



A DMS study found that people who drank two or more cups of green or black tea daily were 30% less likely to have squamous cell skin cancers than were non-teadrinkers.

Persistence pays off for geneticist Conradt

What are we going to find out today?" is the question that energizes Barbara Conradt, Ph.D. A geneticist at DMS, she studies programmed cell death in a roundworm called *Caenorhabditis elegans*. Her lab's latest finding—how asymmetric cell division happens in *C. elegans*—required long, patient observation of mutant worms with minor genetic variations. The finding, which was published in the journal *PLoS (Public Library of Science) Biology*, has long-range implications for identifying ways to kill off cancer cells that defy their predestined death.

Path: The path to virtually every scientific discovery is fraught with frustration. Researchers usually face down failure several times before they achieve success. During her training, Conradt worked on reconstitution of the fusion of vacuoles in yeast. She experienced more than 200 failed attempts before she finally came up with a protocol that worked—a breakthrough that helped establish the current understanding of the molecular mechanism of vacuole fusion. To this day, she recalls not the frustration

of failure after failure but her enthusiasm to get back into the lab every day to try, try again. One "can always learn something from negative data," she notes.

Conradt says if she has learned anything during her career, it is that "little things make big differences." Her meticulous attention to detail allows her to observe things that often escape others. She may not at first be able to explain exactly why one day, after many unsuccessful tries, an experiment works, but she can point to every minute condition she has modified at each step of the way. Such details can easily be overlooked as insignificant. "Good science just takes time," she says. "One has to be patient and open-minded to follow the biology rather than the model in one's mind."

Conradt's passion for science isn't unusual, but her commitment to actually working at the lab bench is. Many principal investigators gradually move away from the bench during the course of their careers and spend more and more time on the administrative work of running their lab. Conradt, however, continues to do experiments. "I just love it," she says. "That is the part that's the most fun." It keeps her up to date on the latest technologies and is also "the best way to see how [others in her lab] are doing and to communicate with [them]."

But she still has to run the lab. When asked how she juggles both science and administration, Conradt chuckles. "Be really organized," she says. "I write a little list, which everyone in the lab makes fun of me about."

Undeterred: But "fun" appears to be the operative word. Conradt expects to be undeterred by whatever failure lies around the next corner, choosing instead to be energized by the success that lies beyond it. TINA TING-LAN CHANG

"One has to be patient and open-minded to follow the biology."

For love of country

Primary-care physicians who live in rural areas are likely to make less than their urban counterparts. So stated two DMS researchers in the *Journal of Rural Health*. They studied data gathered by the American Medical Association and concluded that primary-care doctors in the country work longer hours, see more patients, and rely more heavily on Medicaid reimbursements than do doctors in cities. The authors recommended "increasing incomes, reducing work hours, or some combination of the two" to encourage doctors to leave the pavement for the pasture.



Duck, dog, ditch, dig . . .

Given one minute, how many words could you list that start with the letter "D"? That word game is a test of verbal fluency—the ability to name words in a limited category. Members of the DMS Department of Psychiatry used such tests to examine a possible link between verbal fluency and mild cognitive impairment (MCI), a condition that often progresses to Alzheimer's disease. They reported in *Archives of Clinical Neuropsychology* that there was "an overall decline in verbal fluency performance" among patients with MCI. Their work could help doctors spot the condition earlier, making treatment more effective.



JON GILBERT FOX



Conradt studies cell division in *C. elegans* worms.

For a **WEB EXTRA** with a short video from Yeh's lab that depicts brain cells migrating, see dartmouth.edu/summer08/html/disc_scratch_we.php.



Only 9% of U.S. physicians practice in rural communities, according to the AMA, but 20% of the population lives in rural areas and rural patients tend to be older and sicker.

A scratch on the surface of a big story

Researching fetal alcohol syndrome often involves getting rats drunk. Hermes Yeh, Ph.D., uses mice instead, because mouse genes can be more easily manipulated to test various hypotheses.

Mice, it turns out, are also more sensitive to alcohol. When Yeh and Virginia Cuzon, a doctoral student in Yeh's lab, studied the effects of excessive alcohol consumption on fetal development, they found that mice could tolerate only very low blood-alcohol levels and still have a successful pregnancy.

Low: "There's some serendipity involved in this project," says Yeh. By decreasing the alcohol—so much that they didn't know if they'd see any effect at all—they made a surprising discovery: that chronic exposure to even low levels of alcohol can alter fetal brain development.

A fetus's developing brain is essentially a sea of migrating cells. The cells move to specific locations where they specialize and mature, forming various structures of the brain. Anything that disrupts those migrations can therefore have lasting effects. Alcohol (ethanol) seems to increase the number of certain brain cells—called

GABAergic interneurons—in the embryonic brain, Cuzon and Yeh reported in the February 2008 *Journal of Neuroscience*.

In a mature brain, GABA (gamma-aminobutyric acid) "inhibits things," Cuzon explains. "It kind of keeps the balance of excitatory stuff down to a more manageable level." But when the brain is developing, "GABA's really not playing that role," Cuzon says. "It's doing a whole bunch of different things. It can stop cells from proliferating and [make them] more mature. It can start them migrating." It can also modulate where and how fast they migrate.

"Ethanol is one of the very well-established modulators of the GABAergic system," says Yeh. It causes more GABA to circulate, which, in turn, has a numbing effect. "That's what happens in the adult brain, when everything is all formed and there are a lot of synaptic connections," he continues. "But during development, there are no synaptic connections because things are very immature. The cells are still moving around. . . . Yet we think that alcohol can still work through the GABAergic system to affect GABA receptors or the level of GABA" in the early stages of brain development.

Prolonged: Understanding how ethanol causes these changes is the next step for Yeh and Cuzon. For now, the "take-home message," says Yeh, "is that even a relatively low blood-alcohol level for a prolonged period of time is detrimental to fetal development."

It's difficult to say how applicable the findings in mice are to humans. But pregnant women who regularly consume alcohol, even at a low level, are taking a risk, Yeh believes. It will take a while to determine the size of that risk. "All we've done, really," he says, "is scratch the surface of a big, big story." JENNIFER DURGIN

Even low levels of alcohol can alter fetal brain development.

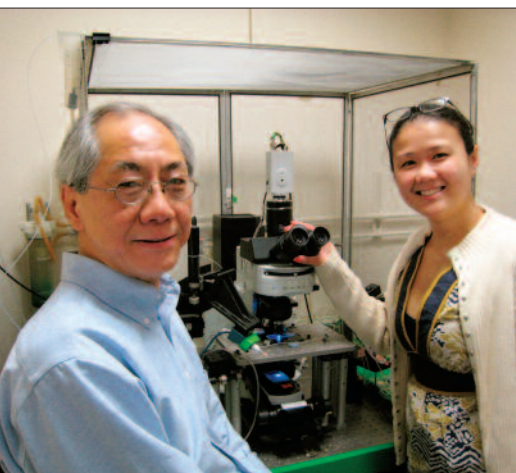
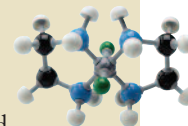
Paging Dr. C-3PO

Robotic-assisted prostate surgery can result in less blood loss and a shorter hospital stay than surgeries performed by sentient beings alone, yet only 7% of hospitals own the necessary equipment. According to DMS researchers, that might be for the best. After examining the costs associated with purchasing a robot—about \$1.5 million—and the time it takes to train a surgeon, they concluded that it simply doesn't make sense for many hospitals to own one. They wrote in *Urology* that although there are advantages to robotic-assisted procedures, "expenditures on a robot are taken from other portions of the health-care system."



Carpe medicamentum

There is no one-size-fits-all drug treatment for epilepsy; some patients suffer serious side effects, while others do not respond at all. But researchers from the Neuroscience Center at Dartmouth reported recently that they had success using uridine—a molecule involved in cell metabolism—to reduce the number and severity of seizures in rats. Just as important was the fact that they did not see any side effects. "These properties," they concluded in the journal *Epilepsy and Behavior*, "make uridine a potentially promising agent for the treatment or prevention of epilepsy."



Yeh, left, and Cuzon looked at fetal brain formation.



The Office of Naval Research awarded DMS's Dr. Joseph Rosen and a colleague \$600,000 to develop a computer to model surgeons' behavior in the OR, with the goal of preventing mishaps.

DMS expert leads the way in dosimetry

In the event of a nuclear accident, terrorist attack, or nuclear war, thousands or even millions of people could potentially be exposed to dangerous levels of radiation. Measuring radiation exposure in an accurate and timely manner would be critical to managing such a crisis. But that's easier said than done.

It's possible to measure radiation exposure using electron paramagnetic resonance (EPR) in a process that's known as dosimetry. However, current EPR instruments are large and not very mobile. Yet without the ability to easily measure radiation, emergency personnel have no way to determine who's received a low dose and doesn't need treatment and who's received a high dose and needs care—until symptoms show up, by which time it may be too late.

For some time, experts have dreamed of having an EPR instrument small enough to carry into the field to triage victims should a nuclear accident or attack take place. Dartmouth researcher Harold Swartz, M.D., Ph.D., an internationally known expert in EPR, is now well on the way to doing just that—developing a portable bio-dosimeter.

Radiation: Swartz described EPR-based bio-dosimetry in a 2007 article for the journal *Radiation Measurements*. He explained that EPR detects the presence of unpaired electrons, and “ionizing radiation generates large numbers of unpaired electron species. While most of these react immediately and disappear, in some materials . . . the unpaired electrons can persist for long periods.” The enamel of teeth is one such material. In 1968, Swartz published a paper showing that EPR could determine radiation exposure by taking measurements of teeth. This was a discovery that, he admits with chagrin, has led some in the field to call him the “Fa-

ther of Dosimetry.” Recently, he has shown that fingernails and toenails also have the same property.

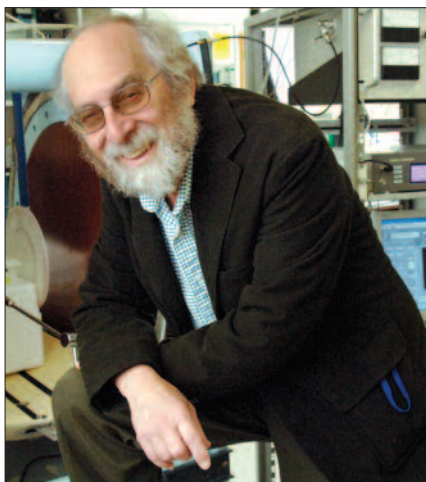
Exposure: The development of a portable dosimeter is understandably of great interest to the Department of Defense (DoD). The DoD's research arm—the Defense Advanced Research Projects Agency, or DARPA—supports research “where risk and payoff are both very high.”

One system uses teeth to measure exposure, the other fingernails.

DARPA has funded four contracts to develop dosimetry systems—two of them with Swartz. One is based on using teeth to measure exposure, the other on using fingernails and toenails.

These contracts are very demanding, according to Swartz. Typical research projects are funded over several years, but the timeline for these is only eight months, plus a month for testing. “It's an impossibly short amount of time,” says Swartz.

But with 40 years of experience in the field, he's as likely to succeed as anyone. With the pressure on, Swartz's group has been making great strides on the project. By October, when the contracts are up, portable bio-dosimeters may be not just a dream but a reality. KRISTEN GARNER



Swartz has been called the “Father of Dosimetry.”

Back and forth

Magnetic resonance imaging (MRI) is an important tool for discovering the cause of lower back pain. “Unfortunately,” DMS researchers wrote in *Spine*, “the relationship between findings on MRI and clinical course remains controversial.” To test the consistency of MRI readings, they asked three radiologists and one surgeon to examine images of 50 patients suffering from a disc herniation. The doctors agreed closely on the severity of the herniations, but they showed greater variability when it came to measuring the length of disc fragmentations, confirming the fact that reading an MRI can be open to some interpretation.



Time-out for tumors

Lung cancer kills more Americans than any other type of cancer, making better treatment options imperative. According to findings from the lab of DMS's Michael Sporn, Ph.D., erlotinib—a drug often used to treat lung cancer—is less effective than two alternatives. Sporn tested erlotinib against two other types of drugs, a rexinoid and a triterpenoid, and reported in *Molecular Cancer Therapeutics* that the latter two “are highly effective for preventing lung carcinogenesis as measured by significant reductions in the number, size, and severity of lung tumors”—more effective than erlotinib. ■

