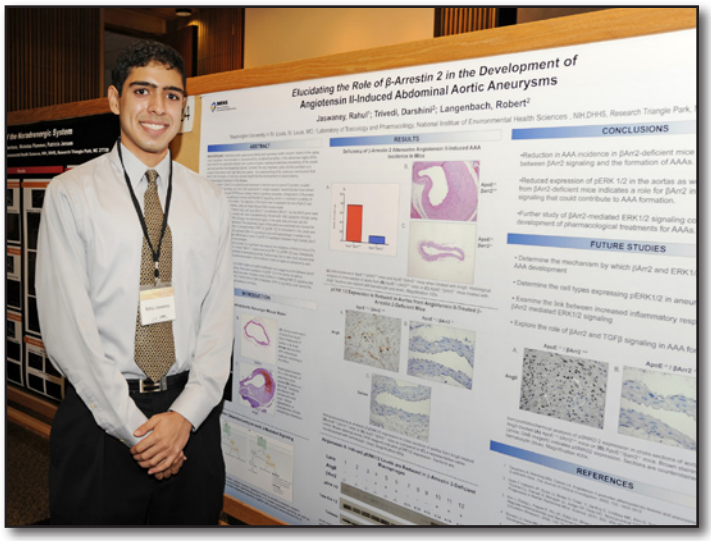
Having the summer program participants in the labs is also a benefit to seasoned scientists, and the Langenbach lab was especially pleased with Jaswaney's work. "Rahul is a very bright, enthusiastic, affable young man, and indeed it has been a pleasure to have had him in our group," said Langenbach.

At an ice cream social later in the day, NIEHS Deputy Scientific Director Bill Schrader, Ph.D., presented awards for the best posters in three categories (see text box). Schrader opened the ceremony by saying, "It was a great morning of science." He also said he hoped that the students enjoyed being at NIEHS as much as NIEHS enjoyed having them here.

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

Amanda Arulpragasam, left, explained her research to fellow intern Neena Davisson. (Photo courtesy of Steve McCaw)

Mount Olive College rising senior Kyle Ham, right, discussed his work on epigenetic regulation of histone H3. (Photo courtesy of Steve McCaw)



Undergraduate poster co-winner Jaswaney said of his project, "It felt like puzzle working and I found it extremely interesting." (Photo courtesy of Steve McCaw)

Fitzgerald, right, whose poster tied with Jaswaney's in the undergraduate category, explained his research to family members. (Photo courtesy of Steve McCaw)

Schrader encouraged the summer intern participants to continue their pursuit of the sciences. (Photo courtesy of Steve McCaw)

High School poster winner Somashekar, right, showed off the award she received from Schrader. (Photo courtesy of Steve McCaw)

Graduate poster winner Dutton, left, accepted his award from Schrader. (Photo courtesy of Steve McCaw)

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Poster competition winners by category

- **High school: Rising senior Greeshma Somashekar — North Carolina School of Science and Mathematics — Mentor Stavros, Garantziotis, M.D., Matrix Biology Group** Inter-alpha-trypsin inhibitor heavy chain 4 (ITIH4) is a serum protein found in the tissue of the lung. The concentration becomes elevated in patients with various types of cancer as well as acute lung injury, making this compound a potential biomarker for these diseases. The challenge for Somashekar was to investigate the functional effects of three ITIH4 domains with regard to cell activation and migration. She was able to create ITIH4 constructs in varying sizes. These constructs will allow further investigation into the functional effects of each of the ITIH4 domains on cell activation and migration.

- **Undergraduate (tie): Rising junior Nicholas Fitzgerald — North Carolina State University — Mentor Ken Tomer, Ph.D., Mass Spectrometry Group** Fitzgerald studied how Anthrax lethal toxin impacted protein expression in macrophages and cardiomyocytes. He found that most of the proteins showed little change from Anthrax lethal toxin exposure. Of the observable changes in macrophages, the most significant change was an up-regulation of stress proteins. In the cardiomyocytes, there was a change in a protein that is a component in endocytosis.

- **Undergraduate (tie): Rising sophomore Rahul Jaswaney — Washington University in St. Louis — Mentor Robert Langenbach, Ph.D., NIEHS Metabolism and Molecular Mechanisms Group** Jaswaney set out to further understand the affect of beta-arrestin 2 (betaArr2) on the occurrence of abdominal aortic aneurysms (AAA). BetaArr2 is a protein that has been known to dampen certain signaling, such as the angiotensin II receptor. These complexes initiate a signaling pathway known for its contribution to a variety of diseases, including AAA formation. He found that a deficiency of BetaArr2 resulted in a reduction in the occurrence of AAA.

- **Graduate: Veterinary student Jack Dutton — North Carolina State University — Mentor Terry Blankenship-Paris, D.V.M., NIEHS Comparative Medicine Branch** Research models often use surgery performed on mice. Historically, surgery has involved multiple injections, which have the potential to cause additional stress and injury to the animal. Dutton's challenge was to develop a formulation of buprenorphine, a treatment for pain, that can be given at the time of surgery and also provide pain relief throughout the recovery period. He found that a gel solution would sustain buprenorphine for longer than the injectable form, maintaining acceptable levels throughout the post-surgery recovery period.

NTA showcases private sector career building

By Melissa Kerr

In today's evolving marketplace, the career path of a scientist is not always as straightforward as it once was. In order for NIEHS employees to feel more confident negotiating their various options, the NIEHS Trainees Assembly (NTA) hosted a Quintiles Open House event July 25, to help young scientists better understand what is available in the private sector.

Postdoctoral fellows and scientists filled Rodbell Auditorium eager to understand the career options available through the RTP-based company Quintiles, which bills itself as "the only fully integrated bio and pharmaceutical services provider offering clinical, commercial, consulting, and capital solutions."

The turn out gratified NTA organizers, since this was the first event of its kind at NIEHS. Although people tended to shun front row seats, seating was tight in the rest of the auditorium. (Photo courtesy of Steve McCaw)

Advice for finding the job

After a brief introduction from NTA steering committee member and event moderator Emily Zhou, Ph.D., Quintiles staff members opened with personal stories of transition from the academic world to their roles at Quintiles. Speakers Maria Schroeder, Ph.D., and Chris Learn, Ph.D., both began their careers in academics, Schroeder at the University of North Carolina at Chapel Hill and Learn at Duke University. Both spoke on transitional roadblocks and how to better overcome them. For a scientist to be acclimated to an alternate role, Schroeder suggested staying informed and investing time into learning how science is changing. "Chance favors the prepared mind," claimed Learn.

Schroeder spoke to a general concern among audience members about how to move, as she did, from academic and regulatory science into private sector science. (Photo courtesy of Steve McCaw)

Quintiles representatives then spoke on the variety of different options available for a scientist who would work with them. Dan Nowell and Angie Giles, both managers of staffing within Quintiles, spoke on their own career choices, as well as how to better make connections within the scientific community. Giles suggested that asking advice from staffing professionals is not only acceptable, but it is actually recommended. Nowell advised any professional in any career path to create a LinkedIn profile. "It is, by far, the most powerful networking tool on the planet," he said.

Quintiles sent a contingent of representatives who talked about the company and its staffing needs. Attendees took full advantage of having so many professionals there to answer questions about the private sector's needs for scientific talent. (Photo courtesy of Steve McCaw)

Another option for career advancement is by placement through Aerotek, a recruitment firm that staffs a wide array of companies throughout the world.

According to representatives Taylor Cook and Ali Ghiassi, Aerotek Scientific is the largest recruiter of scientists within the United States. In the past 10 years, Aerotek has placed 296 former NIEHS employees locally, and 796 have been placed nationally. They also recommended that a prospective employee should keep up with current trends. "You must stay educated about the opportunities in your space," Ghiassi said.

Aerotek recruiters Ghiassi, left, and Crook offered attendees tips for using recruiters to make the job search easier and more rewarding, such as being sure to follow up with recruiters even if the job doesn't work out. (Photo courtesy of Steve McCaw)

Using the rule of three as a guideline for growing in the job

The career path is not over once a person finds a job. Joe Mills, a staffing partner for Global Functional Resourcing at Quintiles, spoke about concepts to keep in mind after an employee starts the first day. He stressed the importance of the first mentor. Mills suggests that the career-building concepts a new scientist could learn from a good mentor are worth much more than the paycheck. He also introduced the rule of three.

Mills explained that in three weeks, employees must master the basics of how they fit into the company. After three months, they should be starting to branch out and learn new aspects of their roles. Then, after three years, employees should start looking into how to take the next step in their careers. "These simple rules will help you make any transition," Mills claimed.

Mills tried to be specific, as in his rule of three, but he also emphasized that situations will vary for individual job seekers. (Photo courtesy of Steve McCaw)

Quintiles Director of Staffing Melissa Hopkins spoke about the company's Global Talent Program and Early Talent Program. She discussed how the summer internship program, currently involving 170 interns globally, invests in the scientists of tomorrow. Hopkins suggested different traits that she looks for when deciding on interns. Aside from a curious mind, she insisted that communication is key. "The Quintiles community is built on direct, honest, competent, and optimistic people," Hopkins emphasized.

The event concluded with an extensive question and answer session, as NIEHS scientists and postdocs explored the specifics of a prospective transition.

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

Zhou showed the stress of moderating the event, but she can now look back to a very successful first in NTA-initiated career development programs. She also served as co-chair of the exceptional 2011 NIEHS Biomedical Career Fair last spring. (Photo courtesy of Steve McCaw)

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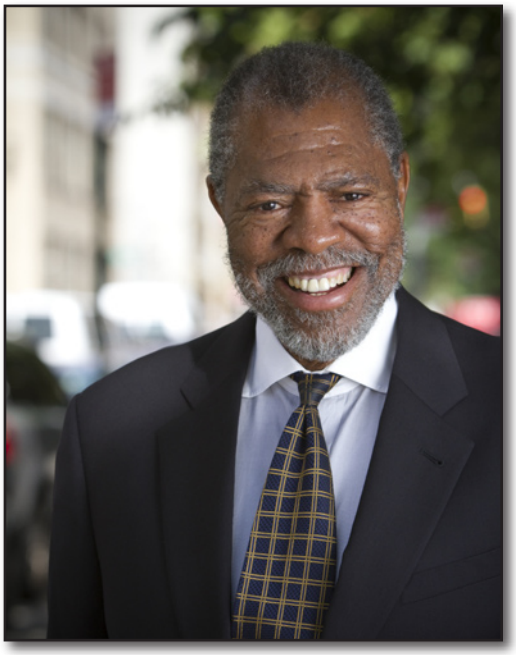
Olden leads school to accreditation

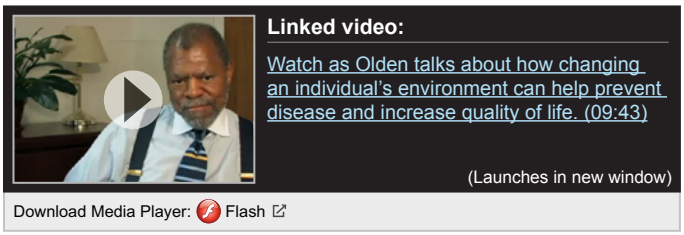
By Eddy Ball

Thanks in great part to the leadership of NIEHS Director Emeritus Ken Olden, Ph.D., the new urban public health initiative at the City University of New York (CUNY) will welcome its first class to a fully accredited school. In a press release issued July 25, the Council on Education for Public Health (CEPH) announced its accreditation of the CUNY School of Public Health (SPH) for a five-year term extending to July 1, 2016. The SPH is a collaboration of Hunter, Brooklyn, and Lehman Colleges, and the CUNY Graduate School.

Olden joined CUNY in 2008 as founding dean of the CUNY School of Public Health and for the past 2 1/2 years has overseen the development of the curriculum and recruitment of 26 tenure-track faculty members. Earlier this year, Olden moved with the school from its temporary home to a new eight-story, 147,000-square-foot green building in East Harlem — a community with one of the highest rates of poverty, and preventable morbidity and mortality in the U.S.



Olden, above, has commuted to New York from his home in North Carolina since the fall of 2008. When he accepted the position, Olden called it "one opportunity I thought I couldn't pass up." He explained that he hopes the school will emerge as "the Mecca, the epicenter for modern public health." (Photo courtesy of CUNY Media Relations)



Addressing a new paradigm in public health

"The goal of CUNY's School of Public Health," Olden said, when he began as dean, "is to train interdisciplinary urban public health researchers and practitioners capable of working across all levels of analysis, disciplines, and social sectors — such as health, education, the environment and criminal justice — to address complex urban public health problems."

According to Olden, to meet the challenges of public health in the 21st century, the discipline needs to think beyond the previous century's focus on infectious diseases and mainstream medicine's preoccupation with drugs and high-tech procedures to treat individuals with disease, to embrace prevention as the most effective strategy for reducing morbidity and mortality and for promoting healthy aging. Olden has explained that the urban setting is where the majority of people in the U.S. and worldwide are encountering the conditions that lead to chronic diseases, such as diabetes and chronic obstructive pulmonary disease (COPD), so it's natural that cities will be the best place to test new strategies for prevention.

As Olden said in a talk earlier this year, "New York is a microcosm of the world," a fertile laboratory for studying the environmental factors that impact health globally and for field-testing ways to eliminate health disparities.

Looking forward

"Once the transition to our new location is complete, my task [here in New York] will be over," Olden said of his work at CUNY. "So, I am looking forward to coming back to North Carolina within the next ten to twelve months."

This will mark Olden's second retirement, first from NIEHS and then from CUNY, but few who know him really think he'll retire in the conventional sense of the word and won't be too surprised if he takes on new challenges after he returns home. Olden travels to Iowa City this month to receive an award for his long-time championship of community participation in the full spectrum of environmental health research. And it's very likely that he'll continue to pursue his passion for advancing public health, health parity, and environmental justice in the years to come.

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Postdoctoral fellow launches career as a scientific coordinator

By Emily Zhou

Jana Stone, Ph.D., left NIEHS July 29 for the scientific coordinator position at the Duke Institute for Genome Sciences and Policy Center for Systems Biology. She was an Intramural Research Training Award fellow in the DNA Replication Fidelity Group in the Laboratory of Molecular Genetics (LMG). Stone's group leader and mentor was senior scientist Thomas Kunkel, Ph.D., who is also the chief of the Laboratory of Structural Biology (LSB).

Stone's successful career transition is a great example of someone taking initiative, finding her passion, and networking in the job search process.

Stone, above, described Kunkel as a great scientist and a wonderful mentor. "I really appreciate that he was able to let me do outside-the-lab activities, which was a tremendous help." Stone encouraged fellows, "Take advantage of career development resources available at NIEHS… and start looking for jobs early." (Photo courtesy of Steve McCaw)

An excellent geneticist

Stone was trained as a yeast geneticist and molecular biologist at the University of North Carolina at Chapel Hill (UNC-CH), where she focused on mismatch repair proteins. At NIEHS, she found that yeast DNA polymerase zeta can independently insert nucleotides opposite lesions in DNA resulting from exposure to environmental agents. Her research led to multiple peer-reviewed publications in major journals.

Stone is also the recipient of a 2011 NIH Fellows Award for Research Excellence. "She has accomplished a lot experimentally," said Kunkel, who was very happy with Stone's contribution as a scientist.

A supportive mentor

When Stone joined the Kunkel lab, she knew that her passion wasn't to be a traditional laboratory researcher. Kunkel said he encouraged her to "network and develop skills that would better position her for an alternative career of her interest." Stone helped plan both the LMG and the LSB annual retreats as well as the NIEHS Biomedical Career fair, for which she helped organize the agenda, recruited alumni panelists, and moderated

panel sessions on careers for PhDs. Commenting on her performance in those roles, Kunkel said, "She's very good at it and enjoyed it."

But Stone didn't stop there. She got more involved with the NIEHS Trainees Assembly (NTA) to develop management and leadership skills. Gradually she found her passion in science education and outreach.

A passion for education and outreach

Stone took part in the NIEHS Summers of Discovery Lecture Series planning committee last year designing curricula on environmental research for summer interns. She taught and led activities for modules on air pollution, health and public policy. Stone also helped recruit and train NIEHS volunteers for the North Carolina DNA Day program. This outreach program, run by the UNC School of Medicine Training Initiative in Biological and Biomedical Sciences, aims to generate interest in careers in public health by having volunteers spend a day teaching high school students about breakthroughs in genetics and genomics.

Networking — the key to landing a job

Knowing her passion and having a portfolio of outreach activities, Stone specifically looked for jobs to fit her communication and organization skill set. After several interviews, she was offered the scientific coordinator position at Duke. "Networking was definitely required to successfully land my job," said Stone. "This job was announced over email and was never posted on the Duke HR [human resources] website. By the time it appeared in the NIEHS fellows' newsletter, I had already applied."

Stone then took the initiative to contact the person she would be replacing to ask specific questions regarding the position. "I could better target my resume and cover letter because many of the job responsibilities weren't listed on the job description," said Stone. "It also made me feel more prepared for the interview."

Exploring resources available at NIEHS

When asked about her advice to NIEHS fellows who are job searching, Stone said, "You have to take the initiative to find opportunities that will help you develop your skill set. Join some activities outside the lab such as the NTA." She also suggested taking on writing opportunities, when possible, because she was asked for both technical and non-technical writing samples during her job search.

(Emily Zhou, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

"Stone is a hard-core, caring, and well-trained molecular geneticist," Kunkel said. "She understands the science. They [staff and students at CSB] are happy to have her, and she's thrilled to be there. This job not only plays to her strength, but also is what she enjoys." (Photo courtesy of Steve McCaw)

Stone's new role as a scientific coordinator at Duke

The Center for Systems Biology (CSB) at Duke includes about 100 faculty and students. In her new job, Stone's responsibilities include helping plan their annual symposium that, this year, will occur at the end of September. She will also be involved with administration and technical writing, including facilitating the center's grant renewal this year.

Another of Stone's responsibilities will be outreach activities. She is currently coordinating a course taught by CSB faculty at North Carolina Central University on complex genetic traits in humans and plants. She is very excited about getting CSB trainees involved in more teaching opportunities to help them in their career advancement.

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Arizona grantee honored for mentoring

By Eddy Ball

NIEHS grantee Patricia Hoyer, Ph.D., was honored with the 2011 Society for the Study of Reproduction (SSR) Trainee-Mentoring Award, during the group's annual meeting July 31-Aug. 4 in Portland, Ore.

Like her own students, Hoyer benefited from mentoring during her graduate work at the University of Wyoming and her NIH postdoctoral fellowship at Colorado State University. Prior to her NIEHS funding, she received early career support as an NIH Career Development Awardee. (Photo courtesy of Patricia Hoyer)

Hoyer is a professor in the Department of Physiology at The University of Arizona (UA) College of Medicine and a researcher in the UA Center for Toxicology and the Southwest Environmental Health Sciences Center. Additionally, she is principal director of an NIH-sponsored T32 training grant titled "Graduate training in systems and integrative physiology."

The trainee-mentoring award recognizes Hoyer as a mentor who has consistently demonstrated a measure of support and guidance to trainees at the undergraduate, graduate, and postdoctoral level that far exceeds the basic responsibilities required of an academic advisor. According to the award website, an additional criterion for the award is that "the nominee has demonstrated a comprehensive knowledge of and passion for reproductive biology and its implications in the broader world of scientific research."

Collectively, Hoyer has trained 25 postdoctoral fellows, and predoctoral and masters students, and has served on the committees of over 80 others.

When he learned of Hoyer's award, the administrator of her grant, NIEHS Cellular, Organ, and Systems Pathobiology Branch Chief Jerry Heindel, Ph.D., said he was gratified to see her mentoring recognized. "One of the goals of all of our funding at NIEHS is to advance the training of the next generation of biomedical researchers, and high-quality mentoring, as exemplified by Dr. Hoyer's success with students, is key to reaching that goal."

Reproductive life span as a global health concern

The theme of the 44th Annual Meeting of SSR was, appropriately enough, "Reproduction and the World's Future," a theme that parallels the research into signaling pathways in chemically induced ovotoxicity supported by Hoyer's grant. Her group studies the mechanisms by which exposure to environmental chemicals can cause a depletion of the finite pool of primordial follicles. Depletion of this pool can lead to premature ovarian failure, or early menopause in women, which is associated with a variety of health disorders and chronic diseases.

Hoyer is studying the chemical 4-vinylcyclohexene and its diepoxide metabolite, VCD, for insights into the effects on ovaries and to characterize the pathways that protect against follicle loss caused by VCD. "The ultimate aim," she wrote in her grant summary, "is to fully understand and identify solutions to prevent premature ovarian failure occurring due to xenobiotic exposures in females."

According to Hoyer, one objective of her research is to promote a greater awareness of ovarian failure caused by xenobiotic exposures in females, to increase appreciation of the global public health impact of the

environment on the reproductive life span in women. Menopause-associated disorders include osteoporosis, cardiovascular disease, metabolic syndrome, type 2 diabetes, and ovarian cancer — diseases that are on the increase worldwide.

Hoyer's initial NIEHS grant award was made in 1998, and it was renewed last year through 2012.

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NIEHS ethics program nominated for excellence award

By Ian Thomas

The NIEHS Ethics Program is being recognized by the U.S. Office of Government Ethics (OGE) for its highly successful Ethics Day event May 25 in Rodbell Auditorium (see story). Presented annually to federal agencies that demonstrate exemplary ethical standards, the award recognizes the superior performance of the NIEHS program, which earned a perfect score of 100 percent compliance with its financial disclosure requirements and ethics training programs.

Prior to joining NIEHS in 2009, Androphy was the executive director of the Tennessee Ethics Commission, where he oversaw its operations and mission, while serving as an advisor for Commission members. (Photo courtesy of Steve McCaw)

"OGE has oversight and jurisdiction over the ethics programs of all federal agencies," explained Bruce Androphy, J.D., director of the NIEHS Ethics Program and a deputy ethics counselor for the NIEHS Ethics Office. "So this nomination means a lot to both the Institute and the ethics staff because, beyond compliance, it justifies the hard work and dedication we put into events like Ethics Day."

Giving ethics a human face and personal touch

Offering a variety of functions and services to NIEHS personnel and administrators, the Ethics Program provides guidance for potential conflict of interest issues, handles matters of public and confidential disclosure, and coordinates ethics training programs, including responsible conduct of research. Despite the ever-growing use of online training and e-learning techniques throughout the federal government, Androphy and his staff believe there should always be a place for in-person, educational events.

"It is our goal to make training fun and meaningful," noted Androphy. "That's why we have activities like Ethics Jeopardy, because it allows people to interact with presenters, ask questions, and get informed on what they can and can't do, in accordance with policy. It also gives them a chance to get to know our staff so that, when the time comes that they need information, they're comfortable coming to us."

Ultimately, it's the hope of Androphy and his office that, through educational events like Ethics Day, they can create a relaxed, stress-free environment, whereby agency personnel are not only encouraged, but content to utilize his staff's expertise in federal and bioethics policy. Therefore, awards such as this one only serve to reinforce his office's commitment to that end.

"Our number one goal is to be a helpful resource for informing personnel on ethics policy as it applies to our daily jobs and responsibilities as government employees," Androphy said. "If we're perceived as being tough, it's not because we like saying no, but rather because we're simply acting in the best ethical interest of NIEHS and the people who make it the world-class organization that it is."

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

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Researcher links economic recession with growing minority health disparities

By Ian Thomas

In an Aug. 9 seminar devoted to the latest in minority health disparities research, scientists and administrators from NIEHS were treated to an informal discussion with one of the field's foremost experts, Irene Dankwa-Mullan, M.D., director of the Office of Innovation and Program Coordination at the National Institute on Minority Health and Health Disparities (NIMHD). Over the course of the hour, attendees covered topics ranging from social, environmental, and biological determinants of health, to current policies surrounding income and educational equality.

Prior to joining NIMHD, Dankwa-Mullan served as the medical director and public health physician with the Montgomery County, Md. Public Health Department. (Photo courtesy of Arnold Greenwell)

"NIEHS has always been committed to addressing health disparities," said NIEHS Chief of Staff Cmdr. Paul Jung, M.D., who hosted the event. "Unfortunately, this issue comes part-and-parcel with environmental health, so it's imperative that our Institute direct resources toward improving health for everyone."

A multifaceted area of health

Health disparities research is a multifaceted area of study, consisting of several key components including basic, clinical, social, and behavioral research, each one conducted with the primary goal of further understanding why health differences exist between various populations. Still, Dankwa-Mullan stressed the importance of remembering that everything is linked.

"Every morning, we wake up and check the Dow Jones to track the economic recession, and yet little is done to track the social recession that's happening at the same time," she explained. "Socioeconomic and psychosocial stresses, such as poverty, poor education, social isolation, and unemployment, can become biologically embedded in a population. These are then transmitted onto future generations, if there is no intervention."

Where science meets policy

One of 27 Institutes and Centers within NIH, the mission of the NIMHD is to coordinate, assess, and lead the NIH effort to reduce and, eventually, eliminate health disparities among minority groups. This is done by promoting biological, physical and social health; fostering emerging programs; disseminating information; and reaching out to minority and other health disparity communities. Ultimately however, Dankwa-Mullan admitted that research alone can only do so much.

Jung, right, arrived at NIEHS in February 2010, after serving as an investigator for the U.S. House Energy and Commerce Committee's Oversight and Investigations Subcommittee. (Photo courtesy of Arnold Greenwell)

"Scientific evidence can inform policies on what must be done but, inevitably, change lies within the policy making process itself," she concluded. "If it could be scientifically proven that raising the minimum wage to $10 per hour would result in more Americans leading healthier, more productive lives, then the burden would still fall on law makers to implement that finding in the form of policy. That can be a challenge and, until this culture changes, the gap in overall health quality between minority populations and the rest of society will always exist."

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

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NIH seeks new ideas for Common Fund Programs

NIH leadership is reaching out to internal and external scientists and stakeholders for ideas about new research programs for 2013, to be supported by its Common Fund, a mechanism enacted into law by Congress through the 2006 NIH Reform Act with the goal of accelerating discovery. NIH is accepting input through Sept. 14 at its strategic planning website.

The Common Fund supports cross-cutting, trans-NIH programs that require participation by at least two NIH Institutes or Centers (ICs) or would otherwise benefit from strategic planning and coordination. The Fund supports exceptionally innovative programs that are inherently high risk but have the potential for high payoff by catalyzing research across all of NIH and in the biomedical research community.

The requirements for the Common Fund encourage collaboration across the ICs while providing the NIH with flexibility to determine priorities for Common Fund support. NIH wants to know about ideas that have the potential to fundamentally change how we think about, support, or do research in a specific field, or to create a new field altogether.

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Superfund awards support early-career researchers

By Anne Johnson

Three budding environmental health researchers are expanding their scientific horizons thanks to a new award established by the Superfund Research Program (SRP). The KC Donnelly Externship Award Supplement, which honors the memory of longtime SRP grantee and celebrated environmental health researcher Kirby Donnelly, Ph.D., supports SRP trainees pursuing translational and transdisiplinary opportunities.

Graduate student Celys Irizarry (Photo courtesy of Celys Irizarry)

Named as winners Aug. 3, Xianai Wu, Ph.D., Alvine Mehinto, Ph.D., and Celys Irizarry are the first recipients of the externship award, which will be issued annually. By supporting talented graduate students and postdoctoral researchers, the award honors Donnelly's dedication to fostering the next generation of environmental health scientists.

"This is a very exciting opportunity for SRP trainees, and we hope that many of them will take advantage of this chance to expand their training experience while working at their SRP center," said NIEHS Health Scientist Administrator Danielle Carlin, Ph.D., who coordinates the award program. "As part of the SRP Strategic Plan, the SRP is focusing on the trainees, because they are the future of environmental health and engineering research."

The externship provides funding for supplies, travel, and housing costs for up to three months, not to exceed $10,000 per recipient, for SRP trainees to pursue opportunities at other SRP centers, government laboratories, and state, local, or tribal agencies.

Postdoctoral fellow Alvine Mehinto (Photo courtesy of Alvine Mehinto)

Promoting translational and transdisciplinary research

The externship awards encourage SRP trainees to explore how their areas of research can be enhanced by translational or transdisciplinary opportunities and experiences. This year's recipients represent a diverse array of environmental health perspectives:

- **Celys Irizarry** is a graduate student at the University of Puerto Rico, Mayagüez campus, through the Northeastern Superfund Research Program. For her externship, Irizarry will work with the U.S. Environmental Protection Agency (EPA) Caribbean Environmental Protection Division and the Puerto Rico Department of Health to collect water-quality data for chemicals that may be associated with preterm birth. Her findings will be used to help the agencies improve their water-quality assessment models. "The KC Donnelly traineeship has provided me with not only the ability to expand my research, but the opportunity to further develop many skills and professional goals," said Irizarry. "It also allows me to establish professional links in the government agencies."

- **Alvine Mehinto, Ph.D.**, is a postdoctoral researcher at the University of Florida. For her externship, she will integrate omics data from her previous experiments on largemouth bass with new research at the University of California, Berkeley on yeast models to study various contaminants' pathways of toxicity. "This externship is an amazing opportunity to bring new dimensions to my studies and use novel computational methods to identify mechanisms of toxicity in living organisms exposed to a variety of Superfund chemicals," said Mehinto.

- **Xianai Wu, Ph.D.**, is a postdoctoral researcher at the University of Iowa, where her research focuses on PCBs and their metabolites. For her externship, she will conduct animal studies at the University of California, Davis to learn metabolomic techniques that are not used in her current laboratory. "The externship award allows me to obtain hands-on training with state-of-the-art metabolomic techniques, which will benefit me both as an Iowa Superfund Research Program laboratory researcher and future regulatory toxicologist," said Wu. "The findings from my experiments will assist with the discovery of biomarkers of PCB 126 exposure that can be used in human biomonitoring studies, and guide the design of laboratory and, ultimately, human studies aimed at dietary interventions to prevent PCB-induced diseases."

Postdoctoral fellow Xianai Wu (Photo courtesy of Xianai Wu)

Externship award recipients will present their research at the SRP annual meeting Oct. 24-26 in Lexington, Ky. The next award application deadline is March 21, 2012. For more information, visit http://www.niehs.nih.gov/research/supported/srp/training/training7_s1.cfm.

Honoring a legacy

Donnelly served as department head of environmental and occupational health at Texas A&M University, before he passed away on July 1, 2009 (see story). During his 30-year career, Donnelly examined environmental exposure and genotoxicity of complex chemical mixtures around the globe, conducting studies in Eastern Europe, China, and across the United States. His scientific contributions and outreach efforts changed many people's perceptions of environmental health problems.

In addition to his scientific accomplishments, Donnelly was a dedicated mentor to his students and postdoctoral researchers. He is remembered for his emphasis on enhancing the impact of environmental health research through transdisciplinary partnerships, translational research, and outreach activities. A gifted leader, Donnelly initiated the SRP Bioassay Network to bring together researchers from six SRP Centers and scientists from EPA Regions and Headquarters. He also championed many community outreach and education activities to improve the health of people exposed to environmental contaminants.

Donnelly was the associate director for the NIEHS-funded Superfund Research Program at Texas A&M University (TAMU). (Photo courtesy of Melany Borsack and TAMU Health Science Center)

(Anne Johnson is on the staff of MDB, a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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SRP celebrates an important milestone

By Rebecca Wilson

In August, the Superfund Research Program (SRP) issued the 200th edition of the SRP Research Briefs. This issue celebrates nearly 15 years of disseminating cutting-edge scientific findings to researchers, regulators, educators, non-profit groups, and environmental and engineering firms across the globe.

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

According to SRP Program Analyst Beth Anderson, the Research Briefs began in 1997 and were inspired by a discussion with Samuel Wilson, M.D., who was the NIEHS deputy director at the time. The Briefs were aimed at U.S. Environmental Protection Agency remedial project managers and risk assessors as a way to share the results of the latest research across the program. Faced with a readership trained in everything from basic biomolecular research to mechanical engineering, the Briefs quickly adopted an informal style that makes even the most complex science accessible to everyone.

"The Research Briefs have been a resounding success with our stakeholders," says Anderson. "They have been an effective tool in disseminating SRP research among those who do not traditionally follow the scientific literature."

Over time, the readership of the Briefs has widened and grown, and now includes subscribers scattered across the globe. Today, there are subscribers from 54 countries, including environmental health officials from 35 federal agencies, 46 state agencies, and 12 local agencies; leaders of five Tribal governments; students, teachers, and researchers from 240 colleges and universities; members of 70 not-for-profit organizations; and employees and affiliates of 82 for-profit engineering and environmental firms.

Media distribution has also expanded. The format of the emails became more sophisticated and graphically intense, print-ready pdfs are now available for each Brief, and, recently, collaborators began adding podcasts. Research Briefs are available on the SRP website as individual web pages and pdfs as well as through iTunes (see Research Brief 198).

To subscribe to the Research Briefs, please send an email to NIEHS contractor Maureen Avakian. Collaborators are also always looking for ideas and feedback, which can be sent to the same email address.

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

Email feedback about Research Briefs

From subscriber Ted Schettler, M.D., science director of the Science and Environmental Health Network

"I can tell you that I regularly forward SRP research findings (your Research Briefs) to several fairly large listserves, reaching many different NGOs [non-governmental organizations] and individuals. This kind of summary is very useful and is much appreciated. I am entirely convinced that reaching community groups/diverse NGOs is essential for helping to develop sound public policy."

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Postdocs receive Gordon Conference travel awards

By Ian Thomas

In recognition of their outstanding work at NIEHS and NTP, postdocs Zhengyu Yin, Ph.D., Huiming Gao, Ph.D., and Mamta Behl, Ph.D., have earned travel awards to present posters of their work at the Gordon Research Conference (GRC), an international gathering held Aug. 7-12 in Andover, N.H.

For more than 75 years, the Gordon Research Conference has offered a variety of uniquely informal meetings each year, where leading minds from around the globe can come together to discuss their work and identify future challenges facing their respective fields. For some, however, it's also a chance to learn new things.

Reflections on the Gordon experience

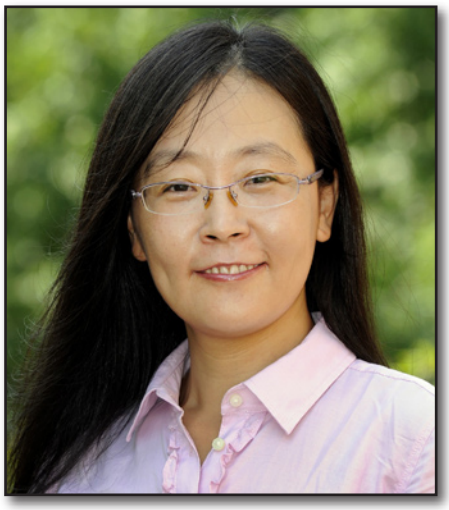
"The Gordon Conference was a remarkable opportunity," noted Gao, a member of the NIEHS Neuropharmacology Group. "Working in such a relaxed and informal setting with both experts and peers was a fantastic experience, and I'm really grateful to NIEHS and the GRC staff for the chance to attend."

"As a toxicologist in training, the Gordon Conference was a great opportunity to step outside of my comfort zone and broaden my knowledge of a number of areas that were previously unfamiliar to me," explained Yin, a visiting fellow with the Institute's Cell Biology Group. "Therefore, conferences like these only serve to better prepare me for my future role as a regulatory toxicologist."

With 460 conferences and seminars slated for 2011 and 2012, GRC meetings will be held in California, Texas, North Carolina, and several states in New England, while international meetings will take place in Italy, China, and Switzerland. Still, for some young scientists, there really is no place like home.

"As a trainee at the NTP, I work with a brilliant and dynamic team of scientists who have contributed heavily to my career in this field," explained Behl, a research fellow in the NTP Toxicology Branch. "The competitive research, constructive criticisms, and great team spirit here provide a phenomenal environment, whereby fellows can expand their understanding of toxicology, grow their knowledge of toxicology testing, and hone their skills as up and coming scientists."

Behl showcased her work, titled "Peripheral Neuropathy in Rats Exposed to Styrene Acrylonitrile Trimer." (Photo courtesy of Steve McCaw)



Gao's work examined the role of neuroinflammation in Parkinson's disease. (Photo courtesy of Steve McCaw)

Yin's study could lead to new therapeutic approaches for radiotherapy and other anticancer procedures. (Photo courtesy of Steve McCaw)

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

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NIEHS seeks director of clinical research

NIEHS is accepting applications through Sept. 30 from senior investigators qualified for a tenured appointment as director of its Clinical Research Program, a senior leadership position within the NIEHS Office of the Scientific Director. The program includes an on-site Clinical Research Unit in Research Triangle Park, N.C., and components at the NIH Clinical Research Center in Bethesda, Md.

NIEHS supports and conducts research that contributes to the basic understanding of biological and chemical processes, the contributions of environmental agents to human disease and dysfunction, and the underlying mechanisms of environmentally associated diseases.

The director of the Clinical Research Program is responsible for the development, administration, coordination, and oversight of investigator-initiated clinical research; provides general advice to the director and scientific director of NIEHS on matters relating to human and clinical studies; supervises the Office of Research Compliance; and develops policies and programs for the conduct of clinical research at NIEHS.

The director of the Clinical Research Program is responsible for creating and maintaining a research environment in which clinical findings influence the direction of laboratory studies, and laboratory findings are applied back to the clinical and clinical research communities.

For more detailed information about the position, duties, and qualifications, visit the Jobs at NIEHS website or contact NIEHS at the following address:

Stephanie Jones (Vacancy Number DIR 11-03)
National Institutes of Health
Office of Human Resources
National Institute of Environmental Health Sciences
P.O. Box 12233, Mail drop K1-01
Research Triangle Park, NC 27709
Email: collinsonj@mail.nih.gov

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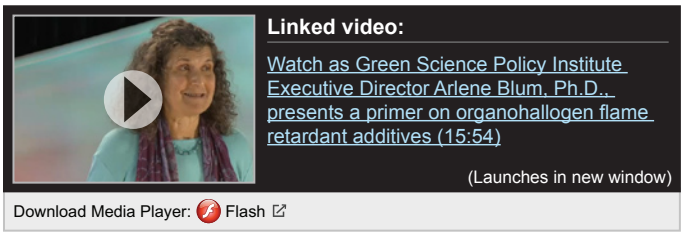
Science Notebook

Birnbaum speaks at Dioxin 2011

By Eddy Ball

NIEHS/NTP Director Linda Birnbaum, Ph.D., was a featured speaker at two sessions during the weeklong Dioxin 2011 in Brussels, Belgium. The presentations were part of the 31st International Symposium on Halogenated Persistent Organic Pollutants (POPs), Aug. 21-25, and a post-symposium Flame Retardant Science and Policy Session sponsored by the Green Science Policy Institute Aug. 26, as part of its Flame Retardant Dilemma series of workshops.

Both of Birnbaum's talks emphasized that NIEHS and NTP are not regulatory agencies. However, she also impressed upon her audience the importance of NIEHS/NTP scientific findings in shaping regulatory decisions by the U.S. Environmental Protection Agency, U.S. Food and Drug Administration, U.S. Consumer Product Safety Commission, and Occupational Safety and Health Administration. (Photo courtesy of Steve McCaw)



Birnbaum spoke on "The Potential Role of Developmental Chemical Exposures in Contributing to the Obesity Epidemic" Aug. 25, which she co-authored with her protégée, Michele La Merrill, Ph.D., of the Mt. Sinai School of Medicine. The next day she explored the question, "How scientists, government, and NGOs [non-governmental organizations] can work together so good science supports public policy."

POPS as obesogens

Birnbaum framed her presentation on obesogens around a hypothesis that may explain the dramatic rise in rates of obesity worldwide, especially in economically developed countries and among urbanized populations. "Early life exposure to environmental chemicals," she speculates, "is a contributing cause of the obesity epidemic, due to the potentially critical role of prenatal and perinatal metabolic programming in later risk of obesity."

In the course of her presentation, Birnbaum reviewed research on the association between outcomes related to obesity and developmental exposure to several POPs in animals and humans. The research included studies of exposure to dioxins, polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDT), hexachlorobenzene (HCB), polybrominated flame retardants, and perfluorinated chemicals (PFCs).

While the results have been mixed, Birnbaum explained, a sufficient number of positive associations have been found to justify additional, longer range studies to explore the connection between early life exposures and outcomes in later adulthood.

"Experimental studies should extend into adulthood," she concluded, "and prospective epidemiology studies should present data with and without adjustment by lipids, if experimental evidence suggests chemicals affect lipid homeostasis."

Birnbaum also urged researchers to evaluate critically non-linear dose response, and build on preliminary findings about the roles of peroxisome proliferator-activated receptor-gamma (PPAR-gamma) and aryl hydrocarbon receptor (AhR) in obesity measures. PPAR-gamma, she explained, is considered a master regulator of adipogenesis, and AhR, the receptor found responsible for essentially all the effects of dioxin and dioxin-like compounds, appears to have an innate role in insulin and lipid homeostasis.

Science and public policy

Birnbaum moved seamlessly from the bench to public health considerations in her second talk in Brussels. She addressed the issue of flame retardants and their potential to affect human health, as a foundation for her discussion of the use of science in regulatory decision-making and the importance of working with communities.

As Birnbaum explained, halogenated fire retardants are a public health concern because of their widespread use in the U.S. in electronics, building insulation, polyurethane foam, and wire and cable. The chemicals have been found in breast milk, and research suggests that they are a potential thyroid hormone disruptor and developmental neurotoxicant. Some brominated fire retardants, she explained, are persistent and found in the blood of humans and animals living as far away from their sources as the Arctic. She cited studies indicating that levels have been doubling every two to five years since the 1970s.

Fire retardants brought Birnbaum to the importance of NIEHS funding for experimental studies in raising awareness of potential public health issues, and the role of NTP gold-standard chemical bioassays in providing science directly for regulatory use. Looking toward the emergence of predictive toxicology, she said, "Biological systems are incredibly complicated, and we need to look for perturbations in various developmental functions and consider multiple important endpoints." To reduce chemical hazards and exposures, the regulatory framework must incorporate all available data.

Birnbaum concluded her presentation with a discussion of the importance of partnerships among NIEHS and the communities and stakeholders who have an interest in how science is used. These communities and stakeholders include organizations performing NIEHS-funded outreach and education, a powerful coalition of grassroots advocacy organizations known as Public Interest Partners, and the larger environmental health community that is the target audience for the NIEHS-funded journal Environmental Health Perspectives.

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Mardis discusses current genomic technologies and cancer models

By Archana Dhasarathy

Elaine Mardis, Ph.D., co-director of The Genome Institute at Washington University in St. Louis, presented a seminar titled "Genomic studies of mouse models of human cancer" Aug. 4 at NIEHS. She was hosted by Jef French, Ph.D., staff scientist and acting chief of the NTP Host Susceptibility Group.

Mardis is a leader in the field of cancer genomics, and directs the Genome Institute's efforts in advancing next-generation sequencing technologies. By comparing the genomes of tumor and normal samples, she maintains, researchers will be better able to identify changes in the genome that lead to cancer, and thus provide more personalized diagnoses and treatments.

The promise of next generation sequencing technologies

Whole genome sequencing has come a long way since the human genome was first sequenced ten years ago. The sequencing technologies available today are powerful enough to allow single base-pair level analysis of changes that occur in the genome of people with cancer.

These analyses include variations in the number of copies of specific genomic regions, mutations in DNA sequence, and other structural variants in DNA. "I'm always amazed that from a 30-fold coverage of the genome you can detect so many different types of alterations," said Mardis. Her lab further validates the information from all this sequencing, to ensure that variations and mutations they've identified are indeed different between normal and tumor samples.

Mardis plays a key role in The Cancer Genome Atlas consortium, which catalogues mutations in cancers obtained through genomic sequencing. (Photo courtesy of Steve McCaw)

Leukemia genomes: Using mice to understand humans

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML), in which an abnormal fusion of parts of chromosomes results in the creation of a promyelocytic leukemia-retinoic acid receptor alpha (PML-RARA) fusion oncogene. While this mutated version of DNA can initiate APL in mice, there are other mutations that are also important for this disease.

In order to identify these other mutations, Mardis' group used a mouse model of cancer, wherein mice expressing the PML-RARA oncogene developed APL. They sequenced the tumor genome of one mouse that developed APL, and were able to identify three mutations important in causing the disease. Importantly, similar mutations were found in both additional mouse samples, as well as in human AML samples, thus helping them discover functionally important mutations in human cancers.

"In humans who have leukemia, you have the luxury of collecting samples from patients throughout the progression of the disease," said Mardis. Samples can be collected at the time of diagnosis, at the start of chemotherapy, and followed up for several months after chemotherapy. Sequencing such samples gives an indication of what kinds of mutations and clonal populations are lost as a result of chemotherapy, and also addresses the question of what mutations arise when tumors relapse.

NIEHS Deputy Director Rick Woychik, Ph.D., had several questions for Mardis following her talk. (Photo courtesy of Steve McCaw)

Breast cancer models

Although scientists understand much about the biology of cancer metastasis, information about the genomic causes for metastasis is still largely unknown. Mardis and her colleagues applied their genomics expertise to analyze both normal and tumor samples from patients with breast cancer. The cells from the biopsy were introduced into mice to produce a xenograft tumor, so they could investigate how the tumor behaved and if it metastasized. The researchers then performed whole-genome sequencing of the trio — normal cells, primary tumor, and mouse xenograft tumor — to search for genomic changes.

They found that the primary tumors differed from the xenograft tumors, mainly in the prevalence of genomic mutations. They also determined that the same type of primary tumor — although from different patients — can develop either into a tumor similar to the primary tumor or a new type of tumor entirely. For instance, a luminal type of breast cancer could develop into a luminal cancer in the mouse xenograft but, in some cases, manifested as a basal type of tumor instead.

French, right, monitored the question and answer session. (Photo courtesy of Steve McCaw)

"If you can detect mutations that are highly specific to a patient, this could lead to personalized medicine and individually tailored therapies," Mardis explained. The results provide insight into how cancer genomes evolve as the disease progresses.

In collaboration with other groups, Mardis is also involved in sequencing other mouse models of breast and other cancers. Thus far, several types of human cancers have been sequenced including leukemia, breast, lung, brain, prostate, multiple myeloma, and ovarian cancers.

Next generation sequencing 101

Whole genome sequencing involves figuring out the precise arrangement of all three billion bases of an individual's DNA. To achieve this goal, sequencing machines first generate short stretches of DNA sequence, called reads, that contain random bits of the genome. Computer programs are then used to map these reads, usually by comparing them to a previously sequenced reference genome.

Several parameters are important for speed and accuracy of sequencing. The first parameter is read length, which refers to the length of sequence generated in each read. Current machines can generate reads between 40 and 150 nucleotides. The longer the reads, the easier it is to align them to the reference genome. Just as in a jigsaw puzzle, the larger pieces are easier to fit into place. Reads that are too short might not map uniquely to the genome, and are, hence, problematic. On the other hand, longer reads may take several extra days to generate. Longer reads are also more expensive and generally less accurate than shorter reads.

Besides read length, the number of sequencing reads that can be produced in a single instrument run for a given cost is another important factor. Current instruments routinely produce tens of millions of sequence reads, with numbers constantly improving as technology develops.

Read coverage refers to the total number of reads needed to ensure that every single base in the genome has been sequenced — the greater the coverage, the better the accuracy. However, this can also make it more expensive. Several groups are in a race to develop cheaper, faster, and more accurate means of whole genome sequencing.

(Archana Dhasarathy, Ph.D., is a postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis.)

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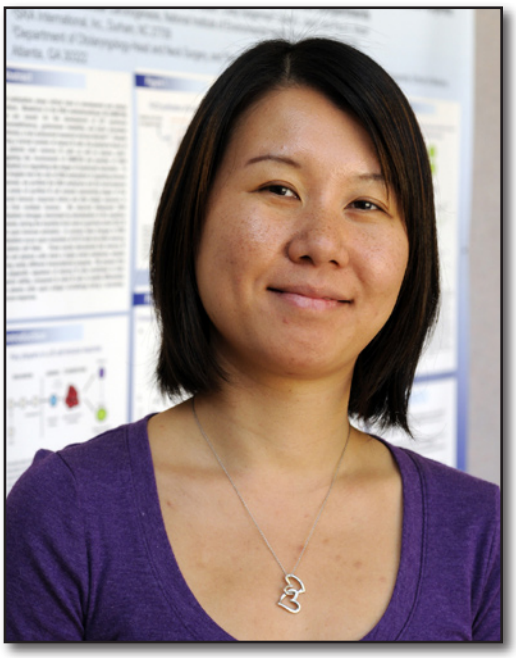
Fellow wins WSA award for research excellence

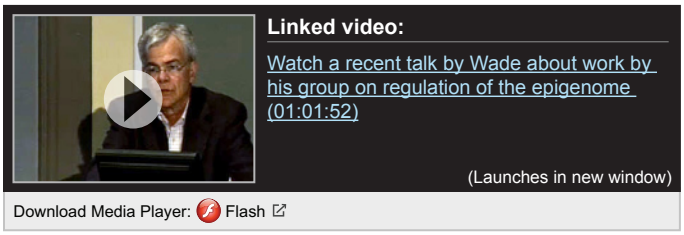
By Archana Dhasarathy

Postdoctoral fellow Anne Lai, Ph.D., has been selected to receive one of two NIH WSA (Women Scientist Advisors Committee) Scholar Awards. Her abstract, titled "DNA methylation primes the memory B cell epigenome for plasma cell differentiation," was selected from a pool of all 2012 female FARE (Fellows Award for Research Excellence) award winners, by a panel of WSA representatives from across the NIH. This is the second year for the award.



Lai said the WSA award came as a very pleasant surprise. (Photo courtesy of Steve McCaw)

Lai is currently an Intramural Research and Training Award (IRTA) fellow in the NIEHS Laboratory of Molecular Carcinogenesis Eukaryotic Transcriptional Regulation Group, headed by Paul Wade, Ph.D. An immunologist by training, Lai successfully applied her knowledge of the immune system towards deciphering the role of epigenetics in the adaptive immune response.



The adaptive immune response

When naïve B cells in the blood encounter a foreign antigen, they respond by active mutation of their antibody-encoding DNA. These mature B cells, now referred to as activated B cells, can then differentiate into a vast number of antibody-secreting plasma cells in specialized structures called germinal centers. The antibodies generated by the plasma cells, which are specific to the invading antigen, help the body launch a counter attack.

In addition to plasma cells, activated B cells can also differentiate into memory B cells, which can more efficiently transition into plasma cells. Memory cells can thus recognize and mount a superior immune response against the same antigen if it is encountered in the future.

Several studies in the past have speculated that epigenetic changes could play important roles in functionally distinguishing the memory cells and naïve B cells from each other. One such epigenetic modification involves DNA methylation, or the addition of a methyl group to the cytosine of a cytosine-guanine (CG) pair in the DNA, which is generally associated with gene silencing.

Epigenetic signatures contribute to the immune response

Lai and colleagues used a genome-wide approach to examine the role of DNA methylation in the adaptive immune response. They purified four different human B cell subsets (naïve, mature, plasma, and memory B cells), representing stages of the immune response before and after antigen exposure, from human tonsils. DNA microarrays were then used to query these cells for differences in their DNA methylation and gene expression profiles.

They found widespread DNA methylation changes between naive and memory B cells, many of which were enriched near immune response genes, implying that DNA methylation was functionally relevant at these genes. This was interesting, because the gene expression profiles of these B cell subtypes are remarkably similar. In contrast, there were fewer differences in DNA methylation between memory B cells and plasma cells, despite their vastly different gene expression programs. The epigenetic differences between naïve and memory B cells may partially explain why memory B cells are more efficient in differentiating into plasma cells.

"Anne's work is significant, because immunologists have long suspected that epigenetics plays an important role in immunologic memory, and there is evidence to support this in T cells. Anne's work provides an indication that this is likely to be the case for B lymphocytes as well," said Wade.

Lai will be presented with a plaque and an award ribbon for her poster during the NIH Research Festival FARE awards ceremony this October.

(Archana Dhasarathy, Ph.D., is a postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis).

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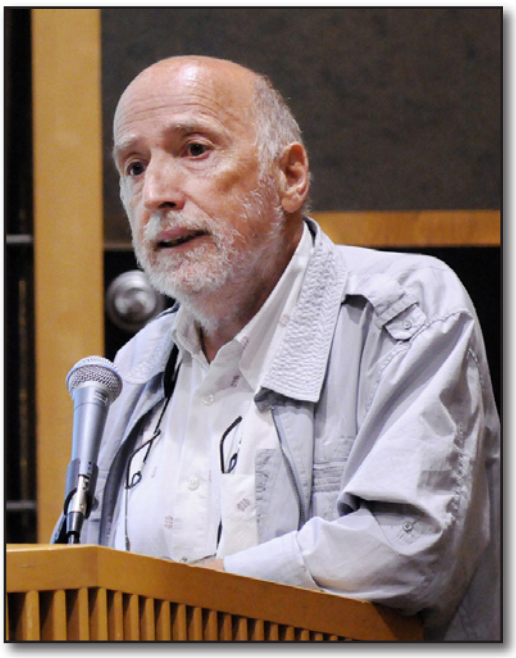
Fuchs discusses replication past DNA damage

By Jeffrey Stumpf

Robert Fuchs, Ph.D., reacquainted himself with many familiar faces at NIEHS and shared his research about mechanisms of replication past damaged DNA, during his talk Aug. 1 at NIEHS. The renowned DNA polymerase expert from the Centre national de la recherché scientifique (CNRS) in France presented his discoveries for the Laboratory of Molecular Genetics (LMG) Fellows Invited Guest Lecturer Seminar Series.



In the course of his presentation, Fuchs also invited postdocs to visit beautiful Marseille, France and study DNA replication past damaged bases in his lab at the Centre national de la recherché scientifique. (Photo courtesy of Steve McCaw)

Environmental factors and carcinogens cause DNA-damaging lesions that, if not removed, block replication by DNA polymerases. The replication machinery must bypass the damage, in a process called translesion synthesis (TLS), or abort replication. Because abort replication leads to genome instability and cell death, TLS is advantageous for cell survival, but is mutagenic.

Fuchs uses the bacterium *E. coli* to study genetic controls that maintain DNA damage tolerance. NIEHS LMG researcher Roel Schaaper, Ph.D., also studies *E. coli* DNA replication and believes that the contribution of multiple polymerases to mutagenesis is important for environmental health.

"The sustained work by Robert Fuchs over the last two decades has been instrumental in teaching us about the roles of the various DNA polymerases," Schaaper explains, "particularly when DNA replication encounters a blocking DNA adduct induced by environmental chemicals or ultraviolet light."

Using plasmids to measure mutagenic TLS

Fuchs pioneered a plasmid-based system that studies the genetic mechanisms for bypassing replication-blocking lesions. The plasmid, a small circular strand of DNA, contains four important attributes:

- An antibiotic resistant gene, to select for cells with plasmids
- A damaged base
- A short region of unique sequence on the strand with the damaged base to identify plasmids that resulted from TLS
- A mutant variant of *lacZ* near the lesion to measure mutagenic TLS as *lacZ* mutations that allow wildtype function to make the colony turn blue

Although plasmids are convenient for genetic engineering, Fuchs is also ready to expand his studies to other replication mechanisms. "In the plasmid system, we can completely measure mutagenic and error-free TLS but not the so-called damage avoidance pathways, and now we are working on a system that will allow us to measure damage avoidance and TLS at the chromosomal level," Fuchs explained.

In addition to hosting Fuchs's visit, Sarah Swerdlow, Ph.D., moderates a stimulating question and answer session after Fuchs's presentation. Swerdlow is a postdoctoral trainee in the NIEHS Mechanisms of Mutation Group, which also studies mutagenesis due to changes in nucleotide pools. (Photo courtesy of Steve McCaw)

Increased dNTP concentration pushes polymerases past the lesion

A long-standing observation from Fuchs' research is that TLS occurs at a low frequency under normal conditions, but 20-fold more frequently after UV exposure. The increase of the levels of DNA polymerase V (Pol V), which is necessary for replicating past the UV-damaged base, is presumably responsible for the increase of TLS. However, when Pol V was artificially induced without UV exposure, TLS frequency remained low. So, what else was necessary for UV-induced TLS?

To answer this riddle, Fuchs reported that UV exposure increases ribonucleotide reductase, the protein that limits the production of the building blocks of DNA or deoxyribonucleotides (dNTPs), and therefore increases dNTP concentration. Strains that increase both dNTP and Pol V concentration in the absence of UV allowed TLS. UV exposure only increases dNTPs 3-fold, but was enough, Fuchs argues, to tip the delicate balance for TLS.

Schaaper, right, and Mark Itsko, Ph.D., left, ponder the conclusions from Fuchs' studies. Schaaper leads the Mechanisms of Mutation Group in which Itsko performs his postdoctoral studies on E. coli genetics. (Photo courtesy of Steve McCaw)

"The level of dNTP is normally low, so we are working in a range where small changes matter," postulated Fuchs.

Small changes in dNTPs matter especially for DNA polymerases. The genome is mostly replicated by DNA polymerase III complexes (Pol III), which contain an exonuclease protein that proofreads mistakes if the wrong nucleotide is incorporated. However, increased dNTP concentration favors replication rather than proofreading,

and affects the interplay among DNA polymerases and exonucleases during TLS.

"What I find fascinating is to understand the genetic control of the response to increasing dNTPs," Fuchs stated. "It's surprising that this hasn't been explored."

Schaaper agrees, "The discovery that elevation of the dNTP levels is part of the DNA damage response, which improves survival at the cost of high mutagenesis, is an important new finding."

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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Michael Resnick, Ph.D., right, takes note of Fuchs' findings during the lecture. Resnick is the head of the Chromosome Stability Group at NIEHS. (Photo courtesy of Steve McCaw)

Study identifies role of mold in asthma development

By Eddy Ball

In a new study funded in part by NIEHS, researchers led by scientists at the University of Cincinnati (UC) found that mold exposure during a critical window of development was associated with a three-fold greater risk for asthma later in childhood. The study appeared in the August issue of Annals of Allergy, Asthma, and Immunology, the scientific journal of the American College of Allergy, Asthma, and Immunology.

Isolating an environmental trigger could lead to better informed preventive efforts to reduce the incidence of asthma, a condition on the rise nationwide and an important public health concern. According to previous studies, asthma is estimated to cause several thousand deaths annually and cost more than $15 billion per year in direct medical expense.

"Early life exposure to mold seems to play a critical role in childhood asthma development," Tiina Reponen, Ph.D., lead author on the study and a UC professor of environmental health, was quoted as saying in a UC Healthnews press release. "Genetic factors are also important to consider in asthma risk, since infants whose parents have an allergy or asthma are at the greatest risk of developing asthma."

"This study should motivate expectant parents — especially if they have a family history of allergy or asthma — to correct water damage and reduce the mold burden in their homes to protect the respiratory health of their children," Reponen said in an interview with Amanda Harper of UC Healthnews. (Photo courtesy of the University of Cincinnati)

The findings also have implications for reducing health disparities, since asthma occurs at higher rates in low-income communities where mold is more likely to occur in residences, especially those without air conditioning. The standardized approach used in the study may offer outreach workers a more sensitive assessment for accurately identifying homes with potentially harmful levels of mold.

Using a standardized approach to quantify mold exposures

The research team analyzed seven years of comprehensive data for 176 children who were a subset of the more than 700 children participating in the prospective Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS), led by Grace LeMasters, Ph.D., who is also the lead researcher on research and training grants from NIEHS. CCAAPS looked at the effects of environmental particles on childhood respiratory health and allergy development. Participants were identified during infancy as at high risk to develop allergies based on having at least one parent with an allergy.

Using the Environmental Relative Moldiness Index (ERMI), a DNA-based tool developed by the U.S. Environmental Protection Agency (EPA) for PCR analysis that measures 36 different molds in floor dust, the team identified homes with a high ERMI rating for exposure to molds. The homes were evaluated when study participants were 1 and 7 years old, and children were evaluated for asthma at age 7, the age at which asthma can be accurately diagnosed.

LeMasters has served as lead researcher on NIEHS grants since 1999 and now oversees three grants to UC. She is also a member of the NIEHS National Advisory Environmental Health Sciences Council. (Photo courtesy of the University of Cincinnati)

Higher moldiness associated with asthma at age 7

Results of the study indicated that the odds of developing asthma were more than two-fold if a child lived in a home with a high ERMI value during infancy. Reinforcing the utility of ERMI ratings of moldiness was another finding from the study, which failed to find an association between visual and olfactory observations of moldiness — a subjective approach — in the homes of children at ages 1 and 7, with asthma diagnosis at age 7.

"This study does not prove that exposures to mold are a cause of asthma," the authors concluded, "but it does provide impetus to reduce the mold burden in infant homes based on the ERMI."

In addition to NIEHS support for CCAAPS, funding for the study was provided by the U.S. Department of Housing and Urban Development and the EPA Communities in Action Asthma Initiative.

Citation: Reponen T, Vesper S, Levin L, Johansson E, Ryan P, Burkle J, Grinshpun SA, Zheng S, Bernstein DI, Lockey J, Villareal M, Khurana Hershey GK, Lemasters G. 2011. High environmental relative moldiness index during infancy as a predictor of asthma at 7 years of age. Ann Allergy Asthma Immunol 107(2):120-126.

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UC grantees' lab-on-a-chip detects toxic heavy metals in humans

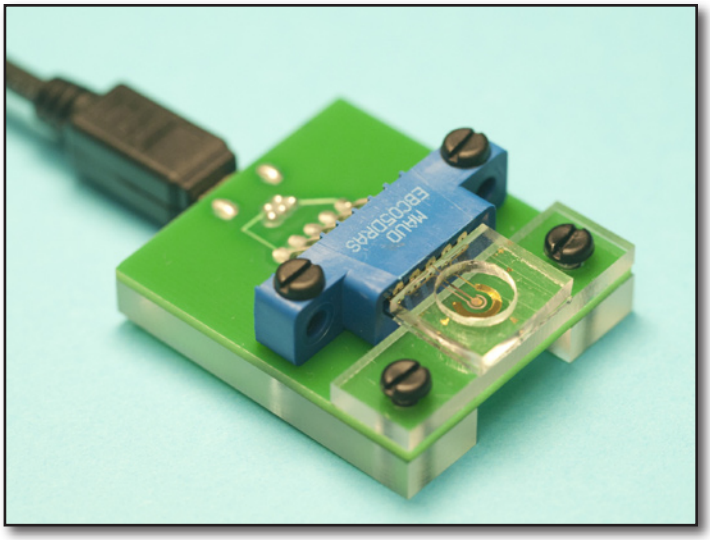
By Ed Kang

An ongoing NIEHS-funded study at the University of Cincinnati (UC) examining the health effects of manganese on children will soon have a new tool at its disposal — an inexpensive, highly accurate, lab-on-a-chip sensor. This new technology can quickly measure not only manganese, but also other metals such as lead and cadmium, from just a few drops of blood.

That the UC study is first to benefit from this innovation is no coincidence. The chip was engineered at UC and its development was also supported by NIEHS.

Portable, inexpensive, and minimally invasive

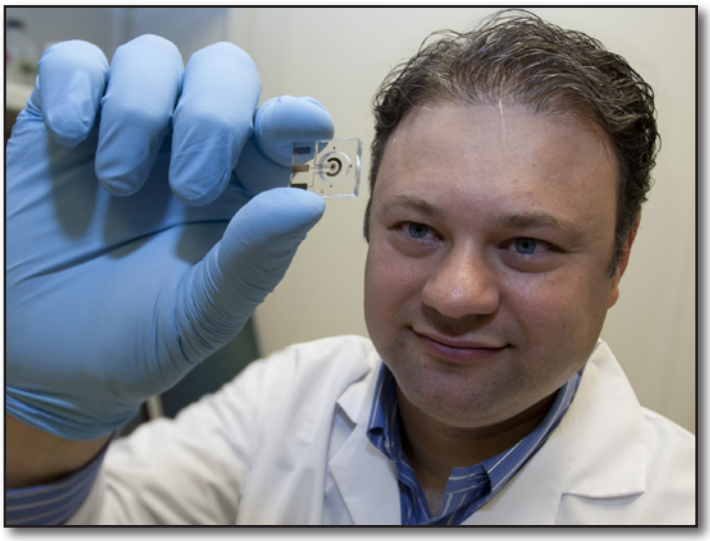
The sensor, dubbed the multi-metal chip, puts a new spin on traditional whole blood analysis, which is the most common method for determining metal exposure for the assessment of health outcomes. But while conventional methods of sample collection can be traumatic for children and relatively slow to produce results, the UC solution will be capable of rapid analysis, 10-15 minutes, of a blood sample of just two drops from a single lancet puncture.



The new sensor efficiently strips highly electronegative heavy metals out of blood to measure their concentration. In a clinical setting, it can give feedback to researchers and families in only a few minutes. (Photo courtesy of Dottie Stover at UC)

"The conventional methods for measuring manganese levels in blood currently requires about five milliliters of whole blood sent to a lab, with results back in 48 hours," said Ian Papautsky, Ph.D., lead researcher and associate professor of electrical and computer engineering at UC. "For a clinician monitoring health effects by measuring these levels in a patient's blood, you want an answer much more quickly about exposure levels, especially in a rural, high-risk area where access to a certified metals lab is limited."

This low-cost and disposable solution will be portable and usable anywhere, continued Papautsky.



Papautsky, above, and his collaborators have developed a new tool that is not only child friendly, requiring only a few drops of blood for testing, but also environmentally friendly. Instead of mercury, the critical electrodes are made from bismuth, a less toxic compound. (Photo courtesy of Dottie Stover at UC)

Targeting manganese

In fact, the concept for a diabetes-like sensor for metals was the brainchild of Papautsky and Erin Haynes, Ph.D., an environmental health researcher with UC, who is studying the exposure and possible effects of manganese on neurological and cognitive development in children. The sensor was initially conceived as a way to easily evaluate the bioaccumulation of manganese in children residing near the Marietta, Ohio area, a rural Appalachian community that is home to a ferromanganese refinery.

Manganese is an essential element in human bodies, but dangerous in excess. Infants and children may be at greater risk for manganese neurotoxicity than adults, and some studies have linked high levels of exposure to movement disorders.

The chip is scheduled for initial field testing in Marietta in 2012 — first on adults, then on children, once the technology has proven safe and effective. Should the practical test be successful, the multi-metals chip will have demonstrated its potential in large-scale settings. Future applications include point-of-care devices where practitioners need immediate feedback on heavy-metal levels such as in clinical, occupational, and research settings.

Public health and research applications

David Balshaw, Ph.D., is the NIEHS program administrator for the grants. "Having a tool like this, that is both cost effective and child friendly, can potentially transform how information is collected in the field," he said. "Any parent will recognize the benefit of a small pin prick that draws 50 times less blood than typical methods."

Balshaw added, "Being able to measure a host of metals and possibly other environmental factors down the road really opens the door to endless public health and research applications."

The concept of the device and its development are profiled in the August issue of the journal Biomedical Microdevices.

Citation: Jothimuthu P, Wilson RA, Herren J, Haynes EN, Heineman WR, Papautsky I. 2011. Lab-on-a-chip sensor for detection of highly electronegative heavy metals by anodic stripping voltammetry. Biomed Microdevices 13(4):695-703.

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

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Highest levels of flame retardant chemicals reported in California pregnant women

By Linh Pham

In a new study, funded in part by NIEHS, a team of scientists reported very high levels of polybrominated diphenyl ethers (PBDEs) and their hydroxylated metabolites (OH-PBDEs) among California pregnant women. Median levels of certain PBDEs and OH-PBDEs were the highest reported to date among pregnant women worldwide.

PBDEs are ubiquitous and persistent flame retardant chemicals found in the environment. Exposure to them during pregnancy poses a public health concern because the chemicals have been linked with neurodevelopmental defects and hormone disruption, according to the authors of the study.

The findings appeared online Aug. 10 in Environmental Science and Technology, the result of collaboration among scientists from the University of California, San Francisco (UCSF), the University of Massachusetts Amherst, and the California Department of Toxic Substances Control.

Zota attributes the high PBDE levels in pregnant women to California's strict flammability regulations that led manufacturers to add flame retardants to a wide variety of products from electronics to furniture, between the 1970s and 2004. She has studied PBDEs since 2008 (see story) and has co-authored a number of studies on the topic. (Photo courtesy of Ami Zota)

Exposure to PBDE linked with defective thyroid hormone signaling

Quoted in a UCSF press release, senior author Tracey Woodruff, Ph.D., said, "These important results, showing that pregnant women in this California population are exposed to high levels of certain

flame retardants, is a key part of our work to understand and address multiple chemical exposures that occur during this sensitive time period." Woodruff is director of the UCSF Program on Reproductive Health and the Environment, part of the UCSF Department of Obstetrics, Gynecology, and Reproductive Sciences.

According to the authors, exposure to flame retardants is a major concern, because people are continuously exposed due to bioaccumulation in the environment. In an interview with the Los Angeles Times the day the study was published, Ami R. Zota, Sc.D., a postdoctoral fellow at UCSF and primary author of the paper, stressed, "It's very hard to avoid our exposures to these products because they're so widespread. Ultimately, we need policy measures."

Woodruff's group found that low-income populations are exposed to higher levels of PBDEs. (Photo courtesy of Tracey Woodruff)

Health disparities of PBDE exposure

Data from this study also support previous findings that U.S.-born low-income populations are more likely to have higher levels of flame retardant chemicals. Economic disparities like this are likely due to older PDBE-treated furniture and poorer housing quality.

As furniture, carpeting, and other household items age, flame retardants are released into the air and dust. California homes have some of the highest reported levels of PBDE chemicals in their household dust. "Blood levels of flame retardant chemicals are two times higher for California residents than for people in the rest of the country," noted Zota, "likely because our state has the most restrictive flammability requirements nationally."

A cohort of women in their second trimester

The team analyzed serum samples collected between 2008 and 2009 from 25 second trimester pregnant women for concentrations of lower- and higher-brominated PDBEs, OH-PBDEs, thyroid-stimulating hormone, free thyroxine, and total thyroxine. This is one of the first studies to measure the hydroxylated metabolites in pregnant women, and also one of the first to examine associations between OH-PBDEs and thyroid hormone disruption. According to the authors, another of several strengths of the study is its focus on a vulnerable, but understudied, population of ethnically diverse and predominately low-income women.

Although the data are preliminary and the sample size limited, the researchers found that higher levels of PBDE were associated with thyroid hormone disruption in pregnant women. Because thyroid hormone is important for pregnant women's health and child development, studying this connection further will be of great importance. "This pilot study lays the basis for larger studies to examine the inter-relationships between PDBEs and OH-PDBEs, TH [thyroid hormone] signaling during pregnancy, and adverse maternal and child health outcomes," the scientists concluded.

In addition to a supplement to an NIEHS grant and an NIEHS career development award, this study was also supported by the Passport Foundation Science Innovation Fund and the Learning Disabilities Association of America.

Citation: Zota AR, Park JS, Wang Y, Petreas M, Zoeller T, Woodruff TJ. 2011. Polybrominated diphenyl ethers (PBDEs), hydroxylated PBDEs (OH-PBDEs), and measures of thyroid function in second trimester pregnant women in California. Environ Sci Technol; doi: 10.1021/es200422b [Online 10 August 2011].

(Linh Pham, Ph.D. is on detail to the Program Analysis Branch of the Division of Extramural Research and Training).

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Superfund webinar showcases trainees

By Eddy Ball

The NIEHS Superfund Research Program (SRP) aired the final installment in its 2011 Trainee Webinar Series Aug. 16, featuring two of its outstanding young environmental engineering researchers. In the approximately three webinars held each year, SRP showcases presentations from poster award winners from the previous SRP annual meeting.

As the webinar host, NIEHS Health Scientist Administrator Danielle Carlin, Ph.D., said at the beginning of the event, "The intent of this webinar series is to increase collaboration and exchange of ideas among our young investigators conducting SRP-funded research and activities, and to hear about their award-winning work."

Some 100 online attendees listened as graduate student Steven O'Connell, of Oregon State University (OSU), presented his work on "Utilizing Silicone Passive Samplers to Expand Environmental Monitoring for the Portland Harbor Superfund, OR." Following his talk, University of Arizona (UA) graduate student Lucia Rodriguez-Freire explored "Biotransformation of Arsenic: The Role of Microorganisms in the Cycle of Arsenic in the Environment."

Rodriguez-Freire expects to complete her doctoral program in 2012. (Photo courtesy of Lucia Rodriguez-Freire)

Optimizing silicone for monitoring additional organic compounds

O'Connell, who is a member of the OSU Food Safety and Environmental Stewardship Program headed by Kim Anderson, Ph.D., described a pilot study conducted along a nine-mile stretch of the lower Willamette River Superfund site. The study was part of an ongoing search for advanced materials to complement passive sampling devices (PSDs) currently deployed in the harbor, which utilize lipid-free polyethylene tubing (LFT) to collect samples of bioavailable compounds in the air, water, and sediment that pose a potential threat to public health.

With a cross-disciplinary approach that combines biology with organic chemistry, O'Connell tested PSDs using silicone as the sampler matrix. O'Connell is interested in developing highly reproducible, cost-effective methods for the detection of semi-polar, or oxygen-containing, organic contaminants, in addition to the non-polar compounds so effectively sequestered by LFT.

O'Connell said there is a need for developing new deployment devices to preferentially sequester polycyclic aromatic hydrocarbons (PAHs) with higher octanol-water partition coefficients, such as oxygenated-PAHs (OPAHs), certain pesticides, and even steroid hormones, personal care products, and pharmaceuticals, commonly found in or near polluted areas. His experiments determined that co-deploying cost-effective silicon-based PSDs offers a good complementary deployment for detection of compounds along the spectrum of octanol-water partition coefficients that LFT is not picking up.

"This is exactly what we wanted to see," he said. "We're getting some of those semi-polar organic compounds we were after."

O'Connell, who splits his time between his OSU lab and his field work collecting samples at a Superfund site, is now in his second year as a graduate student. (Photo courtesy of Steven O'Connell)

Using bacteria to cycle arsenic in the environment

As part of the UA Environmental Engineering program headed by Reyes Sierra, Ph.D., which is involved in studies of the biogeochemical cycle of arsenic in the environment, Rodriguez-Friere's research focuses on innovative ways to utilize microorganisms in the microbial conversion of arsenic in groundwater.

Arsenic in drinking water is a major public health concern worldwide, as exposure has been shown to increase the risk of skin, liver, bladder, and lung cancers. Elevated concentrations are found in many parts of the U.S. naturally and as a contaminant at many Superfund sites.

Rodriguez-Friere is striving to understand the specific chemical processes involved in oxidizing arsenite (As(III)) and reducing arsenate (As(V)). As Rodriguez-Friere explained, understanding the different chemical processes that determine biotransformation is important because speciation affects the mobility and toxicity of arsenic in the environment. "In an arsenic-contaminated aquifer," she said, "most of As(III) will be the water phase, while As(V) will be in the soil phase."

The ultimate goal of research by her group is the development of low-cost bioremediation strategy to utilize the microbial-catalyzed transformation of As(III) to As(V) by three strains of arsenite-oxidizing bacteria that can be applied in bioreactors, permeable reactive barriers, and *in situ* to help protect public health.

Poster Citations:

Lucia Rodriguez-Freire, Wenjie Sun, Reyes Sierra-Alvarez, and Jim Field. 2010. Metabolic Characterization of Three Arsenite-Oxidizing Nitrate-Reducing Bacterial Strains.

Steven O'Connell, Sarah Allan, Glenn Wilson, Lane Tidwell, Kim Anderson. 2010. Utilizing Silicone Passive Samplers to Expand Environmental Monitoring for the Portland Harbor Superfund, OR.

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NIEHS investigator links UV exposure and aging to cataracts and macular degeneration

By Ian Thomas

Genetics, ethnicity, and gender have long since been established as key contributors to ocular disease in adults. However, during a July discussion surrounding her latest work on the effects of light on the human eye, NIEHS researcher Joan Roberts, Ph.D., suggests that the aging process itself, in conjunction with excessive UV exposure, plays a major role in the onset of cataracts and macular degeneration.

"While light itself is not necessarily dangerous to the eye, under the right circumstances it most certainly can be," explains Roberts, a volunteer investigator with the Laboratory of Toxicology and Pharmacology and an expert on ocular disease. "It all depends on the light's intensity, wavelength, mechanism, and the age of the person receiving it."

Presently a professor in the Department of Chemistry at Fordham University, Roberts earned her Ph.D. in organic chemistry from St. John's University in New York, before completing a postdoctoral fellowship in pharmacology at the Albert Einstein College of Medicine. (Photo courtesy of Steve McCaw)

Chromophores — the eye's energy filters

The backbone for Roberts' claim is the progression of ocular changes that occur in many adults age 40 and above, particularly those involving light-absorbing chemicals called chromophores.

"During childhood and young adulthood, chromophores function as energy filters for many of light's harmful effects," Roberts notes. "However, as we get older, the eye encounters a noticeable buildup of phototoxic chromophores such as xanthurenic acid and lipofuscin that, when irradiated, can cause significant damage. Furthermore, this is happening at a time when the body's natural defenses to these agents are in a state of decline, due to a gradual loss of protective antioxidants and enzymes."

Moderating the ravages of aging

In the end, Roberts and her colleagues admit that, while various diseases such as cataracts and macular degeneration may ultimately be inevitable with age, steps can be taken to minimize their effects, if not avoid them altogether.

Conventional thinking has offered a variety of suggestions regarding ocular protection and cataract prevention. Be it wraparound sunglasses with specific UV protective lenses or a steady diet of antioxidant-rich fruits and vegetables, Roberts believes all are good ideas, though she firmly insists that the key to prevention lies in a strictly balanced approach.

"It's important to remember that different antioxidants prevent ocular disease in different ways," she emphasizes. "Omega-3s prevent inflammatory response, while lutein is great for singlet oxygen prevention. Both are wonderful ideas, but only when consumed in the proper amounts. When antioxidants are taken incorrectly, you're actually adding a pro-oxidant, which could conceivably damage the very tissue you're trying to protect."

Nutritional supplementation

Roberts suggests that the following antioxidants may help prevent ocular disease.

- Lutein — 6mg
- Vitamin C — 500mg
- Vitamin E — 400IU
- Zinc — 15mg
- Copper — 2mg
- Omega-3 Fatty Acid — 500mg

"One out of every three people will develop macular degeneration by the time they're 85, so effective prevention is all about starting now," she concludes. "Particularly with younger children whose retinas aren't yet fully protected, let's shut out the lights when we don't need them and eat a little more spinach at dinner. When we're out on the beach or the snow, let's wear the right eyewear to protect us from reflective light. The fact is, most people will develop cataracts by the time they're 70, but, by taking the right precautions, we can at least stave off their effects as long as possible."

Citations for recent research:

Ehrenshaft M, Zhao B, Andley UP, Mason RP, Roberts JE. 2011. Immunological Detection of N-formylkynurenine in Porphyrin-Mediated Photooxided Lens α-crystallin. Photochem Photobiol; doi: 10.1111/j.1751-1097.2011.00979.x. [Online 19 July 2011].

Roberts JE. 2011. Ultraviolet radiation as a risk factor for cataract and macular degeneration. Eye Contact Lens 37(4):246-249.

Wielgus AR, Chignell CF, Ceger P, Roberts JE. 2010. Comparison of A2E cytotoxicity and phototoxicity with all-trans-retinal in human retinal pigment epithelial cells. Photochem Photobiol 86(4):781-791.

Wielgus AR, Collier RJ, Martin E, Lih FB, Tomer KB, Chignell CF, Roberts JE. 2010. Blue light induced A2E oxidation in rat eyes — experimental animal model of dry AMD. Photochem Photobiol 9(11):1505-1512.

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

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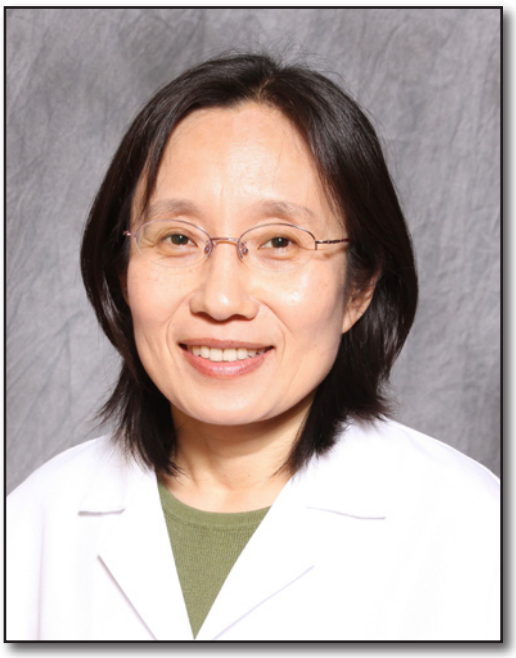
Study suggests nutritional supplements could one day prevent skin cancer

By Ian Thomas

A new study from scientists at NIEHS and the University of Chicago found that decreased levels of phosphatase and tensin homolog (PTEN), a known tumor suppressing protein, led to an increased risk for ultraviolet (UV)-induced, non-melanoma skin cancer in mice. As a result, researchers now believe that, in time, America's number one form of cancer could conceivably be prevented with basic nutritional supplements.



Yu-Ying He is an assistant professor in the Department of Medicine at the University of Chicago. (Photo courtesy of Yu-Ying He)

"Based on our previous studies at NIEHS, we knew going in that UV radiation impaired the expression of PTEN," explained Yu-Ying He, Ph.D., the project's lead researcher and an NIEHS postdoc from 2001 to 2007. "Therefore, with this particular study, we set out to ask three questions. First, what is the function of PTEN in UV response? Next, what is the consequence for PTEN loss? Finally, what is the relevance of this interaction to tumor development and human skin cancer?"

PTEN promotes genomic stability and cellular repair. In this instance, He and her staff found that mediating PTEN levels in mice prior to UVB exposure severely hindered DNA repair in radiation-damaged cells.

"This study provides an important role for PTEN in the earliest stages of tumorigenesis," said Carol Trempus, a co-author on the project and NIEHS biologist since 1992. "Given that mice deficient in PTEN exhibited

accelerated UV-mediated tumor development compared to those with sufficient PTEN levels, this work gives important insights into the early events in UV carcinogenesis. At the same time, it also emphasizes that loss of PTEN may be a predisposing event in human skin tumor development."

Last year, the American Association for Cancer Research estimated that over one million Americans were diagnosed with non-melanoma skin cancer. This comprised 40 percent of all newly diagnosed cases of cancer (see press release). With rates climbing, He is encouraged by her study's results.

"Ultimately, these findings define PTEN as a key genomic gatekeeper in skin cells," she concluded. "If we can begin to identify nutritional and/or pharmacological agents that can effectively increase PTEN activity, this could open the door to many new approaches for prevention and treatment of skin cancer."

Trempus is an alumna of North Carolina State University who works in the NIEHS Laboratory of Respiratory Biology. (Photo courtesy of Steve McCaw)

This study is dedicated in memory of the late Colin Chignell, Ph.D., a dedicated researcher and NIEHS employee of 42 years. Prior to his passing in 2008, Chignell oversaw the Photosensitization Reactions Group in the NIEHS Laboratory of Pharmacology, where this project was initially begun.

Citation: Ming M, Feng L, Shea CR, Soltani K, Zhao B, Han W, Smart RC, Trempus CS, He YY. 2011. PTEN positively regulates UVB-induced DNA damage repair. Cancer Res 71(15):5287-5295.

(Ian Thomas is a public affairs specialist in the NIEHS Office of Communications and Public Liaison)

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Understanding how embryonic stem cells work

By Robin Arnette

In the July 24 issue of Nature Cell Biology, NIEHS researcher Raja Jothi, Ph.D., published a paper that explains how two seemingly opposing mechanisms in embryonic stem (ES) cells actually work together. Jothi said a few papers in the literature suggested that this unique cellular collaboration occurs on a gene-by-gene basis, but his findings were the first to demonstrate that it happens quite frequently on a genome-wide scale.

In a collaborative effort, Jothi and his colleagues in the lab led by Gerald Crabtree, M.D., at the Howard Hughes Medical Institute (HHMI) and Stanford University School of Medicine, wanted to understand how ES cells function given their potential for curing disease. ES cells have the ability to become any cell in the adult body. This capability, known as pluripotency, offers scientists the possibility of treating a host of conditions, such as Parkinson's disease, burns, diabetes, spinal cord injury, arthritis, and amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease.

Using data sets generated at the NIEHS sequencing facility, Jothi, a co-senior author on the paper along with Crabtree, performed the genome-scale analysis. Lena Ho, Ph.D., a graduate student at the time in Crabtree's lab, carried out the experiments. Jothi also shared co-first authorship with Ho on the article.

Jothi is head of the Systems Biology Group in the NIEHS Biostatistics Branch. (Photo courtesy of Steve McCaw)

The players in pluripotency

Jothi provided a little background for the research by saying that the chromatin remodeling complex, esBAF, and the LIF/STAT3 signaling pathway are two critical components required to maintain mouse ES cells in the undifferentiated pluripotent state. esBAF is a multiprotein complex responsible for unwinding tightly packaged DNA so that other proteins can gain access to bind DNA and turn genes on or off in a context-dependent manner.

Jothi said the leukemia inhibitory factor (LIF) pathway, mediated by its downstream DNA binding transcription factor STAT3, is absolutely essential for pluripotency, because it inhibits mouse ES cells from differentiating into mesoderm and endoderm, two of the three primary germ layers of an embryo that is the source of many bodily tissues that include lung, liver, heart and blood cells.

He cited the team's earlier study showing esBAF's colocalization with STAT3 promotes pluripotency, but these latest findings demonstrated that it is primarily achieved by esBAF both working against and in concert with polycomb, a third player in this molecular drama. Polycomb is repressive machinery that silences developmental and differentiation genes when bound to DNA.

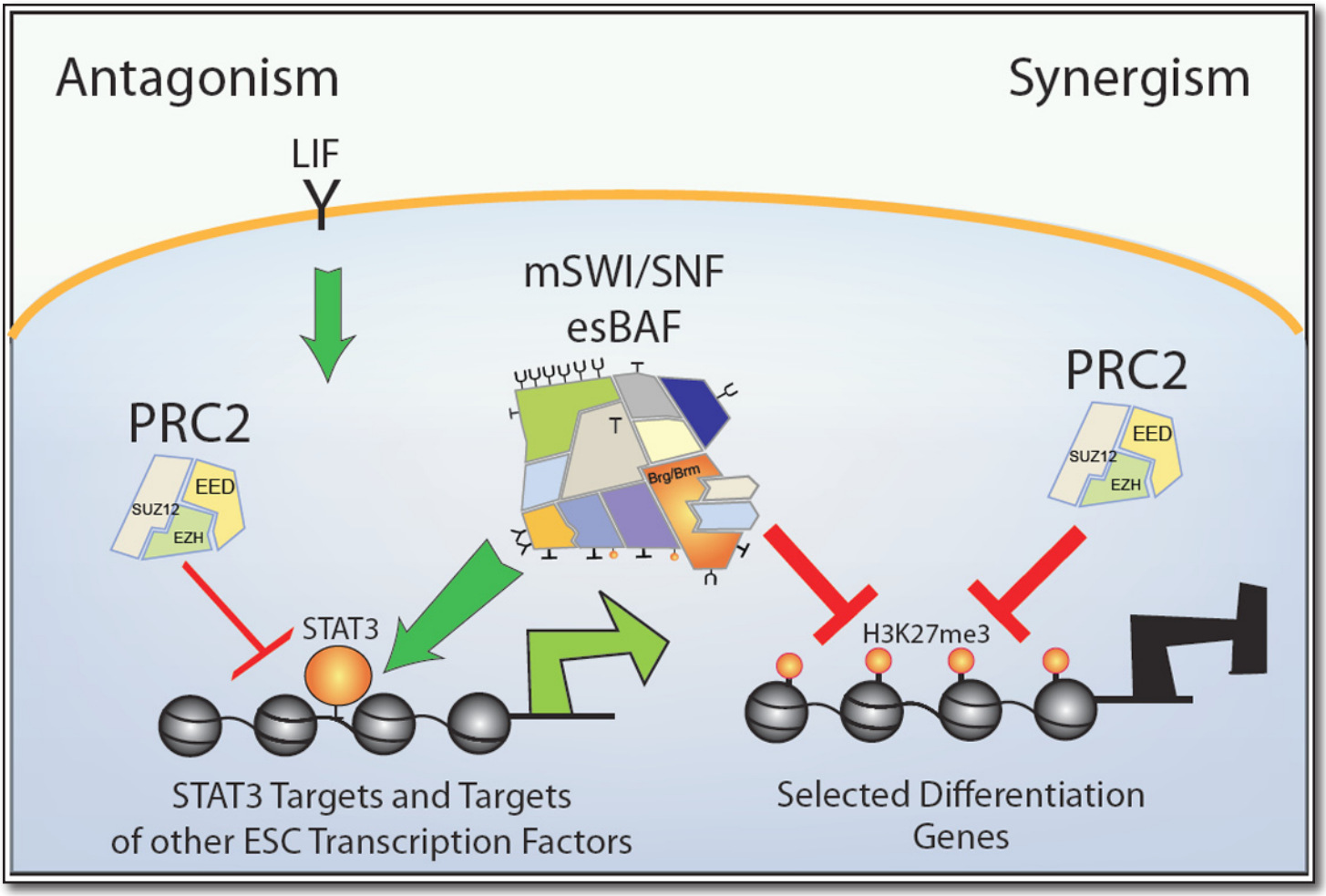
"We wanted to show that esBAF facilitates binding of STAT3 by opposing polycomb and, during our analysis, we started seeing it," Jothi said. "Traditionally, trithorax-group proteins, of which esBAF is a member, and polycomb play antagonistic roles in development but, unexpectedly, we also found that there are instances, like at all four Hox gene clusters, where these two can work together to effectively silence Hox genes and prevent premature differentiation."

Implications for stem cell research

Jothi said that they were a little skeptical when they found that esBAF can facilitate polycomb action, given the traditional view of their antagonistic roles. Fortunately, he and his colleagues were able to demonstrate how these two act both antagonistically and synergistically with the common goal of maintaining pluripotency in ES cells.

Crabtree agreed that the results were very relevant to the field. He said, "The study nicely illustrates the power of modern genome-wide analysis to reverse old biases. All biochemistry and developmental textbooks have polycomb and chromatin remodeling machinery opposing one another. Yet, when one analyzes the entire genome, it is clear that opposition is only a small part of the picture."

Another stem cell expert, Guang Hu, Ph.D., head of the NIEHS Laboratory of Molecular Carcinogenesis Stem Cell Biology Group, believes the paper greatly pushes ES research forward. He added, "This work greatly improved our understanding of the transcriptional control of self-renewal and pluripotency. It may help us understand reprogramming and find better ways to generate pluripotent cells in the future."



Antagonism and Synergism Between esBAF and PRC2 promotes pluripotency
In this model, the chromatin remodeling complex esBAF acts as a general facilitator by providing DNA access in a context-dependent manner. At genes regulated by LIF/STAT3, esBAF facilitates STAT3 binding by antagonizing repressive polycomb action and allowing LIF/STAT3 to activate pluripotent genes. At Hox gene clusters, esBAF facilitates polycomb (PRC2) binding to silence Hox genes. In the absence of both esBAF and PRC2, LIF/STAT3 is able to bind and keep the ES cells in a pluripotent state. (Image courtesy of Raja Jothi)

Citation: Ho L, Miller EL, Ronan JL, Ho WQ, Jothi R, Crabtree GR. 2011. esBAF facilitates pluripotency by conditioning the genome for LIF/STAT3 signalling and by regulating polycomb function. Nat Cell Biol 13(8):903-913.

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NTP researcher wins poster award at conference in Germany

By Ian Thomas

NTP scientist Scott Auerbach, Ph.D., took home top poster honors at the OpenTox 2011 InterAction Meeting for his work on bioinformatics and disease-informing assays. Hosted by the OpenTox community of collaborators and funded by the European Union Seventh Framework Programme, this year's gathering was held Aug. 9-12 at the Technical University of Munich in Germany.

"Most of the work presented at the meeting was focused on computational methods for predicting toxicity," recalled Auerbach, a molecular toxicologist for the NTP Host Susceptibility Branch in the Biomolecular Screening Branch.

Auerbach's work used bioinformatics to link *in vitro* assays to chronic disease processes, such as type 2 diabetes. It then leveraged the assay-disease relationships to identify chemicals with the potential to influence disease processes.

"It's clear that the existing assay data covers certain areas of disease reasonably well," Auerbach explained. "Other areas, such as neurological disease for instance, aren't as well accounted for, in large part due to our limited understanding of certain disease processes and the inherent complexities surrounding them."

Still, Auerbach is happy for the chance to share his work and broaden his research horizons, something he sees as key to the future.

"I'm incredibly grateful for the support I've received here at NIEHS," Auerbach said. "I'm a firm believer that the future advancements of the toxicology field will begin with insights spawned from cross-disciplinary collaborations like this. Therefore, I'm thrilled to have been a part of it."

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison.)

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Auerbach's research, presented with a poster titled "Bioinformatics-based identification of assays that inform on disease hazard," will help NTP select certain chemicals for additional targeted in vivo testing in specific disease models. (Photo courtesy of Steve McCaw)

This month in EHP

By Ian Thomas

A striking cover image of burning forestland serves as a fitting backdrop for the feature news story in the September issue of Environmental Health Perspectives (EHP), "Fields and Forests in Flames: Vegetation Smoke and Human Health." With wildfires increasing worldwide in recent years and expected to increase still more in the near future, there is a need for better understanding of who is most vulnerable to the adverse health effects of smoke and how different types of vegetation smoke differ in toxicity.

In a second story, titled "Climate Change and Infectious Disease: The Future Is Now," researchers examine the evidence for climate-related shifts of vectorborne and other diseases, while preparing the public health community for further changes to come.

In this month's Researcher's Perspective podcast, host Ashley Ahearn sits down with NIEHS Senior Advisor for Public Health John Balbus, M.D., to discuss how the environmental health community is communicating to the public the science of climate change and what it means for human health.

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Featured commentary, reviews, and research this month include:

- Health Impacts of Forest Fire Smoke
- Air Pollution and Cardiorespiratory Events in Infants
- Thirdhand Tobacco Smoke: A Review of the Evidence
- Halogenated Bisphenols Are PPAR Ligands
- Additivity of Pyrethroids on Na^+ Influx
- Bitumen and PAH Exposure Among Ancient Chumash Indians

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

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2012 NIH Director's Award programs funding opportunities

By Eddy Ball

In August, NIH announced that it is welcoming proposals for the 2012 NIH Director's Pioneer Award and New Innovator Award programs for innovative approaches to major challenges in biomedical or behavioral research. Submission deadlines are Oct. 7, 2011 for Pioneer Award applications and Oct. 14, 2011 for New Innovator Award applications.

NIH expects to fund at least 7 Pioneer Awards and 33 New Innovator Awards in summer 2012. To continue its strong record of diversity in these programs, NIH especially encourages women and members of groups that are underrepresented in NIH research to apply.

Pioneer Award program:

- Up to $2.5 million in direct costs over 5 years
- Open to scientists at any career stage

See application instructions in the Funding Opportunity Announcement RFA-RM-11-004. Send any questions to pioneer@nih.gov.

New Innovator Award program:

- Up to $1.5 million in direct costs over 5 years
- For early career stage investigators, defined as those who have not received an NIH R01 or similar grant and are within 10 years of completing their terminal research degree or medical residency.

See application instructions in the Funding Opportunity Announcement RFA-RM-11-005. Send any questions to newinnovator@nih.gov.

The Pioneer Award and New Innovator Award programs are funded through the NIH Common Fund, which encourages collaboration and supports a series of exceptionally high-impact, trans-NIH programs. These programs are managed by the NIH Office of the Director, in partnership with the various NIH Institutes, Centers, and Offices.

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Upcoming bioinformatics conference at Friday Center

By Robin Arnette

The third Toxicogenomics Integrated with Environmental Sciences (TIES) Conference will take place Sept. 15-16 at the University of North Carolina at Chapel Hill (UNC) William and Ida Friday Center for Continuing Education in Chapel Hill, N.C. The two-day event is sponsored by the National Institute of Environmental Health Sciences (NIEHS), the U.S. Food and Drug Administration National Center for Toxicological Research (NCTR), the SAS Institute, and UNC. The international meeting will focus on how bioinformatics and emerging technologies help researchers better understand the environmental influences behind the development and progression of human disease.

The conference theme is "The Biology and Bioinformatics behind Environmental and Toxicologic Influences," and will feature oral presentations and a poster session. Keynote speakers include John Quackenbush, Ph.D., professor of computational biology and bioinformatics at the Harvard School of Public Health Dana-Farber Cancer Institute,; William Slikker Jr., Ph.D., director of NCTR; Rebecca Fry, Ph.D., assistant professor of environmental sciences and engineering at UNC Gillings School of Global Public Health; and Xihong Li, Ph.D., professor of biostatistics at the Harvard School of Public Health.

For more information and to register, visit http://eseconf.sph.unc.edu/TIES2011. Registration for NIEHS and NCTR staff is free.

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Extramural papers of the month

By Jerry Phelps

- Discovery of the seventh and eighth bases of DNA
- Autism and prenatal vitamins
- Microparticle delivery increases efficacy of doxorubicin in treatment of mesothelioma
- Genetic map of African-Americans will aid the study of diseases

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

Discovery of the seventh and eighth bases of DNA

NIEHS Superfund Research Program grantees at the University of North Carolina Chapel Hill have discovered the seventh and eighth bases of DNA. These last two bases, called 5-formylcytosine and 5-carboxylcytosine, are actually versions of cytosine that have been modified by Tet proteins, molecular entities thought to play a role in DNA demethylation and stem cell reprogramming. The finding could have important implications for stem cell research, as it could provide researchers with new tools to erase previous methylation patterns to reprogram adult cells. The discovery also could inform cancer research, as it could give scientists the opportunity to reactivate tumor suppressor genes that had been silenced by DNA methylation.

Citation: Ito S, Shen L, Dai Q, Wu SC, Collins LB, Swenberg JA, He C, Zhang Y. 2011. Tet Proteins Can Convert 5-Methylcytosine to 5-Formylcytosine and 5-Carboxylcytosine. Science; doi:10.1126/science.1210597 [Online 21 July 2011]

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Autism and prenatal vitamins

In a population-based case control study of 566 subjects comparing a group of autistic children to a matched control group of children with normal development, researchers found that mother who didn't take prenatal vitamins were at greater risk of having an autistic child, and certain genetic markers greatly increased the risk.

Researchers examined maternal intake of prenatal vitamins in the three months before conception and the first month of pregnancy, and they looked for genotypes associated with autism. There was a dose/response relationship — the more prenatal vitamins a woman took, the less likely she would have an autistic child. There was no association with other types of multivitamins, and no association with prenatal vitamin intake during months two through nine of pregnancy. Having certain genotypes also increased the odds that a woman would have an autistic child. Children with the COMT 472 AA gene were at increased risk of autism. If their mothers took prenatal vitamins, the odds ratio for the risk of autism was 1.8 — if their mothers didn't, the odds ratio jumped to 7.2. This suggests that the maternal-fetal environment can magnify the effects of a susceptibility gene.

The authors think there are plausible biological explanations. Folate and other B vitamins are critical to neurodevelopment. The gene variants were in one-carbon metabolism pathways, therefore suggesting that methylation mechanisms may be responsible.

Citation: Schmidt RJ, Hansen RL, Hartiala J, Allayee H, Schmidt LC, Tancredi DJ, Tassone F, Hertz-Picciotto I. 2011. Prenatal vitamins, one-carbon metabolism gene variants, and risk for autism. Epidemiology 22(4): 476-485. Story

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Microparticle delivery increases efficacy of doxorubicin in treatment of mesothelioma

NIEHS-supported researchers at the University of Vermont report possible new advances in the treatment of malignant mesothelioma by microparticle delivery of the chemotherapeutic agent doxorubicin. The research was carried out in laboratory animals and builds on previous findings from the same investigators.

Malignant mesotheliomas have a poor prognosis, largely because of their resistance to anti-cancer drugs like doxorubicin and others. The current study investigated the use of acid-prepared mesoporous microspheres (APMS) as a delivery vehicle for doxorubicin. APMS have been shown in previous research to be non-toxic in laboratory animals. The investigators injected APMS-doxorubicin intraperitoneally or directly into subcutaneous tumors. In comparison to doxorubicin alone, APMS-doxorubicin enhanced intracellular uptake of the drug and mesothelioma cell death. In the intraperitoneal-treated animals, decrease tumor numbers and tumor size was achieved with one-third the dose of doxorubicin in the combined form.

This finding suggests that APMS delivery of doxorubicin is an effective treatment for malignant mesotheliomas and reduces the dosage of the drug necessary to achieve tumor regression.

Citation: Hillegass JM, Blumen SR, Cheng K, MacPherson MB, Alexeeva V, Lathrop SA, Beuschel SL, Steinbacher JL, Butnor KJ, Ramos-Niño ME, Shukla A, James TA, Weiss, DJ, Taatjes DJ, Pass HI, Carbone M, Landry CC, Mossman BT. 2011. Increased efficacy of doxorubicin delivered in multifunctional microparticles for mesothelioma therapy. Int J Cancer 129(1):233-244.

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Genetic map of African-Americans will aid the study of diseases

A large multi-institutional team of researchers, including NIEHS grantees, has constructed a detailed genetic map from a population of more than 30,000 African-Americans that will be used to better understand the causes of disease and human evolution. This new map is the first built from an African-American population.

The map holds promise for both broad genome-wide applications and narrowly focused single disease research. It will be helpful in studying diseases with a genetic basis especially those that strike African-Americans frequently, such as hypertension and diabetes. A surprising finding was that the map turned out to be very different than maps based on people of European and other non-African ancestry. The authors think this is due to recombination that has occurred in the U.S. population over the last two or three centuries. It turns out that African-Americans have genetic machinery for recombination that is different than Europeans. The team discovered that a 13 base-pair motif, responsible for many recombination hotspots in Europeans, accounts for only two-thirds as much recombination in African-Americans. The remaining third is connected to a newly identified motif of 17 base-pairs.

These findings are expected to help researchers understand the underlying causes of congenital conditions that occur more often in African-Americans and will also be invaluable in discovering new disease genes in all populations.

Citation: Hinch AG, Tandon A, Patterson N, Song Y, Rohland N, Palmer CD, Chen GK, Wang K, Buxbaum SG, Akylbekova EL, Aldrich MC, Ambrosone CB, Amos C, Bandera EV, Berndt SI, Bernstein L, Blot WJ,

Bock CH, Boerwinkle E, Cai Q, Caporaso N, Casey G, Cupples LA, Deming SL, Diver WR, Divers J, Fornage M, Gillanders EM, Glessner J, Harris CC, Hu JJ, Ingles SA, Isaacs W, John EM, Kao WH, Keating B, Kittles RA, Kolonel LN, Larkin E, Le Marchand L, McNeill LH, Millikan RC, Murphy A, Musani S, Neslund-Dudas C, Nyante S, Papanicolaou GJ, Press MF, Psaty BM, Reiner AP, Rich SS, Rodriguez-Gil JL, Rotter JI, Rybicki BA, Schwartz AG, Signorello LB, Spitz M, Strom SS, Thun MJ, Tucker MA, Wang Z, Wiencke JK, Witte JS, Wrensch M, Wu X, Yamamura Y, Zanetti KA, Zheng W, Ziegler RG, Zhu X, Redline S, Hirschhorn JN, Henderson BE, Taylor HA Jr, Price AL, Hakonarson H, Chanock SJ, Haiman CA, Wilson JG, Reich D, Myers SR. 2011. The landscape of recombination in African Americans. Nature 476(7359):170-175.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training.)

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Intramural papers of the month

By Raluca Dumitru, Ian Thomas, and Angelika Zaremba

- Rodent model examines Parkinson's progression
- Cadmium induces transcription without calcium mobilization
- CAR mediates the activation of *Sult1e1* gene by the garlic extract diallyl sulfide
- A novel mechanism that may underlie learning and memory

Rodent model examines Parkinson's progression

Results from a new study by NIEHS Laboratory of Toxicology and Pharmacology researchers suggest that Parkinson's disease (PD) develops from complex gene-environment interactions. The research team made the finding by creating a mouse model that examined how human alpha-synuclein, a gene mutated in some familial and sporadic PD, interacted with low-grade neuroinflammation.

Using this two-hit rodent model, which involved a genetic lesion and an environmental trigger, investigators discovered that microglia-derived oxidative stress bridged neuroinflammation and alpha–synuclein pathogenic alteration in the mediation of its effects. Furthermore, unlike earlier archetypes, this model reproduced several key factors associated with PD, such as the degeneration of dopaminergic neurons and fibers in the nigrostriatal pathway, while also demonstrating synergistic effects of genetic predisposition and environmental exposures in PD development.

As the second most common neurodegenerative disease in the world, extensive knowledge surrounding a possible gene-environment interaction as a mechanism for Parkinson's progression has previously proven elusive. Therefore, this new model may prove to be an invaluable tool for future PD research.

Citation: Gao HM, Zhang F, Zhou H, Kam W, Wilson B, Hong JS. 2011. Neuroinflammation and alpha-synuclein dysfunction potentiate each other, driving chronic progression of neurodegeneration in a mouse model of Parkinson's disease. Environ Health Perspect 119(6):807-814.

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Cadmium induces transcription without calcium mobilization

Scientists from NIEHS revealed a concentration-dependent effect of cadmium on calcium mobilization and gene expression. These findings have important public health implications because cadmium is a persistent environmental toxicant and exposure to it is associated with several human health conditions, such as kidney dysfunction, cancer, respiratory ailments, and birth defects.

Cadmium affects the expression of hundreds of functionally unrelated genes, by activating multiple signal transduction pathways, but it may also influence the gene expression of second messengers, such as calcium.

Researchers used a protein-based calcium sensor, which was stably expressed in HEK293 cells. Low-level cadmium concentrations were sufficient to induce transcription of cadmium-responsive genes, but did not affect calcium mobilization or increase steady-state mRNA levels of calcium-responsive genes. In contrast, exposure to cytotoxic concentrations of cadmium significantly reduced intracellular calcium stores and altered calcium-responsive gene expression.

The scientists concluded that cytotoxic levels of cadmium activate calcium-responsive transcription as a general response to metal-induced intracellular damage and not via a specific mechanism. The research team plans to further examine the effect of cadmium on human health, by studying the molecular mechanisms that regulate cadmium-responsive transcription at environmentally low-levels of concentration.

Citation: Tvermoes BE, Bird GS, Freedman JH. 2011. Cadmium induces transcription independently of intracellular calcium mobilization. PLoS One 6(6):e20542.

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CAR mediates the activation of *Sult1e1* gene by the garlic extract diallyl sulfide

According to NIEHS researchers, activation of the *Sult1e1* gene by the garlic extract (diallyl sulfide) DAS is mediated by the constitutive active/androstane receptor (CAR). This study is the first to show this interaction and may lead to important discoveries in the prevention of stomach, lung, liver, and colon cancer.

CAR (NR1I3), a member of the nuclear receptor superfamily, is usually activated by numerous xenobiotics and endobiotics. It is involved from drug metabolism to energy homeostasis. DAS can positively regulate the production of various enzymes in the liver. When the investigators exposed wild type mice to DAS, *Sult1e1* was rapidly induced, but exposure to DAS in mice that lacked CAR led to a small induction of the *Sult1e1* gene. Therefore, CAR mediated this interaction.

One other finding in this report is that strong *Sult1e1* induction did not affect the endogenous E2 levels in the blood. Further pharmacokinectical, pharmacogenetical, and biochemical studies are necessary to understand this aspect of the research.

Citation: Sueyoshi T, Green WD, Vinal K, Woodrum TS, Moore R, Negishi M. 2011. Garlic extract diallyl sulfide (DAS) activates nuclear receptor CAR to induce the Sult1e1 gene in mouse liver. PLoS One 6(6):e21229.

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A novel mechanism that may underlie learning and memory

A recent study conducted by researchers at NIEHS identified a novel mechanism that could have broad implications for neurologic disorders such as Alzheimer's disease and schizophrenia. Previous data support the notion that synaptic plasticity plays a major role in certain forms of learning and memory. This work is the first to show that that timing for the release of acetylcholine, one of the major neurotransmitters in the brain, is critical for the plasticity of synapses, or nerve cell connections.

Long-term potentiation (LTP) and long-term depression (LTD) are two well-studied types of synaptic plasticity. LTP strengthens the synaptic plasticity while LTD reduces it. By electrically stimulating different areas of the cholinergic pathway, the authors found that a very small change in the timing of stimulation and, therefore, acetylcholine release, can alter the type of synaptic plasticity inducing either LTP or LTD.

The researchers also generated mice in which the cholinergic neurons selectively expressed a light-sensitive protein. As a result they were able to selectively activate cholinergic inputs and monitor how the release of acetylcholine affected synaptic plasticity. Using this approach they were able to confirm the results obtained with electrical stimulation and, more importantly, were able to modulate the synaptic strength by either inducing LTP or LTD.

Citation: Gu Z, Yakel JL. 2011. Timing-dependent septal cholinergic induction of dynamic hippocampal synaptic plasticity. Neuron 71(1):155-165.

(Raluca Dumitru, M.D., Ph.D., is an Intramural Research Training Award fellow in the Stem Cell Biology Group of the Laboratory of Molecular Carcinogenesis. Ian Thomas is a public affairs specialist in the NIEHS Office of Communications and Public Liaison. Angelika Zaremba, Ph.D., is a visiting postdoctoral fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

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Inside the Institute

Goal exceeded, as NIEHS Feds Feed Families drive concludes

By Eddy Ball

Volunteers at NIEHS collected a record 3,550 pounds of non-perishable food, infant products, and hygiene items, during the 2011 Feds Feed Families food drive, far surpassing the 2010 total of 1,050 pounds and exceeding this year's goal by 50 pounds.

At the collection point in front of Keystone, volunteers showed off donated products, during the July 27 collection. Shown, left to right, are Judy Hanson, Michelle Owens, and Chris Long. (Photo courtesy of Steve McCaw)

NIEHS/NTP Director Linda Birnbaum, Ph.D., said she was gratified by the generosity of employees and impressed by the leadership of organizers Bill Jirles of the American Federation of Government Employees (AFGE) Local 2923, Annette Rice of the Research Triangle Park Chapter of Blacks In Government (BIG), and Monya Wells of the NIEHS Office of Management (OM), in the collection of food for delivery to the Durham Rescue Mission and the Food Bank of Central and Eastern North Carolina.

"We can all take pride in the way NIEHS has given back to the community in this time of need," Birnbaum said. "I want to thank Annette, Bill, and Monya for once again inspiring employees to join in to make the food drive a success, as well as the many people at NIEHS who took time to help their neighbors."

Charles Alden, left, handed over a large sack of donations to Owens, in a scene played out many times during the drive. (Photo courtesy of Steve McCaw)

Answering the call

As they have in past charitable efforts, NIEHS/NTP employees and contractors did their part to make the drive a success, by helping to promote the food drive and make collections at the end of June, July, and August. As the weight of the donations suggests, there was plenty of lifting and moving to go around.

During the drive, which ran from June 28 through Aug. 31, the number of volunteers grew steadily. In addition to the organizers, the volunteers included William Boyd, Juanita Bradley, Sally Fields, Rachel Frawley, Margaret George, Veronica Godfrey Robinson, Dianne Gray, Judy Hanson, Chris Long, Dennis Malone, Jackie Osgood, Michelle Owens, Dudley Riner, VeeVee Shropshire, Mike Tyson, Mitzie Walker, Myra Westmoreland, and Sheila Withers, along with others who pitched in behind the scenes.

Volunteer Rachel Frawley picked up food and other items for loading in the cars that carried the goods to the Durham Rescue Mission and the Food Bank of Eastern and Central North Carolina. (Photo courtesy of Steve McCaw)

Wells, left, and volunteer Juanita Bradley loaded a station wagon with sack after sack of items bound for hungry people in Durham and Raleigh. (Photo courtesy of Steve McCaw)

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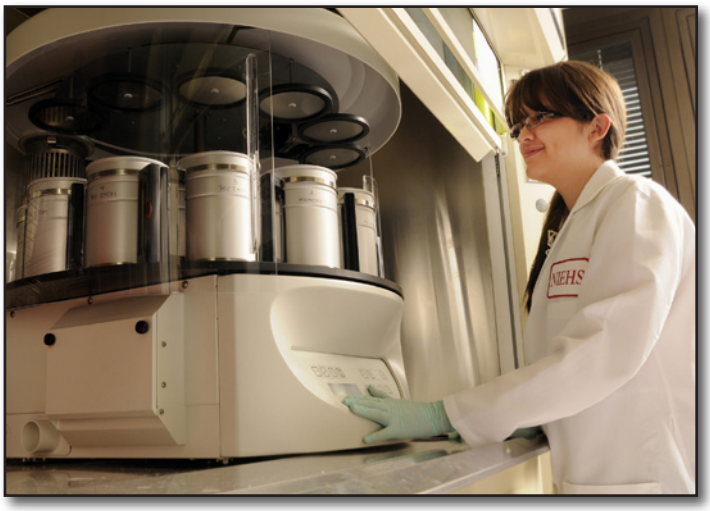
NIEHS mentoring makes summer special for Hispanic intern

By Eddy Ball

From her first contact with NIH up to her last day at NIEHS Aug. 12, summer intern Yasmin Crespo-Mejias enjoyed the support and encouragement of quality mentors —from her colleagues in her lab, the NIEHS Summer Internship Program, and the NIH Hispanic Employment Program.

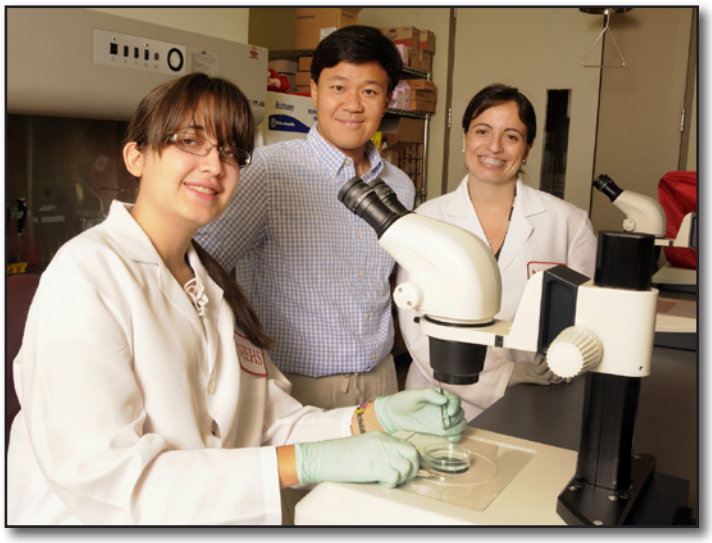
Crespo-Mejias, a junior at the University of Puerto Rico (UPR), was the first intern to train in the NIEHS Reproductive Developmental Biology Group headed by Humphrey Yao, Ph.D. She was one of six interns, five of them working at NIH labs in Bethesda, Md., who benefited from outreach efforts led this spring and summer by Gerard Roman, the NIH equal opportunity and diversity management specialist on-site at NIEHS and manager of the NIH Hispanic Employment Program.



Crespo-Mejias, above, works with an automatic tissue processor, one of several advanced laboratory instruments her internship gave her an opportunity to access this summer. (Photo courtesy of Steve McCaw)

Describing her experience at NIEHS, Crespo-Mejias said, “The resources here are incredible, much better than what’s available for undergraduates at the university. I was able to follow through with designing and carrying

out a controlled experiment, as I got to see how real-world scientific discoveries happen."



Crespo-Mejias, left, was joined at her microscope by Yao, center, and Rodriguez, right. (Photo courtesy of Steve McCaw)

Designing and carrying out a study of endocrine disruption

Crespo-Mejias worked with Yao and others in the group, especially biologist Karina Rodriguez, Ph.D., from June 7, one day after her final exam of the year, to Aug. 12, when she returned home to get ready to begin the fall semester at her university's Rio Piedras Campus the following Monday. During her ten-week internship, she was involved in her summer project, a pilot study testing the hypothesis, "*In Utero* Exposure to Bisphenol A Disrupts Testis Development in Mouse Embryos," as first author on an abstract displayed at the SIP annual poster session July 28 (see related story).

Using CD-1 mice, Crespo-Mejias administered four treatments to pregnant mice — the synthetic estrogen diethylstilbestrol (DES), which has known effects on testis development, as a positive control; BPA in high and low concentrations as experimental dose; and corn oil as a vehicle control. Her preliminary data bore out the hypothesis, suggesting that BPA exposure has an adverse effect on the embryonic development of the testes as shown by histological as well as gene expression analysis.

Taking the next steps

Yao, who was lead researcher on the study, said he was impressed by Crespo-Mejias' understanding of what's necessary for designing an effective study with preliminary data that can be replicated in other laboratories. "Because of Yasmin's careful design," Yao said, "there is strong support for her hypothesis, and we plan to pursue the study with a larger sample size."

The next step for Crespo-Mejias could be presenting her findings at the national conference of the Society for Advancement of Chicanos and Native Americans in Science (SACNAS) Oct. 27-30 in San Jose, Calif. She has applied for a travel grant to display her poster at the meeting, whose theme in 2011 is "Empowering Innovation and Synergy Through Diversity."

Crespo-Mejias said she'd like to come to NIEHS next summer. Then, the next big decision for her will be whether to apply to graduate school or medical school following graduation.

Promoting diversity in science

For Roman, reaching out to young Hispanics is well worth the effort. "It's clear that diversity makes for better science," he explained. "We benefit as a whole from the diverse perspectives that people from different backgrounds and heritages bring to scientific discovery, as well as their often keener awareness of the health disparities that exist in different communities." Roman added that the NIH leadership has repeatedly affirmed its commitment to building an ever more diverse scientific workforce.

A winning combination for quality mentoring

As helpful as the NIH Hispanic Employment Program was for helping Crespo-Mejias find the right scientific fit for her internship at NIEHS, she had little idea that she would also find a perfect match for her mentoring needs here.

This summer, Crespo-Mejias worked side by side with Rodriguez who first came to NIEHS as an undergraduate student at North Carolina State University. She went on to complete her undergraduate work, her Ph.D., and postdoctoral training while affiliated with the Institute. Since joining NIEHS as a permanent employee, Rodriguez has been involved in mentoring postdocs and interns in the Laboratory of Reproductive and Developmental Toxicology. Roman said of her, "If anyone knows something about good science and good mentoring at the NIEHS, Karina does."

Although this was Yao's first year mentoring a summer intern at NIEHS, in his previous position as an associate professor at the University of Illinois at Urbana-Champaign, he had been a mentor in a summer program for minority students that included three young scientists from Puerto Rico.

Other members of the close-knit group, which includes postdoctoral fellows Heather Franco, Ph.D., and Erica Ungewitter, Ph.D., as well as predoctoral fellow Chang Liu, guided her through her summer project. As Yao said, "Yasmin's pilot study involved a lot of work for her in such a short period of time."

Her success, as Rodriguez observed, was rooted in her positive attitude and work ethic. "She was very interested, eager to learn and understand her experiments, and she worked very, very hard this summer on a tough project."

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Remembering Joe Wachsman

By Eddy Ball

Friends and colleagues at NIEHS were saddened to hear of the death of Joe Wachsman, Ph.D., July 10 in Denver, following a brief illness. Wachsman, who was 83 at the time of his death, is survived by his daughters, Dianne Betkowski and her husband Adam of Denver, Nina Alivio and her husband Ben, and Claire Alba and her husband Rennie, as well as Wachsman's sister, Terri Jackson, and seven grandchildren.

Wachsman worked in several groups at NIEHS during his tenure as a special volunteer from the early 1990s and to the mid 2000s. He joined the Institute following his retirement as a professor at the University of Illinois (UI) at Urbana-Champaign and an appointment at the University of North Carolina at Chapel Hill.

After receiving his doctoral degree from the University of California, Berkeley, Wachsman completed a fellowship with the National Cancer Institute before joining UI, where he was also a Research Career Development awardee of the National Institute of Allergy and Infectious Diseases. During his more than 30-year career at UI, Wachsman touched the lives of many students, including NIEHS/NTP Director Linda Birnbaum, Ph.D., who completed her doctorate there.

An intellectual presence at NIEHS

NIEHS pathologist Gordon Flake, M.D., who kept in touch with Wachsman and his family during the years since his retirement from NIEHS, expressed the sentiments of many, when he commented about Wachsman's insatiable curiosity, humor, and enthusiasm for science. "He told me that he lived for the noontime seminars, which he always seemed to grasp and could always be counted on for a question or two at the end."

Wachsman's supervisor during his association with the NTP predictive toxicology project in the mid-1990s, toxicologist Ray Tennant, Ph.D., said of his friend and colleague, "Joe was just plain a good guy with a broad range of interests who would talk science at the drop of a hat." Biologist Carol Trempus, who worked in NTP at the time, added, "He was definitely a presence back in those days."

NIEHS lead researcher and former Deputy Director Samuel Wilson, M.D., was Wachsman's supervisor, when he worked with the Office of the Director (OD) in the early 2000s conceptualizing new research opportunities, especially in the area of oxidative stress. "Joe's interest in oxidative stress and how that impacts environmental health overlapped interest in OD at the time and interest across the Institute in oxidative stress…. He was a person with a great deal of intellectual curiosity and a passion for scholarship."

Wachsman pursued his varied interests in science during his golden years, until his declining health prompted his retirement from NIEHS and move to live near family in Denver. According to members of his family, Wachsman's passion for science was only trumped by his deep love of music. (Photo courtesy of Steve McCaw)

Along with his interest in oxidative stress, Wachsman is remembered for an early paper on epigenetics. Published in 1997 in Mutation Research, the paper explored "DNA methylation and the association between genetic and epigenetic changes: Relation to carcinogenesis," a topic that has stirred widespread interest among the scientific community in the years that followed its publication.

Reflections on a friend and colleague

Even as Wachsman's health declined, said Flake, "He was always researching cures for his own illnesses, and, in spite of all his problems, he always seemed upbeat, like each day was a new day. I'll miss Joe," Flake added. "He was a funny guy, a smart guy, and a friend."

Colleague Tom Hawkins, who worked in policy and communications at NIEHS, described Wachsman as "a warm and engaging human being and intensely interested in the ideas in science." Hawkins also said, "With him, you always knew that science was a growing, learning, evolving discipline."

Another of the people moved by their friendship with Wachsman, NTP geneticist Frank Johnson, Ph.D., said of his late colleague, "He was very open-minded and a true intellectual. He would question anything — he didn't care whether something was a sacred cow or not," Johnson added. "He added a lot to this place."

Notable publications

A microbiologist by training, Wachsman, as Johnson described him, "morphed a bit like a lot of us have," developing interests in toxicology, molecular genetics, and epigenetics over the course of his career. During his time at NIEHS and NTP, Wachsman authored or co-authored several papers, including some memorable reviews:

Wachsman JT, Bristol DW, Spalding J, Shelby M, Tennant RW. 1993. Predicting Chemical Carcinogenesis in Rodents. Environ Health Perspect, 101(5): 444-445.

Bristol DW, Wachsman JT, Greenwell A. 1996. The NIEHS predictive-toxicology evaluation project: Chemocarcinogenicity bioassays. Environ Health Perspect 104(Suppl 5):1001–1010.

Wachsman, JT. 1997. DNA methylation and the association between genetic and epigenetic changes: Relation to carcinogenesis. Mutat Res 375(a):1-8.

Penta JS, Johnson FM, Wachsman JT and Copeland WC. 2001. Mitochondrial DNA in human malignancy. Mutat Res 488(2):119-133.

Copeland WC, Wachsman JT, Johnson FM, Penta JS. 2002. Mitochondrial DNA alterations in cancer. Cancer Invest 20(4):557-569.

(Citations courtesy of Frank Johnson)

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