

# CROET

Putting science to work for working Oregonians



CROET  
2006-2007  
ANNUAL  
REPORT

# Mission, Purpose, and Mandate

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CROET, the Center for Research on Occupational and Environmental Toxicology at OHSU, is dedicated to the promotion of health and safety in the workforce. Through basic and applied research, education, and outreach, CROET seeks to prevent disease and disability among working Oregonians and their families, during their employment years and throughout retirement.

# Message From the Director

This has been a productive period for CROET, but let me begin by telling you how we measure our success each year. We measure CROET in several ways. Most importantly, we measure CROET's efforts in achieving our mission and in the funding we bring into Oregon to tackle the mission. Let me begin with mission-critical issues.

Data for 2007 show for the private sector that Oregon workers suffered the lowest ever recorded work-related injuries and illnesses, the current figure of 5.1 for every 100 full-time employees having dropped steadily from 7.8 in 1997 over the preceding 10 years. Close behind was the Oregon public sector, which reported a total-cases incidence rate of 5.4. Days away from work in 2007 remained at 2.8 and 2.6 in private and public sectors, with the highest rates recorded in transportation and warehousing (5.9), arts, entertainment and recreation (4.7), agriculture, forestry, fishing and hunting (3.9), manufacturing (3.6), and utilities (3.0). (1)

While it is not possible to measure the degree to which CROET has positively contributed to these declining rates of injury and illness among Oregon workers, we can be certain that our research, education, and outreach activities are focused where the need is greatest. In transportation and warehousing, we are pioneering an evidence-based health promotion intervention model for commercial truck drivers, who account for 15% of occupational fatalities, 8% of musculoskeletal injuries and have a 10-12-year shortened life span. The Oregon Fatality Assessment and Control Program spearheaded by CROET addresses several priority workplace sectors, including transportation, logging and workers aged 16-24, who are involved in 15% of all Oregon fatalities. In agriculture, CROET provides short-term training for Oregon's orchard workers while investing in basic research on the long-term adverse effects of pesticides. Health and safety concerns in manufacturing, utilities and other sectors are addressed through CROET's Chemical Risk Information Service and Health and Safety Training Symposia. Broad questions of chemical safety are handled through the Toxicology Information Center, while CROETweb.com provides an occupational safety and health resource directory that covers the waterfront of Oregon industry and commerce.

We are also leveraging every dollar of state support for two federal dollars to explore other conditions that impact the workforce or set up workers for diseases that occur in later life or during the retirement years. These research efforts are focused on the prevention and treatment of cancer, diabetes and neurodegeneration, and they seek to identify factors that increase risk for individuals and identify mechanisms at a fundamental level. For example, brain research on circadian rhythms has great relevance for shift workers. These research programs represent a broad investment in the present and future health and safety of the working people of Oregon and beyond.

There is still much work to do on all fronts! The aging population is increasing the risk of chronic debilitating disease and injury, and Oregon work-related illnesses and injuries while improving are still behind national statistics. CROET will continue to innovate and implement programs with state and federal support that seek to close that gap.

Respectfully submitted,



Peter S. Spencer, PhD, FRCPATH  
CROET Director and Senior Scientist

(1) 2007 Oregon Occupational Injury and Illness Survey Summary. Information Management Division, Department of Consumer & Business Services, December 2008.

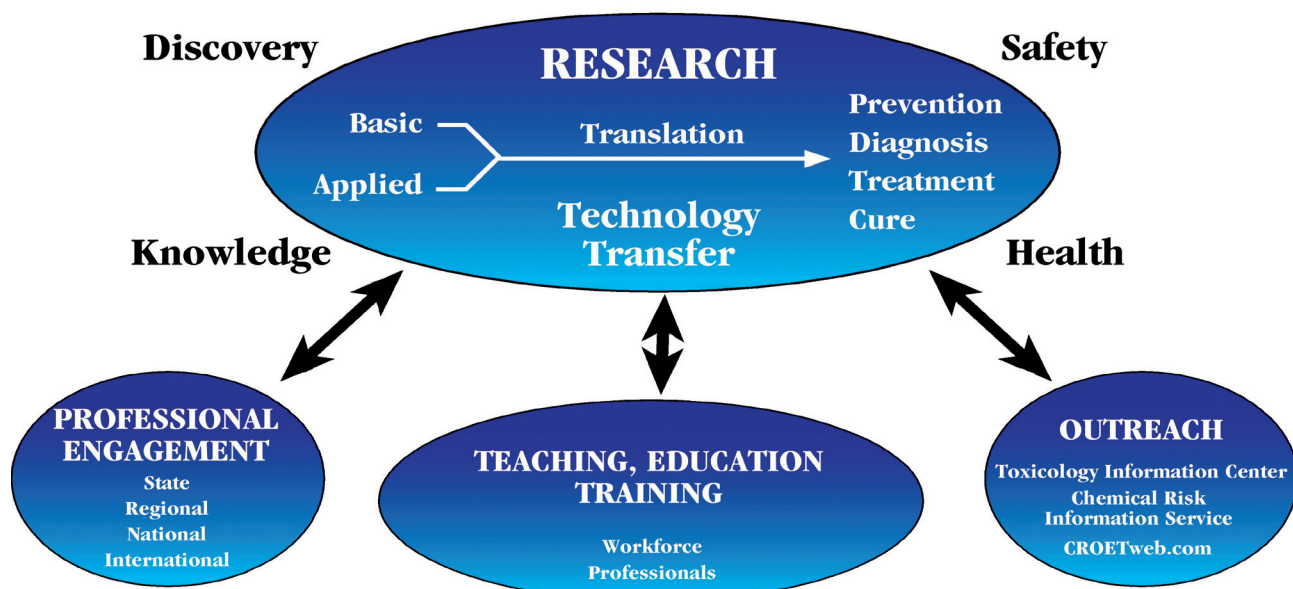
# CROET: a Resource for Oregon

CROET conducts research on the basic biology of workplace-related injury and disease as well as research related to workplace performance and occupational exposure. CROET also participates in doctoral and postdoctoral educational programs to train the next generation of scientists, and provides updates for health and safety specialists to ensure that the latest scientific advances are translated into enhanced workplace safety. Through its outreach efforts, CROET serves as an information conduit to Oregon workers, employers, labor, and the general public.

Applied research addresses workplace hazards, often spurred by specific safety issues of immediate concern to Oregon's workers. Research is focused on surveillance of workplace and environmental problems and on prevention of injury in agriculture, service industries, and construction. This research has short-term payoffs. Examples: (1) identifying unrecognized trends in Workers' Compensation claims, suggesting new prevention priorities; (2) computer-based training has been developed for respirator safety, pesticide exposures, and ergonomics in drywall finishing, and training effectiveness is under study; and (3) agriculture workers are monitored for exposure to pesticides and adverse nervous system health effects, and are given safety training.

Basic research is focused on nerve and muscle damage and repair, occupational/environmental exposures and their consequences, DNA damage, and cancer. This research requires prolonged commitment and synergy among investigators and has a long-term payoff. It is applicable to many diseases and disorders including those associated with the workplace and those that arise from other causes (e.g., genetic, environmental) that plague Oregonians during their working years and into retirement. While this is important for Oregonians, it obviously has a wider impact. Thus, most of the funding for CROET's research in these areas is supported by grants from the National Institutes of Health, Centers for Disease Control, National Institute of Occupational Safety and Health, and from other federal sources. Examples of what CROET scientists are studying include: (1) how nerves grow, how they connect (form synapses) with other nerve cells and with muscles, and how to enhance their regenerative potential — all of which are critical to post-injury recovery; (2) how environmental and occupational exposures trigger DNA damage and cancer, and how mutations in specific genes disrupt cell function; and (3) how the brain and other organs function in normal conditions and following exposure to chemicals and drugs.

***State Mandate:  
Conduct basic and applied research, outreach and education  
to address Oregon's occupational health needs***



# CROET's Areas of Emphasis

## Education and Outreach programs

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### CROET's Education and Outreach Programs have four goals:

- Provide scientifically accurate information on Oregon's occupational issues — continuously on the Internet and daily with scientific interpretation for complex issues through the Toxicology Information Center (TIC)
- Offer educational programs on Oregon's occupational needs to health and safety specialists and medical providers
- Train health professionals who will investigate Oregon's occupational safety and health issues in the future
- Provide the scientific expertise to help Oregon industry and labor evaluate occupational safety and health questions

## Research

### Applications and Outreach

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- Cellular mechanisms that control sleep-wake cycles relevant to shift workers
- Computer-based and other training methods to enhance worker safety training
- Agricultural, construction, high tech, office-related and transportation industries

### Injury and Recovery of the Nervous System and Muscles

- Assessing nerve cell protein dynamics using imaging
- Using nanotechnology to enhance nerve growth
- Factors that govern the accuracy of nerve synapse formation
- Genetic models of nerve maldevelopment

### Chronic Disease and Working Safely

- Effects of pesticide exposures assessed using exposure biomarkers and behavioral testing
- Toxicants that disrupt protein transport in neurons
- Defining and studying models of chronic disease (asthma, neurodegenerative, diabetes)

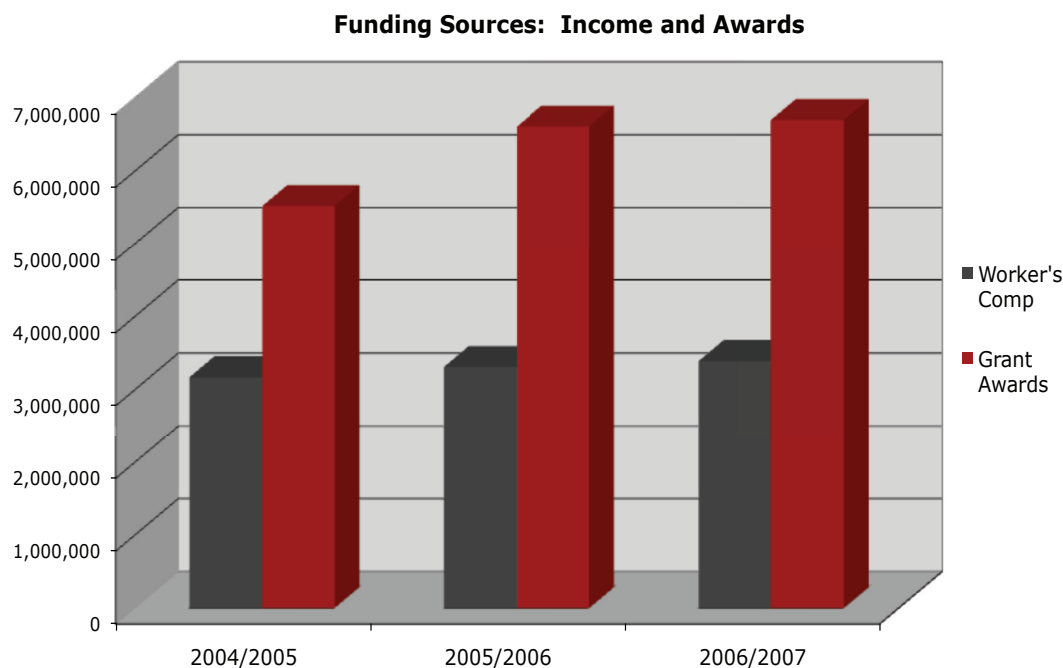
### Integrity of DNA (DNA damage, genetic alterations, and disease)

- Role of DNA repair in protecting the nervous system from effects of chemicals
- Gene silencing and cancer
- Mutations induced by ionizing irradiation, oxidative stress, and other genotoxins
- Ion channel mutations that underlie diseases

# What has CROET done for Oregon?

- **Brought federal dollars into the Oregon economy**

CROET receives base operations funding from the Oregon Workers' Compensation System that, year after year, CROET scientists have successfully leveraged to win federal and other research dollars. For every dollar invested by the State's Workers' Benefit Fund, CROET's world-class scientists have brought an averaged \$2.40 of federal and private grant funding into the Oregon economy (see chart below). Federal dollars for research in Oregon have a significant positive impact on the state's economy. Expenditures for goods and services, as well as the salaries of scientific and support personnel, produce a multiplier effect on the purchase of goods and services and creation of businesses that support the needs of Oregon's research institutions. Moreover, research coming out of CROET has a greater than average impact on the state's economy from the new technologies and jobs that spin off from productive research, as exemplified later in this report. In a study conducted by Oregon State University, multiplier effects on the economy from the infusion of federal grant funds were estimated to range from 2 up to 10 dollars per federal dollar received.



- **Conducted Workplace Studies and Applications Research**

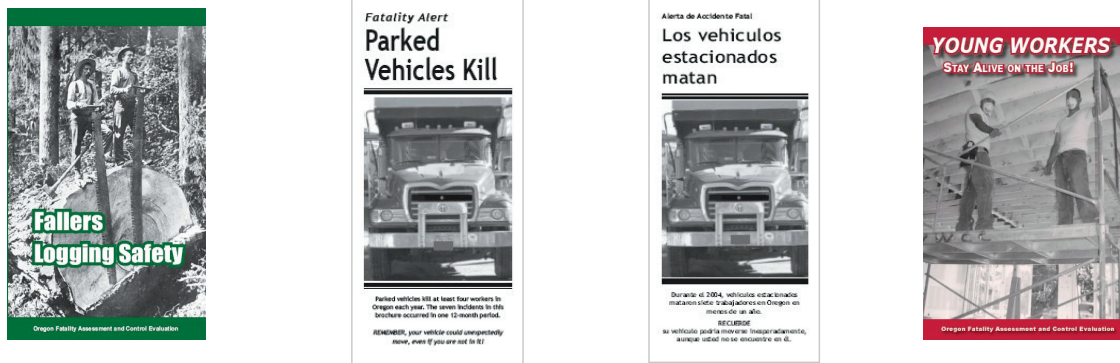
CROET conducts workplace surveys so that prevention and research needs can be identified, and applications research to bring the benefits of science to the workplace floor. It also reaches out to provide education and information to the Oregon workforce and beyond.

## **Oregon Fatality Assessment and Control Evaluation (OR-FACE) Program**

Dr. Gary Rischitelli leads the Oregon Fatality Assessment and Control Evaluation (OR-FACE) program that tracks, investigates, and reports on occupational fatalities in Oregon. In 2006, OR-FACE recorded 79 occupational fatalities in 67 incidents. In 2007, OR-FACE recorded 69 fatalities in 67 incidents. OR-FACE investigates incidents in specific national and local target areas of concern, and between 2006-2007, produced 9 investigation reports with safety recommendations. During 2006-2007, falls became a leading area of concern, and OR-FACE published a hazard alert on falls from elevated work areas, ladders, and suspension from a height. In 2007, OR-FACE published its third annual report summarizing data from 2005, and included an abstract of each incident. The report charted frequencies by age, gender, race/ethnicity, time, month, county, industry, occupation, and event. Principle areas of concern were highlighted in relation to transportation, falls, and contact with objects or equipment. Through its research, OR-FACE has identified several priority areas of concern within specific sectors of the Oregon workforce, including transportation (motor vehicles, trucking), logging, and young workers. Young workers aged 16-24 are involved in



15% of all Oregon fatalities, a finding that inspired establishment of the Oregon Young Worker Health and Safety Coalition, co-sponsored by OR-FACE and the University of Oregon's Labor Education & Research Center (LERC). The Coalition's activities include developing occupational safety and health curricula for teens, disseminating educational materials for teachers, conducting teacher education workshops, outreach to employers, and public information campaigns. OR-FACE investigation reports and other publications are available on the program's website ([www.ohsu.edu/croet/face](http://www.ohsu.edu/croet/face)). Investigation reports from Oregon and other FACE states are also available through the National Institute for Occupational Safety and Health ([www.cdc.gov/niosh/face](http://www.cdc.gov/niosh/face)), which funds the program.



*Examples of publications produced by OR-FACE, 2006-2007*

## Health Promotion Intervention Model Being Developed for Truck Drivers

Safety and Health Promotion for Truck Drivers (SHIFT), a program developed and headed by Dr. Ryan Olson, is a 6-month safety and health promotion program designed for commercial truck drivers. Commercial truck drivers account for 15% of occupational fatalities, 8% of musculoskeletal injuries, and have a 10-12 years shortened life span. Long and unusual work hours, prolonged sitting, limited food choices, and demanding work put drivers at risk for serious illness and injury - most notably heart disease and back injuries. Drivers who joined the SHIFT program completed training and worked toward goals, including weight loss, diet and safe driving. Drivers competed in teams to achieve the largest improvements in health and safety measures, and were rewarded for both participation and high achievement. To help drivers accomplish their health and safety goals, the program included computer-based training, self-management activities and individualized health coaching. This evidence-based health promotion intervention was funded by a National Occupational Research Agenda (NORA) priority grant from the Northwest Center for Occupational Health & Safety. Please visit [www.ohsushift.com](http://www.ohsushift.com) to learn more.

## Self-Assessment and Self-Management Program Helps Truckers Avoid Musculoskeletal Injury

Behavioral self-monitoring (BSM) methods, where individuals repeatedly observe, evaluate, and record aspects of their own behavior, can produce valuable assessment data about injury hazards and near misses. Dr. Ryan Olson has developed and studied BSM assessment with less-than-truckload (LTL) truck drivers. LTL work involves hauling partially loaded trailers, making multiple daily stops, and performing frequent and demanding material handling work in a variety of customer environments. To address this difficulty, Dr. Olson's research team employed two data collection methods: (1) intensive video monitoring, in which direct observation of work habits and environments were achieved through the use of a customized camera system installed in a working trailer and (2) behavioral self-monitoring, in which individuals repeatedly observed, evaluated, and recorded aspects of their own behavior and environmental conditions. Dr. Olson found that each instance of manual material handling increases the potential for severe (hazardous) body postures by 7%, whereas obtaining customer forklift assistance and preventing manual materials handling by palletizing transported materials decreased this potential by 12% and 20%, respectively. Comparisons between experimenter video observations and driver self-observations showed that drivers are quite accurate at self-assessing hazards that are environmental, frequent, and easy to discriminate, but less so at assessing potentially harmful body postures and rare work-related events or environments. These findings suggest areas in which positive interventions can reduce risk for injury, including organizational management of ground stops (e.g. facilitating the use of forklifts), re-engineering handles and steps that lead into trailers, and having workers self-assess the prevalence of certain work exposures. The results of this project are an important step

forward in understanding and preventing musculoskeletal injuries among isolated workers and in advancing our knowledge about the reliability of ergonomic self-assessments.

## Study on Vigilance Performance Enhances Error & Threat Detection

Human performance on visual screening tasks is increasingly important to public and workplace safety. These tasks require human operators to detect rare but potentially dangerous signals or threats on some type of visual display. Examples include: aviation security workers searching for unusual passenger behaviors and prohibited items in luggage; radiologists screening for tumors or other abnormalities in sophisticated body images, and manufacturing workers searching for potentially dangerous and costly deviations in high-tech production processes. Dr. Olson collaborated with Lindsey Hogan and Matthew Bell of Santa Clara University (Santa Clara, California) to develop a simulated baggage-screening task that uses x-ray images provided by the Transportation Security Administration to investigate factors that enhance vigilant search behaviors. It is known that observers in visual search tasks miss threats at increasing rates as threats become less frequent (i.e. anomalous objects such as weapons in luggage are relatively rare). The research team tested a “Vigilance Reinforcement Hypothesis” (VRH), which proposes that signal detection reinforces search behaviors, and predicts more intense searching and better signal detection when signals are abundant. Dr. Olson has completed two laboratory studies that are supportive of this prediction, and has applied to the National Science Foundation (NSF) for funding to support continued work on learning phenomena that could be used to enhance signal detection, such as reinforcing variability in visual search patterns, and using planted signals as an intervention method to sustain vigilant search behaviors.

## Computer-based Training Effective for Immigrant Orchard Workers

W. Kent Anger, PhD CROET Senior Scientist and Associate Director, has been developing and testing the effectiveness of a computer-based training system that is competent across cultures and is now available commercially. It is designed to be effective with the full range of occupational populations, from uneducated (no schooling) immigrant agricultural workers to office workers with graduate educations. Dr. Anger’s lab is shared with staff scientist Dr. Diane Rohlman, whose independent research focuses on neurotoxic effects in young workers and children of workers exposed to pesticides at work. Latinos dominate the agricultural workforce in Oregon and throughout the US. Many have limited years of education in countries with different systems of education than in the US. Drs. Anger and Rohlman have been investigating whether computer-based instruction (CBI) is suitable for this work group, which generally has an average of 5-6 years of education, though some have not been to school at all. Ladder safety was studied in a Latino orchard workforce that reported little computer experience and reported an average 5.6 years of formal education. The orchard workers rated the training highly and their knowledge of ladder safety improved substantially as measured by standardized tests. More importantly, there was a significant increase in safe work practices immediately after training, at 40 days after training and at 60 days, indicating that the learning was durable over time. This demonstrates that an agricultural workforce can learn job safety from CBI, translate the knowledge to work practice changes, and maintain those changes over time. Dr. Anger published this work in the International Journal of Training and Development.

OHSU and Drs. Anger and Rohlman have a significant financial interest in Northwest Education Training and Assessment, LLC, a company that may have a commercial interest in the results of this research and technology. This potential conflict was reviewed, and a management plan, approved by the OHSU Conflict of Interest in Research Committee, was implemented.

## • Continues to be a trusted information resource for Oregon workers

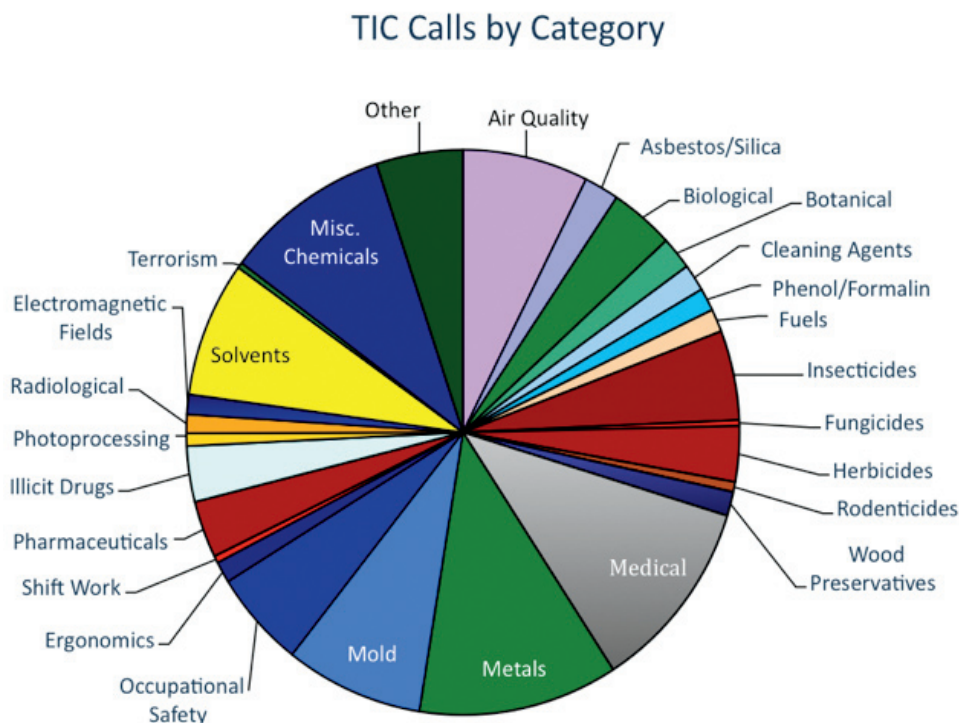
CROET has been proactively engaged in providing timely occupational health and safety information to employees, employers, health and safety professionals, doctors and nurses.

## Toxicology Information Center (TIC)

Directed by Dr. Fred Berman, the TIC provides free scientifically accurate information for those with questions or concerns about chemical, biological, physical or other agents encountered in the workplace and elsewhere. In 2006-2007, Dr. Berman handled hundreds of consultation requests from occupational safety and health professionals, business owners, government agencies, physicians and nurses, the media, and the general working public. Inquiries covered a variety of issues, as shown on the pie chart. Chemical agents of concern included solvents, heavy metals, insecticides, fungicides, and herbicides. Physicians often called seeking information on a variety of potentially occupation-related health complaints.



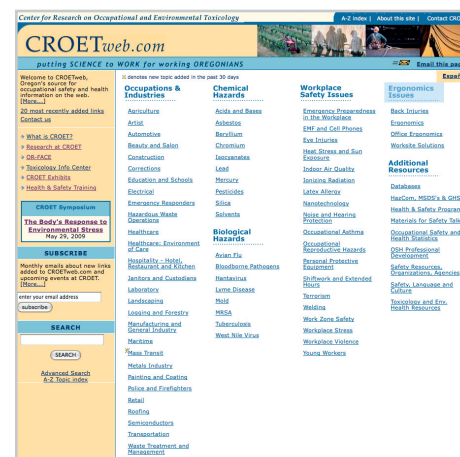
Calls in regard to indoor mold were common as were calls related to acute and chronic medical problems that were attributed to exposure to chemical agents. Each request took from less than an hour up to several days to respond to fully. The TIC is open from 7:30 a.m. to 4:00 p.m., Monday through Friday. Walk-in visitors have access to a variety of resources, including computers, databases, government reports, textbooks, and journals that are devoted to toxicology-related issues.



## CROETweb.com

CROETweb.com is an occupational safety and health resource directory that contains links to over 1200 occupational safety and health resources focusing on day-to-day workplace issues. CROETweb serves thousands of users who regularly bookmark this resource, those who subscribe to the monthly electronic newsletter, and those searching by search engine (e.g. google) for occupational health and safety topics on the web. It is widely recognized and respected by industrial health and other safety professionals as well as the general public. CROETweb was accessed an average 12,000-16,000 times per month for a total of 166,134 'hits' in 2007. This monthly average hit rate has increased yearly since the inception of CROETweb.

- CROETweb added 11 new home page topics, for a total of 83 in 2006  
Hospitality – Hotel, Restaurant and Kitchen; Landscaping; Logging & Forestry; Acids & Bases; Chromium; Avian Flu; Occupational Asthma; Occupational Reproductive Hazards; Materials for Safety Talks; OSH Professional Development; and Safety, Language and Culture.
- An additional 13 topics were significantly revamped in 2007  
Acids and Bases; Asbestos; EMF and Cell Phones; Beryllium; Ergonomics; Office Ergonomics; MSDS Resources; Avian Flu; Healthcare; Solvents; Pesticides; Respirators; Transportation.
- Annual page hits – 2006: 162,838  
2007: 166,134
- More than 1,250 links are posted on CROETweb.com, including Oregon-specific information from OR-OSHA.



## Chemical Risk Information Service

OSHA regulations require employers to maintain Material Safety Data Sheets (MSDS) for hazardous chemicals used in their workplace. This often proves to be a difficult record-keeping task, and it can be burdensome to ensure that employees have quick access to health and safety information in the workplace when they need it. Since 1998, CROET's Chemical Risk Information Service, directed by Dr. Gregory Higgins, has helped a growing number of local and international industries manage and distribute chemical safety information through its Internet-based MSDS management system. CROET's working relationship with the Oregon Poison Center also ensures that employees covered by the program have ready access to medical information in the event of exposure. During 2006-2007, the Chemical Risk Information Service added five new clients, and now provides MSDS management services to 40 municipal, construction, and service companies, most of which are Oregon-based. Also during this period, this program began working with SafetyCal, a chemical labeling company located in Eugene, to begin developing a service to link CROET's MSDS program with their labeling service so that clients can have a one-stop location to meet OSHA right-to-know regulations. Enhancements were made to the CRIS website and database during this period. CROET continues to provide expert MSDS management services at a reasonable cost, which is attractive to both small and large organizations.

## Health and Safety Training Symposia

CROET provides two health and safety symposia per year, one sponsored jointly with Portland State University. Topics are determined based on solicited and unsolicited feedback from the Oregon occupational health and safety professional community. The target audience includes health and safety professionals, occupational nurses and physicians, loss control specialists and human resource representatives, although the targeted group varies based on the symposia topic. The purpose of the symposia is to provide timely, up-to-date presentations, forums and discussions on workplace safety and health issues. CROET presented the following symposia in 2006-2007:

### **Substance Use and Safety in the Workplace**

November 2, 2007, Portland State University, Portland, Oregon

### **Safety at Work in Informal and Non-Traditional Settings: Protecting Vulnerable Workers**

June 8, 2007 at the NECA/IBEW Electrical Training Center, Portland, Oregon

### **Workplace Violence Prevention**

December 8, 2006 at the Native American Center at Portland State University, Portland, Oregon

### **Safety and Health for the Limited English Speaking Workforce: Challenges & Successes**

June 9, 2006 at the Ambridge Event Center, Portland, Oregon

## Regional Health and Safety Conferences

OR-OSHA sponsors the majority of health and safety conferences that CROET attends; these conferences are an important means by which CROET reaches out to working Oregonians. Workers and businesses learn about CROET and what it has to offer, and CROET personnel learn about the needs and concerns of workers and the industries that employ them. Moreover, CROET scientists are often asked to give health and safety presentations in addition to providing conference exhibits. Overall, conferences represent a tremendous networking opportunity for CROET outreach personnel. The following are safety and health conferences attended by CROET during 2006-2007:

### **2006**

- Oregon Governor's Fire Service Summit
- NIOSH/NORA Town Hall Meeting
- Agriculture, Forestry and Fishing
- Bob Bryant Memorial Cascade Occupational Safety & Health Conference
- Oregon Workers' Compensation Educational Conference
- HealthCare Ergonomics Conference
- Central Oregon Occupational Safety & Health Conference
- Southern Oregon Occupational Safety & Health Conference
- Northwest Occupational Health Conference

- NexCon 2006 - Next Generation Construction Summit: Defining the New Critical Path
- Western Pulp & Paper Workers Safety & Health Conference

## 2007

- Oregon Governor's Occupational Safety & Health Conference
- Blue Mountain Occupational Safety & Health Conference
- Central Oregon Occupational Safety & Health Conference
- Southern Oregon Occupational Safety & Health Conference
- Northwest Occupational Health Conference

## "Research to the Public" Exhibit

Jackie Shannon, PhD developed and implemented a "Research to the Public" exhibit as part of the Oregon Museum of Science and Industry's Body Worlds. This interactive exhibit (Nutrition Worlds) provided participants with an opportunity to obtain tailored feedback on their diet, including measurements of height, weight, waist circumference and percent body fat, measurements of blood glucose, HDL, LDL and total cholesterol levels. Participants also had the opportunity to become "research subjects", where de-identified data on diet, body composition, cholesterol measures, and salivary samples for DNA extraction and genotyping were obtained. Over 3000 individuals participated in this project and provided data as part of this "Research to the Public" project. Nutrition Worlds is now being converted into an off the shelf exhibit with the capacity to be used at large health fairs throughout the year. This type of outreach benefits workers and the general public by increasing awareness of factors that contribute to healthy lifestyles and a healthy workforce.

## • Helped build biotech in Oregon

CROET scientists Stephen Lloyd & Amanda McCullough are interested in DNA mutation and the mechanisms cells use to repair DNA damage induced by environmental stresses, including sunlight. Through basic research into the biomolecular mechanisms of ultraviolet (UV) radiation-induced DNA mutation and repair, they have devised and are now developing a novel strategy for preventing UV-induced skin cancer. Since mammals have only one system for repairing sunlight-induced DNA damage, their strategy is to supply skin cells with a second DNA repair system, which can be applied topically as a lotion to the skin. This involves the use of lipid coatings and protein tags that effectively allows the targeting of the DNA repair system to the cell nucleus, where it can be effective, thereby providing an extra level of protection against UV-induced DNA mutation. The technology has been shown in laboratory experiments to almost completely repair UV-induced DNA damage within 2 hours of application. Drs. Lloyd and McCullough have formed a company, Restoration Genetics, Inc., to develop and commercialize this technology as a therapy for prevention of skin cancer. This technology is explained in more detail in CROET Newsletter Vol. 14, #1, which can be downloaded at: <http://www.ohsu.edu/croet/about/pubs.cfm>

## • Became global ambassadors for CROET, OHSU and Oregon workers

### The Global Health Center (GHC)

The newly formed Global Health Center (GHC), housed in the CROET Toxicology Information Center, facilitates OHSU collaboration with the global health community to promote quality and equity in health care at home and abroad. Through the GHC, CROET and OHSU are working with domestic and international communities to develop programs for students, faculty, staff and partners that will promote global health awareness, research, education and advocacy. Dr. Peter Spencer, CROET Director and Senior Scientist, serves as Interim Director of the Global Health Center. Dr. Spencer has long studied the causes and solutions to neglected human diseases in developing countries, and hopes to spawn a new generation of medical and research professionals certified in global health. Built on the principle that there can be an effective two-way exchange on matters such as cultural competency, health education, research opportunities and clinical practice, the long-range goal of the GHC is to maintain a compact, efficient operation on the campus and invest in building healthcare capacity in global communities. In 2007, planning began for transdisciplinary global health courses involving faculty, students and staff. This includes a health and hygiene community exchange program, championed by CROET's Valerie Palmer, that brings Portland's refugees from Africa together with students and faculty from OHSU schools of Dentistry, Nursing and Medicine, and other OHSU-based programs of the OSU College of Pharmacy.

- **Conducted Laboratory Research Aimed at Preventing or Mitigating the Adverse Effects of Workplace Injuries and Exposures**

## **Injury and Recovery of the Nervous System and Muscles**

CROET scientists conduct basic research that examines the causes of injury to nerves and muscles in order to identify protective, preventative, and recovery methodologies for such injuries.

### **New Discoveries on Nervous System Effects of Environmental Pollutants, Statin Drugs, and Pesticides**

Biomarkers allow us to determine when chemical exposures reach a toxic level and identify the need for medical intervention. Dr. Pamela Lein, PhD has discovered that polychlorinated biphenyls (PCBs), a class of known developmental neurotoxicants and environmental pollutants, interfere with neuronal connections in the developing brain by disrupting normal patterns of nerve growth and plasticity (the ability of neurons to change in response to an environmental stimulus). This is the first identification of a specific neurodevelopmental event that is altered by exposure to PCBs. Dr. Lein also discovered that exposure to PCBs during development actually alters the susceptibility of the adult brain to damage caused by lack of oxygen that occurs during a stroke. In a related discovery, Dr. Lein found a novel mechanism by which statins, the commonly prescribed lipid-lowering drugs, decrease neuroinflammation – this effect may explain clinical reports and experimental studies identifying a potential therapeutic effect of statins in diverse neuroinflammatory conditions such as migraine headaches, arthritis and asthma. Dr. Lein also discovered that chlorpyrifos, an organophosphate (OP) pesticide still commonly used in the U.S. and throughout the world, interferes with axonal outgrowth in developing neurons via a unique mechanism that involves interference with the morphogenic activity but not the enzymatic activity of acetylcholinesterase (the enzyme responsible for degrading the neurotransmitter, acetylcholine) – this has important ramifications regarding the use of acetylcholinesterase activity as a biomarker of exposure to toxic levels of OPs.

### **Nerve Support Protein Plays Unique Role in Neuromuscular Development**

By understanding basic mechanisms of neuromuscular development and maintenance, we will learn how to repair muscle and nerve connections damaged in workplace accidents. The wiring of the nervous system during development is coordinated by molecular signals exchanged between neurons, glial cells (support cells which ensheath neurons), and target cells that receive innervation. Bruce L. Patton, PhD is studying signals that coordinate these cellular interactions. His interest is focused on the extracellular proteins that mediate direct contact between neurons, glia, and skeletal muscle fibers. The principal component of the extracellular protein matrix that covers a type of glial cell called the Schwann cell and skeletal muscle fibers is a glycoprotein called laminin. The Patton laboratory discovered four novel types of laminin; two are specifically associated with muscle fibers, and are concentrated at sites of synaptic contact, and the other two comprise the primary scaffold of the Schwann cell basal lamina. Dr. Patton's lab has used a combination of genetic mutational studies in mice and cell and biochemical studies to show that each laminin subtype plays a unique and primary role during neuromuscular development as well as a continuing role in maintaining the mature tissue. For example: laminin-11 localizes nerve terminal differentiation at embryonic synaptic sites in muscle; laminin-9 organizes the active zones (transmitter release sites) in mature motor nerve terminals; laminins-2 and -8 regulate Schwann cell responses to axonal cues during nerve myelination — they act cooperatively to match the number and type of Schwann cells to the number and type of axons; and laminin-2 stabilizes the muscle membrane during contractions. Current research in the Patton lab is directed at determining precise activities (e.g. differentiation, proliferation, signaling, motility support), and the cellular receptors and pathways that mediate the laminins' effects.



## **Chronic Disease and Working Safety**

Chronic disease takes a significant toll on our workforce just as it does in the broader community. CROET research seeks to discover causes of chronic diseases that are produced or exacerbated by workplace factors and identifies processes or procedures that can prevent or ameliorate those diseases and improve workplace safety.

### **Fruit Flies Enhance Our Understanding of Human Neurodegenerative Diseases**

Doris Kretzschmar, Ph.D. is interested in identifying genes and cellular mechanisms that underlie progressive degeneration of the nervous system, such as occurs in Alzheimer's disease. She has used specialized mutant and transgenic *Drosophila melanogaster* (fruit fly) lines to analyze, at the functional and molecular level, a protein called Swiss-Cheese/Neuropathy Target Esterase, which is involved in organophosphate pesticide-induced neuronal degeneration. Dr. Kretzschmar discovered that dysregulation of another cellular protein, known as protein kinase A, when it occurs in the absence of a functional Swiss-Cheese/Neuropathy Target Esterase, leads to neurodegeneration. This finding promises to be of functional significance to our understanding of several important human neurodegenerative diseases. Dr. Kretzschmar is also using her fruit fly model to analyze the physiological and pathological functions of amyloid precursor proteins, which are key factors in the pathology of Alzheimer's disease.

### **Discoveries of Circadian Clock Function Leads to Enhanced Understanding of Sleep-Wake Cycles**

Chuck Allen, PhD, is interested in the brain's circadian clock, which controls our sleep-wake cycles. Disruption of the circadian clock, such as occurs in workers who work odd shifts, plays an important role in increasing our risk for occupational accidents and chronic diseases. Most organisms, from plants to primates, display circadian rhythms, which are daily oscillations of physiological processes. The master circadian clock driving these circadian rhythms in mammals is located in a nerve group within the brain called the suprachiasmatic nucleus (SCN). Each SCN neuron expresses a molecular clock, which must be synchronized to other SCN neurons by neurotransmitter chemicals. Special classes of retinal cells that measure light intensity maintain the time-dependent coupling between the circadian clock and daily light-dark cycles. The long-term goal of Dr. Allen's research is to identify the signaling mechanisms within the SCN and retina that generate and entrain circadian rhythms. In 2006-7, Dr. Allen discovered a variety of cellular mechanisms that control how light-induced signals are processed and passed to areas of the brain that are involved in circadian clock function. A goal of this research is to increase our understanding of circadian clock function so that effective strategies for mitigating the adverse and potentially dangerous effects of shift work and odd work situations can be developed.

### **Organic Solvents Illuminate our Understanding of Neurological Disorders**

Neurotoxic disorders of occupational, therapeutic, or other origin, in which the causative agent is identified, usually present as self-limiting neurodegenerative diseases that impact motor, sensory and other nerve functions. Similarly, some chemical agents, acting alone or aided by a susceptible genetic background, also seem to play a role in the cause of progressive neurodegenerative diseases (e.g., sporadic amyotrophic lateral sclerosis (ALS) and Parkinson's disease). However, the molecular cascade over the long latent period from the beginning of natural disease development to clinical expression is unsolved and a key subject of investigation. Dr. Peter Spencer, Dr. Mohammad Sabri and Dr. Desire Tshala-Katumbay use organic solvents as tools to probe and model, over much shorter time scales, the human neurodegenerative diseases that take such a long time to develop. This requires exploration of the molecular mechanisms underlying the neurotoxic properties of these chemicals, which in turn is helpful in newly identifying hazardous substances in the workplace. New methods to identify and characterize the hazardous properties of chemicals require validation before they can be used to protect public health. One powerful method uses microarrays to capture changes in gene expression of tissues that have been exposed to chemicals and drugs. Microarray technology allows scientists to track the expression of thousands of genes at once. Dr. Spencer and his colleagues joined with six other leading laboratories to determine whether similar results could be obtained when experiments were replicated as closely as possible. The common over-the-counter analgesic acetaminophen was used as the test article because it is well established to produce liver toxicity. The study revealed similarities and some unexplained differences in data generated from different laboratories, but overall new information was captured on the molecular mechanisms under the drug's liver toxicity. The study confirmed the value of microarrays in detecting, characterizing and understanding chemical toxicity. With validation of the method established,



these scientists can now utilize microarrays to understand the pathological changes that occur following short- and long-term exposure to organic solvents.

## **Computational Modeling of Genetic Variation Aids Our Understanding of Occupational Disease**

Dr. Harvey Mohrenweiser is interested in reducing morbidity and mortality in individuals with elevated genetic susceptibility to common exposure-related diseases. Obesity, non-traditional work schedules and age are common exposures associated with increased risk of disease, injury and impaired performance. Such exposures have major negative consequences for health care and Worker Compensation costs for Oregon workers and the cost of doing business for Oregon businesses. Genetic variation has a clear role in modifying the susceptibility of individuals to these exposures; however, the problem of identifying the molecular basis for aberrant disease susceptibility is very complex, especially if the deviation from average disease susceptibility and contribution of multiple genes/variants and exposures are all small. Continued development of new experimental designs and approaches to data analysis will be required to address these complex problems, and they must be conquered if the potential for individualization of health care and medicine is to become a reality. Major progress has been made in identifying “disease causing” genes by studying susceptible families. Through computational and biochemical methods, Dr. Mohrenweiser has predicted that approximately 50% of all gene sequence alterations that have been identified in human genetic variation studies also alter protein function and potentially modify an individual’s risk of disease. This begins to explain the role of family history in predicting disease risk. DNA sequence variation with potential to impact gene expression is commonly observed in studies of DNA repair genes and genes with important roles in the response of cells to environmental agents. Dr. Mohrenweiser successfully employed statistical approaches to identify genetic variants that contribute to variation in the capacity of cells to repair damaged DNA. Genetic variation in DNA repair genes with key roles in repair of DNA damage caused by exposure to sunlight was found to explain about 20% of the variation among individuals at risk for melanoma. This is a very early step in efforts to identify people at elevated risk for this disease, as well as other diseases.

## **Integrity of DNA (DNA damage, genetic alterations and disease)**

Human health and risk for disease ultimately depend on the integrity of our DNA, the genetic material that provides the body’s blueprint for manufacturing proteins that carry out the function of cells and organs. Aberrant forms of DNA can produce inherited diseases, and changes in DNA during life are believed to trigger cancer and many other chronic diseases. Such changes can result from exposure to certain chemicals found in the workplace, in the diet, and in medications. Two broad types of DNA changes are recognized: DNA damage and DNA silencing.

## **Genotoxics Disrupt Neurodevelopment and Induce Neurodegenerative Disease Processes**

Dr. Glen Kisby is interested in the role of DNA damage and DNA repair in neurodevelopment and neurodegenerative diseases, and in the influence of environmental factors (e.g., occupation, stress, diet) on brain tissue DNA repair. Synucleinopathies and tauopathies, neurological diseases that result from the pathological accumulation of alpha-synuclein and tau proteins, are an important neuropathological hallmark of neurodegenerative diseases, including Alzheimer’s disease and the prototypical neurodegenerative disorder, Western Pacific amyotrophic lateral sclerosis/Parkinson-dementia complex (ALS/PDC). The cycad plant has been shown to be a strong causal factor for ALS/PDC. Dr. Kisby has shown that the cycad plant genotoxin, MAM, disrupts cellular processes that regulate tau and synuclein through a DNA damage mechanism. Further investigation of the relationship between MAM-induced DNA damage and tau protein metabolism during early brain development could provide important clues about how cycads contribute to the neurodegeneration in PDC and related neurological disorders (e.g., Alzheimer’s and Parkinson’s disease). Dr. Kisby has also shown that MAM, as well as the chemotherapeutic agent nitrogen mustard, disrupt early brain development through a DNA damage-mediated mechanism. These findings suggest that the specific combination of DNA lesion and DNA repair capacity within a neuron are key factors that determine whether the immature brain is vulnerable to a particular genotoxin. Such factors are expected to be particularly important for understanding how environmental genotoxins or chemotherapeutic agents induce their long-term effects on the developing brain. An understanding of these processes will enable us to avoid workplace/environmental exposures that increase our risk for neurological disease as well as allow us to develop new treatments for such diseases. Following this line of thought,

Dr. Kisby has shown that the brain of aging animals on a caloric-restricted diet is more efficient at repairing DNA damage than animals on an unrestricted diet. This finding indicates that dietary changes can have a positive effect on the DNA repair capacity of the brain, particularly among the aging population.

## **Pesticides May Induce Oxidative Stress and DNA Damage in Agricultural Workers**

Multiple studies have reported associations between exposure to agricultural chemicals and various health outcomes including cancer, Parkinson's disease and other neurological diseases. Oxidative stress and DNA damage have been proposed as mechanisms linking pesticide exposure to these adverse health effects. In recent in vivo and in vitro studies, Dr. Kisby has found evidence that organophosphate pesticides induce oxidative stress and DNA damage in agricultural workers. The method of detecting such changes, called biomarkers, increases our understanding of the link between pesticides and a number of health outcomes (e.g., neurological disorders and cancer). This work has been accepted for publication in the journal *Toxicology and Applied Pharmacology*.

## **Mechanisms Behind Insulin Secretion Diseases Being Uncovered**

ATP-sensitive potassium (KATP) channels are gated by the intracellular nucleotides ATP and ADP, the major energy molecules within cells. As such, they couple cell metabolism to membrane excitability and regulate a variety of physiological processes including insulin secretion, vasodilatation, neurotransmitter release, and cell defenses against cardiac and brain ischemia. Malfunction of KATP channels due to genetic mutations has been shown to cause congenital hyperinsulinism, diabetes, and delayed cardiomyopathy. The primary research focus of Dr. Show-Ling Shyng, Ph.D., is to understand the role of KATP channels in health and disease, in particular with regard to the regulation of insulin and glucose homeostasis. Dr. Shyng has discovered new mechanisms by which mutations affect ion channel function to cause insulin secretion diseases. Her ultimate goal is to develop therapeutic strategies to combat diseases caused by KATP channel dysfunction resulting from genetic mutations or environmental/occupational exposures.

## **Dietary Factors Alter Susceptibility to Cancer**

Jackie Shannon, PhD, uses epidemiologic methods to investigate the role of bioactive food components and metabolic dysregulation in the early stages of cancer development. She is interested in: 1) the role of dietary compounds, including omega-3 fatty acids and sulforaphane (an anticancer, antidiabetic and antimicrobial compound found in cruciferous vegetables) in the early development and prevention of prostate and breast cancer; 2) genetic susceptibility and dietary interactions in breast and prostate cancer prevention; and 3) metabolic dysregulation (including obesity and lipid metabolism) in cancer prevention. Dr. Shannon published her most recent findings on the relationship between omega-3 fatty acids and breast cancer risk. She is building upon her work by obtaining funding to begin one of OHSU's first chemoprevention trials for women newly diagnosed with ductal carcinoma in situ. Her long-term goal is to enhance the overall health of the workforce through the discovery of factors that reduce the incidence of cancer in our population.

## **New Gene Silencing System Facilitates Cancer Research**

Gene silencing occurs when a gene that should be expressed in a cell turns off unexpectedly. It is a common component of cancer. Aberrant gene silencing plays a causal role in cancer because it leads to inactivation of tumor suppressor genes. The endpoints of silencing are fairly well defined: promoter region DNA methylation and repressive histone modifications. Dr. Mitchell Turker has devised a system to trigger and study gene silencing in mammalian cells. The new system will be useful to determine how workplace and environmental exposures could initiate gene silencing and also to identify diets or drugs that could be designed to prevent gene silencing from occurring.

## **Mutation Discovery May Lead to New Skin Cancer Prevention Strategies**

Dr. Mitchell Turker has identified a combination of cellular exposures that lead to an unusual mutation induced by exposure to ultraviolet radiation (UV). Although rare in most cancers, this mutation (termed the tandem mutation) is found commonly in skin cancers and is due to sun exposure. A combination of UVB, which is the damaging form of ultraviolet light found in sunlight, and oxidative stress was shown to effectively induce the tandem mutation. This observation is aimed at developing strategies to prevent skin cancers, such as those that occur among outdoor workers. Dr. Turker is

continuing a long-term project to identify the types of mutations induced by exposure to ionizing radiation. Ionizing radiation is found at low levels in our environment and is used commonly in diagnostic x-rays and in cancer treatment. Knowledge of the types of mutations induced by this form of radiation will be helpful to determine whether a person has been exposed, the consequences of exposure, and to estimate the level of exposure.

## **New Research Discovers Mechanisms Underlying How Tumor Cells Resist Chemotherapy**

Occupational and environmental exposure to chemicals such as butadiene (a major building block in the synthetic rubber and plastics industries) and acrolein (a major contaminant in gasoline and diesel vapors and cigarette smoke) represent a significant health hazard and are classified as human cancer-causing agents. Results from the laboratory group of Stephen Lloyd, PhD, demonstrate the mechanisms by which exposure to these chemicals causes modifications in DNA which leads to mutations and transformation of normal cells into cancer cells. These studies were extended to show that these chemicals undergo complex secondary chemical reactions in which the two strands of DNA can be crosslinked to one another, a form of DNA damage that usually leads to cell death. Crosslinking DNA is one of the major mechanisms by which chemotherapeutic agents kill cancer cells. Even though these chemicals can crosslink the DNA strands, further work in the Lloyd group has shown that cells have special enzymes that can copy DNA even if it is crosslinked. This finding has implications for chemotherapeutic treatment of cancers, providing the first evidence for how cells (especially tumor cells) might resist killing by crosslinking agents.

## **Skin Cancer Prevention Therapeutic Shown to Enhance Repair of Sunlight-Induced DNA Damage in Human Skin**

Even though the Pacific Northwest is generally associated with only modest sun exposure, the state ranks in the top 5 nationally for sunlight-induced skin cancers. This is a significant hazard for working Oregonians. Although the reasons underlying the high incidence of skin cancer in Oregonians are complex, it is well established that sun exposure is the primary cause of non-melanoma skin cancers. It is important to take steps to prevent or at least significantly reduce the onset of this disease. Toward this goal, the research laboratories of Drs. Amanda McCullough and Stephen Lloyd have combined research interests and expertise to develop a potential prevention therapy for these skin cancers. Together, they have patented DNA repair enzymes that, when delivered to human skin cells, rapidly repair sunlight-induced DNA damage. Their investigations have recently shown that when human skin is grown in the laboratory, repair of sunlight damage rapidly occurs when the DNA repair lotion is applied. These studies are aimed at obtaining FDA safety approval for initial human clinical trials.

## **Chronic Low Dose Formaldehyde Exposure Results in DNA Damage Processed by the Homologous Recombination Pathway in Yeast**

Formaldehyde exposure occurs both in occupational settings and household environments. Formaldehyde is a respiratory irritant associated with asthma and “sick building syndrome”, and exposure is associated with the occurrence of nasopharyngeal cancers and DNA damage. In order to identify and characterize the biochemical mechanisms for repair of formaldehyde-induced DNA damage, the McCullough lab is utilizing a yeast model system that allows the entire genome to be screened for genes that confer formaldehyde sensitivity. These studies have identified specific biochemical pathways that protect cells from the cytotoxic effects of acute and chronic formaldehyde exposures, results that will impact the assessment of exposure limits considered safe for humans.

## CROET Expenditures Fiscal Year 2005/2006

Workers' Compensation Expenditures		Federal and Other Grant Expenditures	
<b>Salaries</b>		<b>Salaries</b>	
Salaries - research (16% of all salaries)	857,748	Salaries - research (60% of all salaries)	3,300,887
Salaries - outreach (4% of all salaries)	318,347	Salaries - outreach (<1% of all salaries)	11,335
Salaries - education (2% of all salaries)	90,354	Salaries - education (3% of all salaries)	178,733
Salaries - administration (2% of all salaries)	100,845	Salaries - administration (10% of all salaries)	568,802
Salaries - core services <sup>1</sup> (<1% of all salaries)	24,189	Salaries - core services (2% of all salaries)	102,837
<b>Supporting Services (includes cores)</b>		<b>Supporting Services (includes cores)</b>	
Supplies and equipment	561,514	Supplies and equipment	2,141,090
Miscellaneous support <sup>2</sup>	140,378	Miscellaneous support <sup>2</sup>	132,471
<b>Outreach and Education</b>		<b>Outreach and Education</b>	
Services, supplies and equipment	300,086	Services, supplies and equipment	52,994
<b>Other Expenses</b>		<b>Other Expenses</b>	
Bond principal & interest	353,481	Building operations & maintenance	390,923
OHSU central services	591,750	OHSU central services	197,250
<b>Total</b>	<b>\$3,338,692</b>	<b>Total</b>	<b>\$7,077,322</b>

## Programs Fiscal Year 2005/2006

	Amount paid by W/C	Amount paid by grants	Total Cost
<b>Outreach and Education</b>			
Information dissemination (e.g., TIC <sup>3</sup> , website, newsletters, brochures)	527,570	44,799	572,369
Education & training programs (professional & para-professional)	188,707	464,533	653,240
Chemical risk information service <sup>5</sup>	-7,490	0	-7,490
<b>Basic and Applied Research</b>			
Factors that affect workplace performance	267,053	961,504	1,228,557
Damage and repair of the nervous system and muscle	306,586	827,353	1,133,939
Occupational/environmental exposures and their consequences	384,094	1,451,995	1,836,089
DNA damage, genetic alterations & disease	440,661	1,134,499	1,575,160
Core services support <sup>1</sup>	93,380	256,611	349,991
Non-program-specific expenses <sup>4</sup>	1,138,131	1,936,028	3,074,159
<b>Total Expenses</b>	<b>\$3,338,692</b>	<b>\$7,077,322</b>	<b>\$10,416,014</b>

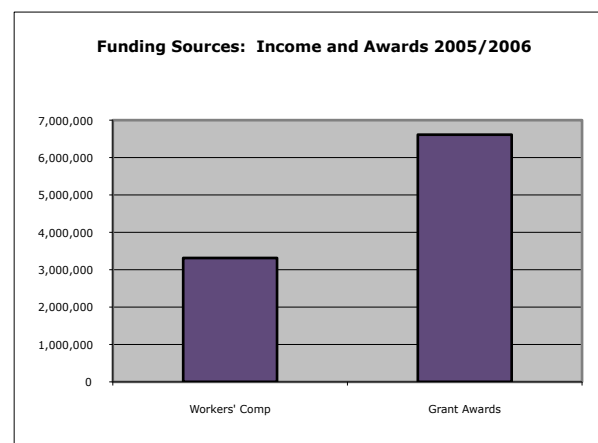
<sup>1</sup> core services - centralized graphics, statistics, imaging, tissue culture and and morphology (pathology)

<sup>2</sup> e.g., office supplies, equipment maintenance and repair, phone rental and line charges

<sup>3</sup> Toxicology Information Center

<sup>4</sup> includes supporting services, administrative salaries, bond principal and interest, OHSU administrative charges, building operation and maintenance

<sup>5</sup> Chemical risk information service is self-supporting and uses carry forward from prior years if needed.



## CROET Expenditures Fiscal Year 2006/2007

Workers' Compensation Expenditures		Federal and Other Grant Expenditures	
<b>Salaries</b>		<b>Salaries</b>	
Salaries - research (20% of all salaries)	1,043,193	Salaries - research (57% of all salaries)	3,023,506
Salaries - outreach (5% of all salaries)	344,783	Salaries - outreach (1% of all salaries)	926
Salaries - education (2% of all salaries)	109,311	Salaries - education (2% of all salaries)	126,864
Salaries - administration (7% of all salaries)	389,205	Salaries - administration (4% of all salaries)	210,727
Salaries - core services <sup>1</sup> (1% of all salaries)	73,781	Salaries - core services (1% of all salaries)	77,621
<b>Supporting Services (includes cores)</b>		<b>Supporting Services (includes cores)</b>	
Supplies and equipment	613,702	Supplies and equipment	1,300,890
Miscellaneous support <sup>2</sup>	153,426	Miscellaneous support <sup>2</sup>	40,658
<b>Outreach and Education</b>		<b>Outreach and Education</b>	
Services, supplies and equipment	305,780	Services, supplies and equipment	33,271
<b>Other Expenses</b>		<b>Other Expenses</b>	
Bond principal & interest	353,031	Building operations & maintenance	0
OHSU central services	150,000	OHSU central services	206,617
<b>Total</b>	<b>\$3,536,212</b>	<b>Total</b>	<b>\$5,021,080</b>

## Programs Fiscal Year 2006/2007

	Amount paid by W/C	Amount paid by grants	Total Cost
<b>Outreach and Education</b>			
Information dissemination (e.g., TIC <sup>3</sup> , website, newsletters, brochures)	585,926	34,198	620,124
Education & training programs (professional & para-professional)	183,766	349,780	533,546
Chemical risk information service <sup>5</sup>	-9,818	0	-9,818
<b>Basic and Applied Research</b>			
Factors that affect workplace performance	286,103	715,787	1,001,890
Damage and repair of the nervous system and muscle	289,367	797,717	1,087,084
Occupational/environmental exposures and their consequences	380,925	880,650	1,261,575
DNA damage, genetic alterations & disease	385,738	1,581,084	1,966,822
Core services support <sup>1</sup>	255,099	105,034	360,133
Non-program-specific expenses <sup>4</sup>	1,179,106	556,830	1,735,936
<b>Total Expenses</b>	<b>\$3,536,212</b>	<b>\$5,021,080</b>	<b>\$8,557,292</b>

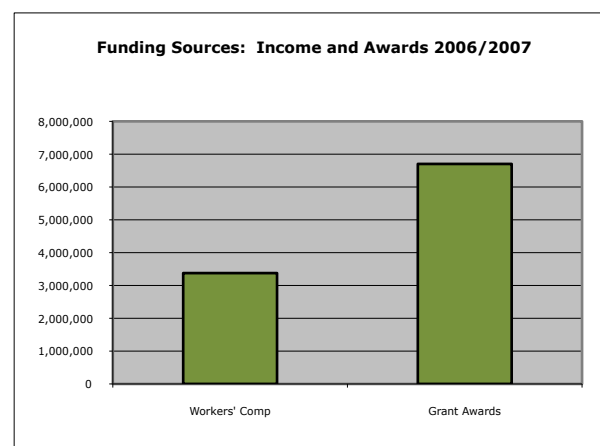
<sup>1</sup> core services - centralized graphics, statistics, imaging, tissue culture and and morphology (pathology)

<sup>2</sup> e.g., office supplies, equipment maintenance and repair, phone rental and line charges

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<sup>4</sup> includes supporting services, administrative salaries, bond principal and interest, OHSU administrative charges, building operation and maintenance

<sup>5</sup> Chemical risk information service is self-supporting and uses carry forward from prior years if needed.





# CROET

The Center for Research on Occupational and Environmental Toxicology (CROET) conducts research, trains health professionals, provides consultation, and offers the public information on hazardous chemicals and their health effects. CROET includes more than 100 scientists and research staff exploring a range of questions relating to prevention of injury and disease - and promotion of health - in the workforce of Oregon and beyond. CROET's Toxicology Information Center (TIC) is staffed to answer Oregonians' questions about chemical and other occupational exposures, and the Center's web site makes health and safety information continuously available through [croetweb.com](http://croetweb.com).

## How to Contact Us

### Mail Address

CROET  
Oregon Health & Science University  
3181 SW Sam Jackson Park Rd, L606  
Portland, OR 97239-3098

### World Wide Web Address

<http://www.ohsu.edu/croet/>

### Telephone

Main CROET number: (503) 494-4273  
Fax: (503) 494-4278  
Toxicology Information Center: 503-494-7366

### E-Mail

General Information:  
[croetweb@ohsu.edu](mailto:croetweb@ohsu.edu)  
Toxicology Information Center:  
[croettic@ohsu.edu](mailto:croettic@ohsu.edu)

For additional copies of this report, call CROET at the numbers listed above or visit [www.ohsu.edu/croet](http://www.ohsu.edu/croet) and click on "About."

## Directors and Scientific Staff, 2006-2007

### Director and Senior Scientist

Peter S. Spencer, PhD, FRCPath

### Associate Director and Senior Scientist

W. Kent Anger, PhD

### Assistant Director for Operations

Gregory Higgins, PhD

### Assistant Director for Business Affairs

Janice Stewart, BS

### Faculty

Charles Allen, PhD  
W. Kent Anger, PhD  
Gary Banker, PhD  
Anne Greenlee, PhD  
Gregory Higgins, PhD  
Glen Kisby, PhD  
Dennis Koop, PhD  
Doris Kretzschmar, PhD  
William Lambert, PhD  
Pamela Lein, PhD  
R. Stephen Lloyd, PhD  
Amanda McCullough, PhD  
Irina Minko, PhD  
Harvey W. Mohrenweiser, PhD  
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Bruce Patton, PhD  
D. Gary Rischitelli, MD, JD, MPH, FACOEM  
Diane Rohlman, PhD  
Jackilen Shannon, PhD  
Show-Ling Shyng, PhD  
Peter S. Spencer, PhD, FRCPath  
Philippe Thuillier, PhD  
Mitchell Turker, PhD  
DongRen Yang, PhD

### Investigators

Robert Irwin, MD, MPH  
Ilena Herrero-Hernandez, MD, PhD  
Stefanie Kaech Petrie, PhD  
Mohammad Sabri, PhD  
Daniel D. Tshala-Katumbay, MD, PhD

### Scientific Staff

Ludovic Alvado, PhD  
Daniel Austin, MS  
Frederick Berman, DVM, PhD  
Heather Fercho, MS

## FRONT COVER

### Top Photo

CROET at OHSU (*photo by Dan Austin*)

### Middle Photo

Electron micrograph of the head of a fruit fly Dr. Doris Kretzschmar uses the fruit fly to model a variety of degenerative diseases of the nervous system (*image taken in the CROET laboratory of Dr. Kretzschmar*).

### Bottom Photo

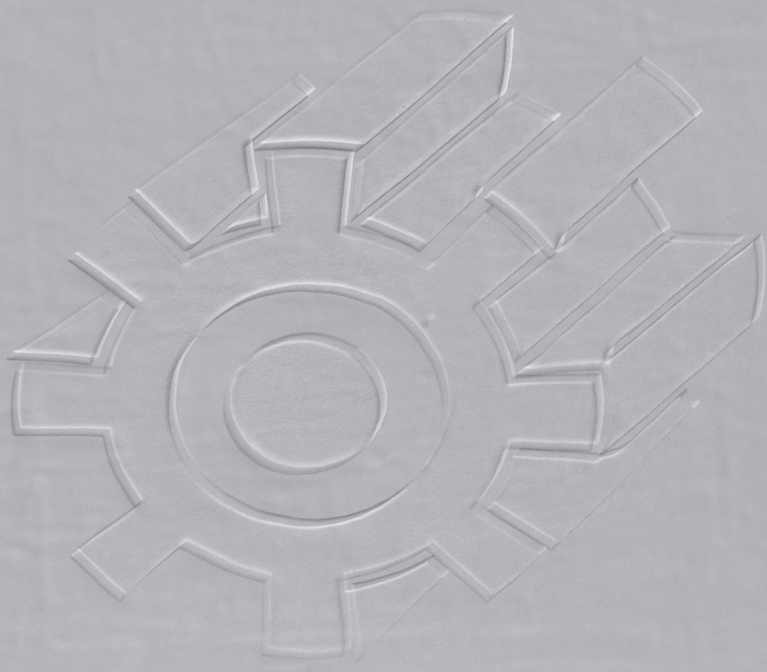
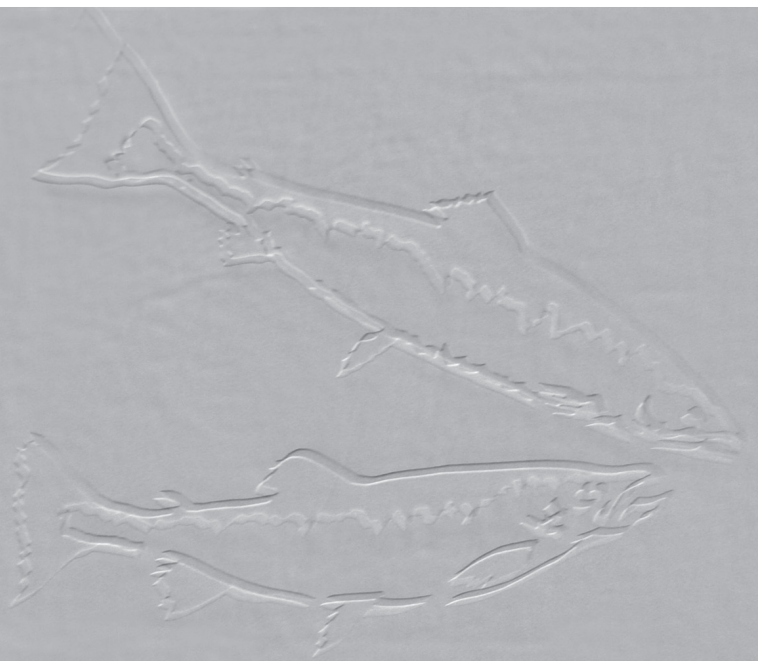
Dr. Ryan Olson is interested in factors that affect safety in the transportation industry. His work with the trucking industry is highlighted on page 9 (*photo of semi trucks by Ryan Olson*).

## BACK COVER

Panel from a marble, granite and glass artwork titled "Vita mensae, Living mind, Life of Thought" by Lawrence Paul Kirkland, located in the CROET Toxicology Information Center (*photo by Dan Austin*).

Karen Fujimoto, BS  
Terry Hammond, MPH  
Chun-Fang Huang, PhD  
Robert Kayton, PhD  
Leena Knight, PhD  
Olena Kolotushkina, PhD  
Mike Lasarev, MS  
Yu-Wen Lin, PhD  
Mykhaylo Moldavan, PhD  
Dede Montgomery, MS, CIH  
Valerie Palmer, BS  
Diane Rohlman, PhD  
Joan Rothlein, PhD  
Bernard Sampo, PhD  
Vladimir Vartanian, PhD  
Izabela Wojnarowicz, MS  
Feifei Yan, PhD  
Erika Zoller, BS





Oregon Health & Science University  
Center for Research on Occupational and Environmental Toxicology  
3181 SW Sam Jackson Park Road, L606  
Portland, Oregon 97239-3098

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