

# Center for Research on Occupational and Environmental Toxicology

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## CROET Hosts Mini-Symposium on Cancer

Cancer is the result of the accumulation of small genetic changes called DNA mutations that can occur in the cells of our bodies. Mutations alter the way our genes are read by the cellular machinery that uses DNA as a blueprint to make proteins. If these mutations affect genes involved in controlling cell division, uncontrolled cell growth will occur and a cancerous growth will result.

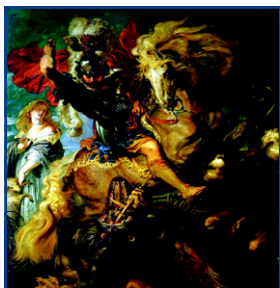
Mutations can be caused by exposure to environmental and occupational agents that bind to or damage our DNA, as well as by endogenous processes that occur normally within a cell. To increase understanding of the types of agents that damage DNA and how cells normally repair this damage, CROET hosted a mini-symposium on April 7, 1999 entitled "Carcinogenesis, Mutagenesis, and DNA Repair." Four speakers were featured and active discussion followed each of the presentations. The audience included interested scientists working at the Oregon Health Sciences University, the Oregon Graduate Institute, and Oregon State University.

The first speaker, Dr. Michael MacLeod from the University of Texas, discussed his research on benzopyrene, a well-known carcinogen found in cigarette smoke and in occupational materials such as coal tar. This chemical is known to bind DNA and cause mutations. However, Dr. MacLeod presented evidence to support his provocative hypothesis that benzopyrene can also cause cancer by blocking the ability of the cell to use DNA to make specific proteins. CROET

(continued on page 2)

### Mini-Symposium (cont. from page 1)

scientist Dr. Mitchell Turker then discussed his research directed at defining the types of DNA mutations that are caused by environmental agents and cellular processes. This talk included a recent observation by members of Dr. Turker's laboratory that oxidative damage can cause a specific type of mutation that is found commonly in many human cancers. Oxidative damage, which is familiar to many of us in the transformation of iron to rust, occurs frequently in cells as a by-product of creating energy and is believed to play a major role in aging. Dr. Turker suggested that his observation might help explain why cancer is more common in elderly individuals.



The next two speakers discussed their research on the ways cells repair DNA damage before it can become a mutation. Dr. Mark Meuth from the University of Sheffield Medical School in England talked about an important DNA-repair pathway called mismatch repair. This pathway is used by cells to make sure the DNA molecule has each of its four possible "letters" in the correct order. If even one letter is out of place, the cell makes an incorrect protein. The final speaker, Dr. Isabel Mellon from the University of Kentucky, discussed how abnormal changes in DNA repair pathways, including mismatch repair, can lead to a variety of human diseases, most commonly cancer.

The mini-symposium format functioned well to inform the scientific community about cutting-edge research in the fight against cancer that is taking place at national and international laboratories, and at CROET. A good time was had by all!

### WWW World Wide Web

- <http://www.aacr.org> (American Society for Cancer Prevention)
- <http://www.cancer.org/> (American Cancer Society)
- <http://www.nih.gov/sigs/dna-rep/whatis.html> (Review of DNA repair)
- <http://www.cancergenetics.org/dnafix.htm> (Genes involved with DNA repair)
- [http://www.eur.nl/fgg/ch1/gen\\_research/general.html](http://www.eur.nl/fgg/ch1/gen_research/general.html) (Molecular basis and biological impact of genome stability/instability)

## GRANTS

CROET faculty and staff have received several grants since our fiscal year began in July. The amounts listed are received over the duration of the grant, which is typically 1-5 years.

Faculty	Title	Direct Costs
Banker, GA	Multidisciplinary Training in Neuroscience	\$766,580
Turker, M.	Cancer, Aging and Mutation	\$1,196,870
Patton, B.	Medical Research Foundation of Oregon	\$25,000

## SYMPOSIUM

### Substance Abuse in the Workplace

February 11, 2000 Portland Conference Center, Portland, Oregon

Substance abuse is a serious problem that affects many Oregonians. This symposium will provide useful information for employees and employers on the following topics:

- Overview of Substance Abuse Problems - Gary Jacobsen, MD
- Overview of Addiction - Jerry Schnell, PhD
- Identifying Addiction in Co-workers - Anne Thureson, MSW, CSW
- Drug Testing Issues - Jana Wolfgang, MS, C-SAPA
- Impact on Performance - Bob Rosen, MD
- Resolving the Problem - Anne Thureson, MSW, CSW  
EAP/The Systems Approach  
Steps a Supervisor Can Take
- Panel Discussion - All speakers

Information, directions, registration forms, contact:

Joanne Brown at (503) 494-2514 or <http://www.croetweb.com>

Registration is \$75 (includes lunch).

Reduced registration for Oregon State government agencies, educational institutions, labor unions, and companies with fewer than 25 employees.

## COMMUNITY

### In Memoriam

CROET recently lost one of its own when Gregg Komma passed away on June 10, 1999. Gregg joined Dr. Glen Kisby's laboratory in 1998 as a Research Assistant. Although only with us at CROET for a short while, Gregg quickly established himself as a skilled researcher, mentor, and friend to the staff and students at CROET. He was also a dedicated family man, complete with stories and pictures of his fiancée, children, and grandchildren that he proudly shared whenever the opportunity presented itself. We all remember Gregg's friendly manner and willingness to help out no matter what the task. For some of us, it was only at his memorial service that we learned of his long struggle with chronic pain and illness. In retrospect, we marvel at his positive attitude and strength of character that were always evident to those of us who had the privilege to work alongside him. Although he will be sorely missed, all of us at CROET will remember Gregg's contributions to the center. Let us also strive to keep Gregg's memory alive at CROET by following his example as a scientist, mentor, and friend.

## UNLOCKING SECRETS OF THE BODY'S INNER CLOCK

## RESEARCHERS DISCOVER KEY CONTROL MECHANISM FOR AN AREA OF THE BRAIN THAT REGULATES SLEEP

Much of what determines whether you sleep well or badly happens in a tiny area of the brain consisting of just a few thousand nerve cells, or neurons. Now, researchers in CROET, working together with other scientists at OHSU and in San Antonio, Texas, have discovered that a chemical produced within the brain can slow the activity of those cells almost to a stop, thereby affecting the body's reaction to light and darkness. The research, published in the March 15 issue of *The Journal of Neuroscience*, opens an entirely new avenue of investigation directed toward an understanding of the molecular basis of sleep disorders and problems related to natural light cycles, such as shift work and jet lag.

The research focuses on an area deep in the brain called the suprachiasmatic nucleus (SCN), which is about the size of a pinhead. The SCN is known to regulate the circadian rhythm — the normal 24-hour cycle of sleep and wakefulness. When neurons in the SCN are damaged or their activity is altered, the sleep cycle is disrupted. For example, a normal consequence of aging is a deterioration of sleep quality and difficulty in tolerating shift work; this reflects alterations in the circadian pacemaker or in the response of the pacemaker to environmental stimuli.

Dr. Charles Allen and his colleagues recently identified a novel peptide neurotransmitter that modulates the light input and modifies the SCN's pacemaker cell activity. Together with CROET Scientist Dr. Richard Allen and Dr. David Grandy, an Associate Professor in the Department of Physiology and Pharmacology, Dr. Charles Allen has investigated the role of the heptadecapeptide orphanin FQ in the modulation of circadian rhythms. Orphanin (also known as nociceptin), is a peptide, or combination of amino acids — the basic building blocks of proteins. Orphanin is active in the brain, where it plays a role in feeding and drinking behavior, nursing and reproductive behavior, and in the regulation of body temperature and reward, among other things. Orphanin acts as a neurotransmitter, a kind of messenger that tells cells how to act. While its role elsewhere in the brain is still being studied,

the CROET research shows clearly that orphanin acts on all the cells in the SCN.

Collaborating with the OHSU research teams, Dr. Michael Rea of the Biological Rhythms and Integrative Neurosciences Research Institute tested the effects of orphanin on the SCN of hamsters. First, normal hamsters were exposed to light before their normal waking time. The circadian clock

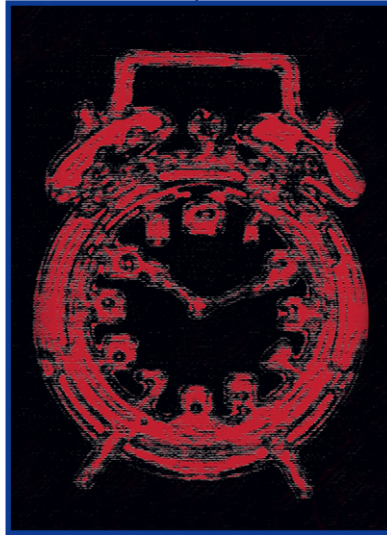
adjusted to the light; in other words, the hamsters woke up earlier. Then, orphanin was injected into some of the animals.

Even when consistently exposed to light before they would normally wake up, their circadian clock did not shift, suggesting orphanin was blocking the process that normally converts light into a brain signal telling the animal to wake up.

Light is the most important signal that regulates the biological clock. There's a direct connection between our eyes and the clock. In fact, the orphanin system is found in the retina as well as the SCN. While the exact mechanism that keeps the clock adjusted to natural light cycles is not

known, the latest research findings suggest that the light signal excites the neurons in the SCN, while orphanin inhibits them.

Understanding that the orphanin-SCN system exists is the first step. The next step is to determine the physiological mechanism by which orphanin modulates the circadian cycle. The ultimate hope is that these discoveries will lead to better treatments for sleep disorders. The OHSU research was funded by the National Institutes of Health and by the "Research for the Future" program of the Japan Society for the Promotion of Science.


**WWW** World Wide Web

<http://www.ohsu.edu/croet/occtrans.html> (from the CROET Transportation Page)

<http://www.ohsu.edu/croet/allenc/allenc.html> (CROET)

<http://www.chronotherapy.com/> (Searle)

<http://www.circadian.org/> (Circadian Rhythm Laboratory)

<http://www.cbt.virginia.edu/tutorial/GLOSSARY.html> (Circadian rhythm glossary)

<http://www.stanford.edu/~dement/circadian.html> (Circadian rhythm disorders-Stanford)

# C A L E N D A R

Send calendar notices to [altschud@ohsu.edu](mailto:altschud@ohsu.edu) or  
FAX to (503) 494-4278

## Partnerships for Health in the New Millennium January 24-28, 2000 Washington, DC

Contact: Partnerships for Health in the New Millennium c/o Social & Health Services Ltd, 11426 Rockville Pike, Suite 100 Rockville, MD 20852, Fax: (301) 984-4256, E-mail: [partnerships@health.org](mailto:partnerships@health.org) Website: <http://www.health.gov/partnerships>

## 10th Annual Construction Safety Conference and Exposition February 15-17, 2000 Rosemont, IL

Rosemont Convention Center, Rosemont, IL (800) 552-7744.  
Website: <http://www.buildsafe.org>

## Managing the Terroristic Threat February 21-February 23, 2000 Houston, TX

Dealing with a terrorist incident. Website:  
<http://www.fightterror.com> Email: [indfire@myriad.net](mailto:indfire@myriad.net)

WWW

### World Wide Web

[http://www.fireworld.com/conference\\_info.html](http://www.fireworld.com/conference_info.html)

## The 15th Annual Industrial Fire World Conference and Exposition (2000 IFW) April 10-April 13, 2000 Houston, TX

Adam's Mark Hotel, Houston, TX. A training conference for the industrial fire, safety, and emergency response professional.

## American Industrial Hygiene Conference and Exposition (AIHCE) May 19-May 26, 2000 Orlando, FL

Over 10,000 occupational health and safety experts from all over the globe discuss and debate the latest issues in technical sessions, roundtables, and forums. Website:  
<http://www.aiha.org/conf.html>

## American Society of Safety Engineers Conference and Exposition June 25-June 28, 2000 Orlando, FL

To provide attendees the opportunity to address key issues facing EHS professionals, improve professional skills and knowledge, prepare for new EH&S challenges, share experiences.

## International Ergonomics Association and Human Factors and Ergonomics Society July 30-Aug 4, 2000 at the San Diego Marriott

WWW

### World Wide Web

<http://www.asse.org/annual.htm>

# O U T R E A C H

CROET provided exhibits at the following conferences this fall.

## Snake River Occupational Safety & Health Conference Ontario, OR September 28-30, 1999

## 9th Annual Southern Oregon Occupational Safety & Health Conference Medford, OR October 13-15, 1999

## 9th Annual Oregon Pulp & Paper Workers, Safety & Health Conference Eugene, OR November 30, December 1-3, 1999

# C R O E T W E B U P D A T E

Watch our site! The CROET website grows every week.

### New on the Site

Connect from our home page at "[www.ohsu.edu/croet](http://www.ohsu.edu/croet)"

- New CROET chemical survey analysis web pages. New format, and it now includes all Oregon counties (click "surveillance" under "outreach").
- Join our mailing list and/or request CROET information. Fill out the "mailing list" form under "outreach" to be added to our mailing list.
- Access to MSDS sheets as well as chemical safety links (click "MSDS Sheets" under "outreach"). We now have an extensive list of free MSDS sites.
- New Health and Safety pages for your industry:
  - Transportation
  - Restaurant/kitchen health and safety page
  - Pulp and paper (updated)

### Dr. Mitch Altschuler joined CROET earlier this year.

He will help evolve the website into new areas.

### We have a SECOND address!

We have added an easier-to-remember website address:

"<http://www.croetweb.com>"

We also still reside at our familiar OHSU address:

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

So you don't have to change your link to us. We have simply added an easy-to-remember address which will automatically send you to our website at OHSU.

# Center for Research on Occupational and Environmental Toxicology

CROET, the Center for Research on Occupational and Environmental Toxicology at the Oregon Health Sciences University, conducts research, provides consultations, and offers information on hazardous chemicals and their health effects. CROET includes more than 80 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 chemical and other occupational exposures.

## How to Contact Us

### MAIL ADDRESS

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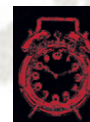
### VISITING SCIENTISTS

Masayuki Ikeda, PhD  
Koji Teshima, PhD  
Ting Huawang, PhD  
Zhen BoHan, MD

Cover: St. George is fighting the dragon, which represents any dreaded enemy, in this case cancer. The painting is by Peter Paul Rubens, from 1606-7. It is owned by the Museo del Prado, Madrid. Image provided by Carol Jackson Fine Art web gallery.



The clock symbolizes the body's circadian rhythms.



Stylized rendition  
of the New  
Carissa sinking.



## NEW CARISSA

On February 4, 1999, the New Carissa, an empty wood chip ship, became grounded off the coast of Coos Bay, Oregon. The bow section has been towed out to sea and sunk (on the second attempt), but the stern is still beached near Coos Bay. To date, approximately 70,000 gallons of diesel and heavy fuel oil have been released.

### Health and Safety Issues

While many Oregonians first thought was the danger to the environment, human health was also jeopardized. The initial spill response and beach clean-up exposed crews to all the dangers faced by the environment, in concentrated form when they entered the lurching ship. Because the temperatures were low, the oil was extremely viscous and the diesel volatilized quickly, there was minimal concern for inhalation. However, protection was needed to prevent dermal contact with heavy oil and diesel. Long term safety and health issues surrounded the crews working on the beaches in cold, wet, windy weather. Efforts were made to keep workers off the beach near high tide. Numerous physical hazards were encountered while working on the beached ship (movement, physical hazards). Stress associated with the length of the events and the unpredictable turns of events.

### Burning the Oil

After initial attempts to refloat the ship failed, the decision was made to burn onboard fuel. This created a very different kind of hazard to crews placing explosives (Department of Defense demolition experts) and working in confined spaces. Potential hazards were presented to the surrounding communities if plumes of smoke blew inland. The burn effort was closely coordinated with the Coos County Health Department to minimize this concern.

Weather conditions were good for the burn. Smoke didn't significantly impact the local communities. The bow section, which still contained an estimated 135,000 gallons of oil, was successfully towed out to sea and sunk by a Navy torpedo. Concerns were also raised about potential hazards to sport and commercial fishermen, and those consuming local shellfish.

### Effects on Wildlife

On February 11th, the Oregon Department of Agriculture closed shellfish harvesting in Coos and Douglas counties until potential human health effects could be assessed. Shellfish were tested for polycyclic aromatic hydrocarbons (PAHs), which are carcinogenic. "Safe" and "unsafe" levels of PAHs were derived. Composite samples were collected from February 10 - March 6. The initial oyster samples showed elevated PAH levels, which declined with time. This is consistent with the scientific literature about oil contamination and oyster beds. No sample exceeded reopening criteria. The highest PAH-containing samples were found to be contaminated with pyrogenic components NOT related to the New Carissa (e.g., creosote). Samples of clams and mussels fortunately revealed very low levels. Commercial and recreational shellfish harvesting reopened on March 4th.

The New Carissa beaching could have had far more extensive impacts to our environment, and it could have posed much greater safety and health hazards for the dedicated workers who controlled the spill and towed the hull to open ocean. We were lucky, at least luckier than we might have been. Reducing the likelihood of another such beaching not only protects our environment, but also Oregonians in the workplace and at home.



### WWW World Wide Web

<http://www.newportnet.com/carissa/> (New Carissa Joint Information Center)

<http://www.eastside.coos-bay.k12.or.us/Carissa/> (News from a local high school)

<http://www.oregonlive.com/special/newcarissa.html> (News on this ship)

<http://www.abcnews.go.com/sections/science/DailyNews/carissa990312.html> (News)

