CROET Center for Research on Occupational and Environmental Toxicology

NEWSLETTER

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Czech Woman's Harvest by Faye Cummins

INSIDE

OHSU

Where Healing, Teaching and Discovery Come Together

OHSU OREGON HEALTH & SCIENCE UNIVERSITY

CROET Named To $37 Million Research Consortium

Grant award, spearheaded by CROET, makes OHSU one of five centers studying gene-environment contributions to disease

Oregon Health & Science University (OHSU) has been selected as one of five university research centers to pioneer development of the National Institutes of Health Toxicogenomics Research Consortium (TRC). Representing a fundamental change in our approach to toxicology, toxicogenomics is a revolutionary new scientific discipline that studies the role of gene-environment interactions in disease and dysfunction. The OHSU component -- spearheaded by CROET, in concert with the School of Medicine's Department of Pediatrics and Doernbecher Childrens' Hospital -- will focus on neurotoxicogenomics and child health. Other participants in this national consortium include research scientists at the Massachusetts Institute of Technology, the Fred Hutchinson Cancer Research Center at the University of Washington, Duke University and the University of North Carolina.

OHSU received the center grant as a cooperative agreement from the National Institute of Environmental Health Sciences (NIEHS), a component of the National Institutes of Health (NIH). NIEHS and CROET at OHSU have complementary missions of reducing the burden of disease and dysfunction by defining how environmental and occupational agents adversely impact health. NIEHS has slated a total of $37 million to fund the new consortium for an initial period of 5 years. OHSU will receive $7.25 million, one-fifth of which will be used to fund collaborative studies at the Boston Biomedical Research Institute. Last year, NIEHS awarded CROET a Superfund Basic Research center grant that will interact with the new TRC initiative.

To conduct their research, scientists at OHSU and other participating TRC centers will utilize genome and protein-profiling technologies. These groundbreaking methods will allow the consortium to understand how cells of various organisms respond to environmental factors. Chemicals that disrupt human brain development and induce neurodegeneration are the common interest of scientists in the CROET-Pediatrics research partnership at OHSU. The university's bioinformatics resources will play an important role in this research by organizing and compiling the tremendous amount of data generated by the research programs.

One of the consortium's goals is to develop standards and practices for the newly developed science of toxicogenomics that will allow researchers to generate consistent data in a suitably equipped laboratory anywhere in the world. The five participating centers and NIEHS scientists will seek inter-laboratory validation of experimental results by conducting specific experiments using common research protocols. A TRC Steering Committee, with membership from the five cooperating university centers, the NIEHS, and a NIEHS-appointed contractor, will oversee the research collaboration. The Steering Committee will apply its collective knowledge to accelerate the pace of discovery and promote the identification of gene-expression signatures associated with chemical-induced disorders, such as organic solvent neuropathy. Gene signatures will be entered into a publicly accessible NIH Environmental Genome database for use in developing strategies to prevent and treat environmental diseases.

Results gained through the synergistic interactions of researchers in the TRC will help improve public health through better risk detection and earlier intervention in disease processes. CROET researchers see benefits in sorting out why some chemicals are bad actors and others not, and how workplace chemicals and other exposures interact to trigger illness.

"Exposures early in life may result in health disorders evident at birth, during development or in later life" says Dr. Peter Spencer, senior scientist and director of CROET. "A greater understanding of the impacts of natural and synthetic chemicals on human development will minimize illness in the population and provide for a healthier workforce." Drs. Charles Roberts and Srinavasa Nagalla, respectively professor and assistant professor of Pediatrics in the School of Medicine (SOM), will also play a leading role in the new research center. Other OHSU members of the team include Richard Allen, Ph.D. (CROET) Stephen Back, M.D. (Pediatrics, SOM), Christopher Dubay (Medical Informatics, SOM), Gregory Higgins, Ph.D. (CROET), Michael Lasarev, M.S. (CROET), Glen Kisby, Ph.D. (CROET), Jodi Lapidus, Ph.D. (Public Health and Preventive Medicine, SOM), and Mohammad Sabri, Ph.D. (CROET and Neurology, SOM). Harvard Associate Professor Jeffrey Miller, Ph.D., completes the multidisciplinary research team.

TOXICOGENOMICS IS...

Toxicogenomics is a scientific field that aims to study the complex interaction between the cell's **genome** (the sum total of all genes), chemical, physical and other agents, and disease. When the body's cells are exposed to a stress, drug or toxicant, they may respond by altering the pattern of expression of genes within their chromosomes. Genes are transcribed into messenger RNA (**mRNA**), which is in turn translated into proteins that serve a variety of cellular functions in response to the exposure. The production of protein encoded by a given gene may be increased, decreased, or remain unchanged, depending upon the type of exposure and the needs of the cell.

A technology that is central to the field of toxicogenomics is known as **DNA micro-array,** which allows scientists to monitor the activity of thousands of genes simultaneously. This technology will help define the complex regulatory circuitry within a cell, tissue or organ and give scientists a global perspective on how an organism responds to a stress, drug, or toxicant. The data generated will provide information about cellular networks of responding genes, define important target molecules associated with the toxicity mechanism, and provide **biomarkers** for epidemiological studies. Ultimately, this information may allow us to identify new ways to reduce or prevent disease by controlling biochemical and molecular functions that have been perturbed by environmental chemicals. DNA micro-array technology will undoubtedly become a major tool in environmental medicine, because it will also improve our diagnostic and prognostic capabilities for specific diseases as well as our ability to examine drug interactions, sensitivities and effectiveness. This technology will also aid research on alternative model testing procedures and support the development of new toxicity screening processes.

DNA microarray technologies will permit the design of experiments in the occupational and environmental sciences to clarify whether:

- specific toxicants have unique gene expression profiling signatures;
- different cells in different tissues have profoundly different response signatures for a given toxicant;
- different species show similar, overlapping or distinct patterns of gene responses to a toxicant;
- a specific toxicant signature is altered depending upon the stage in the developmental process or defined health condition;
- responses to complex chemical mixtures in the workplace can be defined by their gene expression profiling signatures;
- responses to chronic low doses of toxicants or environmental pollutants can be measured by gene expression profiling;
- specific gene polymorphisms can be identified that are characteristic of an increased susceptibility to substances that induce occupational or environmental diseases.

DEFINITIONS:

Genome The sum total of all genes.

mRNA Messenger RNA: the chemical message by which information encoded in genes is translated into proteins, which in turn do the work of the body.

DNA micro-array A technology that enables scientists to simultaneously monitor the activity of tens of thousands of genes within the genome.

Bioinformatics The application of computer technology to the management of biological information generated from microarrays.

Biomarker A biological measure of an individual's susceptibility to, exposure to, or effect resulting from, an environmental agent.

Gene polymorphism Multiple variations of a specific gene that occur within a population.

Occupational Exposure to Paint

The next time you think about it, take a look around at all the objects that are painted, varnished or otherwise finished with some type of coating. Cars, roadways, signs, buildings, furniture - you name it - paints are a significant, if largely overlooked, part of our modern world. But to those engaged in coloring and coating the objects around us, paints and solvents pose a potential health hazard if appropriate safety measures are not observed.

TYPES OF PAINTS

Many different types of compounds are used in paints. However, most contain three primary ingredients: thinners, which evaporate once the paint is applied; binders, which hold the constituents together and onto the painted surface; and pigments, which are the ingredients that give paint its color and improve its durability. Water-based paints, including latex, tempera and poster paints, are the least hazardous of the major classes of paints. They typically contain latex or alkyd binders, biocides, plasticizers, drying agents and surfactants. Solvent-based paints contain thinners that are volatile compounds, such as toluene, xylene, light petroleum spirits and various ketones and alcohols. They are often used in spray paint products because they have a low viscosity and dry rapidly. Oil-based paints contain mineral spirits as the thinner. They dry more slowly, but provide a superior and more durable coverage than water- and solvent-based paints. Specialty paints, many of which are powder-based, contain a variety of ingredients, including isocyanates, polyurethane or epoxy resins.

HEALTH EFFECTS OF PAINT EXPOSURE

People occupationally engaged in painting may be at risk for a variety of acute and/or chronic health problems. Dermatitis and allergic skin sensitization are common manifestations of paint exposure. Rhinoconjunctivitis (eye, nose and throat irritation) is also common among people who apply water-based paint and is reported to occur in 43 % of those applying polyisocyanate-containing paints. Chronic inhalation of paint fumes has been associated with reduced pulmonary function, increased incidence of respiratory symptoms and an ilevated risk of mortality from nonmalignant respiratory disease. Moreover, isocyanates and reactive dyes, such as those derived from azo, anthraquinone and phthalocyanine compounds, may induce a more serious allergic reaction in the pulmonary system.

Acute and chronic neurologic effects are known to occur as a result of excessive exposure to solvent- and oil-based paint fumes. Headache, lightheadedness and fatigue are commonly reported after acute exposures. More severe acute exposures, such as may occur in poorly ventilated areas, can produce loss of balance, amnesia, confusion and lethargy. Workers chronically overexposed to paints and solvents are at risk for a "toxic encephalopathy" known as Painter's Syndrome or Organic Solvent Neuropathy. Symptoms of Painter's Syndrome include memory impairment, difficulty concentrating, fatigue, headache, dizziness, apathy, depression, anxiety and personality changes. These symptoms may be poorly reversible after exposure stops.

Ingesting solvent-based paints and inhalating their vapors may cause gastrointestinal irritation, nausea and diarrhea. Liver toxicity, as indicated by elevated blood hepatic enzyme levels, may occur. Liver cell damage has been observed after even a single exposure to polyurethane-based paint fumes. Chronic overexposure to paint has been associated with liver fibrosis and an increased risk of death from nonmalignant upper gastrointestinal tract disease.

The blood and bone marrow may be targets in paint-induced toxicity. Polyurethane-based paints are known to produce transient depression of the major blood-forming elements in the bone marrow, even after single acute exposures. Although lead is no longer used in paints, anemia and neurological symptoms may develop after exposure to lead-based paint chips or dust, which may be inhaled or

ingested during paint-stripping projects. A variety of other heavy metals used as pigments in paints, such as chromium, cadmium and nickel, can also be toxic to the blood, nervous system and internal organs.

Subcutaneous injection of paint, lacquer or other material by high-pressure spray guns can cause severe tissue injury despite a relatively benign initial appearance. Injection injuries produce tissue necrosis and blood thrombosis, resulting in the need for amputation in 60 to 80 percent of cases. These injuries occur most commonly to the hands and digits. Thus, paint injection injury should be regarded as a serious surgical emergency.

In addition to the above risks, persons chronically exposed to paints may be at increased risk for cancer. Painters are one of the occupational groups most at risk for bladder cancer, and have an increased risk of laryngeal and esophageal tumors. Prolonged repeated paint exposure has been associated with an increased risk for myelogenous leukemia and multiple myeloma as well as for bile duct, bowel and rectal cancer. In one epidemiologic study, painters who never wore masks or respirators were at a five-fold excess risk for lung cancer as compared to a control population not exposed to paints.

REDUCING THE HAZARDS OF PAINTS

In order to avoid potential health risks, it is important to become familiar with the chemicals that are contained within the paints you are using, their potential hazard, and how to avoid them. This information can be found in the Material Safety Data Sheet (MSDS), which is required to be available for every paint product used in a workplace.

In addition to the precautions outlined by the MSDS, a few sensible safety guidelines are applicable to all paint products. Ideally, priming and painting should be done in a properly maintained spray booth or room. Always position yourself so that the object being painted is between you and the exhaust fan, and always keep the spray gun pointed away from your body.

Personal protective equipment is vital to ensuring your continued good health. These include respirators, eye protection and protective clothing. Two types of respirator, air-purifying and atmosphere-supplying, are commonly used in spray painting. It is important to use the correct type of respirator for the job being done and the type of chemicals being used. Air-purifying respirators are not effective unless they contain a filter cartridge designed to absorb the specific chemicals contained within the paint. These cartridges must be replaced when vapors can be smelled within the mask, when they become difficult to breathe through, or when their specified lifetime has been exceeded. Atmosphere-supplying respirators are required in some paint spraying operations, especially when painting in confined spaces (e.g. within tanks or a ship's hold) or when urethane paints are used. Whichever respirator is used, it must fit properly to ensure adequate protection. Proper respirator fit may require the removal of facial hair in areas contacting the mask. A computer-based training program on respiratory protection is available on CD-ROM from OR OSHA's resource center in Salem.

Safety goggles should always be worn to protect the eyes from over-spray or splashing. Coveralls and appropriate gloves are also important to reduce injury to the skin and prevent absorption of toxic solvents into the body. Protective clothing and gloves should be washed frequently to prevent chemicals from accumulating, especially around cuffs where they can easily contact the skin. Barrier creams are available for use on the hands, face and neck. Finally, head wear should be worn to prevent solvent absorption through the scalp.

For more information on paint and solvent safety, contact CROET's Toxicology Information Center at 1-800-457-8627 or visit our web site at http://www.croetweb.com

KUDOS

CROET Employee Shares AWSEM Knowledge and Enthusiasm with Middle School Girls

Greta Glover, a CROET employee and OHSU neuroscience graduate student who works with Dr. Gary Banker, took time out in March to introduce twelve girls from Whitford Middle School to CROET neuroscience. With help from Dr. Ginger Withers and Dr. Stefanie Kaech-Petrie, Greta showed the girls around three educational stations in the lab: dissection and anatomy, cell biology, and the microscope. The event was part of the AWSEM (Advocates for Women in Science, Engineering, and Mathematics) program that originated out of the Saturday Academy program of the Oregon Graduate Institute. Greta, who also volunteers with KIDS (Kids Interested in Discovering Science), was contacted by AWSEM through the OHSU neuroscience graduate program in which she is enrolled. She plans to present another educational program to AWSEM participants this Spring.

CROET High School Research Apprentices Win Awards, Acceptance to Harvard and Stanford University

Korri Thiessen, a high school student from Oregon Episcopal School in Beaverton, won several research awards as a result of her research apprenticeship with CROET's Dr. Glen Kisby. Korri took the first place overall award at the Oregon State Fair Science Expo for a presentation, titled The Influence of Stress and Age in APE Neuroprotein-Correlated Base Excision DNA Repair. She was awarded a medallion and a certificate from the U.S. Army and was invited to compete in the Gerontology Category of the International Science and Engineering Fair in San Jose, CA. At this event, Korri won Overall Best of Division from both the U.S. Army and Navy, 2nd Place in the Gerontology Category, and an Honorable Mention Overall from the American Psychological Association. Her prizes for these awards totaled over $13,000, which will be used for Korri's college education.

Jessika Lora, a high school summer student who came to CROET through the OHSU Multicultural Affairs' Research Apprentice Program, has been courted by both Harvard and Stanford universities. Jessika participated in Stanford's Youth Environmental Science Program after working this summer on an epidemiological study conducted by CROET's Dr. Linda McCauley. In the study, Jessika learned about measuring pesticide-exposure biomarkers in children of migrant farmworkers. Jessika accepted Stanford's offer of admission, and plans to pursue a career in medicine.

Another participant in the CROET summer program, Joshua Foster, took the time recently to express his gratitude to his mentors in CROET. Joshua worked with Juan Muñiz and Julie Richman, whose research supports Dr. McCauley's epidemiological studies. "Juan and Julie made sure that I always knew what I was doing and why I was doing it," writes Joshua, who plans to continue studying science when he goes to college. "There is only so much you can learn in textbooks and this job allowed me to learn what science, especially chemistry, is all about."

The CROET Summer Student Program began in 1993, and has brought many Oregon students into the world of science. The program accepts both college and high school students, of which there are 40-50 applicants each year.

Center for Research on Occupational and Environmental Toxicology

CROET, the Center for Research on Occupational and Environmental Toxicology at Oregon Health & Science University, conducts research, provides consultations and offers information on hazardous chemicals and their health effects. CROET includes approximately 100 scientists and research staff exploring a range of questions relating to health and the prevention of injury and disease in the workforce of Oregon and beyond. CROET's Toxicology Information Center is open to the public and is staffed to answer Oregonians' questions about hazardous substances in the workplace and elsewhere. CROET's website also provides answers to questions about industries found in Oregon through links on a series of pages devoted to industry-specific topics.

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Czech Woman's Harvest
by Faye Cummins

CROET Newsletter Will Feature Oregon Artists

From classical art, to volcanoes, to nerve cells, the CROET newsletter has traditionally contained a picture on its cover. In the next several editions, we will be including the works of a variety of Oregon artists. In this newsletter, we feature the work of Corvallis elementary school teacher and artist, Faye Cummins.

CROET HEALTH AND SAFETY SEMINARS

Building Effective Training Programs

Has tentatively been rescheduled for presentation in March

Internet Sleuthing

Hands-on Internet information workshop
Limited to five students per class
Second Friday of each month, 1-3PM

For information, contact CROET at:

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OUTREACH

CROET is providing exhibits at the following conferences.

Cascade Safety, Health & Environmental Conference

March 12-14, 2002
Hilton Eugene & Conference Center, Eugene, OR

For more information, see the following web site.
http://www.cbs.state.or.us/external/osha/educate/conferences/confer.htm

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