Environmental Factor
Your Online Source for NIEHS News

April 2008

NIEHS Spotlight

Spirit Lecture Celebrates Achievement and Work-Life Balance

The Spirit Lecture Series, sponsored by the NIEHS Diversity Council, has honored women scientists who were not only leaders in their respective fields, but who were also able to balance science, community, volunteerism and mentoring. This year's speaker, Lisa Alvarez-Cohen, Ph.D., embodied the same indomitable spirit and delivered a lecture that combined how she succeeded in science with her work in the field of environmental engineering. ...read more

NIEHS Marks International Women's Day

On March 10 in Rodbell Auditorium NIEHS celebrated women scientists and their contributions by marking International Women's Day. The event highlighted the scientific and personal achievements of foreign-born women scientists working in NIEHS labs with a program of talks and panel discussion. ...read more

RAISE Recognizes the Contribution of Women Scientists

Two scientists with a similar background on paper — a strong publication record, adequate teaching service and an exceptional history of training young scientists, for example — should have about the same chance of receiving a merit-based award or being awarded tenure. However, according to a national study, if review committee members know that one of the applicants is a woman, her chance of winning the award or gaining the promotion decreases dramatically. ....read more

Science Notebook

Epidemiologist Calls for Revitalizing Toxicology

For Devra Davis, Ph.D., the war on cancer is a prime example of the way economic and social forces can shape scientific inquiry and public health policy — and highlights the shortcomings of today's toxicology. ...read more

The Role of Hormones in Breast Cancer and Metastasis

Breast cancer researcher Kathryn B. Horwitz, Ph.D., presented the most recent talk in the 2007-2008 NIEHS Distinguished Lecture Series on March 11 in Rodbell Auditorium to a capacity audience. The talk, titled "Hormonal Regulation of Breast Cancer: Stem Cells and Metastasis," was hosted by John Cidlowski, Ph.D., supervisory biologist in the NIEHS Laboratory of Signal Transduction. ...read more

New Directions in Autism Research Funded by NIEHS

Support from NIEHS is enabling researchers at NIEHS and across the country to make important discoveries that may help unravel the mysteries of the complex syndromes grouped as Autism Spectrum Disorders (ASD). New studies have been published in the past few months by NIEHS-funded investigators involved with the Childhood Autism Risks from Genetics and Environment (CHARGE) project and their colleagues. ....read more

NIEHS Spotlight

Looking Ahead to Legal and Ethical Implications of Epigenetics

If bioethicist Mark Rothstein, J.D., is successful in his mission, the legal and scientific communities may be able to consider new research findings about the growing list of diseases related to epigenetics with at least some appreciation of their legal and ethical implications. ...read more

Exploring the Impact of HIV and AIDS on African American Women

Along with plenty of straight talk about the impact of HIV/AIDS on African American women, the audience at the NIEHS Black History Month Observance February 29 in Rodbell Auditorium heard a series of speakers who argued for greater participation of African Americans in clinical trials. ...read more

NIEHS Again Rated a Top Workplace for Postdocs

In the latest annual *Scientist* magazine ratings of top places to work for postdoctoral fellows, NIEHS again placed among the top government institutions and ahead of any other NIH Institutes or Centers (ICs). Survey respondents praised NIEHS for its strengths in the areas of career development opportunities and facilities and infrastructure. ...read more

Suk Speaks at Symposium Honoring Paul Lioy

A symposium honoring *Environmental Health Perspectives (EHP)* Associate Editor Paul Lioy, Ph.D., was held at the Environmental and Occupational Health Sciences Institute (EOHSI), which is funded in part by NIEHS, on Friday, Marcy 7, 2008. Lioy was the recipient of the Fifth Annual Distinguished Alumni Award from the Rutgers University Graduate School. ....read more

Extramural Research

Extramural Update

In November 2007, the NIEHS Division of Extramural Research and Training (DERT) held its Annual Science Retreat, focusing on understanding Translational Research and the ability to bridge research findings from one domain to another. With subsequent refinement, the draft framework initiated at that retreat has become a useful evaluation metric that provides insight into the maturity and potential of a given field with regard to translation. ...read more

Extramural Papers of the Month

- Black Carbon Air Pollution May Lower IQ
- Mitochondrial Protein Mortalin and the Progression of Parkinson's Disease
- Identical Twins: Are They Really Identical?
- Flaxseed Improves Outcome from Lung Injury

Intramural Research

Intramural Papers of the Month

- Hormones Can Affect the Expression of Cardiac Genes
- Singlet Oxygen Production Indicates Site of Irradiation Damage
- Cell Surface Receptor Involved in Innate Immune Response
- Silicone Implants, Connective Tissue Disease and Monoclonal Gammopathies

Inside the Institute

Social Justice for People with Disabilities

According to NIEHS Bioethicist David Resnik, J.D., Ph.D., most people respond initially to the issues of accommodation for people with disabilities on the level of personal ethics. ...read more

New Triangle Roadway Proposed for 2010

Triangle residents who work in Research Triangle Park (RTP) know that the daily commute can be a test of patience at times. That's why the North Carolina Turnpike Authority (NCTA) wants to construct a six-lane, median-divided toll roadway called the Triangle Parkway. ...read more

Calendar of Upcoming Events

- **April 3 -4 (Offsite Event)** in Natcher Conference Center, NIH Campus, Bethesda, Md. — Joint NIEHS SBRP-WETP Technical Workshop and WETP Spring Awardee Meeting: "Reducing Risk and Protecting Public Health Through Research and Training"
- **April 4** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, featuring Joe Piven, M.D., topic TBA
- **April 7** in Rodbell Auditorium, 10:00 – 11:00 — Laboratory of Molecular Genetics Seminar Series, featuring Joann Sweasy, Ph.D., speaking on "Aberrant Base Excision Repair and Cancer"
- **April 11** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, speaker and topic TBA
- **April 15 -17 (Offsite Event)** at Embassy Suites, Washington, D.C. — 2nd Annual CounterACT Network Research Symposium
- **April 17-18 (Offsite Event)**, Bol, Island of Brač, Croatia — International Workshop on Diagnostic Criteria in Endemic (Balkan) Nephropathy
- **April 18** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series with Jonathan Patz, M.D., topic TBA
- **April 22** in Rodbell Auditorium C, 10:00 – 12:00 — "Xeriscaping and low water requiring native species for your garden" presented by UNC Habitat Gardens Curator Chris Liloia
- **April 22 – 24** — Earth Week activities will include speakers, joint programs with EPA, a house plant exchange, and live music with musicians from both EPA and NIEHS; times and locations TBA.
- **April 24** in Rodbell Auditorium, 10:30 – 11:30 — "The drought, water conservation, water resources and the future," by James Lim, Durham Water Authority
- **April 25 (Offsite Event)** in the US EPA Main Building, RTP Campus, 8:45 – 4:30 — 11th Annual NIEHS Biomedical Career Fair
- **April 25** in Rodbell Auditorium, 9:00 – 10:00 — Frontiers in Environmental Sciences Lecture Series, featuring Francois Guillemot, Ph.D., topic TBA
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Spirit Lecture Celebrates Achievement and Work-Life Balance

By Robin Arnette

The Spirit Lecture Series, sponsored by the NIEHS Diversity Council, has honored women scientists who were not only leaders in their respective fields, but who were also able to balance science, community, volunteerism and mentoring. This year's speaker, Lisa Alvarez-Cohen, Ph.D., embodied the same indomitable spirit and delivered a lecture that combined how she succeeded in science with her work in the field of environmental engineering. Her talk, titled "Application of Omics-Based Tools and Microarrays to Optimize Bioremediation," took place on March 7 in Rodbell Auditorium. This seventh annual Spirit Lecture was co-sponsored by the Frontiers in Environmental Sciences Lecture Series and was part of several activities that celebrated Women's History Month.

Alvarez-Cohen presented the 2008 Spirit Lecture. (Photo courtesy of Steve McCaw)

Alvarez-Cohen is the Fred and Claire Sauer Professor and Chair of the Department of Civil and Environmental Engineering at the University of California at Berkeley. She said she was humbled and honored to be chosen as a Spirit Lecturer and acknowledged the role that NIEHS played in her career. "The majority of the research that I'll be talking about today was funded by NIEHS through the Superfund program to a center at UC-Berkeley," she said. "I'm incredibly grateful to the institute for supporting this work."

Molly Vallant, Chair of the Spirit Lecture Committee, provided a stirring welcome address for the combined Spirit and Frontiers in Environmental Sciences Lecture. (Photo courtesy of Steve McCaw)

Alvarez-Cohen was anxious to jump into the science portion of the talk, but before she did, she offered advice on how to be successful in science. Among the essentials were being able to evolve as a scientist, prioritizing one's life and only doing work that one is passionate about. However, the most important skill was being able to get out of one's comfort zone. She recalled a turning point in her life when doing so changed her way of thinking and living.

When Alvarez-Cohen was in graduate school, she and a friend had planned to backpack across Europe one summer, but her friend backed out at the last minute. Alvarez-Cohen had never traveled anywhere at that point, but she decided to go anyway. "I spent the entire first day in London crying," she said. "I wanted to get back on

the plane and come back to my comfort zone." Since she couldn't get another flight until the next morning, she decided she would venture out and attend a play that evening. When she did, she saw that she wasn't the only adventurer in town. "When I stood in line, I met all of these other people who were also backpacking that summer. It made me realize that I didn't have to always do things I was comfortable doing," she stated.

Beth Anderson, a program analyst for DERT's Center for Risk & Integrated Sciences, listened intensely to this year's Spirit Lecture. (Photo courtesy of Steve McCaw)

One area where Alvarez-Cohen is comfortable is tracking environmental contaminants. Her lab employs molecular tools to optimize bioremediation, which means using microorganisms to remove dangerous chemicals that leak from underground tanks. She said the reason why the nation's groundwater resources weren't contaminated with gasoline and other solvents was because of naturally occurring soil microorganisms that biodegrade them. "These versatile organisms live in complex communities that break down contaminants and pass them on to others that continue the degradation," she explained.

Chris Portier, Ph.D., moderated the Q&A portion of the lecture. (Photo courtesy of Steve McCaw)

During bioremediation, Alvarez-Cohen works with *Dehalococcoides*, a bacterium that breathes chlorinated ethenes and other chlorinated materials. If perchloroethene (PCE), a highly toxic solvent and the predominant ingredient in dry cleaning solution, leaks into the soil, *Dehalococcoides* can break it down into ethene, a safe and environmentally-friendly compound. The reaction happens when the team biostimulates or injects an inexpensive organic such as lactate or whey into the ground. The fermenting organisms in the soil use the organic to make hydrogen, acetate and vitamin B12 — the products that *Dehalococcoides* need to grow. Alvarez-Cohen noted that if contaminated field sites don't have indigenous *Dehalococcoides* colonies present, the team could add enriched cultures of the bacteria to the soil in a process called bioaugmentation.

The lab's overall goal is to use biomarkers based on ribosomal genes to measure the numbers of *Dehalococcoides* at field sites and use quantitative functional genes to distinguish between different *Dehalococcoides* strains and their functions. Team members also use reverse transcription to quantify cell mRNA expression and microarrays to identify important growth conditions for the bacteria.

Return to Table of Contents

NIEHS Marks International Women's Day

By Robin Arnette

On March 10 in Rodbell Auditorium NIEHS celebrated women scientists and their contributions by marking International Women's Day. The event highlighted the scientific and personal achievements of foreign-born women scientists working in NIEHS labs with a program of talks and panel discussion.

The International Women's Day panel: (L-R) Yang, Kadiiska, Li and Kinyamu. (Photo courtesy of Steve McCaw)

"International Women's Day has been recognized globally as a time to reflect on progress, to call for change and to celebrate acts of courage and determination of ordinary women who have made extraordinary achievements," said Sharon Hrynkow, Ph.D., associate director of NIEHS. Hrynkow welcomed what she called the "small but mighty" audience to the event.

The scientists gave 20 minute talks that were followed by a panel discussion moderated by Darlene Dixon, head of Comparative Pathobiology at NIEHS, and Molly Vallant, a biologist in the NTP. A networking reception, sponsored by the Office of the Director at NIEHS, the NIH Foundation, the Society for Women's Health Research and the United Nations Foundation, immediately followed the program. The scientists's stories combined their love of science with the challenges they've overcome to succeed in their fields.

Hrynkow was excited to host NIEHS's first celebration of International Women's Day. (Photo courtesy of Steve McCaw)

Maria Kadiiska, M.D., Ph.D., is a staff scientist in the Free Radical Metabolism Group with Principal Investigator Ron Mason, Ph.D., but she started her career as a physician in her native Bulgaria. Since then she has co-authored more than 100 publications, been invited to speak at more than 65 conferences and co-chaired many scientific sessions at national and international meetings. She is also the leader of the NIEHS international BOSS project for validating biomarkers of oxidative stress. She said she's been lucky to have worked with so many talented scientists, and she pointed out all of the good ones had one thing in common — a passion for science. "It is not how much you do, but how much love you put into doing it," she said.

Harriet Kinyamu, Ph.D., is a staff scientist in the Chromatin & Gene Expression Group with Principal Investigator Trevor Archer, Ph.D. A native of Kenya, Kinyamu is interested in understanding the role of the 26S proteasome in gene expression, but her career in science was almost derailed during her graduate school years. "I was in the process of being deported when a colleague alerted me to an open position in a lab in

London, Ontario," she remarked. That lab turned out to be Archer's group, and a year and a half later, Archer and Kinyamu made the move to NIEHS.

Xiaoling Li, Ph.D., is head of the Mammalian Aging Group and studies the environmental cues involved in age-related diseases. She was born in China and majored in biochemistry at Beijing University. Like the other women of this panel, Li wasn't afraid to study abroad, even though the language barrier made things difficult. Nevertheless, Li's doctoral advisor at Johns Hopkins encouraged her to continue working. Li said, "He told me the only thing that really matters is the science. If I excel in that, the language will come later." It seems her advisor was right; her improved English skills and her outstanding science landed her a position at NIEHS.

Ivana Yang, Ph.D., is a National Heart, Lung and Blood Institute staff scientist, but she started at NIEHS as a member of the Environmental Lung Disease Group formerly headed by David Schwartz, M.D. For the past three years, she's tried to identify novel innate immune genes, but that struggle was nothing compared to her college days. Yang grew up in Sarajevo, which is now capitol of Bosnia-Herzegovina (formerly Yugoslavia), but she was an undergraduate at the College of William and Mary when the Bosnian war began in 1992. "Those were the hardest four years of my life because I didn't know if my family was doing okay or not," she said. After the conflict, her family moved to Montreal, so seeing them whenever she wanted became a reality.

The panelists, like many other foreign-born scientists, had to overcome a whole host of roadblocks on the path to success, but their hard work, strength and optimism — traits common to many women trailblazers — carried them through.

Return to Table of Contents

Dixon was instrumental in organizing the panel discussion. (Photo courtesy of Steve McCaw)

Lily Hong, a biologist in the NTP. (Photo courtesy of Steve McCaw)

RAISE Recognizes the Contribution of Women Scientists

By Robin Arnette

Two scientists with a similar background on paper — a strong publication record, adequate teaching service and an exceptional history of training young scientists, for example — should have about the same chance of receiving a merit-based award or being awarded tenure. However, according to a national study, if review committee members know that one of the applicants is a woman, her chance of winning the award or gaining the promotion decreases dramatically. Gender bias is a reality in the world, especially in science, but a group of women scientists hope to change that.

Hrynkow stressed the importance of the RAISE project. (Photo courtesy of Steve McCaw)

According to its Web site, the Recognition of the Achievements of Women in Science, Medicine and Engineering (RAISE) Project is "a campaign to increase the status of professional women through enhanced recognition of the achievements of women in science, technology, engineering, mathematics and medicine." The RAISE Project highlights the fact that awards and prizes are important as recognition for scientific achievement. Despite the marked rise of women receiving M.D.s and Ph.D.s in science, the disparity between scientific awards given to men and women still exists. In a study of almost 800 awards and prizes in science, technology, mathematics and medicine, The RAISE Project has established that over 55 percent have rarely, if ever, been given to women. Such analysis confirms the reality of gender bias and is the impetus for a wide ranging effort to improve the success of professional women.

Pincus encouraged the audience to nominate a woman for an award listed on the RAISE Web site. (Photo courtesy of Steve McCaw)

On March 10 Stephanie Pincus, M.D., founding director of RAISE with the technical assistance of Florence Haseltine, M.D., Ph.D., Director of the Center for Population Research at NICHD and co-founder of the Society for Women's Health Research, presented "RAISE-ing the Status of Women in Science" in Rodbell Auditorium. Pincus and Haseltine said biases persist when it comes to rewarding women for their scientific accomplishments, and they encouraged everyone in the audience to nominate a woman for one of the awards listed on the RAISE Web site. The RAISE Project is sponsored by the Society for Women's Health Research.

When asked to comment after the program, Sharon Hrynkow, Ph.D., associate director of NIEHS and leader for NIEHS's first month-long series of events marking Women's History Month said, "Women at early stages of their careers need to understand the value of formal recognition, how to nominate and how to be nominated.

This insight will carry them at every stage of their path, and this is why the RAISE project is so important." Hrynkow was pleased that the audience included several male colleagues, including NIEHS and NTP Acting Director Samuel Wilson, M.D., whose support and encouragement for Women's History Month events, she said, was outstanding.

Acting Deputy Director of NIEHS and NTP William A. Suk, Ph.D., M.P.H., said it was encouraging that the numbers of supportive scientists were on the rise, but more could be done. "What I don't see is a truly concerted effort on the part of all scientists to mentor and encourage young women scientists starting at an earlier age," Suk said. "NIEHS should try to emulate the outstanding mentoring programs that occur across the country."

Suk and Haseltine looked over the data regarding women scientists and award rates. (Photo courtesy of Steve McCaw)

Senior Investigator Mitch Eddy, Ph.D., was one of several male colleagues who attended the RAISE seminar. (Photo courtesy of Steve McCaw)

Return to Table of Contents

Looking Ahead to Legal and Ethical Implications of Epigenetics

By Eddy Ball

If bioethicist Mark Rothstein, J.D., is successful in his mission, the legal and scientific communities may be able to consider new research findings about the growing list of diseases related to epigenetics with at least some appreciation of their legal and ethical implications. That was one of the themes in the NIEHS grantee's February 26 presentation at the annual Rabbi Seymour Siegel Memorial Lecture in Ethics and Law— and in the panel discussion which followed. Rothstein's talk, titled "Exposed Today, Grandchildren Pay," was held at the Duke University School of Law.

Rothstein, who is a distinguished professor of law and medicine at the University of Louisville, was joined by a group of Duke

"Epigenetics highlights the effects of inequality in living and working conditions, as well as a range of disparities in societal advantages," Rothstein argued as he described the implications on environmental justice. (Photo courtesy of Steve McCaw)

University panelists that included NIEHS grantee and recognized authority on epigenetics, Randy Jirtle, Ph.D., professor of Radiation Oncology at Duke Medical Center; Robert Cook-Deegan, M.D., director of the Center for Genome Ethics, Law and Policy (GELP); and Lauren Dame, J.D., GELP associate director and associate of the Trent Center for Bioethics, Humanities and History.

Opening with the now familiar definition of epigenetics as the study of heritable changes in gene expression that are unrelated to DNA sequence variation, Rothstein explored the impact of new discoveries on regulation and liability, intergenerational equity, eugenics, environmental justice, privacy and confidentiality, and equitable access to health care.

Although Rothstein elaborated on the many complex challenges in epigenetics research and its many unanswered questions, he was nonetheless adamant in his call for scientists, legal scholars and ethicists to start now to prepare for the impact of the new findings. "Law and ethics do not do well in catch-up mode," he reminded the audience, "and science does not wait."

Rothstein noted that epigenetics shares a subset of issues associated with the mapping of the human genome, which he said was arguably the first scientific effort to build in a bioethical component from the outset. However, as his talk made clear, these shared issues hardly exhaust the range of concerns arising from the study of epigenetics, a biological process that by definition operates at the intersection between genes and environment, impacting ethical and legal concerns related to both.

As Rothstein explained, epigenetic modifications are caused by such environmental factors as exposures to chemicals and radiation, diet and lifestyle that mark DNA, either turning on or turning off gene expression. Although epigenetic modifications are potentially reversible — and some are actually beneficial to the organism — they can be passed from generation to generation with potential transgenerational health effects presenting years later in descendents of the individuals who were exposed.

Like genetics, epigenetics raises important issues related to privacy, discrimination, employment and the right to know. The new science also raises concerns

In her introduction, Coleman said of Rothstein, "It would take me most of the time, literally, allotted for this lecture to mention all of his accomplishments and honors." (Photo courtesy of Steve McCaw)

During Rothstein's talk, Dean Levi, center, sat with sponsor Allen Siegel and his wife, Rochelle, right, and panelist Dame, left. (Photo courtesy of Steve McCaw)

Panelist Jirtle, right, addressed the complexities of interpreting epigenetic research findings: "I can't extrapolate… [epigenetic responses in one strain of mice] even to another strain, let alone to other species of animals." (Photo courtesy of Steve McCaw)

about eugenics, a movement devoted to improving the human species through controlled mating, because it will likely be possible at some point in the future to test individuals for epigenetic alterations. With this ability to identify these modifications will come the danger of results being used as a justification for encouraging or requiring testing of individuals — and as a rationale for controlling the lives of people so affected.

Because the changes are triggered by environmental exposures that may be preventable and potentially reversible, issues surrounding epigenetics research also include individual responsibility, legal liability, health disparity and environmental justice. At the present time, Rothstein argued, we are just beginning to articulate the necessary questions about the obligations individuals and society as a whole may have for the health and well being of the most vulnerable people in society and their descendants, generations into the future.

The Siegel Lecture is held each year at the Duke University School of Law. The lecture is sponsored by labor lawyer and former Duke Law Professor Allen Siegel, a member of the Duke Law class of 1960. The lecture series honors the memory of Siegel's brother, Rabbi Seymour Siegel, a noted scholar of ethics and theology who died in 1988. The lecture was introduced by Dean David Levi, J.D., and hosted and organized by Professor Dorianne Coleman, J.D. Rothstein's talk and previous Siegel Lectures are available as webcasts courtesy of the School of Law.

"The science is changing," insisted Cook-Deegan. "It turns out that genes aren't as simple as we thought they were." (Photo courtesy of Steve McCaw)

On the positive side, observed Dame, "Epigenetics will help bring back environment as an equally important player in health." (Photo courtesy of Steve McCaw)

Like many of the students who made up the bulk of Rothstein's audience, this young man seemed to struggle with the connections between the unfamiliar world of laboratory research and the arena of contemporary legal and ethical issues — as well as with his course and bar exams. (Photo courtesy of Steve McCaw)

Veteran legal scholars in the audience, such as Duke's Jerome Reichman, J.D., center, the Bunyan S. Womble Professor of Law, also appeared eager to hear Rothman's arguments about the impact of the new science on the legal community. (Photo courtesy of Steve McCaw).

Exploring the Impact of HIV and AIDS on African American Women

By Eddy Ball

Along with plenty of straight talk about the impact of HIV/AIDS on African American women, the audience at the NIEHS Black History Month Observance February 29 in Rodbell Auditorium heard a series of speakers who argued for greater participation of African Americans in clinical trials. Sponsored by the NIEHS Office of Clinical Research and the RTP Chapter of Blacks In Government (BIG), the event featured four women involved in the prevention and treatment of patients with HIV/AIDS and related diseases.

NIEHS Administrative Officer Kim Peterson, center, and fellow choir members sang as the audience took their places in the auditorium. Rice led the singers, and NIEHS Project Officer Jennie Foushee provided piano accompaniment. (Photo courtesy of Steve McCaw)

The program opened with a moving choral presentation of James Weldon Johnson's "Lift Every Voice and Sing," led by NIEHS Stem Cell Biologist and BIG member Annette Rice. NIEHS Project Officer and President of the RTP Chapter of BIG Veronica Godfrey welcomed the audience to the annual program on health disparities in the African American community. Rice introduced the panelists and gave an overview of the program.

Rice was serious about keeping the program on schedule. As the event came to a close, however, her lighter side emerged as she joked, "I'm going to ask Dr. Stavros come up to give us his last name so we'll all know how to pronounce it." (Photo courtesy of Steve McCaw)

In the first presentation, North Carolina Central University Professor La Verne Reid, Ph.D., surveyed the history of HIV/AIDS in the United States, risk factors for the disease and trends of new infections. She pointed to the disparity in the African American community, which makes up 13 percent of the population but 50 percent of new cases.

Reid introduced a theme that would be echoed by speakers throughout the event: the need to overcome complacency about HIV/AIDS, to engage in honest dialogue with sex partners, to practice safe sex and to get tested routinely — and re-tested as often as necessary. "HIV testing should be as normal as taking your temperature," she said.

Testing of a related kind was the topic of a talk by North Carolina Department of Health and Human Services Nurse Consultant Elizabeth Zeringue, a specialist in tuberculosis (TB) and TB/HIV co-infection. Zeringue tries to combat widespread complacency and ignorance about TB, which she said kills someone somewhere in the world every 20 seconds. "HIV dramatically increases the risk of tuberculosis when a person is co-infected," Zeringue told the audience.

Director of the Maria Parham Medical Center and Infectious Disease Specialist Michelle Collins Ogle, M.D., took consideration of the disease a step farther to include African American patients treated at her rural clinic, people who cope with HIV/AIDS every day of their lives. Ogle focused on the barriers to their participation in clinical trials, including a long history of medical abuse of minorities. One of the main reasons minorities don't get involved in clinical trials, she concludes, is "they don't trust the government."

To underscore the effects of health disparity, Ogle presented the dramatic differences in rates of treatment/participation in clinical trials by HIV/AIDS patients who are African American, 33 percent/ 21 percent; Hispanics, 15 percent/11 percent; and whites, 49 percent/62 percent.

Godfrey acknowledged the major role played by Marian Johnson-Thompson, Ph.D., in putting the program together. Godfrey also urged audience members to do their part: "We are stewards, [and] you might be the person to change someone else's life." (Photo courtesy of Steve McCaw)

The final panelist is a participant in an AIDS Clinical Trial at Duke University Medical Center, who was not identified to protect her rights to privacy and to comply with the Institutional Review Board stipulations governing her clinical trial. She explained her reasons for bucking her community's widespread distrust of the medical system by undergoing treatment and participating in clinical trials. Her narrative gave the audience an opportunity to hear a first-hand account of the experiences of an African American woman with HIV/AIDS. With her unaffected eloquence, the participant infused an emotional appeal into the program that reinforced the statistics presented by the rest of the panelists.

According to the participant, African Americans who volunteer for clinical trials not only help themselves by getting innovative treatments they would not get otherwise and increase the understanding of racially influenced differences in drug metabolism. As the participant explained, there are also other important reasons: "I just wanted to give back something to show my gratitude to the ones who went before me, to the people who marched and protested and, in other words, acted up."

A veteran public health educator, Reid gave the audience several disturbing statistics. "The HIV case rate for black women is 24 times that of white women," she said. "HIV/AIDS is the leading cause of death among African American women ages 25 to 34." (Photo courtesy of Steve McCaw)

The program concluded with a question-and-answer session and comments by NIEHS Clinical Research Unit Director Stavros Garantziotis, M.D., who expressed the support of Acting Director Sam Wilson, M.D., and Acting Clinical Director Darryl Zeldin, M.D., and reaffirmed his group's commitment to greater diversity in clinical research populations.

During her talk, Zeringue told the audience, "The most important message we give to anyone when we talk to them about tuberculosis is that it is curable and HIV, if they are co-infected, is treatable." (Photo courtesy of Steve McCaw)

Ogle put the issues into historical perspective. "There have been so many other things that have happened since that blunder [the Tuskegee syphilis experiments] that give communities of color reasons not to trust." (Photo courtesy of Steve McCaw)

The clinical trial participant described her sense of history and obligation. "I wanted to pay tribute to the ones who dealt with stigma and discrimination head on by paving the way for me and other people to walk." (Photo courtesy of Steve McCaw)

Shown during the question-and-answer session, Garantziotis delivered the closing words of the program. "Educational programs, such as today's," he remarked, "are very important… for education of both the public and medical professionals." (Photo courtesy of Steve McCaw)

Return to Table of Contents

NIEHS Again Rated a Top Workplace for Postdocs

By Eddy Ball

In the latest annual *Scientist* magazine ratings of top places to work for postdoctoral fellows, NIEHS again placed among the top government institutions and ahead of any other NIH Institutes or Centers (ICs). Survey respondents praised NIEHS for its strengths in the areas of career development opportunities and facilities and infrastructure.

Diane Klotz, Ph.D., acting director of the NIEHS Office of Fellows Career Development (OFCD), saw the results as an indication of the Institute's holistic approach to training. "I believe the NIEHS continues to do well because we strive to create a real sense of partnership between our postdoctoral fellows and our administration where the training, education and career development of postdocs is concerned."

"The NIEHS has created an infrastructure that supports the career development of its postdoctoral fellows not only scientifically, but professionally as well," Klotz said of the Institute's highest rated strength. (Photo courtesy of Steve McCaw).

The newly elected chair of the NIEHS Trainees Assembly (NTA), Postdoctoral Fellow Stephanie Nick McElhinny, Ph.D., was also gratified by the high rating the Institute received in regard to career development. "The strength of career development at NIEHS is a testament to the phenomenal efforts of OFCD Director Diane Klotz and her predecessor, Debbie Swope," Nick McElhinny observed. "Career development opportunities were strong for only three institutions ranked ahead of NIEHS in the survey, which I see as evidence that NIEHS is clearly ahead of the curve in keeping in touch with the changing needs of postdoctoral fellows."

NIEHS placed sixteenth in the ranking, ahead of NIH, which was rated number 29, and the National Cancer Institute, which came in at number 33. The *Scientist* offered several caveats about the survey results and tried to put the results into perspective. "No attempt has been made to measure the statistical significance of the results," wrote author Jonathan Scheff. "The difference between, say a 10th ranked and a 15th ranked institution may be insignificant."

Nick McElhinny was elected unanimously as NTA chair. Previously, she served on the planning committee for the annual NTA Biomedical Career Day. (Photo courtesy of Steve McCaw)

The Institute ranked behind only three other government institutions that pay their postdocs higher salaries. Two Department of Defense Sandia National Laboratories sites, which pay their postdocs $77,800 annually, ranked third and tenth. The Institute's neighbor, the U. S. Environmental Protection Agency in Research Triangle Park, which pays its postdocs an average of $64,265 per year, was ranked eleventh in the survey.

During a year of flat budgets for NIH ICs, some of the highest ranked institutions increased benefits and compensation for their postdocs. Examples include the Whitehead Institute,

which promised a $9,000 per year raise to first year postdocs earlier this year and an eight percent retirement contribution, and the Woods Hole Oceanographic Institute, which added dental insurance.

"While every institution would like to see itself at the number one position," Klotz reflected, "there is always room for improvement even at the top of the list, and this type of survey is more of a friendly reminder of what we do well and where we can make those improvements than anything else."

Survey Methodology

The web-based survey received ratings from more than 3,000 postdoctoral fellows. The 82 U.S. institutions and 17 international institutions that received 5 or more responses were included in the rankings. Institutions are rated according to eleven criteria:

- Quality of Training and Mentoring
- Career Development Opportunities
- Quality of Communication
- Networking Opportunities
- Value of the Postdoc Experience
- Quality of Facilities and Infrastructure
- Funding
- Equity
- Remuneration and Compensation
- Benefits
- Family and Personal Life

Return to Table of Contents

Suk Speaks at Symposium Honoring Paul Lioy

A symposium honoring *Environmental Health Perspectives (EHP)* Associate Editor Paul Lioy, Ph.D., was held at the Environmental and Occupational Health Sciences Institute (EOHSI), which is funded in part by NIEHS, on Friday, March 7, 2008. Lioy was the recipient of the Fifth Annual Distinguished Alumni Award from the Rutgers University Graduate School. This distinguished award is given to a faculty member who has made significant contributions in the Physical, Mathematical and Engineering Sciences. Lioy has been instrumental in establishing the strong translational research program in exposure assessment/exposure modeling at EOHSI and has given EOHSI an internationally recognized presence in these disciplines.

The focus of the symposium was Exposure Science and featured three distinguished speakers. William Suk, Ph.D., acting deputy director of the NIEHS, presented "Approaches to Exposure Sciences by the NIEHS" to a standing-room only audience. His presentation was followed by Morton Lippmann, Ph.D., professor of Environmental Medicine at New York University Medical School, who discussed "Paul Lioy's Contribution to the Sciences of Human Exposure Assessment." The final speaker was Bernard Goldstein, M.D., professor of Environmental and Occupational Health and former dean of the University of Pittsburgh's Graduate School of Public Health, who presented "The Challenges of Integrating Exposure Science and Risk Policy."

Lioy is professor and vice chair, Department of Environmental and Occupational Medicine, UMDNJ-Robert Wood Johnson Medical School (RWJMS). He is deputy director for Government Relations at the EOHSI, which is jointly sponsored by Rutgers University and UMDNJ. He is the division director for Exposure Science and, with Panos Georgopoulos, Ph.D., directs the Center for Exposure and Risk Modeling. In 1985, he started the first academically-based program in the world on Exposure Assessment (now Science) research, and in 1992 he and Christopher Uchrin, Ph.D., established the first doctoral program in Exposure Science, a joint program of UMDNJ and Rutgers University

Lioy received the International Society of Exposure Analysis Jerome Wesolowski Award for Lifetime Achievement in Exposure Analysis in 1998, and in 2003, he was the recipient of the Frank Chambers Award for lifetime achievement in Air Pollution from the Air and Waste Management Association. In 1999, he was elected to the International Academy of Indoor Air Sciences, and the same year was elected as a Fellow of the Collegium Ramazzini, Carpi, Italy. He is one of the founders of International Society for Exposure Analysis and served as President from 1993-94. Recently, Lioy was appointed co-chair of the New Jersey University Consortium for Homeland Security Research and is a member of the New Jersey Domestic Security and Preparedness Planning Group.

He is a member of the Science Advisory Board of the US EPA and currently a member of the Homeland Security Advisory Committee. Lioy has also been a member of the National Academy of Sciences Board of Toxicology and Environmental Studies and was chair of the National Research Council's Committee on Exposure Assessment. Lioy was a member of the US-Canada International Joint Commission Air Quality Advisory Board (1992-2007). He was the vice chair of the EPA and CEQ WTC Expert Technical Panel (2004-2005).

Currently, he is the associate editor of *Environmental Health Perspectives* and the *Journal of Exposure Science and Environmental Epidemiology*. He has published more than 235 peer-reviewed articles, two books and numerous book chapters and editorials.

Return to Table of Contents

Science Notebook

Epidemiologist Calls for Revitalizing Toxicology

By Eddy Ball

For Devra Davis, Ph.D., the war on cancer is a prime example of the way economic and social forces can shape scientific inquiry and public health policy — and highlights the shortcomings of today's toxicology. An epidemiologist at the University of Pittsburgh, Davis outlined her argument in an NIEHS Frontiers of Environmental Sciences/ Women's History Month Lecture March 3 in Rodbell Auditorium titled "The Need to Revitalize Toxicology: Lessons from the Secret History of the War on Cancer."

Davis was candid about the shortcomings of current standards for burden of proof in toxicology. "We always need more research," she said, "but you can hold up uncertainties like a cross to the vampire and say, 'Wait, we'd better do nothing.'" (Photo courtesy of Steve McCaw)

The host of Davis' talk, NIEHS Acting Director Sam Wilson, M.D., introduced the speaker, describing Davis as "an old friend of mine" and "one of the most influential and thoughtful leaders in field of environmental cancer research." Wilson praised Davis' contributions to environmental public health through raising public awareness and performing community outreach and through her steadfast commitment to uncovering the truth about environmental triggers of cancer.

Davis began her talk by acknowledging the 60th anniversary of the Killer Fog of Donora, where Davis grew up and where in one five-day period of time in 1948 a fog of industrial air pollution settled on the Monongahela River, killing 20 people. When she finally learned about it — "People didn't want to talk about it," she noted — the Killer Fog became the first of many emblematic events that would shape her career in environmental oncology.

Wilson pondered Davis' answer to his question about her community outreach. He was enthusiastic about the quality of what he described as her "great, great talk." (Photo courtesy of Steve McCaw)

The Killer Fog of Donora and cancers caused by environmental exposures led Davis to reassess the role of toxicology in preventive medicine and public health. "The motto of my work is that we have to learn from the past because we want the future to be different from the past," she explained. "And Donora is my past."

Davis traced the war on cancer back to the first x-ray of Bertha Roentgen in 1892, the death of Clarence Dally, Thomas Edison's assistant, in 1904 from radiation poisoning, and the death of Marie Curie from radiation-induced leukemia. By1936, Davis said, scientists, such as pioneer cancer investigator Ángel Roffo, had presented convincing evidence linking cancer to newly synthesized hormones, x-ray and solar radiation, coal tars and soot, benzene, and cobalt and uranium mining.

"I think it's extraordinary to go back and realize how much was known," Davis continued, "and how much good scientific evidence the scientists had to back up their warnings. They actually had studies and very detailed studies," including *in vitro* and *in vivo* toxicology, clinical case reports and descriptive epidemiology.

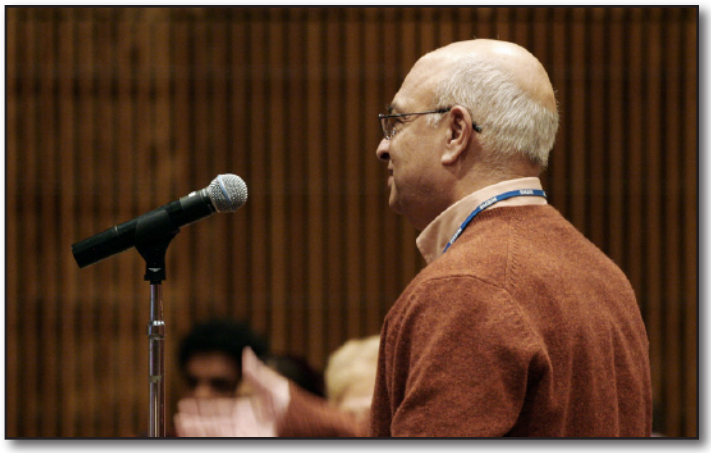
According to Davis, industry funding influenced health research organizations and professional groups to ignore the growing body of evidence about environmental influences on cancer. The public's attention was effectively diverted from prevention to the search for the elusive "cure for cancer" and to development of such gimmicks as the "safe cigarette."

Davis has used what she learned to develop several proposals for revitalizing toxicology. One involves creating a Truth and Reconciliation Commission, much like the one established in South Africa, to clear up the quagmire in the field of toxicology. By offering protection from punitive damages, such a commission, she reasons, would encourage disclosure of the information industries already have on file about the dangers of their products.

Davis also proposes a fee on products suspected of causing harm to fund more research by government and greater use of high-throughput screening as other ways to help expand toxicology's knowledge base.

Yet another proposal calls for revision of what currently constitutes the burden of proof for deciding whether compounds may be harmful to humans. "Randomized control trials work for drugs, but they don't work for life because life is a mixture," she argued. "Missing data should not be confused with absence of proof of harm."

As a member of the NIEHS Laboratory of Experimental Pathology, Visiting Fellow Saija Savolainen had an obvious interest in Davis' topic. (Photo courtesy of Steve McCaw)



"How do we clone people like you? There is such a big shortage," asked Rajendra Chhadbra, Ph.D., group leader of the National Toxicology Program's Toxicology Group.

After most of the audience had left the auditorium, Chris Portier, Ph.D., continued the conversation with Wilson and Davis. Portier is the director of the NIEHS Office of Risk Assessment Research and organizer of the FES lecture series. (Photo courtesy of Steve McCaw)

Davis also discussed cancer-related effects of CT scans (see text box below), aspartame and Ritalin. She concluded the talk with a description of the way her university's Cancer Institute is helping with the greening of Pittsburgh by making more environmentally responsible choices about sanitation and energy.

Avoidable Cancer Risk of CT Scans

One of Davis' recent concerns is unnecessary exposure to radiation in computerized tomography (CT) scans. Her article on the topic appears in the winter 2008 issue of Healthy Choices, Healthy Lives.

Davis and colleagues at the University of Pittsburgh Cancer Institute Center for Environmental Oncology have joined members of the radiological community in speaking out on the overuse of such scans, which can expose patients to radiation at levels great enough to eventually cause cancer as they age — especially children, who are far more vulnerable than adults.

A pediatric head CT scan, according Davis, can produce radiation equivalent to 400-6000 standard chest (PA/lateral) x-rays. Even the comparably "low-level" emissions from a screening mammogram expose patients to 20 to 300 times the radiation in a chest x-ray.

The American College of Radiology has called for national standards for training and certifying CT technicians and expanded educational programs for practitioners. Radiologists are warning the medical community of the possibility of a sharp increase in radiation-related cancers unless the number of CT scans is reduced in non-emergency situations.

Davis acknowledges the value of the CT scan as a tool for saving lives and avoiding exploratory surgery. However, physicians need to explore alternative diagnostic tools, such as MRI or ultrasound, before ordering procedures that involve the use of radiation.

"We have an opportunity here to take this technology, which we now understand can be used for good and has negative consequences as well," Davis reasons, "and marshal it in a much smarter way."

Return to Table of Contents

The Role of Hormones in Breast Cancer and Metastasis

By Robin Arnette

Breast cancer researcher Kathryn B. Horwitz, Ph.D., presented the most recent talk in the 2007-2008 NIEHS Distinguished Lecture Series on March 11 in Rodbell Auditorium to a capacity audience. The talk, titled "Hormonal Regulation of Breast Cancer: Stem Cells and Metastasis," was hosted by John Cidlowski, Ph.D., supervisory biologist in the NIEHS Laboratory of Signal Transduction.

Horwitz, Distinguished Professor of Medicine & Pathology at the University of Colorado Health Science Center in Denver, Colo., was the first person to show that breast cancer cells contained progesterone receptors. She prefaced her talk by explaining why it was important to understand the roles of estrogen (ER) and progesterone

receptors (PR), and hormones, in metastasis. "The problem with breast cancer is that women don't die of the primary disease of the breast; they die of their metastasis."

Metastasis is defined as the spread of a cancer from the initial site to the rest of the body. Horwitz said that the metastases that spread from the primary tumor to lymph nodes and more distant sites contain ER or PR, or both. Her lab has developed methods that help shed light on the metastatic process.

Many metastatic tumors travel to the lymph nodes, so Horwitz's research group created a model system for studying lymph node metastasis using the ER^+ breast cancer cell lines T47D and MCF-7. Human breast cancer cells that were ER^+/PR^+ were flagged with green or red fluorescence using retroviral vectors. ER^- cancer cells were used as controls. Because team members wanted to understand the effects of estrogens and progestins in their experiments, they implanted the fluorescent tumor cells into the mammary glands of immune deficient mice that had undergone an ovariectomy or ovary removal. Some of these mice were given hormone (estradiol) treatments and some were not.

"After six weeks, you could see red or green tumor cells migrating up the lymphatic system in mice treated with estradiol, so these are clearly estrogen-dependent tumors," Horwitz explained. "In the no estradiol control mice, the tumors didn't grow and no lymph node metastases occurred. The tumor cells weren't dead, just dormant."

Distinguished Lecturer Horwitz fielded questions from the audience. (Photo courtesy of Steve McCaw)

Horwitz and lecture host Cidlowski. (Photo courtesy of Steve McCaw)

Horwitz's studies indicated a difference between lymph node tumors and primary tumors with regard to estrogen resistance. To study this in detail, tumors from the mammary gland and the lymph nodes of the same mouse were grown in the presence of estradiol. Some mice were kept on estradiol, while in other mice, the estradiol was withdrawn. The difference between the two would define the estrogen-regulated genes. The tumors were harvested and the DNA was extracted and placed on microarray chips.

Microarray analysis revealed that many more estrogen-regulated genes were expressed in the primary tumor than in the lymph node tumor. "Therefore, the lymph node appears to be a protected area in which the ER is working differently than it does at the primary tumor site," Horwitz said. "In other words, the microenvironment or the part of the body where the tumor resides does have an effect on estrogen regulation."

Horwitz concluded her talk with data on breast cancer stem cells, progenitor cells that undergo several rounds of asymmetric division before forming a tumor. She knew these cells expressed $CD44^+/CD^{24-/low}$, but her work determined that breast cancer stem cells also contained cytokeratin 5 (CK5), were ER^-/PR^- even in ER^+/PR^+ cancers, and could differentiate into the ER^+/PR^+ cancer subtype. This means that if a patient has an ER^+ breast

cancer that contains ER$^-$ stem cells, standard therapies such as anti-estrogens or aromatase inhibitors will shrink the tumor, but they won't affect the stem cells.

"We'll have to figure out a way to kill these stem cells without affecting normal stem cells," Horwitz remarked, "but it gives us hope that we could possibly cure a disease like breast cancer by targeting the appropriate cells with the appropriate drugs."

Return to Table of Contents

New Directions in Autism Research Funded by NIEHS

By Eddy Ball

Support from NIEHS is enabling researchers at NIEHS and across the country to make important discoveries that may help unravel the mysteries of the complex syndromes grouped as Autism Spectrum Disorders (ASD). New studies have been published in the past few months by NIEHS-funded investigators involved with the Childhood Autism Risks from Genetics and Environment (CHARGE) project and their colleagues. To promote further collaborative efforts in the field, NIEHS is also participating in the Interagency Autism Coordination Committee on Autism Research.

One of these new studies found an increase in plasma levels of the hormone/cytokine leptin in children with early onset and regressive autism that may be the first biological marker that can distinguish the two forms of the disorder. A second study identified immunological factors in mothers that could be linked to autism in the very earliest stages of life. A third study identified for the first time specific patterns of gene expression in autistic children that differentiate them from normally developing children in the general population. The researchers were also able to distinguish between autistic children with early onset or regressive autism using gene expression patterns.

A new study is about to be launched with support from NIEHS to identify very early environmental exposures that might contribute to the development of autism. The Early Autism Risk Longitudinal Investigation (EARLI) Network aims to follow 1,200 mothers of children with autism at the start of a new pregnancy and document the development of their newborn siblings through age three.

This study will provide a unique opportunity for studying possible environmental risk factors for autism and biomarkers during different developmental windows, as well as an opportunity to investigate the interplay of genetic susceptibility and environmental exposure. A number of such exposures, ranging from suspected neurotoxicants to medications taken during pregnancy, could potentially be investigated with data and samples collecting through EARLI.

There has been significant public interest in the potential role of the vaccine preservative thimerosal in the recent increase in the prevalence of autism spectrum disorders. In an effort to replicate findings reported in a 2004 publication on the strain-dependent neurodevelopmental effects in mice from thimerosal exposure,

a group of NIEHS-funded researchers repeated the experiment. They applied rigorous methodology to enable collection of additional toxicological endpoints and behavioral assessments. The investigators' systematic and objective approach added important and reliable scientific evidence to the ongoing discourse about the effects of the preservative.

Taking CHARGE of Autism Research

Initiated in 2002, the CHARGE Study represents the first large-scale, population-based and case-control epidemiologic study of autism. The study is based at the University of California (UC) Davis, housed at the university's Medical Investigation of Neurological Disorders (MIND) Institute and linked to the laboratories at its Center for Children's Environmental Health. CHARGE studies have addressed a wide spectrum of environmental exposures and genetic and epigenetic susceptibility factors and their interplay. In 2003, the study set out to recruit 1,000 to 2,000 children with differing patterns of development. Investigators sought to enroll a population of children with autism, children with developmental delay who do not have autism, and children from the general population. In 2006, the study included 1,240 subjects.

CHARGE studies have explored the phenotypic heterogeneity of Autistic Spectrum Disorders (ASD) in an effort to understand the extent to which several conditions with distinct etiologies and pathogenic mechanisms may be involved. Researchers have investigated similarities and differences in developmental delays in affected children and how those delays skew the incidence ratio of four boys to one girl often observed in ASD. Exploration is underway of co-morbidity patterns in ASD, such as gastrointestinal problems and sleep disturbances.

In an attempt to delineate the mechanisms of pathogenesis, CHARGE investigators have utilized extensive interviews with parents, laboratory analysis of blood, urine and hair specimens, and prenatal labor and delivery, neonatal and pediatric records. The research also takes advantage of animal models of autism and *in vitro* investigations of immune and neurogenic cells.

Over the years, CHARGE has worked to build an infrastructure that can support multiple investigations of autism and related neurodevelopmental disorders. Because of the large number of cases of autism in the CHARGE study, it may be comparable with what can be expected in unselected birth cohorts of 100,000. Collaborations with other population-based efforts are currently under way, such as the national Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) study, which offer potential opportunities for replication and data pooling.

Citation: Hertz-Picciotto I, Croen LA, Hansen R, Jones CR, van de Water J, Pessah IN. 2004. The CHARGE study: an epidemiologic investigation of genetic and environmental factors contributing to autism. Environ Health Perspect 114(7):1119-1125.

Elevated Leptin and Inflammation in Autism

Most of the hormone leptin is produced in fat cells. This has led to the association of the neuroendocrine mediator with regulation of energy intake and energy expenditure, including the regulation (decrease) of appetite and (increase) of metabolism, and hence to overweight and obesity conditions.

However, as the study by UC Davis immunologist Judy Van de Water, Ph.D., and her colleagues explains, there is evidence from earlier studies to demonstrate the production of leptin also by inflammatory cells. Researchers have shown in animal studies that leptin deficiencies can shift the immune response and result in defective cell-mediated and humoral immunity.

Working on the hypothesis that "an altered immune response may impact other biological systems including the neuroendocrine and nervous systems," the investigators compared plasma leptin levels, measured as nanogram/

milliliter (ng/ml), in a population of children with careful documentation of autism and age-matched controls. Controls included children with and without developmental disabilities. Because of the association between body mass index (BMI) and leptin, the research team controlled for BMI-for-age, a modified calculation that is a more relevant measure for a pediatric population.

While the researchers found that leptin levels were significantly higher in children with autism than in typically developing controls, they also discovered a dramatic difference among the autistic children themselves. When the subjects with autism were further categorized by symptom cluster, children with early onset autism showed significantly higher median and interquartile range levels of leptin than did children with clinical regression: 2.62 (1.12 – 4.38) versus 1.38 (.061 – 2.69) ng/ml. The investigators also found that children with the regressive form of autism were not significantly different when compared with controls, both typically developing and developmentally delayed.

This study is the first report of a potential biochemical marker in autism that may be able to differentiate between disease phenotypes. The investigators acknowledged that it is still undetermined whether leptin levels are a cause or secondary phenomenon of the condition. However, they concluded, "these findings provide a framework for further longitudinal studies to investigate changes in leptin levels over the lifetime of the disorder."

Citation: Ashwood P, Kwong C, Hansen R, Hertz-Picciotto I, Croen L, Krakowiak P, Walker W, Pessah IN, Van de Water J. 2008. Brief Report: Plasma Leptin Levels are Elevated in Autism: Association with Early Onset Phenotype? J Autism Dev Disord 38(1):169-175.

IgG Antibody Transfer and Early Neurodevelopment

The search for a biochemical marker of autism moved forward with another recent investigation of maternal plasma IgG antibodies against human fetal and adult brain proteins, also led by Van de Water. According to the investigators, the antibodies, which can easily cross the placental barrier, may be able to react to fetal 'self'-proteins to give the fetus a subset of the maternal adaptive humoral immune system proteins. These proteins could possibly produce an autoimmune reaction in the infant which could then impact fetal neurodevelopment.

Researchers studied 61 mothers of children with autistic disorder (AU) and 102 matched controls with typical developing (TD) children or children with non-ASD developmental delays (DD). Separating proteins by weight, they looked for patterns of reactivity in the range of 20 to 220 kilo-daltons (kDa) — a measure of molecular weight used in chemiluminescent visualization of marker bands.

The investigators found patterns of reactivity against fetal, but not adult, brain clustered at two points, 37kDa and 73kDa, that differentiated between mothers of AD children and mothers of TD and DD children. Autoreactivity to a protein at approximately 37kDa was found in 26 percent of mothers of AD children compared to 2.5 percent of mothers of DD children and 8.1 percent of mothers with TD children, yielding a 5.69-fold odds ratio associated with this band.

When reactivity against proteins at both molecular weights was studied, 11 percent of mothers of AU children showed the results at 37kDa and 73kDa, while no mothers of TD or DD children showed that pattern of reactivity. Significantly, 86 percent of the mothers of AU children with reactivity to the pair of bands had children with the regressive form of the disease.

The team found support for their hypothesis that there is a potential role for maternal IgG antibody transplacental transfer during pregnancy and subsequent binding to fetal brain cells as a cause of autism in some children. They also discovered a possible biomarker that may be able to predict the development of a specific phenotype of the disease.

The results led Van De Water to comment, "We are …optimistic that in the future a prenatal test and therapeutic intervention preventing IgG exposure during pregnancy could protect some children from ever getting autism."

Citation: Braunschweig D, Ashwood P, Krakowiak P, Hertz-Picciotto I, Hansen R, Croen LA, Pessah IN, Van de Water J. Autism: Maternally derived antibodies specific for fetal brain proteins. Neurotoxicology epub 2007

Gene Expression Patterns in Autistic Children

A precedent-setting CHARGE investigation of gene expression patterns in autistic children could give researchers new insights into the biological foundations of the disease and may be an important step in identifying new targets for therapies.

Led by UC Davis neurologist Frank Sharp, M.D., the investigation was the first to use genomic profiling of whole blood successfully to pinpoint differential gene expression patterns that distinguished autistic (AU) children, diagnosed by both the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview, from general population (GP) children. The team also was the first to identify gene expression patterns that differed between children with the major phenotypes or subsets of AU, the early onset without regression (A-E) and the regressive forms (A-R) of the disease.

The subject population included 61 children enrolled in the ongoing CHARGE study: 35 diagnosed with AU; 14 diagnosed with Autism Spectrum Disorder (ASD), a term used for children who do not meet the full behavioral criteria for AU; and 12 typically developing GP children, age and gender matched, with no evidence of ASD. RNA was isolated from blood drawn in the afternoon and analyzed for gene expression patterns.

Results indicated that the autistic groups (AU, A-R, and A-E) shared 11 differentially expressed genes in natural killer (NK) cells, many of which belong to the natural-killer cytotoxicity pathway identified in the Kyoto Encyclopedia of Genes and Genomes. The authors observed that "the importance of these findings is that NK cells are a primary, innate defense against viral, bacterial, and parasitic infections or malignant transformation."

A secondary finding, but one of importance in the diagnosis of forms of AU, involves differentially expressed gene patterns that differ between A-E and GP children, a set of 140 genes, and between A-R and GP children, a set of 20 genes. Gene expression data supporting different forms of AU, the authors concluded, "may be able to help define the etiology, genetics and clinical phenotype, as well as the outcome, in autism."

Citation: Gregg JP, Lit L, Baron CA, Hertz-Picciotto I, Walker W, Davis RA, Croen LA, Ozonoff S, Hansen R, Pessah IN, Sharp FR. 2008. Gene expression changes in children with autism. Genomics 91(1):22-29.

Mice Models of Thimerosal Toxicity

In the long and often frustrating search for what environmental factors might trigger autism (AU) and autistic spectrum disorders (ASD), concerned parents and some researchers have speculated that vaccine-level exposure to ethylmercury in thimerosal-preserved childhood vaccines could play a role. Advocates of the thimerosal connection hypothesized that deficits in immune function among some children may make their developing nervous systems vulnerable to pervasive developmental toxicity, leading to AU and ASD.

While relevant data in humans are lacking, a 2004 study of the autoimmune-susceptible SJL/J mice strain conducted by Mady Hornig, M.D., and associates at Columbia University's Mailman School of Public Health, reported findings consistent with the notion that immune dysfunction can exacerbate the effects of thimerosal. Their study found gross morphological changes in the hippocampus as a result of early post-natal injections of thimerosal.

A research team that included NIEHS Neurotoxicology Group Head G. Jean Harry, Ph.D., attempted to replicate Hornig's findings, given the significance of this approach of an augmented response to toxicants as a function of underlying immune status. The team consisted of researchers experienced in the design and conduct of developmental neurotoxicology studies and with expertise in morphological and statistical analysis. The animal studies were conducted in laboratories at the University of California Davis and used a similar injection schedule to that reported by Hornig. SJL/J pups from 51 different litters were injected with five different solutions according to a regimen that modeled childhood vaccination schedules.

A within-litter dosing design was utilized to control for the large impact that maternal factors, both genetic and behavioral, have on the neurobehavioral functioning of the offspring. Tissue mercury levels were used to confirm that there was no cross contamination within the litters from the pups injected with thimerosal.

The first group received a dose of thimerosal (1X thimerosal) comparable to the maximum dosage a child could have been exposed to with thimerosal-preserved vaccines against hepatitis B, diphtheria tetanus pertussis (DPT) and hemophilus influenza B (HiB). A control group received a phosophate-buffered saline vehicle (VEH). The other groups received, respectively, vaccine alone (VAC), 1X + VAC, and 10X + VAC to evaluate the effects of different levels of thimerosal and the different components of vaccines.

After the mice had completed the injection schedule, the research team evaluated survival, body weight growth indices of early development and hippocampal morphology. They put the mice through a battery of behavioral tests related to core neurological deficits, including social interaction, sensory gating and anxiety.

In one cohort of mice, total mercury levels were measured in blood, brain and kidney at two time points selected based upon previous work by the UC Davis lab and Harry lab at NIEHS. Morphological examination of the hippocampus was conducted using an advanced computerized methodology of unbiased stereology performed by an expert in the field. In all cases, data collection and analysis were conducted on coded animals and samples to maintain a totally unbiased assessment with investigators blind to individual animal treatment groups. The code was maintained during the statistical analysis as well.

In contrast to the Hornig study, the mice in this study maintained overall good health and showed no adverse behaviors. The researchers found no evidence of structural abnormalities in the hippocampus or of neurobehavioral changes in activity levels or social behavior in the offspring as a result of the injections of thimerosal, by itself or in combination with VAC. As expected, pups injected with the higher 10X and 10X + VAC showed higher blood levels of mercury; however, the other results were similar to the lower exposure groups.

Citation: Berman RF, Pessah IN, Mouton PR, Mav D, Harry J. 2008. Low-Level Neonatal Thimerosal Exposure: Further Evaluation of Altered Neurotoxic Potential in SJL Mice. Toxicol Sci 101(2):294-309.

Future Directions: Networking for a Large-Scale Epidemiological Study of Gene-Environment Interactions

The Early Autism Risk Longitudinal Investigation (EARLI) Network promises to pull together several lines of research from earlier CHARGE investigations and explore new directions in a ten-year study of mothers of autistic children and their newborn siblings that combines epidemiology and basic laboratory research. The network includes an administrative center at the Drexel University School of Public Health, a data coordinating center at the University of California Davis, a central lab and repository at Johns Hopkins School of Public Health, and field sites in Philadelphia, Baltimore, the San Francisco Bay area and Davis, Calif.

The network plans to implement a core epidemiologic data collection protocol focusing on prospective documentation of exogenous exposures, continuous ASD behavioral domains during pregnancy and early life, collection and banking of biological samples and follow-up of the newborn siblings through 36 months of age.

Researchers will gather data on ASD diagnoses, continuous ASD behavioral domains and other behaviors that may be associated with ASD.

Principal Investigator Craig J. Newschaffer, Ph.D., of Drexel University, listed four "exemplary specific aims" to be addressed in the study:

- Determine whether markers of maternal autoimmune status, measured during pregnancy, at delivery and at six months post-partum, are associated with autism risk
- Determine whether *in utero* exposure to persistent organic pollutants is associated with autism risk
- Explore maternal and child epigenetic marks as predictors of ASD risk
- Assess whether polymorphisms of *ADRB2*, which may affect brain development, and *in utero* ADRB2 agonist exposure are associated with autism risk and explore potential interaction of genotype and exposure

Data collected in this large study are intended to serve as a resource for ongoing epidemiologic investigation of potential risk factors and risk biomarkers for ASD well into the future.

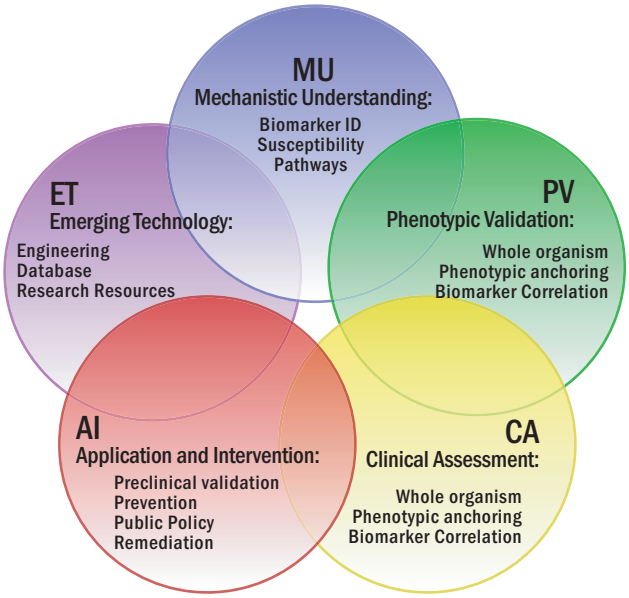
Return to Table of Contents

Extramural Update: A Framework for Translational Research at NIEHS

In November 2007, the NIEHS Division of Extramural Research and Training (DERT) held its Annual Science Retreat, focusing on understanding Translational Research and the ability to bridge research findings from one domain to another. With subsequent refinement, the draft framework initiated at that retreat has become a useful evaluation metric that provides insight into the maturity and potential of a given field with regard to translation.

The goal of the 2007 retreat was to provide a framework for developing translational and interdisciplinary research related to environmentally relevant exposures and diseases. Discussions focused on generating a consensus definition of Translational Research, developing an evaluation framework for categorizing the portfolio, initiating a process for prioritizing areas that are ripe for translation and identifying approaches to stimulate interdisciplinary translational research.

Draft Framework for Translational Research



In developing the framework, NIEHS program staff identified five broad domains to categorize research in the grant portfolio (see figure). These domains included the development of emerging technologies, mechanistic understanding of the effects of environmental factors, phenotypic validation of those effects at the level of the whole organism, clinical assessment of environmental causes of disease at the human or population level, and the application of these research findings in both clinical and public health interventions. During the retreat, it became apparent to the staff that translational research is not a linear process in which investigators move

directly from one level to the next in progression, ending with the application and intervention; rather, it is an overlapping cascade with researchers frequently integrating work at multiple levels in an effort to gain true understanding of the significance of their research findings.

This draft framework was used to evaluate four representative topics within the NIEHS grant portfolio – DNA repair (as a model basic science mechanism), cardiovascular disease (as a model disease), skin (as a model organ system) and arsenic (as a model toxicant). Each of these areas included projects working at all stages of the framework, with a large number of these projects focusing on interdisciplinary efforts. DERT staff concluded that the framework is helpful for understanding better the translational process of grant-funded research projects and potential applications for research findings.

Contact: David Balshaw, Ph.D.; balshaw@niehs.nih.gov

Return to Table of Contents

Extramural Papers of the Month

By Jerry Phelps

Black Carbon Air Pollution May Lower IQ

Children who live in neighborhoods heavily polluted by automobile traffic typically have lower IQs and score worse on other intelligence and memory tests than children in healthier environments, according to a new study by NIEHS supported researchers. While the respiratory and cardiovascular effects of air pollution are well documented, this study is one of the few that have explored the possible neurodegenerative effects of air pollution.

Researchers reported dramatic differences in the 202 children eight to eleven years old from the Boston, Mass. area in the study. The more heavily exposed children were to black carbon, the lower their scores on several intelligence tests. For example, the average IQ of the most heavily exposed children was 3.4 points less than children with low exposure. When the researchers adjusted for the effects of parents' education, birth weight and exposure to tobacco smoke, the associations remained. The effects were roughly equivalent to those seen in children whose mothers smoked ten cigarettes per day while pregnant.

The researchers speculated that the harmful effects may be caused by the inflammatory and oxidative effects of the black carbon particles. These findings suggest that additional research is warranted to investigate the effects of air pollution on the development of intelligence in children and on cognitive decline for people of all ages.

Citation: Suglia SF, Gryparis A, Wright RO, Schwartz J, Wright RJ. 2008. Association of black carbon with cognition among children in a prospective birth cohort study. Am J Epidemiol 167(3):280-286.

Return to Table of Contents

Mitochondrial Protein Mortalin and the Progression of Parkinson's Disease

NIEHS-supported researchers employed combined proteomic and labeling techniques to identify a protein, mortalin, that may be involved in the progression of Parkinson's disease. Using brain tissue samples from deceased Parkinson's patients at various stages of the disease and comparing those to samples from age matched controls, they isolated many proteins that had differential expression and found that mortalin was decreased in late stages of the disease.

Parkinson's disease is a progressive neurodegenerative condition that currently afflicts more than one million people in the United States alone and strikes about one percent of all people over the age of 60.

Mortalin is a multifunctional protein involved in mitochondrial energy generation and in protection from oxidative stress. In previous work, these investigators demonstrated that mortalin expression is associated with other proteins thought to be involved in Parkinson's disease including alpha-synuclein.

This study employed a novel proteomic method to study the mechanisms of Parkinson's disease progression. Using pathological samples from diseased Parkinson's patients, the study verified that mortalin is decreased in brain tissue at advanced stages of the disease. Further studies are necessary to determine mortalin's role and mechanism of action in the progression of Parkinson's disease.

Citation: Shi M, Jin J, Wang Y, Beyer RP, Kitsou E, Albin RL, Gearing M, Pan C, Zhang J. 2008. Mortalin: a protein associated with progression of Parkinson disease? J Neuropathol Exp Neurol 67(2):117-124.

Return to Table of Contents

Identical Twins: Are They Really Identical?

In groundbreaking research, an international team of scientists, including NIEHS-funded investigators, has shown that identical or monozygotic twins are indeed not genetically identical as was previously thought. Until now, environmental factors were thought to be the reason that one twin might develop an illness such as Parkinson's disease while the other remained healthy. The current study suggests that other factors may be in play.

The team studied 19 pairs of monozygotic twins and found subtle differences in their DNA due to copy number variation (CNV). CNV occurs when segments of DNA are missing or when extra copies of segments are inserted in the DNA sequence. Previous research suggested that CNV may play a bigger role in health and disease than previously thought, and one recent study proposed that sequence variation involving CNV may actually be more important than single nucleotide polymorphisms.

DNA differences due to CNV could tell researchers if a missing gene or multiple copies of a gene are implicated in the onset of a disease. If one twin develops a disease and the other doesn't, the region of their genetic sequences that are different could offer a target for further investigation to discover the genetic underpinnings of the disease.

Citation: Bruder CE, Piotrowski A, Gijsbers AA, Andersson R, Erickson S, de Ståhl TD, Menzel U, Sandgren J, von Tell D, Poplawski A, Crowley M, Crasto C, Partridge EC, Tiwari H, Allison DB, Komorowski J, van Ommen GJ, Boomsma DI, Pedersen NL, den Dunnen JT, Wirdefeldt K, Dumanski JP. 2008. Phenotypically concordant and discordant monozygotic twins display different DNA copy-number-variation profiles. Am J Hum Genet 82(3):763-771.

Return to Table of Contents

Flaxseed Improves Outcome from Lung Injury

NIEHS investigators have determined that flax-seed oil helps to combat the adverse respiratory effects seen in a mouse model of ischemia-reperfusion injury. Mice undergoing experimental ischemia-reperfusion lung injury fed ten percent flax seed in their diets showed improved arterial blood oxygenation, increased levels of protein in bronchoalveolar lavage and lower levels of oxidative lung damage than mice fed diets without flax seed supplementation.

Flax is a blue flowering plant that is grown on the Western Canadian prairies for its oil-rich seeds, one of nature's richest sources of omega-3 fatty acids. Nearly every system in the body can benefit from flax seed oil's natural antioxidant properties, including the cardiovascular, immune, circulatory, reproductive and nervous systems.

This study raises the possibility that flax seed may be a useful antioxidant therapy for treating chronic inflammatory lung diseases. Preliminary studies suggest that human ingestion of just 25 grams of flax seed results in the same blood level of the active ingredients seen in the mouse study. Also, if the bioactive components of flax seed could be isolated and formulated for rapid administration, administering it to both donors and recipients in lung transplantation procedures might reduce the incidence and severity of injury and primary graft failure.

Citation: Lee JC, Bhora F, Sun J, Cheng G, Arguiri E, Solomides CC, Chatterjee S, Christofidou-Solomidou M. 2008. Dietary flaxseed enhances antioxidant defenses and is protective in a mouse model of lung ischemia-reperfusion injury. Am J Physiol Lung Cell Mol Physiol 294(2):L255-265.

Return to Table of Contents

Intramural Papers of the Month

By Robin Arnette

Hormones Can Affect the Expression of Cardiac Genes

Researchers from NIEHS and the National Heart, Lung, and Blood Institute (NHLBI) determined that the gene for lipoprotein lipase (LPL), an enzyme that hydrolyzes lipids in lipoproteins, is regulated by estrogen in cardiac tissue. The study was funded by the NIH Intramural Program and published in a recent issue of *Endocrinology*.

Earlier studies had demonstrated that estrogen, acting through the estrogen receptor beta (ERβ) had a protective effect on the heart. In this research article, the research team extended its studies to show that estrogen had direct effects on gene regulation in the heart. Team members treated heart tissue from ovarviectomized female mice with estrogen or vehicle (control) for two hours. Team members froze the hearts, isolated RNA and measured LPL expression using real-time PCR. The estrogen-exposed hearts exhibited a significant increase in LPL mRNA, but this stimulation could be inhibited by the addition of progesterone or an estrogen receptor antagonist.

Sequence analysis of the LPL gene indicated that an estrogen response element possibly existed in the first intron. Further studies indicated that ERα and ERβ interacted strongly with the proposed sequence.

LPL is an essential regulator of fatty acid uptake in the heart, and altered LPL expression, due to the influence of estrogen and progesterone, could lead to cardiac malfunction. These studies provide valuable information on the role that hormones play in gene regulation.

Citation: Liu, D, Deschamps A, Korach KS, Murphy E. Estrogen-enhanced gene expression of lipoprotein lipase in heart is antagonized by progesterone. Endocrinology 2008 Feb;149(2):711-716.

Return to Table of Contents

Singlet Oxygen Production Indicates Site of Irradiation Damage

Cellular proteins are often damaged after a cell has been irradiated with UV or visible light, and scientists may use one of the mediators of this damage, singlet oxygen, to indicate which parts of the cell were affected. That's according to NIEHS researchers who published their results in *Photochemistry and Photobiology*. The work was supported by the NIH Intramural Program.

In earlier studies, the group had irradiated rose bengal (RB)-stained keratinocytes using visible light and had successfully detected singlet oxygen, but it was unable to determine exactly where the singlet oxygen had been produced in the cells. Therefore, the team tried again, this time using immuno-spin trapping to visualize the site.

The experiment involved the following reactions. When cells are exposed to singlet oxygen-generating dyes such as RB, protein hydroperoxides (POOH) are produced. In the presence of metal ions such as copper, POOH is converted to POO• and PO•, which both react with 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO), a nitrone widely used in spin trap detection of free radicals. The keratinocytes were stained with DMPO antibody and a fluorescently-tagged anti-rabbit IgG and subjected to confocal microscopy. The results indicated that the singlet oxygen was being produced around the nucleus.

This work provides specific knowledge about the distribution of singlet oxygen, and therefore, damage after irradiation.

Citation: He Y-Y, Council SE, Feng, L, Bonini MG, Chignell CF. Spatial distribution of protein damage by singlet oxygen in keratinocytes. Photochem Photobiol 2008 Jan-Feb;84(1):69-74.

Return to Table of Contents

Cell Surface Receptor Involved in Innate Immune Response

In an article published in *The FASEB Journal*, researchers from NIEHS and Harvard University reported that scavenger receptor class-A (SR-A), one of the eight subclasses of scavenger receptors, is responsible for binding viral double-stranded RNA (dsRNA) and initiating cellular pathways involved in innate immune response. The work was funded by the NIEHS Intramural Research Program.

Prior to this report, scientists knew that dsRNA induced signal transduction pathways inside the cell, such as NF-κB and MAPK, which led to the regulation of inflammatory cytokines. However, they didn't know how it was done. Team members radiolabelled polyinosinic:polycytidylic acid (poly I:C), a synthetic double-stranded

RNA that is used to model viral infections *in vivo*, and used it in competition assays. The results indicated that poly I:C competitively bound to SR-A. In addition SR-A antibodies and ligands inhibited internalization of poly I:C into cells.

This study indicates that SR-A is a novel receptor on the surface of lung epithelial cells that participates in innate immunity. The findings suggest that eventually researchers may be able to develop new therapeutics that will target the receptor and prevent viral infection.

Citation: Limmon GV, Arredouani M, McCann KL, Corn Minor RA, Kobzik L, Imani F. Scavenger receptor class-A is a novel cell surface receptor for double-stranded RNA. FASEB J 2008 Jan;22(1):159-157.

Return to Table of Contents

Silicone Implants, Connective Tissue Disease and Monoclonal Gammopathies

The results of a case-control study determined that silicone implants pose no increased risk of monoclonal gammopathies to women. The work, published in *Arthritis Research & Therapy*, was carried out by researchers from NIEHS, the NIH Clinical Center, the University of Michigan Medical School and the University of Utah Medical Center. The project was funded by the FDA Office of Women's Health and the Intramural Programs of the NIH (Clinical Center and NIEHS).

Previous studies had suggested a link between the appearance of abnormal serum proteins, including monoclonal gammopathies, also called paraproteins, in women with silicone breast implants. However, these investigations did not take into account the presence of connective-tissue disease (CTD). To address the issue, the team studied several groups of women at tertiary-care academic centers and performed serum protein determinations and immunofixation electrophoresis on the women's blood to detect monoclonal gammopathies.

Team members determined that women with implants, either with or without CTD, had lower serum globulin and immunoglobulin levels than women without implants, but overall there was no increased risk of paraproteinemia for women with implants. This study represents the first comprehensive study of serum proteins in women with silicone implants and CTD.

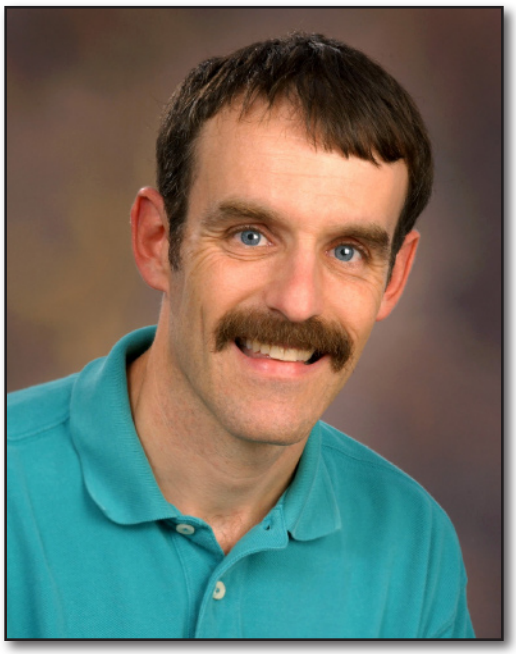
Citation: Csako G, Costello R, Shamim EA, O'Hanlon TP, Tran A, Clauw DJ, Williams HJ, Miller FW. Serum proteins and paraproteins in women with silicone implants and connective tissue disease: a case-control study. Arthritis Res Ther 2007 9(5):R95.

Return to Table of Contents

Social Justice for People with Disabilities

By Eddy Ball

According to NIEHS Bioethicist David Resnik, J.D., Ph.D., most people respond initially to the issues of accommodation for people with disabilities on the level of personal ethics. However, as Resnik explained in his March 4 talk on "Disability and Social Justice," laws such as the Americans with Disabilities Act (ADA) and formal statements of public policy also reflect the tenets of major theories of social justice. Resnik's talk was sponsored by the NIEHS Disability Advocacy Committee (DAC) and hosted by DAC Chair Alicia Moore.



Resnik underscored the difficulties of defining society's obligations to its members who have disabilities. "These are not cut and dried matters of law," he argued. (Photo courtesy of Steve McCaw)

"One way of thinking about the issues of treatment of the disabled," Resnik observed at the beginning of his talk, "is to think about it from the point of view of how I should treat individuals with disabilities." This viewpoint considers questions of respect, dignity and equal opportunity, often with specific people in mind.

However, Resnik continued, the larger question is what society owes people with disabilities. This question involves more abstract reasoning about people with disabilities as a segment of a society and is impacted by theories about the most effective role for government.

According to Resnik, the question also brings up the even larger question of what is a fair or just society. "Scholarship in this area has focused on social institutions," Resnik said, "how a government operates, how businesses operate, how the health care system operates, how the educational system operates."

Looking at stipulations in the ADA, Resnik commented on the ambiguity of its wording in regard to such terms as "a physical or mental impairment" and "a major life activity" because these terms are somewhat vague. The terms imply, but don't define, a standard of normality. Disabilities, Resnik said, can be biological, social and cultural.

Some disabilities, such as deafness, are contextual as well. "There are some people in the deaf community," Resnik added, "who do not consider deafness as a disability" because they view disability as a product of society. In a society of deaf people, deafness is not a disability.

There is also ambiguity in the requirement for "reasonable accommodation." As Resnik noted, institutions with functional historical buildings sometimes can't give people with disabilities

Moore has been recognized at the NIH level for her contributions to equal opportunity and reasonable accommodations at NIEHS. (Photo courtesy of Steve McCaw)

equal access without the "undue hardship" of undertaking prohibitively expensive major alterations, and they have often been permitted to use a lower standard to achieve compliance with the ADA.

Because America is a country established in the environment of eighteenth-century social thought, the tenets of three well-known social theories of the time run through debates about the rights and treatment of people with disabilities. Resnik identified these important influences on law and policy as Libertarianism, Egalitarianism and Utilitarianism.

Libertarianism, which is identified with the philosopher John Locke, values the concepts of individual rights and limited government. Egalitarianism, which is associated with Jean Jacques Rousseau, the French Revolution's Rights of Man and, in the nineteenth century, Marxism, values equal opportunity and more equal distribution of wealth. Egalitarian thinkers typically envision a larger role for government to control the excessive exercise of individual rights at the expense of others.

In marked contrast to the theories of Locke and Rousseau, Utilitarianism, developed by Jeremy Bentham and his follower John Stuart Mill, supports the concept of the greatest balance of good for the greatest number. Resnik compared Utilitarianism to cost-benefit analysis in economics and pointed to the practice of triage on the battlefield as an example of pursuing the greatest social good.

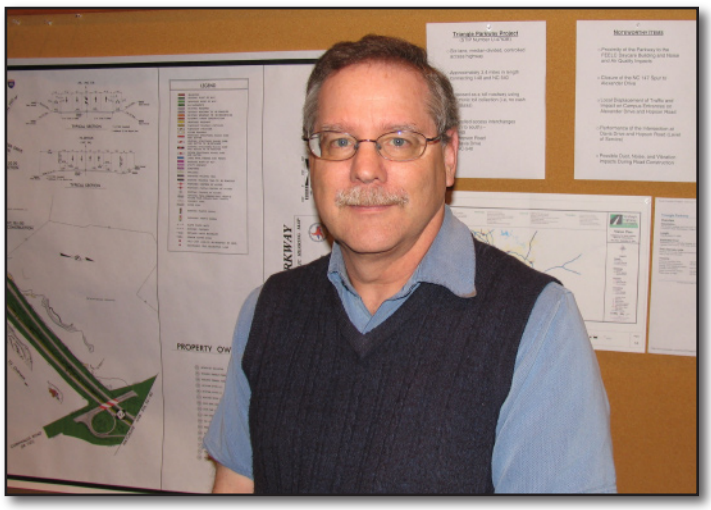
As he concluded the talk, Resnik commented on the strengths and weaknesses of the theories and his own preferred blend of ideas. "I actually think the best approach would be equality of opportunity, the sort of Egalitarian approach," he maintained, "but with some practical or utilitarian constraints recognizing that we can't do everything. There really are some economic and technological and other limits on what we can do."

Return to Table of Contents

New Triangle Roadway Proposed for 2010

By Robin Arnette

Triangle residents who work in Research Triangle Park (RTP) know that the daily commute can be a test of patience at times. That's why the North Carolina Turnpike Authority (NCTA) wants to construct a six-lane, median-divided toll roadway called the Triangle Parkway. The NCTA and the North Carolina Department of Transportation say the new 3.4 mile freeway, which will extend between NC 540 and I-40, will improve commuter mobility and accessibility to RTP while reducing congestion on NC 55 and NC 54, two other north-south roads that serve the area. The funds generated from the tolls will pay for the construction.



Merkle answered questions from NIEHS employees about the proposed roadway. (Photo courtesy of Robin Arnette)

The NCTA issued an Environmental Assessment, a document that addresses the positive and negative impacts of the project on the environment, and held a public meeting at the Sigma Xi Auditorium on March 25. NIEHS employees had an opportunity to ask questions about the plan at an informational session held in Rodbell C on March 19. Scott Merkle,

chief of the NIEHS Health and Safety Branch, led the assembly. “We’re trying to make sure that the employees who commute here everyday are aware of what these changes might bring about if this project gets constructed as proposed,” he said. Merkle stressed that plans for the parkway are still a work in progress and depend on successfully completing the Environmental Assessment process, securing gap funding from the North Carolina General Assembly and approval from the local metropolitan planning organization (MPO).

According to the project planners, the roadway will also alleviate future traffic strains as more people move to the Triangle, but some residents are wary. “Since the planned Triangle Parkway route brings it within 350 feet of our [FEELC] childcare center classrooms and play areas, parents are concerned about noise and air quality impacts,” said Gary Bird, Ph.D., staff scientist in the Laboratory of Signal Transduction and member of the FEELC parent board. The Environmental Protection Agency and NIEHS are working together to submit joint comments on the project.

Construction contracts are scheduled to be awarded in July 2008 with the roadway opening to traffic in fall 2010. The public may submit questions or comments regarding the proposed Triangle Parkway until April 8. Please see the project Contact Us page for more information.

Return to Table of Contents

NIEHS
National Institute of
Environmental Health Sciences

The e-Factor, which is produced by the Office of Communications and Public Liaison, is the staff newsletter at the National Institute of Environmental Health Sciences. It is published as a communication service to NIEHS employees. We welcome your comments and suggestions. The content is not copyrighted. It can be downloaded and reprinted without permission. If you are an editor who wishes to use our material in your publication, we ask that you send us a copy for our records.
• Director of Communications: Christine Bruske
• Writer-Editor: Eddy Ball
• Science Editor: Robin Arnette