

FEATURED ACTIVITIES of DERT May 2003

MEETINGS

Symposium on Children's Environmental Health: Identifying and Preventing Environmental Risks

February 24-26, 2003

Natcher Conference Center, NIH Campus, Bethesda, Maryland

For three days, scientists, community members, members of advocacy groups and representatives of the media came together to discuss what is known about environmental health threats to children, how well we are translating important scientific findings to the public and how we can share our information more effectively with the press and media. The symposium, which included 250 attendees and over 40 speakers, was divided into five key topic areas: respiratory disease and air quality, neurological impairments, childhood cancer, birth defects and endocrine disruption. There were also special sessions on obesity and nutrition, built environment, autism, fetal origins of adult disease and international perspectives.

In each session, lead speakers from laboratories, organizations that care deeply about the health of children, and from policy arenas summarized the state of the science, shared success stories from outreach and translational programs that work, and defined the gaps to fill in order to reduce morbidity and mortality among children exposed to hazardous substances.

The work of the NIEHS supported Children's Environmental Health and Disease Prevention Research Program was highlighted throughout the three days in scientific sessions and with poster presentations. Meeting highlights were published in *the April issue of Environmental Health Perspectives*. A more comprehensive meeting report is being written for future publication.

Meeting Highlights

- Dr. Phillip Lee, former Assistant Secretary of DHSS was the keynote speaker. He spoke about children's vulnerabilities to toxic substances and the impact neurodevelopmental diseases, such as ADHD, have on children and their families in terms of school performance, drop out rate, future drug abuse and risk of suicide. A number of environmental agents could contribute to this disease, and are not well studied. Dr. Lee also talked about manganese, which is an essential element that is added in high levels to infant formula and could be dangerous to infants.
- Other speakers discussed lead and mercury as classic neurotoxicants and how much our understanding about the threats to childhood development have come from understanding the mechanism of these metals.
- The systemic effects of air pollution were discussed, noting that it is not just detrimental to children's respiratory health, but new data indicate the components of air pollution may contribute to pregnancy loss, reduced birth weight, cancer, sudden infant death syndrome and cardiovascular disease in adulthood.
- Risk factors for childhood cancers were discussed and the process of developing new risk assessment cancer guidelines considering adult and childhood risks was also discussed.
- Representatives from organizations such as the Learning Disabilities Association, the Birth Defects Research for Children, Children's Environmental Health Coalition, etc., put forth the public

perspective and discussed actions that these groups are taking to raise awareness for these issues. Attendees joined in the discussion during break out sessions.

- A three-pronged approach to children's environmental health was articulated by Dr. Kenneth Olden, Director of NIEHS: Identify the risk factors, reduce exposure, and translate this information into public health policy and the practice of medicine.

Environmental Factors in Autoimmune Disease

February 4-5, 2003

Durham Marriott at the Civic Center, Durham, North Carolina

Autoimmune diseases are chronic, potentially life-threatening conditions. There are more than 80 recognized autoimmune diseases, which include systemic lupus erythematosus, glomerulonephritis, multiple sclerosis, autoimmune thyroiditis, rheumatoid arthritis, and myositis. Although some of the conditions afflict only small numbers of individuals, as a group autoimmune diseases represent an important public health concern. The common characteristics of these diseases are immune responses directed against normal tissue or cellular components, which are normally protected from immune attack and the resultant inflammatory response. Although genetic susceptibility and exposure to infectious agents have been identified as possible contributors to autoimmune disease and have been extensively studied, these factors cannot account for most cases. This suggests the likelihood of exposure to environmental agents as an etiologic factor, and research has linked environmental agents with autoimmunity. Human studies have shown an association between exposure to vinyl chloride, silica, and organic compounds. Likewise, experimental studies have shown numerous immunologic changes, related to autoimmunity, induced by exposure to metals, polycyclic aromatic hydrocarbons, and mycotoxins. Possible mechanisms for environmentally induced autoimmunity include molecular mimicry, alteration of lymphocyte signaling, and interference in the development of tolerance to "self" antigens. Despite the accumulation of these research data, there are still gaps in knowledge, including how to link results from human and animal studies.

The goals of the workshop were to get input from the environmental health science and autoimmune research communities on the most appropriate and productive directions for research in the area of environmentally related autoimmune disease. The format of the workshop, which included six breakout sessions, was designed to enhance interactions among research scientists that will lead to identification of gaps in knowledge, appropriate questions for future research, innovative uses of existing technology and ideas for new technologies (including animal models), and types of collaborations needed to address these issues.

Meeting Highlights

The workshop was attended by over 100 participants, including basic scientists, epidemiologists, clinicians, and disease advocates. It was in part a grantees' meeting, to allow some of the awardees from the 1999 RFA, "Environment / Infection / Gene Interactions in Autoimmune Disease," to present findings from these studies. There was also a session consisting of six breakout groups focused on the following topics: Gene-Environment Interactions, Altered Antigens, Immune Modulations, Signal Transduction, Translational Research: Systemic Autoimmune Disease, and Translational Research: Organic-Specific Diseases. The two primary outcomes of the meeting were:

- While experimental animal data are strong, many more human studies, epidemiologic and clinical, are needed to link environmental exposure to autoimmune disease.
- Greater efforts are needed to establish collaborations between epidemiologists and clinicians, on the one hand, and basic scientists on the other.

Hopefully, the workshop can generate interest in this field among epidemiologists and encourage the types of collaborations in which data from basic research and human studies can inform further research in the other discipline.

The products of this meeting will include a workshop report to serve as a framework for future program planning and a publication of the workshop highlights.

Human Health Effects of Phthalate Exposure Workshop

March 26-27, 2003

Radisson Hotel, Research Triangle Park, North Carolina

For something so ubiquitous in the environment of most Americans, phthalates are poorly understood. The compounds are used in everything from time-release capsules and children's toys to plastic tubing and pesticides.

Recently, researchers learned that exposures to phthalates are much more common in humans than first thought. An analysis of the latest National Health and Nutrition Examination Survey (NHANES) data on body burden by researchers at the Center for Disease Control and Prevention revealed that a majority of Americans are exposed and some at significantly high levels.

In fact, levels of phthalates are generally highest in children and women of reproductive age. These exposure levels create the potential for developmental effects in the fetus and children. For this reason, understanding the health effects of phthalate exposure in humans may be important for protecting populations at risk. Researchers, however, would be just as interested to confidently know that phthalates are harmless to humans.

Compared with many other chemicals in widespread use, the research gaps for phthalates are relatively extensive.

Dr. Kimberly Gray, NIEHS/SPHB, and Dr. Russ Hauser, Harvard School of Public Health, organized and convened the workshop, which was sponsored by the office of the Director, NIEHS, and co-sponsored by Harvard's Environmental Health Center. The multidisciplinary workshop was designed to describe the current state of knowledge on the health effects of phthalates, to identify gaps and deficiencies in that knowledge base, and to identify future directions for exposure assessment, toxicologic and epidemiologic studies.

The conference assembled some of the nation's leading phthalate researchers across disciplines to address many of the issues and focus the future research agenda regarding phthalates.

Meeting Highlights & Recommendations

The workshop was divided in to three sessions: Toxicology & Mechanisms, Exposure Assessment and Epidemiology. Learning objectives and discussion points were prepared for each presentation, and these were used as talking points for the one-hour open discussion that followed each session. The following is an abridged summary list of questions, comments and future recommendations discussed at the workshop.

- Rodent endpoints need to be better harnessed for human studies. It is unclear what animal models indicate for humans. In particular, researchers should look at what cholesterol data might indicate. Short-term problems need to be identified that could be studied now.

- Gaps exist in all models of endpoints. Researchers need endpoints that can be extrapolated to humans. Species differences between reproductive effects and liver effects make extrapolation very difficult. More data on developmental differences in species is desirable.
- Human markers need to be identified if indicated. For example, placenta blood and amniotic fluid should be studied. Different biomarkers for males and females may be required. A better understanding of how male and female effects compare on a mechanistic and molecular level will help. Gene changes that offer hope for potential molecular markers need to be identified.
- Better methods should be developed to look more carefully at the varying effects of different phthalates. Which exposure routes are most important for each of the phthalates needs to be defined.
- Researchers would like to see all sources of potential phthalate exposure identified. This includes the range and concentration of phthalates in assorted products.
- Diet is still thought to be the largest source of phthalate exposure but it has hardly been studied due to experimental difficulties in accurately making such assessments. However, this may be a key area to explore, especially in terms of specific routes of exposure and contamination of food sources.
- Participants hope a better sharing of questionnaire approaches will result from the workshop. Questions linger about how to best sample urine and best store samples for stability. Researchers might investigate the stability of urinary phthalate metabolite levels in individuals over time.
- Leading researchers would like to see expanded use of NHANES data. On a population basis, differences in phthalate metabolism will likely be a big factor. Populations with the highest exposures should be targeted for study. Though phthalates are not persistent in the body, life time exposures may be important for human effects and should be considered. Susceptible subpopulations such as neonates should also be targeted for study. Genetic polymorphisms likely to be of interest should also be identified.

NIEHS Worker Education & Training Program (WETP)

4th National Trainers Exchange - Training for Change: Changing Our Training

March 26-28, 2003

Rosen Centre Hotel, Orlando, Florida

“Worker Training” is a constantly changing field, particularly in the area of occupational safety and health where scientific research, regulatory and legislative initiatives, and innovations in educational methodology are applied on an almost daily basis. With funding from the NIEHS WETP, 18 different awardee consortia, representing over 80 individual organizations, have developed one of the most highly skilled networks of trainers in this country. As these expert trainers are in the forefront of this dynamic profession, staff organized a two-day conference entitled the National Trainers Exchange, for them to showcase new translational methods and techniques and to share and evaluate their current practices. The NIEHS WETP believes that this Trainers Exchange is important in advancing the profession of occupational safety and health training; therefore, the proceedings from this conference were carefully documented and will be published in the near future by NIEHS National Clearinghouse for Worker Safety and Health Training on their website at <http://www.wetp.org>.

The 4th National Trainers Exchange was the largest held by the NIEHS WETP with over 250 health and safety trainers participating in 40 interactive workshops and plenary sessions. This year, based on extensive input from trainers and consortia, these sessions were concentrated in the areas of Advanced Training Technologies (e-learning), Instructor Development, Life Skills and Literacy, Weapons of Mass Destruction (WMD) and Emergency Response. Each workshop/plenary was organized according to adult

learning principles and included, as appropriate, participatory activities, hands-on demonstrations of particular training techniques, skill building exercises, or facilitated discussions of technical issues.

Of special note were those workshops in the Life Skills, Instructor Development and the WMD/Emergency Response tracks. The Life Skills sessions conducted by Xavier University and the Laborers-AGC Education & Training Fund on "Cultural Awareness and Competence" allowed many trainers to grapple with sensitive issues of cultural stereotyping including race, age, abilities, and language and how it impedes training within our diverse workforce. Each session provided attendees, especially instructors, with a series of tools that can be used in re-shaping their own classroom and teaching environments.

The WMD sessions on "Critical Incident Stress Management" (CISM) and "What You Need to Know About Bioterrorism Diseases" also received very positive evaluations. The CISM model by the International Association of Firefighters shared the key elements for effective stress management before, during and after critical incidents. This CISM approach was instrumental in addressing the concerns of firefighters at the 255 firehouses in New York City after September 11. The Community College Consortium conducted the bioterrorism session, which included presentations, facilitated discussion and covered biological agents, exposure routes, emergency response requirements, personal protection needs, long and short-term health impacts and fatality rates.

The application of scientific knowledge is fundamental to the field of occupational and safety and health. The National Trainers Exchange is one excellent example of this application. The NIEHS WETP expects to conduct another exchange in the spring of 2005.

Healthy Environments for Children: The Promotion of Collaborative Research

February 3-5, 2003

Pattaya, Thailand

This meeting, which was chaired by Dr. Suk, was a follow-up to the "International Conference on Environmental Threats to the Health of Children: Hazards and Vulnerability," held in Thailand in March, 2002. Exposure to deleterious chemicals pose significant health effects worldwide but especially to maternal and child populations. This meeting addressed new scientific data and research results on children's vulnerability, discussed how to improve the current health conditions of children, and promoted the protection of children's environmental health. Scientific and methodological approaches to understanding mechanisms by which chemical substances pose a risk to human health and the environment were identified for international action. Products from this meeting will identify and resolve key issues with regards to mechanistic research, exposure assessment, risk assessment, risk management, and health effects.

The meeting, though largely regional in scope, focusing on children's environmental health issues most relevant to the South-East Asia and Western Pacific regions, provided a forum for interactions among environmental health scientists whose activities focus on research, public health, education, and environmental exposures as related to children's health. It also provided an opportunity to work directly with academic institutions, government organizations, and industry in the area on specific children's environmental health issues.

Besides international organizations including WHO and the United Nations Environment Program, and South-East Asia organizations and industries based in China, Vietnam, Japan, Singapore, and Thailand, there was co-sponsorship by NIEHS, U.S. EPA, U.S. Trade and Development Agency, and USAID. In conjunction with this meeting in Thailand, Dr. Suk traveled to Hanoi, Vietnam, to assist in the planning of a conference to be held next year that will focus on exposure monitoring and remediation technologies as detailed in the Memorandum of Understanding (MOU) between Vietnam and the U.S on scientific issues surrounding Agent Orange/Dioxin.

DETR PAPERS OF NOTE

Rod-Shaped Eye Cells Die When Exposed to Lead

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R01ES12482 and P42ES10337

Background: Some health effects of lead, cognitive and behavioral impairments, high blood pressure, and kidney disorders, are well known and documented. However, the effects lead has on rod-shaped photoreceptor cells, or rods, of the retina are not well or frequently studied. Rods assist in seeing in dim light. The other type of retinal cells, cones, are responsible for color and spatial vision. Cones are used primarily in daylight and for activities such as reading. A person can lose up to 20% of their rods and not experience any functional loss of vision. However, for people who need to see clearly at night or for people who are losing their rods due to disease or injury, finding a way to prevent the rods from dying could be critical.

The results of a previous research project conducted by this research team demonstrated that 7-10 year-old children whose mothers had elevated levels of lead in their blood during the first trimester of pregnancy developed retinal abnormalities. It isn't clear whether the children's rods are dying, but there are unique abnormalities in the children. These researchers continued their studies by examining the retinas of lead-exposed mice.

Advance: The animal study demonstrated that the rods died from lead-induced apoptosis. Lead triggers an increase in calcium entering the mitochondria, which in turn induces the production of Bax, a "death factor" protein. Bax then causes the release of cytochrome C, which initiates DNA damage and subsequent cell death. Electron micrographs confirmed that more gates or contact sites, thought to be associated with cytochrome C release, were open in cells of the eyes from the lead-exposed mice. Other studies found that an excess of an anti-death protein called Bcl-xL completely blocked the death of the rod cells and maintained normal mitochondrial function in the rods throughout adulthood.

Implication: Over expression of Bcl-xL prevented the effects of Bax and reduced the formation of contact sites preventing the release of cytochrome C. For people losing rods because of retinitis pigmentosa, diabetes, or traumatic injury, finding a way to increase the concentration of Bcl-xL or a similar factor in the eye could prevent cell death.

Citation: He L, Perkins GA, Poblentz AT, Harris JB, Hung M, Ellisman MH, Fox DA. Bcl-xL overexpression blocks bax-mediated mitochondrial contact site formation and apoptosis in rod photoreceptors of lead-exposed mice. *Proc Natl Acad Sci USA*. 2003 Feb 4;100(3):1022-7.

Breakthrough in Understanding Disease-Causing DNA Instability

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R01ES05508

Background: Genes in normal individuals contain short lengths of trinucleotide repeats in which a combination of nucleotides, the building blocks of DNA, are repeated a number of times, usually less than 30. Research has identified 18 human genetic diseases associated with expansion of the number of these repeats, sometimes numbering in the thousands. Fragile X syndrome, myotonic dystrophy, and Huntington's disease are few of these devastating diseases, which become increasingly severe and have earlier onsets in successive generations, a process known as anticipation. Scientists have theorized that if the cause of the repeat expansion can be discovered, there is hope in preventing them from occurring.

Advance: Researchers at Texas A&M University recently discovered that a repeat associated with spinocerebellar ataxia type 10 (SCA 10) is unlike any repeat identified to date. The repeat is made up of 10 nucleotides in the sequence (ATTCT)_n·(TAAGA)_n. Experiments demonstrated that the repeat unpairs and acts as a false site of DNA replication.

Implication: While it remains to be seen if repeats associated with other expansion-related diseases support incorrect DNA replication initiation, this finding gives researchers a new target on which to focus. It also sheds light on the mechanism of repeat expansion and may lead to further discoveries on how to prevent and repair these genetic defects.

Citation: Potaman VN, Bissler JJ, Hashem VI, Oussatcheva EA, Lu L, Shlyakhtenko LS, Lyubchenko YL, Matsuura T, Ashizawa T, Leffak M, Benham CJ, Sinden RR. Unpaired Structures in SCA10 (ATTCT)_n·(AGAAT)_n Repeats. *J Mol Biol.* 2003 Feb 28;326(4):1095-111.

Calcium Supplements Lower Blood Lead in Nursing Mothers

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R01ES07821, P42ES05947, P30ES00002

Background: Exposure to lead from a variety of sources has been known for centuries to cause adverse health effects. Children are especially vulnerable to learning and behavioral deficits resulting from lead exposure. Pregnancy and breast-feeding are known to cause a marked turnover of lead stored in bones, which account for 95% of lead found in adults. Therefore, lactation places women and their breast-fed infants at an increased risk of lead exposure. Dietary calcium supplements have been shown to reduce fetal lead exposure; however no reports in the literature exist of testing this hypothesis with a properly conducted clinical trial. To address this issue, these investigators conducted a double-blind randomized clinical trial to determine if taking 1,200 mg of calcium each day lowered blood lead levels in lactating women.

Advance: Calcium supplementation produced a small reduction in blood lead levels. The effect was more apparent for women with higher bone lead levels and who were more compliant with taking the supplements. Women with high bone lead levels experienced a 16% decline in blood lead levels.

Implications: This trial demonstrates that calcium supplementation may be effective in decreasing blood lead levels in lactating women. Because dietary lead absorption and bone lead mobilization are likely to be similar during pregnancy and lactation, calcium supplementation is likely to reduce lead exposure to the fetus as well. This kind of intervention is not intended to be a substitute for public health efforts to reduce environmental lead exposure from all sources; however, it may constitute an important secondary prevention effort, because dietary lead exposure is difficult to eradicate and lead exposure from long-lived bone stores is likely to persist for decades.

Citation: Hernandez-Avila M, Gonzalez-Cossio T, Hernandez-Avila JE, Romieu I, Peterson KE, Aro A, Palazuelos E, Hu H. Dietary calcium supplements to lower blood lead levels in lactating women: a randomized placebo-controlled trial. *Epidemiology.* 2003 Mar;14(2):206-12.

Component of Plastic Linked to Chromosome Damage in Mice

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R21ES11172

Background: Bisphenol A (BPA) is a widely used component for the production of polycarbonate plastics used in food and beverage packaging and dental sealants. Though it is a man-made compound, BPA has hormone-like properties that mimic the effects of naturally produced estrogens. Recently, the accidental use of a harsh detergent used to clean animal cages led to the release of small amounts of BPA. Mice housed in the cages were exposed to the compound resulting in meiotic disturbances in the oocytes from the mice. This finding was later replicated in a controlled experiment.

Advance: Researchers in the Department of Genetics at Case Western Reserve University noticed the abnormalities and went looking for an answer. When the detergent was determined to be the cause, the researchers dosed mice with environmentally relevant doses of BPA. Eggs from the dosed animals showed increases in problems of meiosis including disorganized or unaligned chromosomes, and an abnormal number of chromosomes, a condition known as aneuploidy.

Implication: The kinds of chromosomal abnormalities resulting from both the accidental exposure and the controlled experiment are leading causes of miscarriage, congenital birth defects and mental retardation in humans. Although no direct conclusions can be drawn on human health effects without further study, these results do raise concerns because another study in Germany indicated pregnant women are exposed to similar amounts of BPA. These findings provide the first conclusive link between mammalian aneuploidy and an accidental environmental exposure. The study also suggests that the mouse oocyte may provide a sensitive system for the study of reproductive toxins.

Citation: Hunt PA, Koehler KE, Susiarjo M, Hodges CA, Ilagan A, Voigt RC, Thomas S, Thomas BF, Hassold TJ. Bisphenol a exposure causes meiotic aneuploidy in the female mouse. *Curr Biol.* 2003 Apr 1;13(7):546-53.

Gene-Environment Interaction: Effect of Polymorphisms on Biomarkers in Coal Miners

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P01ES09606

Background: Oxidative stress is a harmful condition that occurs when there is an excess of free radicals, not enough anti-oxidants, or both. Studies have shown that free radicals contribute to many diseases including asthma and chronic obstructive pulmonary disease (COPD), diseases of the aging, such as Alzheimer's and Parkinson's disease, and tissue damage resulting from diabetes.

Genetic factors may also play a part in the susceptibility to oxidative stress. Genetic polymorphisms have been implicated in differences in responses to environmental agents, but the interactions between genes and oxidative environmental agents involved in the development of human lung diseases have been largely unexplored. The overproduction of reactive oxygen species (ROS) from cigarette smoking and long-term exposure to dust and particles causes chronic airway inflammation. Inflammation is essential in the development of many airway diseases such as asthma, COPD, and coal workers' pneumoconiosis (CWP). This research team decided to investigate whether polymorphisms in two genes coding for tumor necrosis factor (TNF) and lymphotoxin ? (LTA), proinflammatory cytokines implicated in the progression of chronic lung disease, modify lung response to oxidants in an epidemiologic study of 253 coal miners.

Advance: A significant interaction was observed in miners with high oxidant exposure and a polymorphism in the *TNF* gene on red blood cell glutathione activity. No interaction was observed among workers with low exposure. Results also showed an association of CWP prevalence with a polymorphism in the *Lta* gene in workers with low catalase activity. Catalase is an enzyme that breaks down ROS like hydrogen peroxide. No association was seen in those with high catalase activity nor were any other significant associations observed.

Implication: These results provide the first demonstration of the involvement of genetic polymorphisms of two genes in the control of physiologic responses from exposure to oxidative stressors. The study suggests an interaction of genetic background with environmental exposure and intermediate responses are important in the development and progression of chronic pulmonary diseases such as coal worker's pneumoconiosis.

Citation: Nadif R, Jedlicka A, Mintz M, Bertrand JP, Kleeberger S, Kauffmann F. Effect of TNF and LTA polymorphisms on biological markers of response to oxidative stimuli in coal miners: a model of gene-environment interaction. *J Med Genet.* 2003 Feb;40(2):96-103.

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Surfactant Gene Expression Recovered after Inhibition of Nitric Oxide

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R01ES10562 and P30ES06096

Background: Although one of the simplest biological molecules in nature, nitric oxide (NO) has found its way into nearly every phase of biology and medicine ranging from its role as a critical endogenous regulator of blood flow and thrombosis to a principal neurotransmitter mediating erectile function to a major pathophysiological mediator of inflammation and host defense. These major discoveries have stimulated intense and extensive research into a vast array of fields including chemistry, molecular biology, and gene therapy.

NO has been proposed as a therapeutic agent for acute lung injury. The administration of low levels of NO preferentially dilate vessels in the lung to improve oxygenation of the blood. However, the role of NO in acute lung injury remains controversial because overall mortality is not reduced in adults. NO formation in the lungs may be detrimental to recovery. This is illustrated by clinical studies where inhibitors of the NO synthase enzyme restored pulmonary function. These investigators explored the function of NO in mice with nickel-induced acute lung injury.

Advance: Nickel exposed mice with acute lung injury were given either a saline control treatment or a NO synthase inhibitor (*N*^ε-nitro-L-arginine methyl ester; L-NAME). The saline treated mice exhibited multiple endpoints of acute lung injury while those that received the inhibitor had better survival, lower NO synthase activity, and lower levels of cytokine release, an indicator of inflammation. Surfactant protein gene expression initially decreased in both groups but recovered in the inhibitor group.

Implication: This work builds upon previous studies of acute lung injury that indicated inhibition of NO synthesis restores pulmonary function. These findings suggest inhibiting NO formation during acute lung injury may be protective possibly by limiting NO synthase-mediated vascular permeability, cytokine production, and causing later restoration of proper surfactant production.

Citation: McDowell SA, Gammon K, Zingarelli B, Bachurski CJ, Aronow BJ, Prows DR, Leikauf GD. Inhibition of nitric oxide restores surfactant gene expression following nickel-induced acute lung injury. *Am J Respir Cell Mol Biol.* 2003 Feb;28(2):188-98.

Identification of Possible Human Liver Tumor Suppressor Genes

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T32ES07017

Background: Several distinct regions of human chromosome 11 demonstrate loss of heterozygosity or confer tumor suppression in chromosome transfer studies in specific types of human tumors, including liver cancer, suggesting the presence of multiple tumor suppressor genes on this chromosome. By developing a model in which human chromosome 11 was introduced into a rat liver tumor cell line this laboratory was able to create a new cell line that exhibits suppression of tumorigenicity. Using this model system, the investigators were then able to employ a candidate gene approach to identify potential human liver tumor suppressor genes.

Advance: Thirty-eight genes have been mapped to this region of chromosome 11 by the Human Genome Project. Three of these genes were uniformly expressed by an index panel of suppressed microcell hybrid cell lines, which identified them as candidate liver tumor suppressor genes. In preliminary analyses in four human carcinoma cell lines, the transcript of one gene, p53-induced protein (PIG11), was lost or significantly decreased in two of the lines identifying this gene for potential involvement in some human liver carcinomas.

Implication: This study increased the knowledge of genes located in the liver tumor suppressor region of chromosome 11 and identified several candidate liver tumor suppressor genes from this region. Further characterization of these candidate genes may provide further insight into the role of this region of chromosome 11 in the pathogenesis of human liver cancer.

Citation: Ricketts SL, Carter JC, Coleman WB. Identification of three 11p11.2 candidate liver tumor suppressors through analysis of known human genes. *Mol Carcinog.* 2003 Feb;36(2):90-9.

Lead and Age Reduce The Fertilizing Ability of Sperm

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Andy Wyrobek, Ph.D. and Brenda Ezkenazi, Ph.D., Univ. Cal. Berkeley, P42ES04705

Background: Human sperm are fragile creatures, but there are so many in a single ejaculate, odds are good that one will find the target—the egg. However, over the past 15-20 years, the scientific community has been alarmed over the drastic decreases in human sperm concentrations reported in some scientific publications. Environmental agents have been shown to reduce sperm concentrations and viability in laboratory animals. Increasing age is known to be a factor in fertility reduction in women in part because of the finite number of oocytes women have at birth. Lead is known to reduce fertility in animal models, but a direct link between lead exposure and human fertility has not been established.

Advance: In two separate studies published in the same issue of *Human Reproduction*, two NIEHS-supported teams reported the harmful effects of age and lead exposure on human sperm. In the study on age, semen volume, motility, and the ability to swim in a straight line declined with age. Although the sperm concentration remained relatively constant, these decreases in function suggest that fertility starts dropping when men are in their 20s and continues to diminish for the rest of their lives. In the lead exposure study, lead was measured in the seminal plasma of 140 partners of women undergoing *in vitro* fertilization. Men with higher levels of lead had decreases in sperm counts and were more likely to have damaged sperm less likely to fertilize an egg.

Implication: These results present clinicians with additional information to consider when evaluating couples with unexplained fertility. Given the need for sperm function tests to predict the outcome of *in vitro* fertilization attempts, and to help in determining the appropriate course of infertility treatment, infertility clinics should consider measuring lead in semen of the partners of women undergoing *in vitro* fertilization.

Citations:

- Benoff S, Centola GM, Millan C, Napolitano B, Marmar JL, Hurley IR. Increased seminal plasma lead levels adversely affect the fertility potential of sperm in IVF. *Hum Reprod.* 2003 Feb;18(2):374-83.
- Eskenazi B, Wyrobek AJ, Slotter E, Kidd SA, Moore L, Young S, Moore D. The association of age and semen quality in healthy men. *Hum Reprod.* 2003 Feb;18(2):447-54.

Destruction of Oxidized Proteins

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R01ES03598

Background: The accumulation of damaged proteins is a characteristic of aging cells and many age-related conditions such as Alzheimer's disease. Unless these proteins are repaired or removed from cells, they often impair proper cell function and can lead to cell death. Cells contain complexes of enzymes designed to breakdown these proteins known as proteasomes. Proteasomes not only degrade harmful accumulations of damaged proteins, but they also breakdown short-lived regulatory proteins important in a variety of basic cellular processes.

Advance: For the most part, proteasomes recognize, unfold, and digest proteins that have been marked for degradation by the attachment of multiple molecules of ubiquitin. This ubiquitin-proteasome pathway functions widely in intracellular protein turnover. However, recent research sponsored by NIEHS at the University of Southern California has shown that a form of the proteasome known as 20 S can carry out protein degradation without the ubiquitinylation. This research, done in intact cells in culture, builds on previous findings in this laboratory.

Implications: The focus of this research team is the role of free radicals and oxidative stress in biology. In particular the lab is focused on oxidative stress during aging and aging pathologies such as Parkinson and Alzheimer's diseases. The results reported here describe a novel method for the destruction and removal of oxidatively damaged proteins. Although very basic in nature, this study provides insight into normal cell functioning, may lead to discoveries of how disease of aging impair these functions, and possibly provide clues to how these diseases may be prevented or treated.

Citation: Shringarpure R, Grune T, Mehlhase J, Davies KJ. Ubiquitin conjugation is not required for the degradation of oxidized proteins by proteasome. *J Biol Chem.* 2003 Jan 3; 278(1):311-8.

Chemical Driven Premature Ovarian Failure

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R01ES06999, R01ES08430, and F32ES11941

Background: Exposure to certain industrial chemicals has been shown to cause premature death of the stockpile of female germ cells mammals are born with. If this effect occurs in women as well, it could cause premature menopause leading to other hormonally related conditions. This was the focus of a previous report by these investigators (*Nat Genet.* 2001 Aug;28(4):355-60). In the earlier report compounds known as polycyclic aromatic hydrocarbons (PAHs), but not dioxin, were shown to signal through the Ah receptor/Bax-regulated pathway leading to oocyte death.

Finding: In a new report the investigators have expanded their work to include the environmental agent 4-vinylcyclohexene diepoxide (VCD). VCD is a by-product of the manufacture of plastics, rubber, flame retardants, and pesticides. VCD has also been shown to also cause premature death of immature

follicles from the ovaries of rats and mice. The current study shows that mice lacking the Bax gene retained more of their follicles than wild-type females when exposed to VCD. The same was true for mice lacking genes for the enzymes caspase-2 and caspase-3; enzymes essential in the life cycle of follicles.

Implication: These results add to the tremendous progress that has been recently made in understanding the cellular and molecular events responsible for oocyte death and follicle depletion under normal and pathological conditions. Future research aimed at finding natural substances that will modify or incapacitate these proteins may lead to methods to prevent oocyte loss in response to the natural aging process and from exposure to environmental agents.

Citation: Takai Y, Canning J, Perez GI, Pru JK, Schlezinger JJ, Sherr DH, Kolesnick, RN, Yuan J, Flavell RA, Korsmeyer SJ, Tilly JL. Bax, caspase-2, and caspase-3 are required for ovarian follicle loss caused by 4-vinylcyclohexene diepoxide exposure of female mice in vivo. *Endocrinology*. 2003 Jan;144(1):69-74.

Hand to Mouth—Ingestion of Pesticides by Children Living on the US/Mexico Border

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University of Medicine and Dentistry of New Jersey and Texas A&M University

P30ES05022 and P30ES09106

Background: Many studies have shown that children are exposed to environmental chemicals including pesticides through different mechanisms and sometimes in greater amounts than adults. This can be especially troublesome in agricultural communities where the potential for pesticide exposure is higher than in the general population. Clearly, the potential for toxicity is dependent on the dose children receive. Children in general spend more time in contact with surfaces prone to pesticide contamination such as floors and soils. The pesticides are transferred to the hands and then ingested when mouthing behavior occurs.

The purpose of this study was to evaluate relationships between exposure to organophosphate containing pesticides in children living in border agricultural communities and dose levels determined by measuring metabolites in urine.

Advance: Seventy-six percent of house dust samples and 50% of hand rinse samples contained pesticides. Urine samples from all 52 children contained at least one pesticide metabolite and 95% contained metabolites of two or more pesticides. Younger children and infants had higher concentrations of urinary metabolites than older children. Levels of pesticides on the childrens' hands were more closely associated with urine concentrations than were housedust samples.

Implication: This study demonstrates the elevation of pesticide contamination in children living in border communities. The levels were higher in younger children suggesting the need for study in younger infants. The level of pesticides found on the childrens' hands was correlated higher with urine concentrations than housedust samples suggesting it is a better estimate of exposure. Little is known about the health hazards from long-term exposure to these chemicals. The findings presented illustrate the importance of continued study of environmental pesticide exposure and its possible involvement in chronic illness among children living in agricultural communities along the US/Mexico border.

Citation: Shalat SL, Donnelly KC, Freeman NC, Calvin JA, Ramesh S, Jimenez M, Black K, Coutinho C, Needham LL, Barr DB, Ramirez J. Nondietary ingestion of pesticides by children in an agricultural community on the US/Mexico border: preliminary results. *J Expo Anal Environ Epidemiol*. 2003 Jan;13(1):42-50.1

Lead-Induced Learning Impairment Reversed by Environmental Enrichment

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Background: Lead is a potent environmental neurotoxicant with a long history of exposure in children. The developing brain is highly susceptible to lead exposure and long-term deficits in cognitive function are the principal effects of lead exposure in children. Despite significant and effective efforts to reduce lead levels in the environment, 1 in 20 children living in the U.S. have blood lead levels known to produce long-term learning deficits. Chelation therapy is the primary method used to treat lead poisoned children; however, recent studies have shown that while it is effective in reducing blood lead concentrations, it has little impact on reversing the cognitive deficits caused by lead.

It is widely known that a disproportionate number of children at-risk for lead exposure live in low socioeconomic environments. The work of these investigators asked whether an enriched and social environment that stimulates brain function could modify the learning impairments and molecular deficits identified in the brains of lead-exposed laboratory rats.

Advance: The experiments showed that environmental enrichment consisting of housing rats in larger cages with toys, platforms, tunnels and a running wheel reversed the long-term deficits in learning in lead-exposed animals. The investigators also determined two specific molecular events in the brain that may be responsible for the improvement in cognitive function. The lead-exposed rats housed in enrichment cages expressed the induction of a nerve growth factor, brain-derived neurotrophic factor. This nerve growth factor is important for nerve cell survival and synaptic plasticity. Secondly, they found that environmental enrichment reversed the deficits of a component of a key neural cell receptor, N-methyl-D-aspartate receptor subunit 1, in the brains of lead-exposed rats. These molecular changes induced by environmental enrichment were present in the hippocampus, a brain region important in learning and memory and known to be targeted by lead.

Implication: This work demonstrates for the first time that learning impairments in lead-exposed rats can be reversed by environmental enrichment even after the exposure has occurred. The model provides an avenue for further study of molecular events involved in lead neurotoxicity and offers new insights in ameliorating the effects of lead on learning in children.

Citation: Guilarte TR, Toscano CD, McGlothan JL, Weaver SA. Environmental enrichment reverses cognitive and molecular deficits induced by developmental lead exposure. *Ann Neurol.* 2003 Jan; 53(1):50-6.

STAFF ACTIVITIES

Drs. McClure, COSPB; Paul Van Look , WHO; Phyllis Leppert, NICHD; and Henry Gabelnik, CONRAD-U.S. AID; co-organized the Invitational Nature 2003 Supplemental issue entitled: "Fertility" which appeared simultaneously in *Nature Cell Biology* Vol. 4(S1):S1-S63 and *Nature Medicine* Vol. 8(S1):S1-S63 and included the review entitled: "Environment, lifestyle and infertility - an Inter-generational Issue", by Drs. R.M. Sharpe and S. Franks.

Dr. Sassaman, OD, presented at the Society of Toxicology's annual meeting as part of the Education Committee's forum on grantsmanship. She described the NIH extramural process and discussed current and future directions of the Institute's grants program. Also on the program was Dr. Elaine Frances, who presented on the USEPA's extramural programs. Dr. Sassaman also participated with Drs. Olden and Wilson in a noon forum on the NIEHS for grantees and interested constituents.

Dr. McClure, COSPB, coauthored with *Dr. Heindel, COSPB*, *Dr. Philip Mirkes*, University of Washington, and *Dr. Miriam Saunders* an article entitled: "Developmental Toxicology in the 21st Century: Multidisciplinary Approaches Using Model Organisms and Genomics" which appeared in the *Journal of Births Defects Research (Part A, Clinical and Molecular Teratology)*, Vol.67:21-34, 2003.

The Advisory Committee for the National Center for Toxicogenomics held its first meeting at NIEHS on May 28. *Dr. Sassaman* presented the extramural Toxicogenomics Research Consortium component of the trans-institute program, and *Dr. Van Houten, PAB*, also participated in the discussion.

A Town Meeting on "Oceans and Human Health" was organized by the Marine and Freshwater Biomedical Research Center at the University of Miami was held February 27. This was followed the next day by a "Hollywood Squares" event at a local special high school which featured *Dr. Olden* as a "celebrity." Attending the events from DERT were *Drs. Sassaman, Tyson and Deary* and *Mr. O'Fallon*.

Dr. McClure, COSPB, co-chaired the organizing committee for the NIEHS-supported 1st Annual International symposium entitled "Embryonic Stem Cell Biomedicine: the Journey from Mice to Patients," which was held May 15-17 at the Pittsburgh Development Center/Magee-Women's Research Institute following the "2003 Frontiers in Human Embryonic Stem Cells (lecture/laboratory) Training Course" supported by NIH (<http://pdc.magee.edu/events/>).

Dr. Suk, CRIS, co-chaired the "Children's Susceptibility to Environmental Agents Symposium" at the Environmental Mutagen Society annual meeting in Miami, Florida, May 11th, and presented the paper entitled "Children's Health and the Environment."

Dr. Thompson, CRIS, presented the opening talk at the 12th International Symposium on Pollutant Responses in Marine Organisms (PRIMO¹²) in Tampa Florida on May 9. The purpose of PRIMO¹² was to provide a forum for presentation, discussion and publication of original research in mechanisms of toxicity, development of biomarkers, biotransformation, and assessment of biochemical, cellular, immunological and reproductive effects of chemical pollutants in aquatic organisms. The PRIMO¹² Symposium was open to individual scientists, postdoctoral fellows and students interested in these areas of mechanistic aquatic toxicology.

Dr. Suk, CRIS, participated at the 4th International Conference on Environmental Mutagens in Human Populations (4th ICEMHP), May 4-8, in Florianopolis, Brazil. This Conference was designed to identify solutions to human environmental health problems and to facilitate the establishment of sustainable collaborative programs around the world. The overall goal is to reduce mutagen-induced environmental disease. *Dr. Olden* gave the keynote address. The conference participants included an international gathering of biomedical scientists. *Dr. Suk* co-chaired the Symposia "Children's Environmental Health," and delivered the talk within that Symposia entitled "Environmental Hazards to Children's Health in the Modern World." The Symposia within this Conference provided a better understanding of the nature of environmental threats to assist in the development of strategies to prevent harmful exposures to children, and assisted in focusing the research community at looking at issues of childhood exposure and disease and prevention.

Dr. Weis, CRIS, and *Dr. Heindel, COSPB*, in conjunction with staff from DIR, organized an international conference on *Metabolic Profiling: Application to Toxicology and Risk Reduction* held at the NIEHS on May 14-15. The conference was designed to define the state of the science for the emerging technology of metabolomics/metabolomics and its application to environmental health research, and to identify future directions for exposure assessment, toxicology and clinical medicine.

Mr. Hughes, WETB, participated in and presented at the CDC Chemical/Radiation Preparedness Workshop in San Francisco, California on May 5-6. As part of the Interstate Chemical Terrorism

Working Group, NIEHS staff is assisting in a national survey of public health preparedness of state and local health departments for response to terrorist attacks and other disasters.

Dr. Gray, SPHB, participated in Effective Strategies of Asthma Interventions in Bethesda, Maryland, on April 4. This meeting was organized by CDC and hosted by NHLBI. It brought together a diverse group of participants such as asthma coalitions and Federal Agencies that conduct asthma interventions, as well as researchers actively implementing intervention studies of asthma, including clinical, community-based, and population-based research. The objectives of the meeting were to define criteria to successfully identify effective asthma strategies, to determine mechanisms that would facilitate the dissemination of these interventions, and to identify issues related to implementation and evaluation of successful asthma interventions.

Dr. Weis, CRIS, presented at a workshop entitled *Metrology and Standards Needs for Gene Expression Technologies: Universal RNA Standards* hosted by NIST-FDA on March 28-29 at Stanford University. Dr. Weis presented on "Applications of Standards to Harmonize Data Laboratories and Microarray Platforms."

Dr. Weis, CRIS, presented at two sessions of the Science Education Program's *Rx for Science Literacy* Workshop on March 25. The workshop was co-sponsored by the NIEHS and North Carolina Association for Biomedical Research. Her presentation was titled "Toxicogenomics: Genomic Science to Understand Biological Response to Environmental Stressors."

Dr. McClure, COSPB, accepted an NIH appointment to the NIH Office of Dietary Supplements Strategic Planning Committee for FY 2004-2009. He presented an invitational plenary lecture on "DHHS Public Health Perspectives of Dietary Supplement Risks and Safety Issues" at the May 8-9 stakeholder's meeting convened by the Office of the Director, NIH.

Dr. Heindel, COSPB, has been an invited speaker at three local SBIR workshops sponsored by the North Carolina Small Business Technology Development Center and the specific University Sponsored Activities Programs. These half day workshops were held February 13 at NC A&T, March 27 at UNC Wilmington and April 9 at East Carolina University. At each workshop Dr. Heindel gave two presentations, one entitled, "Overview of the NIH and NIEHS SBIR Programs and Interests" and another entitled, "SBIR grantsmanship: or How to Swim with the Sharks and Survive." Each workshop was attended by 30-40 university scientists and local small business representatives interested in generating SBIR funds.

Mr. Hughes and Mr. Winchel, WETB, presented at the EPA Emergency Support Function #10 Coordination for National Hazmat Disasters Committee in Washington, DC on April 9.

Drs. McClure, COSPB, and Sassaman, OD, co-organized and co-hosted, in conjunction with U.S.-EPA counterparts, the April 4 orientation meeting for the NIH Extramural Associates (EA) Program which provided an extensive research, training and career development programs orientation and facilities tour for the NIEHS and the EPA. NIH EAs are senior administrators/faculty of research capable Historically Black College or University (HBCU), Women's, or other minority organizations nominated in a grant application by an eligible organization's President or CEO, who successfully complete either a short-term (1-3 Months) or long-term (6-12 Months) EA training program in sponsored research administration held annually at the NIH.

Dr. Shreffler, COSPB, participated in the Undergraduate Education Program for Minority Students on March 9 at the Society of Toxicology Meeting in Salt Lake City, Utah. She discussed the Graduate and Short Term Training programs supported by the NIEHS and provided information on fellowship opportunities for underrepresented minorities.

Mses. Duke, Mason, Garcia, Russell, Winters, Ricci and Mr. Dwight Dolby, GMB, attended the North Carolina Society of Research Administrators Annual Meeting, March 3-5 in Chapel Hill, North Carolina. At the meeting, Ms. Duke presented an NIH update. *Mses. Garcia and Russell* presented a Training Grants Update.

Dr. McClure, COSPB, co-organized with *Dr. Straus*, Director, NCCAM, NIH, and *Dr. Coates*, Director, ODS-OD/NIH, an independent external review committee evaluation of the Trans-NIH Botanical Research Centers program sponsored by NIEHS, NCI, NCCAM, NIDDK, NICHD and ODS-OD/NIH. The committee membership included senior NIH, USDA, and NIH supported expert consultants. *Dr. Bernard Goldstein*, NAEHS Council member, chaired the committee. *Dr. Martin Philbert*, an NIEHS grantee, served as a neurosciences expert consultant member. The committee review, held February 21, will yield a report to the Office of the Director, NIH.

Mr. Hughes, WETB, and staff conducted its Spring 2003 Awardee Meeting in Orlando, Florida on March 26. At the meeting over 100 individuals participated by interacting with NIEHS staff during the NIEHS Update and attending breakout sessions pertaining to specific grants and program topics such as A-133 Audits, Financial Management, Sub-Recipient Monitoring, Supplemental Awards, Life Skills/Remedial Education Training, Curricula Development and Redesign of the WETP Data Management System. As a result of recommendations from the WETP Strategic Plan (http://www.wetp.org/oldchfiles/awardee_mtgs/fall01/stratplanE.pdf), a new session format called Health and Safety Rounds was introduced. The Health and Safety Rounds are a new participatory series of sessions that are meant to address relevant topics on health and safety and management issues. Staff attending the workshop and participating in various activities included *Ms. Beard, Mr. Outwater, Ms. Thompson, WETB, and Ms. Duke, GMB*.

Mr. O'Fallon, SPHB, provided oversight in the development of an exhibit booth for the Community Outreach and Education Program. The booth made its debut at the National Science Teachers Association annual national convention in Philadelphia, Pennsylvania on March 24-27. The booth will be exhibited at the American Public Health Association conference this Fall and at the Society of Toxicology conference in March 2004. This booth helps NIEHS promote COEP as a larger program, as well as increase awareness of the outreach and educational materials offered by the 26 COEPs across the country.

Mr. Hughes, WETB, participated in and presented at the Federal Disaster Response Meeting in Arlington, Virginia on February 26. Representatives from EPA, NIOSH, OSHA, and RAND Corporation also shared their perspective on federal disaster response.

Dr. Tyson and Mr. O'Fallon, SPHB, organized the annual Environmental Health Sciences as an Integrative Context for Learning grantee meeting, held in Miami, Florida, February 26-27.

Dr. Gray, SPHB, was invited to the Veterans Administration ALS registry steering committee meeting and to present the data from the study, "Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans" in Washington, DC on February 13. She also presented on NIEHS' ongoing efforts to facilitate research in the area of environmental exposures and ALS.

Mr. Hughes, WETB, presented at the 13th Annual Construction Safety and Health Conference and Exposition in Chicago, Illinois on February 11. *Mr. Hughes* moderated a session entitled "Training Skilled Support Personnel at Federal Disaster Sites."

UPCOMING MEETINGS and WORKSHOPS

Ms. Beard WETB, will host a Brownfields Focus Meeting in Research Triangle Park, North Carolina on May 20. This meeting will focus on strengthening and promoting the strategic plan for Brownfields issues. All NIEHS/WETP Brownfields Minority Worker Training Awardees will participate in this meeting. Staff attending and participating in the meeting includes *Mr. Hughes, Mr. Outwater, and Ms. Thompson, WETB*.

Drs. Packerham, Gray, and Maull, SPHB, in conjunction with the Harvard Comparative Mouse Genomics Center, are organizing a scientific symposium under the auspices of the Environmental Genome Project titled "Genes, Environment and Disease." This meeting will be held June 7-9 in Boston, Massachusetts at the Harvard School of Public Health. The scientific symposium is designed to examine the role of genetic variation in gene-environment interactions, emerging technologies used in the study of genetic variation, and examine issues of ethics and social consequences related to the discovery of environmentally responsive genes in human populations. This is an open meeting, with opportunities for other scientists to present their results at a poster session. The Comparative Mouse Genomics Centers Consortium and Molecular Epidemiology grantees are invited to attend a round-table discussion at the end of the meeting to foster dialogue and stimulate discussion among this multidisciplinary group of scientific experts about issues related to studying genetic susceptibility of environmentally induced diseases in the laboratory research to the human population studies, and to stimulate collaborative efforts that may lead to new directions of the EGP.

The National Institutes of Health (NIH) Director's scientific symposium/workshop entitled "NIH Research: Recent Progress and Future Promise of Human Embryonic Stem Cells" will be held June 12 on the NIH campus in Bethesda, Maryland (<http://www.masimax.com/nihstemcells/>). The workshop highlights NIH conducted hESC research in an NIH town meeting style.

Dr. McClure, COSPB, is part of the organizing committee and will moderate the session on "Differentiation into placental and neural cells."

The Eighth International Congress on Toxic Combustion By-Products," will be held June 17-19, in Umea, Sweden. The goal of the Congress is to provide an international forum to discuss topics on the origins, fate, and health effects of combustion. This field has gained significant relevance to worldwide environmental policy, as risk-based programs increasingly rely on the ability of advanced scientific research to provide mechanistic, diagnostic, and analytical answers to complex problems concerning air toxic exposure. The Congress proposes a forum for advanced learning through emphasis on internationally known invited speakers and advanced scientific and engineering research. Researchers and practitioners have the opportunity to interact and discuss recent developments and future goals in the control of combustion by-products and the effects of exposure on human and ecological health. NIEHS's Superfund Basic Research Program, US EPA, Coalition for Responsible Waste Incineration, University of Umea, the United Nations Environment Program (UNEP), and the World Health Organization (WHO) are co-sponsoring the meeting. The previous Congress (Seventh International Congress on Combustion By-Products: Origins, Fate, and Health Effects) was held at NIEHS and chaired by *Dr. Suk, CRIS*, who helped to organize the 8th International Congress in Umea.

STAFF CHANGES

Recruitments:

Dr. Dennis Lang joined NIEHS as the Deputy Director of the Division of Extramural Research and Training in March. Dennis comes to us from the National Institute of Allergy and Infectious Diseases in Bethesda where he served for ten years as the director of NIAID's enteric diseases program. His work at NIAID consisted of a basic and clinical research portfolio aimed at understanding bacterial and viral pathogenesis and at developing new preventive and therapeutic strategies against a group of organisms that contribute to the worldwide diarrheal diseases burden. NIAID, NIH and FDA awards for his achievements recognized his work there. Prior to that, he spent two years as a scientific review administrator for the NHLBI. Dr. Lang received his training in microbiology and biochemistry at Syracuse

and Cornell Universities. He spent nine years as an assistant/associate professor in the Department of Microbiology at the University of Cincinnati College of Medicine where his research was focused on membrane bioenergetics in *Bacillus* and on chemically induced mutagenesis and transformation of mouse and human fibroblasts. Dr. Lang left academe in the early 90's to assume a leadership role in a start-up biotechnology company where he headed a research group that engineered *Bacillus* organisms to express foreign genes and to produce unique peptides from *in vitro* synthesized genes. His government service at NHLBI began in 1991.

Dr. Leslie Reinlib has joined SPHB as a Program Official. He is working with the forthcoming Breast Cancer and the Environment Research Centers and is the Overall Coordinator of the Environmental Genome Project. Dr. Reinlib received a Doctorate in Naturwissenschaften (Natural Sciences) from the Laboratory of Biochemistry at the distinguished ETH Zurich (Swiss Federal Institute of Technology). He has experience in cellular imaging and protein biochemistry and has applied basic science approaches to clinical questions, such as the cellular basis for Cystic Fibrosis, Crohn's Disease, heart failure, and the neuronal effects of alcoholism. After faculty positions at The Tufts University and The Johns Hopkins University Schools of Medicine, Dr. Reinlib moved to an administrative position with the NIH National Heart, Lung, and Blood Institute. There, he oversaw a broad spectrum of grants in basic and clinical research concerned with cardiovascular and lung diseases and was an Executive Council Member and NIH representative to the Heart Failure Society of America. At NHLBI, Dr. Reinlib was a Team Leader of the Programs for Genomic Applications and helped establish it as a national resource for future genomics studies as they apply to heart, lung, blood, and sleep disorders.

Mr. Rodney (Peppy) Winchel, Jr. MPH, has joined WETB for a three month rotation as part of the NIH Presidential Management Intern (PMI) Program. While in DERT, he is serving as the coordinator for the Weapons of Mass Destruction Supplemental Awards. Originally from Wisconsin, Mr. Winchel earned a BA in Biology from Illinois Wesleyan University. He served four years in the US Army as a Medical NCO. He earned his Masters of Public Health from Northern IL University. During the fall of 2001, Mr. Winchel served as the Illinois American Red Cross State Disaster Volunteer Coordinator, including being assigned as a local disaster volunteer coordinator in New York City. Immediately prior to his appointment to NIH as a PMI, he served as a program manager for a homeless/crisis services organization of North Chicago. Mr. Winchel is pursuing administration and management of biodefense and disaster research programs, especially communicating evidence-based knowledge to responders and the public.

Departures:

Dr. Allen Dearry, SPHB, departed from DERT on April 3 to join the NIEHS Office of the Director as the Associate Director for Coordination, Planning, and Translation. *Dr. Collman*, has been named Acting Branch Chief of the branch.

Ms. Laura Williams-Boyd, GMB, retired on March 31 after almost 35 years with the government. She had been with GMB nine years.

Ms. Sandi Manness, RCB, retired on March 31 after 32 years of government service. She had been in RCB for the past 17 years.

Ms. Helen Watson, GMB, retired on May 3 after more than 25 years of government service. She had been with GMB for almost 18 years.