

University of Kentucky Research

Summer 2008

Odyssey

ταυ. αἰ. εἰς τὴν αὐτὴν καὶ τὸ τοιο
μὲν πόλιν οὐκ εἶναι τὴν Ἰακχίαν· ἀλλ' ἔστι
τὴν μὲν οἱ λεγόμενοι ἀδελφοὶ τοῦ Ὀδυσσεύος
αὐτοῦ δὲ εἰς τὴν Ἰακχίαν· οὗτοι τὸν Ἰακχίαν
ἐκ τῆς πόλεως τοῦ πατρὸς πλῆθον· ἀπομῆναι
ἐκ τῆς πόλεως· ἐκ τῆς πόλεως οὐκ εἶναι τὴν
δοῦ ἀναρρεῖται κατὰ τοὺς ἀνθρώπους· ἐκ τῆς πόλεως
αἰμαρτίαν· τότε τοῦ πατρὸς σώματι καὶ τὸν τῆς πόλεως καὶ
τὴν πῆνυθρον πρὸς τὴν μητέρα μεθίστηται· ἡ δὲ αὐτοῦ
ἀθανάτοιοι ποιεῖ καὶ σωοίσει· τὴν μὲν πῆνυθρον τῆς
πόλεως· κίρκελιν δὲ τῆς πόλεως·



Resurrecting the Iliad

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Armed with a robot-mounted laser scanner, two UK researchers from the Center for Visualization and Virtual Environments travel to Venice, Italy, to realize their goal of offering Homer's Iliad to the world with the click of a mouse.

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blood test licensed



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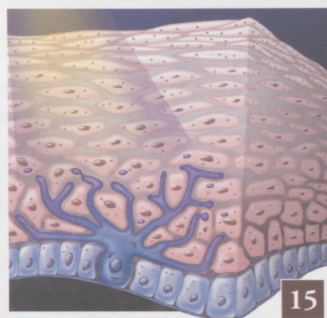
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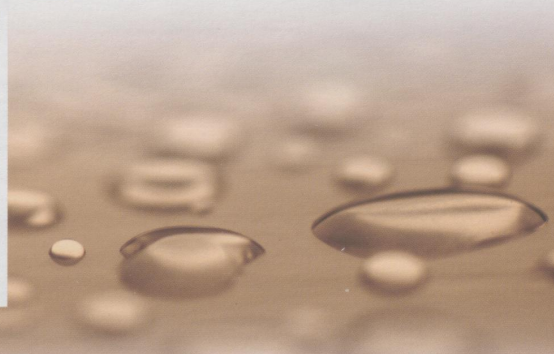
Timothy McVeigh showed the world that ammonium nitrate (AN) can be a deadly weapon. Preventing another Oklahoma City-like blast is what UK scientist Darrell Taulbee aims to do in a project to create a fertilizer that won't have nearly the blast impact of AN.



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Triggered by a snapshot she took 14 years earlier of a memorial statue that belonged to a Kenyan tribesman, Monica Udvardy turns detective to return African art to its rightful owners.



Tracy Is UK's New Research VP

Jim Tracy, UK's new vice president for research, knows exactly when he got bit by the science bug. His grandfather, a mapmaker and self-taught geologist, is responsible, Tracy says.

"We'd be driving along the highway, come to a cut through the hills, and he'd stop on the side of the road. We would walk up to the layers of rock, and he'd tell me about the different layers and why they had formed the way they did. Some of my earliest recollections are of him handing me a flower or showing me a bee or scooping up a handful of dirt to show me slime mold. I can almost guarantee you that I was the only first grader in Ohio who could scientifically explain slime mold," says Tracy with a smile.

Tracy says he was *almost* a Kentuckian by birth. He was born and raised in the small community of Portsmouth—"as far south as you can go in Ohio." His father was a professor of English, and Tracy grew up surrounded by books. There was never any doubt, he says, that he would get a college education.

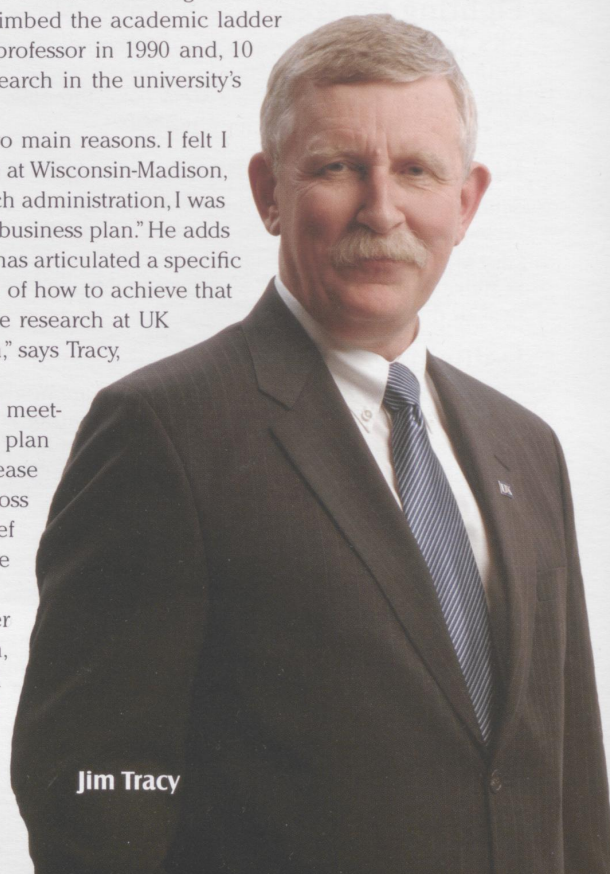
His vita: a B.S. in chemistry and physics from Bowling Green State University (1972) and a Ph.D. in biochemistry from Purdue (1976). He did a seven-year stint as a research assistant professor in geographical medicine—studying drugs to treat tropical diseases—at Case Western Reserve University before taking a position at the University of Wisconsin-Madison, where he became one of the founding members of the School of Veterinary Medicine. Tracy climbed the academic ladder at Wisconsin-Madison and became a full professor in 1990 and, 10 years later, became associate dean for research in the university's School of Veterinary Medicine.

"I was interested in coming to UK for two main reasons. I felt I had accomplished everything I'd wanted to at Wisconsin-Madison, and in looking for a new position in research administration, I was extremely impressed with Dr. Todd's Top 20 business plan." He adds that UK is the only school he knows of that has articulated a specific goal like this and drawn up a detailed plan of how to achieve that goal. "All efforts toward these goals advance research at UK and benefit citizens of the commonwealth," says Tracy, who has been at UK since last October.

One of his priorities is to work toward meeting the goals of the university's strategic plan for 2006 to 2009, including efforts to increase interdisciplinary research collaborations across campus, he says. "My primary role as chief research officer is to create a climate where discovery and learning can flourish."

"With wide-ranging experience at a top-tier public university, Dr. Tracy brings the vision, experience and energy needed to steer UK toward its Top 20 research goals," says UK Provost Kumble Subbaswamy.

—JW



Jim Tracy

Fasting Can Reduce Brain-Injury Impact

Researchers at the University of Kentucky have found that fasting within the first 24 hours of a moderate traumatic brain injury reduces the damage to brain tissue and improves cognitive function.

Using rats as their model system, a research team led by Patrick Sullivan of the UK Spinal Cord and Brain Injury Research Center found that fasting after such an injury increases the amount of brain tissue that is preserved. This dietary therapy also preserved the rats' ability to use and develop spatial memory, indicating that the tissue spared is functional.



Laurie Davis

"In this study we were primarily interested in the preservation of mitochondrial function since mitochondria are the powerhouse of the cell and responsible for the production of most of the energy used by the cell," explains Laurie Davis, a graduate student and lead author on the article reporting these findings, which appeared in the *Journal of Neuroscience Research*.

The UK team also investigated ketone bodies, which are produced by the liver from fat in response to a prolonged decrease in glucose levels. Giving the animals ketones increased preservation of brain tissue compared with a control group of untreated animals.

"In previous studies, we showed that ketones preserve mitochondrial function after neuronal injury," Davis says. "This finding could indicate that ketosis, the production of ketones, is the underlying mechanism responsible for the beneficial effects of fasting after brain injury, and could represent a potential therapeutic intervention for the treatment of traumatic brain injury."

—Dan Adkins, UK Public Relations

Saliva Can Help Diagnose Heart Attack

Early diagnosis of a heart attack may now be possible using only a few drops of saliva and a new nano-bio-chip, according to findings from a team of scientists at the UK colleges of dentistry and medicine, University of Louisville, University of Texas Health Science Center at San Antonio, and University of Texas at Austin.

Since 2006, UK researchers have tested saliva from 56 people who had a heart attack and 59 healthy subjects for 32 proteins associated with atherosclerosis, thrombosis and acute coronary syndrome. The findings from the ongoing study show that not only are biochemicals associated with these conditions in higher concentrations in saliva of heart attack victims, but specific salivary biochemicals are as accurate in the diagnosis of heart attack as current blood serum tests, conducted when a patient having a heart attack is admitted to the hospital.

This new device takes advantage of the recent identification of a number of blood serum proteins that are significant contributors to—and indicators of—cardiac disease.

"These are truly exciting findings, since use of these tests could lead to more rapid diagnosis and faster entry of patients into treatment scenarios that can save lives," says Craig Miller, a scientist with the UK Center for Oral Health Research. His colleague Jeffrey Ebersole says, "We are rapidly meeting our goal of

identifying compounds in saliva that are diagnostic of heart attack."

The nano-bio-chip test could someday be used to analyze a patient's saliva on board an ambulance, at the dentist's office or at a neighborhood drugstore, helping save lives and prevent damage from cardiac disease. The device is the size of a credit card and can produce results in as little as 15 minutes.

"Many heart attack victims, especially women, experience nonspecific symptoms and secure medical help too late, after permanent damage to the cardiac tissue has occurred," says John McDevitt, a UT-Austin professor of chemistry and biochemistry, and designer of the nano-bio-chip. "Our tests promise to dramatically improve the accuracy and speed of cardiac diagnosis."

Cardiovascular disease is the leading cause of death in developed countries, including the United States. In 2008, an estimated 770,000 Americans will have a new coronary attack, and about 430,000 will have a recurrent attack.

—Ann Blackford, UK Public Relations



Glen Simmons, University of Texas

Microneedles Enhance Drug Delivery

In a first-of-its-kind study involving human subjects, researchers at the University of Kentucky College of Pharmacy and the Georgia Institute of Technology have demonstrated that patches coated on one side with microscopic needles can facilitate transdermal delivery of a drug that normally cannot pass through the skin.

By painlessly punching a series of microscopic holes in the outer layer of skin, microneedles promise to expand the range of drugs and vaccines that can be delivered transdermally. And microneedles offer other advantages over oral or injected drugs, including an ability to produce therapeutic drug levels with lower doses.

Transdermal drug delivery has proven successful in a number of applications, including pain management and hormone replacement, but has been limited to a narrow range of compounds that easily pass through the skin.

Daniel Wermeling, associate professor in the UK pharmacy practice and science department who led this work, says, "This proof-of-concept study shows that microneedles work in humans for transdermal drug delivery." He emphasizes that microneedles present a new opportunity to deliver current and future biotech drugs, which are almost exclusively proteins, peptides, vaccines, and antibodies. Because these types of drugs are large molecules and/or water soluble, they can't pass through the skin and must be delivered with a hypodermic needle.

The research team included microneedle inventor Mark Prausnitz (Georgia Institute of Technology), Wermeling and UK colleagues David Hudson (psychiatry department fellow), Audra Stinchcomb (pharmaceutical sciences associate professor), and Stan Banks (a pharmacy graduate student).

Working with a small group of healthy volunteers, the UK researchers first prepared a section of skin on each subject's arm by pressing and removing thumb-sized patches that contained 50 stainless steel microneedles, each about 1/40th of an inch in length. Next, gel containing naltrexone, a skin-impermeable compound used to treat opiate and alcohol addiction, was applied to the prepared area and covered by an adhesive patch and protective dressing.

The concentration of the drug in each subject's bloodstream was monitored for 72 hours. The researchers quickly saw levels of the drug reach pharmacologically active concentrations, and those levels remained steady for at least 48 hours in the six test subjects.

Control subjects were treated in the same way, but without the microneedle preparation prior to application of the naltrexone gel. None of the control subjects had detectable levels of the drug in their bloodstream.

Microneedle administration also reduced the amount of drug required to reach therapeutic levels, replacing a 50 milligram tablet with 10 to 12 milligrams of drug in the gel. Use of the microneedles also produced steady bloodstream levels of the drug, without the initial peak that occurs with oral delivery.

"There are a number of ways microneedles can be used," says Prausnitz, who has been developing the devices for more than 10 years. "This study addressed the simplest use of microneedles—the needles are inserted and removed from the skin, and a drug patch applied. To understand how broadly microneedles can be used in medicine, we will also need to study delivery of other therapeutics, such as lidocaine, insulin and flu vaccine."

—Ann Blackford, UK Public Relations





Sparking an Early Interest in Reading

A class of 4th graders in Kent Island, Maryland, in 1986 changed Janice Almasi's life. Almasi, now the Carol Lee Robertson Endowed Professor of Literacy in the UK College of Education, had been reading about the benefits of peer book discussions, so she tried that approach in her classroom.

"As I witnessed the outcome—nine year olds debating the interpretation of a line in a book and actually listening intently to each other's understanding of the text—a chill shot down my spine," Almasi recalls. After teaching that class, she knew she would go into full-time doctoral study and knew exactly what her work would focus on.

For the past 17 years, she has been studying the learning environments of elementary classrooms and the discussions that follow when students read. She created a model where students interact as if they're members of Oprah's Book Club, rather than answering questions directed to them from the teacher, the traditional approach almost all of us experienced.

In her most recent study of this peer-discussion model, Almasi selected schools where kindergartners, first graders, second graders, and third graders were divided into experimental and comparison groups. A Tennessee school served as the rural site, and schools in New York as an urban site and a suburban

site. Around 860 children were a part of this study, which followed them from kindergarten through third grade. The experimental group practiced peer discussion; the comparison group read and discussed texts in the more traditional way, responding to teacher-directed questions.

One goal was to measure any difference in attitude toward reading and motivation to read of children in the two study groups. To determine this, Almasi used two different measures—an attitude survey and a motivation-to-read profile. Although she found only a modest change in students' attitudes in the two groups at the end of the study, she saw significant differences in their motivation to read. "The children in the peer discussion group viewed reading as significantly more important and valuable," Almasi says.

Another intriguing facet of this study was the socialization patterns of the children in the two groups. "Before we started the study, we confidentially asked the students who in class they would choose to work, play or read with. Usually there were a handful of 'social stars' in the class that almost all of the other children wanted to do things with. Then there were several whom nobody picked—the 'isolates.' There was a pattern of elitism. Would our program impact these patterns? That's what we wanted to find out."

At the beginning of the study, Almasi says, the patterns in the experimental and control group were very similar in terms of social stars and isolates. But by the end of the three-year study, there were almost no isolates in the experimental group and even fewer social stars. "The reading discussion groups became more egalitarian. The children listened to and respected the opinions of all of the other children," Almasi says. She adds that if peer discussion of text continues, a longer-range effect of this change in socialization might be an extended sense of equality among students and less of a tendency toward forming cliques.

"The peer discussion model, based on democratic principles of discussion, breaks the mold of teacher-centered education."

Almasi's work in reading methods, reading theory and reading research design has recently been nationally recognized. Later this year she will join the board of directors for both the National Reading Conference and the International Reading Association.

—Michaela Riley

Soil Sciences Superstar Comes to UK

Here's Paul Bertsch, the newest hire in UK's Department of Plant and Soil Sciences, by the numbers. Published articles: more than 150 in environmental chemistry, biogeochemistry, toxicology and soil physical chemistry, and mineralogy. Invited presentations and seminars: over 200. Other talks and published abstracts: over 300. Recognitions and awards: nearly an uncountable number. And though his career is far from finished, he's already won two Career Achievement Awards. (Oh, and he's also the new president of the Soil Science Society of America.)

So how did UK snag this superstar?

"The one constant in my career so far as a scientist is an intense interest in solving important problems through an interdisciplinary approach," says Bertsch, a professor of environmental chemistry and toxicology, from his office in agriculture north. "During the interview process, I saw a lot of inter-connection between disciplines here, and I was pleased to be offered an opportunity to help establish an interdisciplinary program in environmental research." He adds that he was also impressed with the university's Top 20 by 2020 plan.

Bertsch is no stranger to the UK campus. He earned his doctorate here in soil physical chemistry-mineralogy in 1983 and worked as a research specialist and assistant professor in the agronomy department for nearly two years after that. "So, yes, this is a homecoming of sorts," he says, "though UK has changed quite a lot in 24 years. From what I've been able to tell, every department in the sciences is stronger and there's been an obvious expansion, lots of new construction," he adds, nodding beyond his window to the noise of the UK hospital addition being built.

Kumble Subbaswamy, UK provost, says, "With his extensive experience in building and leading interdisciplinary programs in environmental science, Dr. Bertsch will be able to build on UK's current efforts to reach nationally competitive levels in this area of critical importance to Kentucky." Bertsch is the College of Agriculture's first hire under the provost's initiative to recruit world-class scientists to the university.

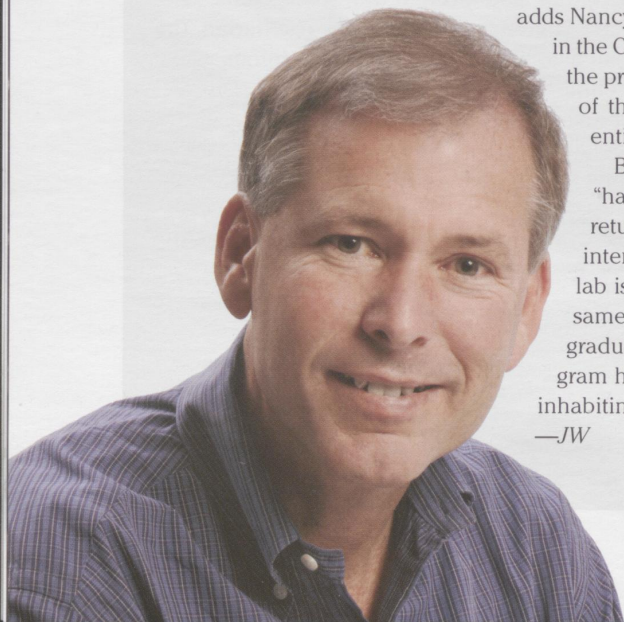
Scott Smith, the dean of the college, sees the hiring of Bertsch as fitting in with agriculture's strategic goal of being a leader in environmental sciences. "As the college moves aggressively to advance our work on management of natural resources, Paul Bertsch will provide a focal point for faculty leadership of those efforts," Smith says. "His hire will complement and grow the programs of the Tracy Farmer Center for the Environment."

"Environmental sciences is an area the college already has a good bit of strength in, and this could take us to another level,"

adds Nancy Cox, associate dean of research in the College of Agriculture, who chaired the provost's committee that conceived of the idea to recruit renowned scientists to the university.

Bertsch admits plainly that he's "happy to be here," and says his return to the university involves an interesting déjà vu coincidence. "My lab is currently being renovated—the same lab I worked in when I was a graduate student in the doctoral program here. It's a bit eerie to think I'll be inhabiting the same space."

—JW



Mighty Mouse Fights Cancer

A mouse resistant to cancer, even very aggressive types, has been created by researchers at the University of Kentucky. The breakthrough stems from a discovery by UK professor of radiation medicine Vivek Rangnekar and a team of researchers who found a tumor-suppressor gene called Par-4 in the prostate. The researchers discovered that this gene performs the slickest trick an anti-cancer agent can: it kills cancer cells, but not normal cells.

Funded by several grants from the NIH, Rangnekar's study is unique in that mice born with this gene don't develop tumors. The mice grow normally and have no defects. In fact, the mice possessing Par-4 actually live a few months longer than lab mice without the gene, indicating that Par-4 mice have no toxic side effects.

"We originally discovered Par-4 in the prostate, but it's not limited to the prostate. The gene is expressed in every cell type that we've looked at, and we've seen that it induces the death of a broad range of cancer cells, including, of course, cancer cells in the prostate," says Rangnekar. "The interesting part of this study is that this killer gene singles out cancer cells. It will not kill normal

Lung Cancer Blood Test Licensed

Lung cancer research by two University of Kentucky faculty members, featured in *The Wall Street Journal* and on the global radio program *The Voice of America*, is now moving an important step closer to the marketplace. Markey Cancer Center researchers Edward Hirschowitz and Li Zhong have spent the last five years working on a blood test that has been 85 percent accurate in predicting non-small cell lung cancer (NSCLC) years before the cancer could be detected by a CT scan.



cells, and there are very few selective molecules out there like this."

To further investigate the potential therapeutic benefits of this selective assassin, Rangnekar's team put it into the egg of a mouse. That egg was then implanted into a surrogate mother. "The mouse itself does not express a large number of copies of this gene, but the pups do and then their pups start expressing the gene," says Rangnekar exuberantly. "So we've been able to transfer this activity to generations in the mouse."

To further establish the power of Par-4, his group removed the gene from several mice. The result: tumors developed in various tissues of the animal.

Rangnekar speculates that this gene may one day be transplanted into a patient's bone marrow to fight cancerous cells in the body. This process could be combined with chemotherapy and radiation, which on their own have highly toxic effects on healthy cells, in order to lower toxicity. But Rangnekar admits there is much more work to be done before this research can be applied to people.

"I look at this research from the standpoint of how it can be developed to benefit the cancer patient, and that's what keeps us focused," says Rangnekar. "The pain that cancer patients go through—not just from the disease, but also from the treatment—is excruciating. If you can treat the cancer and not harm the patient, that's a major breakthrough. That's happening with these animals, and I think it's wonderful."

The research was published in the journal *Cancer Research*. Rangnekar holds the Alfred Cohen, M.D., Endowed Chair in Oncology Research and serves as the associate director for translational research at the UK Markey Cancer Center.

—JW

Approximately 213,000 people are diagnosed with lung cancer each year, and 85 percent of those will die within the first five years of diagnosis. Kentucky has the highest incidence of and death rate from lung cancer—49 percent higher than the national average.

The Maryland-based company 20/20 GeneSystems Inc., which develops diagnostic products for early disease detection, has entered into an agreement with Ortho-Clinical Diagnostics (OCD), a Johnson & Johnson company, to license—and ultimately market—the Hirschowitz and Zhong blood test. The agreement provides 20/20 with funding for further development of the blood test as well as incentives to market it.

The researchers have been awarded \$1.5 million in funding for the development of the test from various sources and recently received an additional four years of funding from the National Institutes of Health. Hirschowitz says moving this test from the laboratory to the clinic involves assuring the reliability and applicability to the general population (with more patients, different demographics). Studies currently are under way to confirm the reliability of the test on a larger group of blood samples. If successful, 20/20 plans to introduce the test within the next year. It would become the first blood test to predict cancer since the prostate specific antigen test was introduced in the 1970s.

"Only 25 percent of non-small cell lung cancer is diagnosed at an early, curable stage," says Jonathan Cohen, president and CEO of 20/20. "By partnering with world leaders like OCD we hope to help establish the first accurate blood test for lung cancer that can detect the disease years earlier than the current gold standard."

The test identifies panels of antibodies generated by the body's immune system in response to very early stage NSCLC. Studies have shown that the presence and amounts of these antibodies in the blood predicted NSCLC with 85 percent accuracy, suggesting that the disease may be present three to five years before reaching the necessary size needed for diagnosis by a CT scan.

—Amy Ratliff, UK Public Relations

When Kathryn Rutland, a UK student working toward a master's degree in public health, walked into Don Gash's office in the fall of 2003, he couldn't have guessed that they would soon be launched on a medical investigation that would for the first time convincingly link a common degreasing agent with Parkinson's disease.

"Some months before, I had suggested that as part of her coursework Kathryn do a detailed clinical history of 10 patients who were part of a study here on Parkinson's disease," says Gash, chairman of UK's anatomy and neurobiology department. "Her focus was on possible genetic factors that caused the onset and progression of the disease. But after she talked with the man known then as Patient Number 10, she rushed to my office and convinced me that, instead, we should focus on a possible environmental factor that might cause Parkinson's."

Rutland explained to Gash, an affable man who has been studying Parkinson's disease for nearly 30 years, that this patient had cleaned grease from metal gauges at a Berea, Kentucky, factory for 25 years, dipping the gauges in a vat of trichloroethylene, or TCE, a chemical solvent. It soaked through his cotton gloves, when he wore them, and into his skin. It splashed onto his clothes, and he breathed in its vapors. The man, whose name is Eddie Abney (he later went public with his story) was sure that his exposure to TCE was the cause of his Parkinson's disease and added

that several of his co-workers had also developed Parkinson's—especially those who had been closest to the vat.

"Kathryn really caught fire on this trail of clues, and it helped that she has a detective's mentality," says Gash. He was familiar with previous research on the possible toxicity of TCE and papers published on other toxic substances that might cause Parkinson's, and he directed Rutland to these sources. TCE had been identified as an environmental contaminant in at least 852 of the 1,430 Superfund priority sites listed by the EPA. Superfund is the federal government's program to clean up the nation's uncontrolled hazardous waste sites. There was also a recent assessment by the National Academy of Sciences on the health risks of chronic exposure to TCE and nervous system toxicity which, the EPA admitted, was not well understood by scientists.

"And there were some relevant scientific studies," Gash says, "including a breakthrough study in 1982 that has been referred to as the Case of the Frozen Addicts." He sets the scene. "Hospital emergency rooms in the San Francisco Bay area were suddenly confronted with mysteriously 'frozen' patients—young men and women who, though conscious, could neither move nor speak." Doctors were baffled until neurologist J. William Langston, recognizing the symptoms of advanced Parkinson's disease, administered L-dopa—the only known effective treatment—and 'unfroze' his patient.

The Mystery of the Toxic Workplace

by Jeff Worley

"Langston determined that his patient and five others had all used the same tainted batch of synthetic heroin, laced with a toxin that destroyed an area of their brains essential to normal movement. The same area, the substantia nigra, slowly deteriorates in Parkinson's disease."

A more recent study in Germany was also revelatory. In 2002, researchers at the University of Würzburg found that in rats TCE was converted to a neurotoxin that led to mitochondrial dysfunctions—mitochondria are the cells' power sources—in substantia nigra dopamine neurons. The team speculated that this TCE conversion could be the linchpin for an environmental TCE-induced Parkinson's disease.

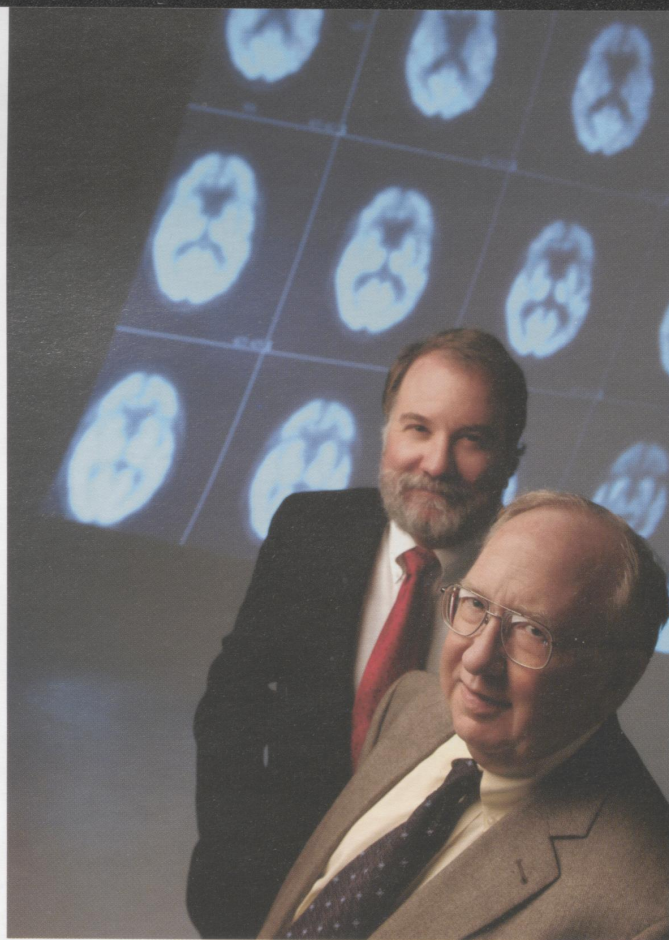
Gash suggested that Rutland talk with former workers at the Berea factory, which is no longer open, to see if there was a TCE-Parkinson's connection. "We realized that for the first time, researchers could work with a 'cluster' of human subjects to see if this connection could be established," adds Gash.

Recruiting the Research Team

The first step in this investigation was to secure Institutional Review Board (IRB) approval for the project—any study that involves human subjects or animals must be approved by UK's IRB. With this approval, Gash, who directed the project, asked his colleague John Slevin, a professor of neurology and molecular and biomedical pharmacology, to join the research team. Slevin, who has worked at UK for 27 years and has headed up several previous Parkinson's trials at UK, was intrigued by this possible TCE-Parkinson's connection and eagerly joined in. Scott Prince, an expert in environmental health in UK's College of Public Health, was brought in, too, to help develop a questionnaire focused on symptoms of Parkinson's.

"This investigation included a tour de force of UK researchers, working through the Morris K. Udall Parkinson's Disease Research Center of Excellence," says Greg Gerhardt, a professor of anatomy and neurobiology, and director of the Udall Center. "The project involved 13 researchers—some of the top people we have here at UK," he adds. Gerhardt's role in this study was to help coordinate the project and review critical data.

With IRB approval and the research team in place, Slevin began by examining Eddie Abney, the foreman

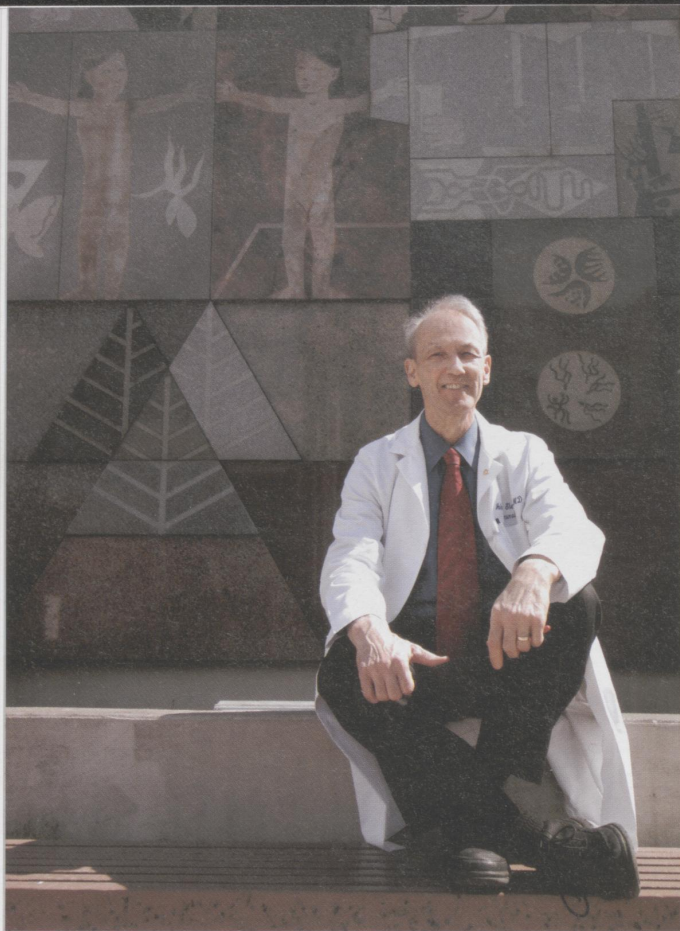


Greg Gerhardt (left) and Don Gash in the UK anatomy and neurobiology department have been collaborating for over 14 years to better understand, and fight, Parkinson's disease. Gash directed the recent project focused on the connection between trichloroethylene (TCE) and Parkinson's disease.

at the Berea plant, and his two co-workers who were closest to the TCE vat. Slevin found that all three had Parkinson's disease. The following case studies of these co-workers show the common thread of coming in direct contact with TCE and close proximity to the TCE vat.

Case 1: A 49-year-old man with 25 years' exposure to TCE, and no family history of the disease. He routinely submerged his arms to the elbows in the TCE vat to clean metal parts. He had had blepharospasm, a twitching of the eyelid, and "tics," uncontrolled repetitive movement, for 10 years and had probably had Parkinson's for seven years.

Case 2: A 76-year-old man at the time of his death, with 25 years' exposure at the plant to the TCE who worked closely with Case 1. He also routinely submerged his arms to the elbows in the vat and suffered tremor, balance and cognitive problems, and



John Slevin, a UK professor of neurology and molecular and biomedical pharmacology, examined 30 former plant employees who had worked with and around TCE. He diagnosed three workers with Parkinson's disease and 24 others with symptoms of the disease. "This is a phenomenally high percentage," he says.

involuntary movement four years before diagnosis of Parkinson's. He had two siblings who also had the disease.

Case 3: A 56-year-old woman with 29 years' exposure to TCE and no family history of Parkinson's. She shared similar work experience with subjects 1 and 2, and sat at a work station adjacent to the TCE vat. She received parts that were often wet with TCE from subjects 1 and 2. She had shown parkinsonian symptoms for five years. Her tongue movements caused "communication difficulties."

The researchers now wanted to gather information about the other co-workers. Prince and Rutland developed a questionnaire which—thanks in large part to a list of names and phone numbers Abney passed along to the researchers—was mailed to 134 former workers. Sixty-five co-workers responded, and of these, 21 reported at least three Parkinson symp-

toms—slowness of movement, stooped posture, trouble with balance, slow walk or dragging feet, rigidity or stiffness, tremor, or decreased facial expression. Twenty-three respondents reported one or two of these signs, and 21 reported no symptoms. Fourteen of the 21 workers who reported three or more signs and 13 co-workers without any symptoms agreed to participate further in the study.

"We were pleased that so many agreed to come in," says Slevin. "Another man, the foreman who worked alongside Abney, would have come in, too, if he had been able. Unfortunately, he was dying—from Parkinson's disease."

Slevin completed physical and neurological exams, and rated the patients according to the Unified Parkinson's Disease Rating Scale, which measures mental ability, physical behaviors and mood. He also evaluated the fine motor speed of each subject.

Slevin says that he didn't really expect to find that anyone in this group would have Parkinson's. After all, in the United States only one or two people in a thousand have the disease, with the prevalence increasing after age 60. But Slevin's examinations led to further sad surprises. In addition to the three workers earlier diagnosed with Parkinson's disease, 24 of the other 27 workers had symptoms. The 14 employees who self-reported Parkinson's symptoms performed significantly more slowly than normal controls—age-matched people without signs of the disease—on the test of fine motor speed. Even more startling, the group of 13 who reported themselves asymptomatic also performed significantly more slowly than normal controls, though not as slowly as their 14 co-workers.

"This is a phenomenally high percentage," says Slevin, his voice underlining the word "phenomenally." "Parkinson's disease is certainly more common in older people, but even in the over-65 general population, it affects only one in 100 people."

"Through this 'case-finding study' with this cluster of workers at the Berea plant, we were able to establish for the first time a strong potential link between chronic TCE exposure and parkinsonianism," says Prince.

The Rat Studies

To complement the human studies and perhaps further establish TCE's effect on the nervous system, the research team used adult male rats. Previous studies had shown that damage to the mitochondria leads to the degeneration of dopamine neurons in Parkinson's disease. How would TCE affect these basic energy producers in the rat brain?



In a study using rats, Patrick Sullivan found that TCE significantly reduces enzyme activity in the substantia nigra, the midbrain lesion site in Parkinson's disease, and that dopamine neurons in this region were also damaged.

This is when Gash brought in another top UK researcher, Patrick Sullivan, who Gash calls the university's "mitochondrial guru."

Sullivan's work is focused on spinal cord and traumatic brain injury, and developing novel therapeutic interventions targeted specifically at mitochondria to treat these injuries.

"Parkinson's is typically thought of as a mitochondrial disease, with what we call Complex I being severely impaired," says Sullivan, an associate professor in anatomy and neurobiology, and associate director of UK's Spinal Cord & Brain Injury Research Center. "Complex I is the first step of the energy chain, the gatekeeper for ATP production. Without a well-functioning Complex I, the cells don't efficiently make ATP, which is what they need to drive the energy train."

The rats were given high doses of TCE five days a week for six weeks. The high doses replicated in weeks what may require years of exposure in humans, Gash explains. The animals were then anesthetized, and Sullivan, with the help of Jignesh Pandya, a research scientist in Sullivan's lab, dissected brain and liver sections to obtain mitochondrial samples.

"The results strongly showed that TCE significantly reduces Complex I enzyme activity in the substantia nigra and that dopamine neurons in this region were damaged," says Sullivan.

"It's important to recognize that this study was not a large-scale epidemiological investigation," Gash adds. "But the results demonstrate a strong potential link between chronic TCE exposure and parkinsonianism."

And now what?

Gash and Gerhardt plan to follow the health of the former plant workers, even those that were asymptomatic, to see if TCE exposure has long-term effects. They also hope that the EPA will take good notice of this study in their periodic review of carcinogens and other toxic substances.

"The most important thing our study did was connect the dots," Gash says. ■

A UK Center of Excellence

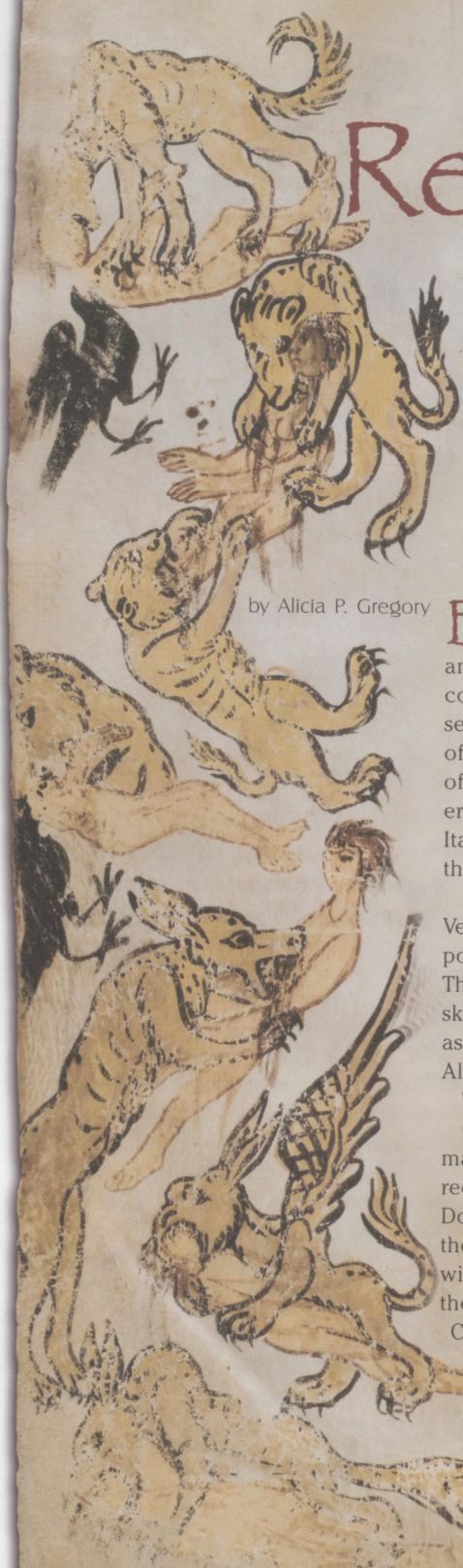
The University of Kentucky Morris K. Udall Parkinson's Disease Center of Excellence, one of 12 Udall Centers in the United States and the only such center in Kentucky, was established in 1999. In 2005 the Udall Center received \$6 million in funding for the next five years from the National Institute on Neurological Disorders and Stroke.

The Parkinson's Disease Research Centers of Excellence program was developed in response to Senate Bill 535, also known as the Udall bill in honor of former Congressman Morris K. Udall, who died in 1998 after a long battle with Parkinson's disease.

"The Udall Center has enabled our research teams to develop a new approach for treating Parkinson's disease, which likely would not have been possible without this support," says center director Greg Gerhardt, who came to UK in 1999. "This new treatment approach is one of the first to try to slow the progression of Parkinson's and possibly restore function to part of the brain affected in the disease."

Working through the Udall Center, nearly two dozen research faculty, scientists and postdocs are looking for ways to repair damage to the brain. Projects include work on a protein called glial cell line-derived neurotrophic factor (GDNF) as a potential therapy for advanced Parkinson's disease, pioneering research on the causal relationship between exposure to TCE and Parkinson's, and illuminating work on Neurturin, a trophic factor that is a close cousin to GDNF in animal models of Parkinson's.

"Patients and their families in Kentucky have benefited from the increased emphasis on Parkinson's disease research and novel treatments," says Gerhardt.



Resurrecting the Iliad

Homer's Epic Poem Lives Anew Digitally

by Alicia P. Gregory

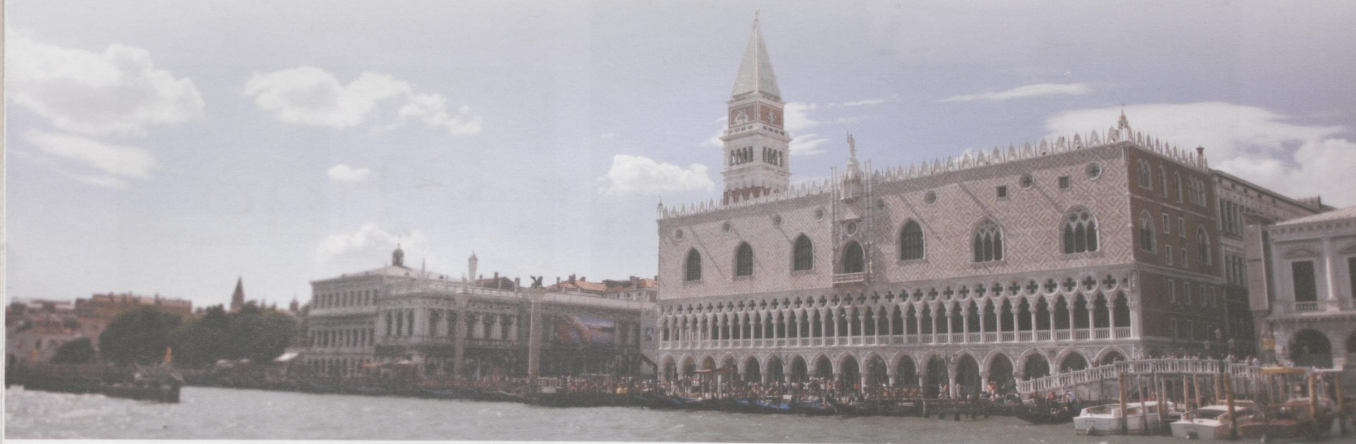
Brent Seales says the enormity of what they were about to do hit him as the waterway opened up into the Grand Canal, and the famed Piazzetta San Marco came into view. Seales, a UK computer scientist, was a member of a team of 20 classicists, conservators and photographers from across the globe who stepped off the water taxi that day in May 2007. Their trip, the culmination of five years of negotiations, brought them to the nexus of eastern and western scholarship—the Biblioteca Marciana in Venice, Italy—to realize their goal of offering the Iliad to the world with the click of a mouse.

Since the 15th century the Marciana library has housed the Venetus A—the oldest surviving complete text of Homer's epic poem that glorifies and laments the death of young men in battle. The Venetus A is from the 10th century A.D., but the Byzantine goat skin parchment includes notes and comments that reach back as far as the 3rd century B.C., to the work of Homeric scholars in Alexandria, Egypt.

The text is beyond priceless.

Only a handful of people had ever seen the actual Venetus A manuscript, and only a slightly larger group had access to the most recent photographs of the precious text. In 1901 Italian scholar Domenico Comparetti sliced each of the Venetus A's 645 pages off their binding, pressed them between glass, and photographed them with black and white film. But these photographs turned many of the tiny scholarly notes into mere smudges. So Harvard University's Center for Hellenic Studies (CHS), a Washington D.C.-based group of Greek scholars, led the push to take new high-resolution photos of the manuscript.

An illustration of people being devoured by lions springs to life in the new color photographs of the Venetus A, the oldest complete manuscript of Homer's Iliad.



Technology Meets Antiquity

Back in Kentucky, Ross Scaife, a UK Greek scholar and longtime collaborator with the CHS, had spent the last 15 years of his career championing open scholarship—freely distributing images and texts in a digital format for the widest possible audience. The images of most ancient texts are restricted on a pay-per-use basis. A pioneer in applying technology to antiquities, Scaife was a founding editor of the Stoa Consortium for Electronic Publication in the Humanities (this umbrella project set the standard for open-access, digital humanities publication) and the Suda On Line, a web database for work on Byzantine Greek semantics.

And it was Scaife who forged the Iliad collaboration, bringing CHS scholars together with the UK computing team of Seales and Matt Field.

Scaife and Seales were co-investigators on EDUCE, a project that uses non-invasive scanning technology to virtually unwrap objects that can't be physically unwrapped, like the delicate, charred scrolls from the Herculaneum library that were destroyed by the eruption of Mount Vesuvius in 79 A.D. Scaife recognized the potential of applying this technology to the Venetus A. Seales explains, "Our role was to capture the exact 3-D shape of every crinkled page."

"The 3-D scans were just one more way to preserve the document in its current state," says Field, who wielded the laser scanner mounted on a robotic arm. Field has a B.S. in computer science from UK and now works full time on the staff of the university's Center for Visualization and Virtual Environments, which is directed by Seales. "There's a lot of bend and warp to those pages. In 1901, they cut and physically flattened each page under glass. There's no way you'd even consider doing that now!"

So a 3-D scanner was just one piece of gear Seales and the CHS team carried from the water taxi to the Marciana library.

Venice in Springtime

May and June were the only months the Marciana library would allow the fragile Venetus A out of the vault (the only climate-controlled section in the 15th-century building), due to the relatively low heat and humidity. But even then the team had to fight the elements (with air conditioning, dehumidifiers and a ventilation system) by constructing a makeshift studio in a small storage room on the library's second floor. They set up a specially designed metal cradle for the book, lights with shutters that could be closed when the photographer was not shooting, and calibrated the robot-mounted laser. This was a particularly tricky task, Field says, because each time anyone on the second floor took a step, the whole floor vibrated.

Setup took an entire week, but soon the team was in a 100-page-per-day groove. The conservator's gloved hand would turn the page, the photographer would shoot it with a 39-megapixel digital camera, Field would scan each page by "painting" the page with strips of laser light, and the classicists would review each digital photo for readability.

The team finished imaging the manuscript ahead of schedule, so they were able to shoot close-ups and ultraviolet shots that the scholars hoped would improve the readability of text in certain places, revealing writing that had



A crown tops a column of text in the 1901 Comparetti photo (inset). The 2007 photo reveals how much of the crown has disappeared.



UK's Matt Field scans the text of the *Venetus A* with a laser scanner mounted on a robotic arm. This painstaking process captures the 3-D shape of the page.

been smudged out and letters that had worn away. The skin of the parchment absorbed ultraviolet (UV) light, and the ink reflected the light, which helped to differentiate the ink from its background.

Digital Treasure Trove

In the end, the team had 700, 40-megapixel digital photos. Now the burden lay on the shoulders of the UK team. Back in Kentucky at the Center for Visualization and Virtual Environments, grad student Eric Cooker cleaned up the 3-D scans while Field and fellow programmer Ryan Bowman wrote the software to register—precisely overlay—the images.

This software lined up the new color photographs with the UV and close-up shots, as well as the 1901 Comparetti photos. Then the software essentially “pasted” the high-resolution photographs onto the 3-D scan of the page and pressed it against a virtual plane to flatten it—giving even more clarity to the tiny scholarly notes.

Bowman shows two examples of what this process allows you to see: “If you look at the edge here, there’s something that looks like a smudge under normal lighting, but if we switch to ultraviolet, we can see a note. And on this page, here’s the 1901 version with an illustration of a crown. Now the new photo: the crown has almost completely evaporated.”

The just-released web-based version of the *Venetus A* uses an interface that allows the user to zoom in and zoom out on the manuscript. This kind of interactivity requires a significant amount of bandwidth—a fast rate of data transfer—so the entire collection of images is housed on a server at the CHS and a mirror server at UK.

Chris Blackwell, one of the classicists from the Center for Hellenic Studies who went to Venice, says, “When I look at everything that’s in the *Venetus A*—the illustrations, the comments in the margins, the comments in the narrow margins, the comments between the lines, the little summaries of each chapter, the conclusions on each chapter—it really makes me



**Ross Scaife
(1960-2008)**

“Ross and I found a real partnership that went deep,” Brent Seales says. “He got involved

with EDUCE—Enhanced Digital Unwrapping for Conservation and Exploration—because he was a Greek scholar and most of the Herculaneum manuscripts are Greek. He loved the potential of this project to rediscover the wisdom of the ancient world and share it through today’s technology.” (Seales is currently doing test scans on one of these Herculaneum fragments, on loan from the Sorbonne in Paris.)

With the *Venetus A* project and the impending Herculaneum discoveries, Seales says his colleague was very close to realizing his dreams. “It’s hard to accept that he could get so sick at the point when he was on the cusp of finally achieving things for which he’d been planning and working for years. But Ross made me see that life is less about achieving than it is about becoming.”

Allen Ross Scaife, 47, professor of classics at the University of Kentucky, died of cancer on March 15, 2008, at his home in Lexington, Kentucky.

think that the scribe who copied it out in the 10th century was trying to make the equivalent of the ‘deluxe DVD version’ of the *Iliad*. He took every single thing he had at his disposal about the *Iliad* and put it all together in this one, very compact package made of goat skin and written in ink.”

“The ability to see what’s been disappearing over the past 100 years, and the chance to do an apples-to-apples comparison of every page gives scholars so much more information than just a photograph,” says Seales. “We think it’s fantastic that the actual original images—not just degraded, pixilated copies—are available for any scholar.”

To experience the digital *Venetus A*, visit <http://chs75.harvard.edu/manuscripts>. ■

Bathing suits. Check. Beach toys. Check. Sunglasses. Check. Sunscreen. Don't need it.

Soon Mom and Dad may have one less item to pack for the family trip to the beach—sunscreen. Instead, about a week before they head to Orlando, the whole family will smear on a special lotion that naturally tans their skin. But more important than the tan is the built-in UV protection. The University of Kentucky's John D'Orazio is doing the basic science work behind this revolutionary approach to stop skin cancer.

By repairing a defect in the chemical pathway that tells cells which kind of melanin (pigment) to produce, D'Orazio turned "blond" mice black. And one day the science behind this discovery may tan and protect vacation-bound families and sun-worshippers.

How did D'Orazio, a clinical pediatrician and scientist at the Markey Cancer Center, get into tanning research? "For me, the pitch was the fact that childhood sun exposure, particularly blistering sunburns, is the biggest risk factor for melanoma later in life." Melanoma is the most common cancer in young adults between ages 20 and 30, and the primary cause of cancer death in women between 25 and 30. And then, he adds, there was the curious observation that people with albinism—no pigment at all—don't get melanoma.

D'Orazio explains that pigmentation plays a big role in skin cancer. Take three groups of people, the first with dark skin (say from Africa or India), the second with fair skin (say from Ireland) and the third with albinism. "Now look at the cancer risk. There are two basic carcinoma categories. In the first category, there's basal cell carcinoma/squamous cell carcinoma—these account for over a million cases a year in the United States and don't kill you, you just get them cut out—versus the bad guy melanoma." It makes up less than 10 percent of the total cases of skin cancer, but three-quarters of the deaths.

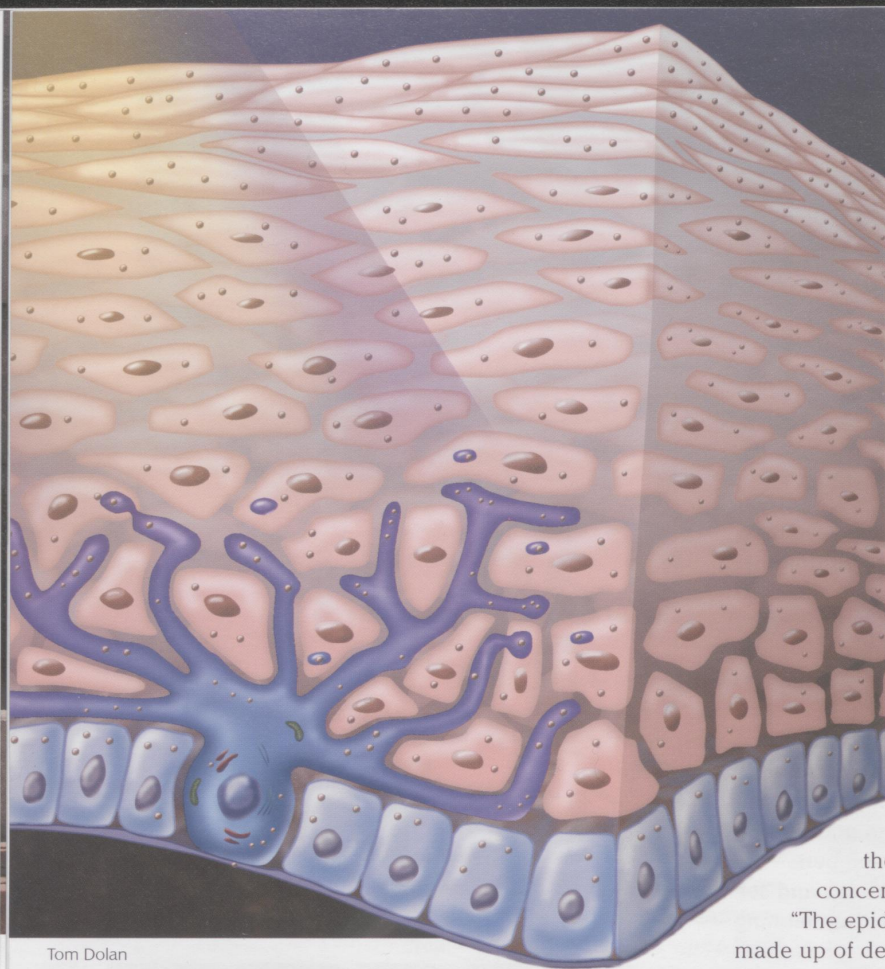
D'Orazio says, "So guess what? If you're dark skinned, you don't get either kind of cancer. If you're fair, you're at high risk for both kinds. And if you have albinism, you're at the highest risk for basal cell/squamous cell carcinoma, but you won't get melanoma."

Why zero pigment equals zero melanoma was the driving question behind his work in David Fisher's

Fighting Cancer with a Safe Tan

by Alicia P. Gregory





Tom Dolan

Childhood sun exposure, particularly blistering sunburns, is the biggest risk factor for melanoma later in life.

lab at the Dana-Farber Cancer Institute in Boston before D'Orazio came to UK four years ago. "David, one of the top three melanoma researchers in the world, got me interested in figuring out a way to protect kids from melanoma." This research led to a landmark September 2006 paper in *Nature* that demonstrated an experimental lotion could protect "fair skinned" mice against UV damage. "But before we get to the mice, let's look at your skin," he says picking up a marker.

"Your skin is made up of layers," D'Orazio explains, as he draws several wavy lines with small and large circles. "These big circles are keratinocytes—they make up 90 percent of skin cells. They proliferate down here at the lowest layer, and as they mature they

Melanocytes (dark blue cells) distribute pigment, a.k.a. melanin (tiny brown spheres), to the keratinocytes (peach cells). Keratinocytes make up 90 percent of skin cells, and as the keratinocytes are pushed up to the surface by new cells beneath them, the melanin gets more and more concentrated. John D'Orazio explains: "Skin rich in one type of melanin, called eumelanin, absorbs the UV light before it can get down to the danger zone where the melanocytes live." Skin cancer happens when UV light mutates cells in the danger zone.

lose their nuclei, bind tightly to each other, and pick up melanin—pigment—from melanocytes, the only cells that produce it." He adds that one melanocyte can interact with 30 to 50 of these keratinocytes. And as the keratinocytes are pushed up to the surface by new cells beneath them, the melanin gets more and more concentrated.

"The epidermis—the top layer of your skin—is made up of dead keratinocytes, jammed with melanin, that seal in the skin." He draws a sun with an arrow down to the epidermis with a big "UV" next to it. "Skin rich in one type of melanin, called eumelanin, absorbs the UV light before it can get down to the danger zone where the melanocytes live." Skin cancer happens when UV light mutates cells in the danger zone.

This eumelanin is a natural sunscreen. "I call it that because it's not something you apply. It's in your skin. You couldn't get rid of it if you wanted to ... well, unless you're Michael Jackson," he laughs. "If you're dark skinned you have eumelanin, and remember these folks don't get either kind of skin cancer. If you're blond or red haired, lots of freckles, burn easily, you have pheomelanin, and can get both kinds of cancer."

But if you have albinism, you don't have either of these types of melanin because your body doesn't make the enzyme, tyrosinase, that leads to melanin production. And people with albinism are at very high risk for non-melanoma skin cancers, but they don't get melanoma.

"UV exposure is clearly linked to melanoma, but nobody understands how," D'Orazio adds. He and his peers across the country, however, suspect melanoma risk may be related to pheomelanin in the skin.

To get at the mechanisms behind which kind of melanin is made, D'Orazio used genetically modified mice that differed only in key genes that caused them to have eumelanin (black mice), pheomelanin (blond mice) or no melanin (albino) to study the UV responses and DNA damage in each group.

It all comes down to a signaling molecule—a chemical involved in transmitting information between cells—known as cyclic AMP (adenosine monophosphate). Cyclic AMP carries signals from the cell surface to proteins within the cell and triggers a cascade of gene and enzyme actions that produce eumelanin. When there's a defect in this signaling process, pheomelanin is made instead.

D'Orazio found that by using a drug to bypass this defect, he could make his blond mice black. He created a lotion containing a compound called forskolin, which is made from the root of a plant called *Plectranthus barbatus* grown in the foothills of the Himalayas, used for centuries worldwide in traditional medicines, and used in labs since the 1970s. Within a couple of days of applying the lotion to the backs of these mice, he started to see the blond mice turn black. "The black skin is caused by eumelanin production, so we essentially repaired that signaling defect pharmacologically." He found that the more you apply, the greater the UV protection, and that the protection lasts for a few weeks. "It takes a month for all your skin cells to renew, so it gradually works its way out of the skin just like a natural suntan."

But it's not likely that a forskolin-based lotion will end up on your drugstore shelf. "Human skin is much thicker than mouse skin. The problem is getting the drug down to the melanocytes." He adds, if you took enough of forskolin orally to get the needed concentration, you'd probably have diarrhea. Not a vacation-friendly side effect. "We used this drug as proof-of-principle. Whether another compound that can tickle this cyclic AMP pathway in the same way ends up on the shelves will depend on whether a safe, deliverable drug can be found that works in humans." That's what Magen Biosciences, founded by David Fisher, is trying to do.

Along with top scientists from Harvard and MIT, D'Orazio is on the scientific advisory board of this Massachusetts-based company that is identifying and developing novel treatments for dermatological disorders. "Magen is handling the consumer product side, while we're using our mouse model to continue to tackle the basic science questions of how UV light causes DNA damage and leads to melanoma.

"Our mouse study has implications for protection against UV light, and more cosmetically sunless tanning. We didn't set out to get rich or put tanning salons out of business. Our goal is cancer prevention." ■

John D'Orazio, a clinical pediatrician and scientist at the UK Markey Cancer Center, is fighting skin cancer before it starts with a lotion that optimizes skin's natural pigment to prevent UV damage.



The winning design has tall, H-shaped towers. This rendering shows the bridge as it will appear when it is completed in 2020.



Democratic Bridge Building

by Doug Tattershall

Ted Grossardt learned about democratic decision-making on the family farm in Claflin, a town of 700 people in the middle of Kansas. This community is guided by the farmer cooperative, an institution that strongly supports farm families. After graduating from college, Grossardt returned to work on the family farm and also served on this cooperative.

Central Kansas might seem a long way from Central Kentucky and the Kentucky Transportation Center, a

research center in the UK College of Engineering, but Grossardt's work on improving public satisfaction with bridges and other public projects was inspired by his work on the co-op.

"The idea that large groups of people can effectively make decisions is something I grew up with," says Grossardt, who came to UK in 1993 to pursue a doctorate in geography and worked at the Transportation Center while completing his degree. His experience with the farmer cooperative has served him well,

Working through the Kentucky Transportation Center in the UK College of Engineering, Ted Grossardt (right) and John Ripy have involved hundreds of citizens in public meetings to help select the design of two new bridges.

he says, in a current project involving hundreds of citizens at public meetings in northern Kentucky and southern Indiana who have helped select the design of two new bridges.

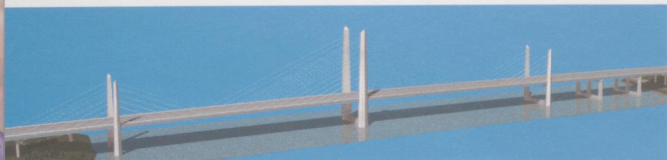
The high-profile Louisville-Southern Indiana Ohio River Bridges project, which began in 2004 with a targeted completion date of 2020, will result in the building of two new bridges over the Ohio River, one of which will be in downtown Louisville adjacent to the Kennedy Bridge. The project is funded by a combination of federal, Kentucky and Indiana tax dollars, and its cost of \$4.3 billion makes it the fifth largest infrastructure project in the nation. Because of the new bridge's prominent location, the state required formal public input into the design.

Compiling useful public information is easier said than done because of the many design factors involved. The bridge structure might be a truss, arch, box, or cable stay. The height might be low, medium or high. The gateway, or the appearance as one crosses the

bridge, might be H-shaped (with sides not touching at the top) or A-shaped (sides touching). The design might be symmetrical or asymmetrical, based on the positioning of the piers, the upright supports that anchor the bridge to the rock bed below the river. And the design may be visually open and simple, or complex in appearance.

These design elements create hundreds of options. A straight vote on all of them would almost certainly fail to present a clear winner, and such a ballot would stymie even the most conscientious citizen.

This project is being guided by a team that includes Grossardt, Keiron Bailey, a UK doctoral graduate now in the University of Arizona Department of Geography and Regional Development, John Ripy, information systems manager at the Transportation Center, and UK graduate students. Grossardt, Bailey and Ripy developed a system they call Structured Public Involvement to draw out public preferences for the design of the bridges.



The winning design (left) and the runner up for the downtown Louisville bridge were determined by input from 170 citizens.



The heart of the process is a 40-minute public meeting. "The goal of this meeting is to get useful, informed feedback from the public," Grossardt explains. "Engineers have long used such meetings for public works projects, but the meetings we hold are focused on getting the public involved in the decision-making process itself." Attendees are given a handheld electronic keypad and are shown only a limited number—20 to 30—of the hundreds of bridge design possibilities, electronically rendered into a photo of the actual environment.

When attendees see a bridge, they are asked to react to it on their keypads, giving it a rating of 1 to 10. This range allows for a more accurate rating than simply "yes" or "no," and allows Grossardt and his team to determine degrees of reaction. Another advantage of using keypads is that the people at the meeting see immediately what designs the others in the group prefer.

Grossardt sees at least three advantages of Structured Public Involvement: it allows a large group to get involved, it provides a model that allows participants to handle multiple and sometimes complex variables, and it can be used with many engineering issues—from bridges to street patterns to urban development to highway routes. "It has always been a challenge to get the public involved in these design decisions, mostly because the people who came to such meetings questioned whether their input would really count," Grossardt says.

With the data gathered from 170 people who attended four public meetings in 2006, the research team moved from an intuitive sense of what the public preferred to a scientific valuation of public preferences, and the researchers came to several conclusions. In the scoring on the Louisville bridge, the people at the meetings favored an open, H-shape gateway if the bridge was going to be a tall arch, but preferred a closed, "basket-handle" arch for a shorter

bridge. Conversely, if the bridge was a cable-stay structure, they preferred the shorter designs to be open, or H-shaped. They also wanted the new bridge to match the height of the other bridges around it, but wanted a simpler design because that stretch of the Ohio is already so visually busy. The design for the downtown bridge was chosen, with citizen input, in December 2006.

"This was an intelligent process that showed us what characteristics people liked and didn't like," says J.B. Williams, project manager and vice president of the Michael Baker Corporation's Louisville office. "Ted and his team didn't just throw up some bridges and say, 'Which one do you like?' Structured public involvement requires us to create more renderings, but in the end gives us more intelligent information."

The SPI process has already been used for several public works projects with results that are specific to the community and the project at hand, Grossardt points out. For example, where the Louisville bridge project showed a public preference for a relatively simple bridge design, another bridge project at Land Between The Lakes yielded a much different result. The 300 participants in that process preferred something more monumental, an architectural statement in an environment dominated by nature.

Grossardt emphasizes the point that while the public gets to vote on the design, the designer maintains creative control. "This process doesn't dictate the design—it supports the design decisions."

In his farming days, Grossardt participated in decision-making that balanced the work of cooperative managers and the input of a board of farmers elected by other area farmers. "I've been surprised that this business model has not been used more," he says. "It makes the organization listen to its members, and that's what happens here with Structured Public Involvement. It allows people to take a proprietary interest in how their community looks and functions." ■

University Research Professors 2007-2008

by David Wheeler

University Research Professors

Jayakrishna Ambati: Working to Cure Macular Degeneration

JK Research Professor Jayakrishna Ambati loves solving puzzles. When he was 10 years old, shortly after moving to the United States from Vellore, India, his father noticed this interest and often challenged him with "brain teasers." Now a father himself, Ambati displays a framed photo of his wife and one of his daughters on his busy desk. At UK, Ambati has put his problem-solving abilities to work as a professor of ophthalmology and visual sciences, publishing two major discoveries recently in the prestigious journal *Nature*.

He made the first discovery, about blood-vessel growth, in collaboration with his brother, Balamurali Ambati, an ophthalmology researcher at the University of Utah. One reason human beings have good vision is that blood vessels in the human eye normally stop growing before reaching the cornea. But the question of why blood vessels behave this way puzzled researchers until the Ambati team solved the mystery.

"This has been the single outstanding question in all of vascular biology," says the UK researcher, behind stacks of papers and journals that threaten to topple from his desk. The reigning hypothesis was that a variety of molecules joined together to block blood vessel growth, but Ambati discovered that a single protein was responsible.

"Through a series of studies over five years, we established with tremendously compelling evidence that this protein was singularly essential for keeping the blood vessels away from the cornea," he explains. The protein, called Soluble Vascular Endothelial Growth Factor 1 (S-VEGF Receptor 1), cancels out the work of blood-vessel-inducing VEGF. The finding could be key to a future cure for macular degeneration. "If we can bring the promise of blindness elimination one day closer, at least from this one disease that my lab focuses on, then that's tremendously rewarding, more rewarding than any paper," he states emphatically.

A more recent discovery by Ambati revolutionized the gene research field by clarifying the 2006 Nobel Prize-winning discovery of RNA interference.

To regulate proteins, the body creates entities called "small interfering" RNAs (siRNAs), which bind to the RNA of specific genes, preventing the production of particular proteins. Because numerous diseases are linked to protein overproduction, this Nobel Prize discovery intrigued some pharmaceutical researchers, who thought they could turn off individual disease-causing genes with synthesized siRNAs.

But Ambati discovered that siRNAs have a downside: they can have systemic side effects. In the case of macular degeneration, the drugs don't just inhibit unwanted blood vessel growth in the eye—they inhibit blood vessel growth in other parts of the body, too. In tests done by Ambati's lab on mice, synthesized siRNAs prevented skin wounds from healing as quickly as they should.

Ambati says that his discovery points to the need for caution when using new technologies such as siRNAs. "We can't rush headlong into injecting drugs into people without understanding how they work."

For Ambati, all biomedical research is a search for what works, or to put it more grandly, for truth. "It's a way to assemble the pieces of the truth that are dispersed. In some ways, it's like a big jigsaw puzzle that you can gradually assemble with patience, insight and diligence."

But there's one mystery Ambati does not expect to solve. "Here's the real puzzle." He smiles, pointing to the framed photograph of his daughter. "That is the greatest, most mysterious science experiment that there is: How the mind of that little creature works." ■



Richard Kryscio: Science by the Numbers

Richard Kryscio's relationship with biostatistics began when his elementary school class lined up for a mysterious shot in the 1950s. "They took us into this dark hallway," says Kryscio, UK biostatistics department chair in the College of Public Health. "We were all equally scared." The shot turned out to be the polio vaccine, whose success was proven through biostatistical analysis. "Children were randomized to either get a placebo shot or get the vaccine, and scientists demonstrated unequivocally that the vaccine prevented this disease." His eyes brighten. "Biostatistics helped wipe it out."



Today Kryscio is on an interdisciplinary mission, working with experts in neuropsychology, aging and biostatistics to wipe out another disease: dementia. Unlike the fight against polio, the battle against dementia has progressed slowly. But Kryscio believes that biostatistics can help scientists better understand dementia, and thus have more weapons to fight it. Having been named a University Research Professor, he can now dedicate even more resources to the challenge.

Biostatistics emphasizes order, and Kryscio, appropriately, seems to embody this trait—from the neat shirt and tie that he wears at work to his careful explanation of his research interests. "Ultimately we'd like to answer the question that a lot of investigators are interested in: What is the probability that a person will become demented in their lifetime?"

Previously, poor scores by an elderly person on a memory test were seen as a guarantee of future dementia, but Kryscio's team reframed the debate. "Our data shows that the early stages of mild cognitive impairment are not necessarily a path to dementia," he notes. "People can and do recover from it." For example, an elderly person might score poorly on a memory test simply because of a bad day. "Looking at the neuropsychological tests, we realized that people can have a memory impairment for a variety of reasons. Someone might have passed away in their family, and that sadness affects test performance. So when you test them a year later, they score in the normal range."

Realizing that there are few promising treatment options for dementia, Kryscio has begun to devote more attention to prevention. "There are some things you can't do anything about," Kryscio emphasizes. "You're going to get older, and you can't change what you inherited from your parents. So we're looking for modifiable risk factors." For example, he is investigating the role that antioxidants such as vitamin E and selenium might play in preventing the disease.

Whether designing a specific Alzheimer's study or promoting biostatistics in general, Kryscio brings order and progress wherever he goes. "A very satisfying moment for me professionally has been the creation of the Department of Biostatistics, because it gives biostatistics a standing like any other academic department here on campus." He folds his arms and smiles. "We went from nowhere to somewhere, and I think the future's pretty bright." ■

The UK Board of Trustees first awarded University Research Professorships in 1977. The goal of these \$35,000, one-year professorships is to enhance scholarly research and awareness of UK's research mission by recognizing outstanding faculty.

Peter Nagy: Advancing Science—One Move at a Time

In his younger days, Peter Nagy spent hundreds of hours honing his chess skills. When he was 17, he played in the final match for the chess championship of Sopron, Hungary, his native country. He won.

Today, Nagy works as a professor in plant pathology at the University of Kentucky. He no longer competes in chess championships, but he's quick to point out the similarities of chess and science.

"Like a chess player, a scientist has to have an initial plan but be flexible when that plan doesn't work out. Both have to adapt and use situational strategy. And a scientist, like a chess player, 'wins' by utilizing his resources well," says Nagy, who still retains a noticeable Hungarian accent.

At UK, Nagy's lab focuses on Tombusviruses, small model RNA viruses of plants, to identify the viral and host players in replication and to unravel the mechanism of virus replication. RNA replication is the central process in viral infections, Nagy explains, which in the case of Tombusviruses is a robust process and leads to the production of millions of progeny viruses in a single cell in a day. He hopes that a better understanding of viral replication will lead to improved antiviral



strategies and enhanced resistance against virus diseases in plants.

Nagy's team has gained international attention recently by publishing a host-virus study involving yeast cells and the "tomato bushy stunt virus." A yeast cell has 6,000 genes, and Nagy's team performed genome-wide experiments involving the interaction between this particular virus and every one of these genes. "This way, you can systematically ask the question, 'What is the virus doing without that gene?'" he explains. Most of the time, when one of the yeast genes was deleted, the virus did not replicate as well. "But in some cases, the virus was actually happier, there was much more replication, and those are probably the genes the host cell uses to fight back the viral infection."

Nagy eases into a smile when he describes an unexpected discovery by his lab in this work: the viruses were not only replicating in the yeast, but actually evolving. "Most of the time evolution is being judged by millions and millions of years. But here, we saw evolution in front of our eyes; it was happening within hours." When a virus detected that a certain gene was missing in the yeast, this virus started to "play evolution," Nagy says. "The new virus sequences started to compete with each other, which was truly remarkable."

Importantly, Nagy's group was able to take the findings from the yeast experiments and reproduce the results in a plant system. In other words, Nagy found that the virus-host interaction was similarly affected by both the yeast gene and its equivalent plant gene. Nagy and other scientists hope this fact will lead to discoveries about viruses in humans.

Such progress is already under way. After Nagy published his findings, Japanese scientists began studying the influenza virus replication in yeast, citing his work and using his methods. In all, Nagy has about 1,500 citations in scientific journals.

This year he received the Ruth Allen Award from the American Phytopathological Society. This prestigious award recognizes "an outstanding, innovative research contribution that has the potential to change research in plant pathology." ■

Fighting Relapsed Leukemia

by Jeff Worley

When cancer returns, it can come back with a vengeance. And older people are particularly susceptible to cancer's return because their immune systems aren't generally as strong as those of younger patients.

The University of Kentucky's Markey Cancer Center is conducting a clinical trial for elderly and relapsed Acute Myeloid Leukemia (AML) patients with the goal of helping this group of patients live longer. Dianna Howard, a physician-researcher in the Department of Internal Medicine, is leading this study.

AML is a cancer of the white blood cells, characterized by the rapid proliferation of abnormal cells that accumulate in the bone marrow and interfere with the production of normal blood cells. AML is the most common acute leukemia affecting adults,

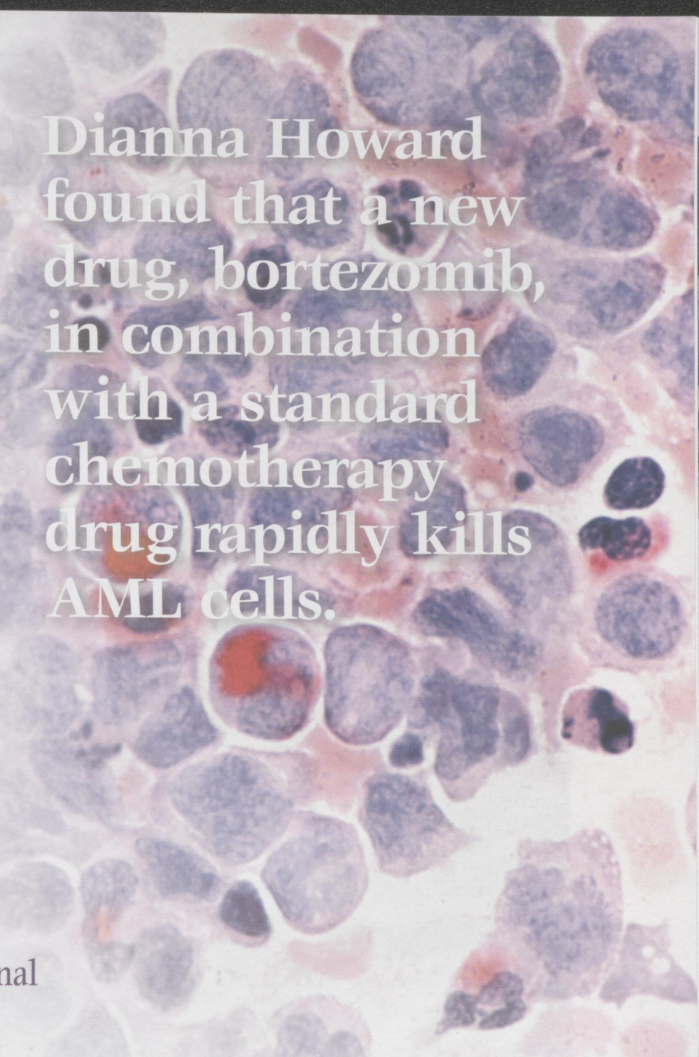
and its incidence increases with age.

Howard and her team found that the combination of a new drug, bortezomib (Velcade), with a standard chemotherapy drug, idarubicin, rapidly kills AML cells, including AML stem cells—the cells thought to be responsible for leukemia relapse in the majority of patients. The drug combination also offers the potential for remission with fewer side effects than other traditional combinations. Bortezomib interrupts the biological signals that keep AML cells alive and makes them more likely to die when treated with idarubicin. With the same drug combination, normal stem cells, the cells responsible for producing normal blood cells, are not killed.

"We demonstrated that this novel combination of drugs could kill leukemia cells in the Petri dish, so we were eager to move into clinical trials," says Howard, who has been on the faculty at Markey since 1999.



Dianna Howard's son, Will, was diagnosed with Acute Lymphoblastic Leukemia when he was 9. The good news? He's been in remission for over four years now.



Dianna Howard found that a new drug, bortezomib, in combination with a standard chemotherapy drug rapidly kills AML cells.

"We're now heading up a Phase I trial to determine a safe dose of these drugs in our 15 patients, and once we do that we'll look at the efficacy of the drug combination and expand the number of patients in the study."

Howard says this clinical trial is particularly important because in the past about half of adults over age 60 that were diagnosed with leukemia were never offered therapy for their disease, since the perception of the therapy has been that an effective dose of drugs would be too toxic. "That view is changing, and we're trying to be a part of that change," says Howard, who has seen some encouraging signs so far in the study. "With this combination of drugs, some of our patients have gone into complete remission, which in a Phase I study is somewhat remarkable—you don't expect remissions with such low dosages."

Leukemia Research: Up Close and Personal

In December 2003, Howard's research became personal, very personal: Her 9-year-old son, Will, was diagnosed with Acute Lymphoblastic Leukemia (ALL). ALL is a fast-growing type of leukemia in which too many immature white blood cells congregate in the blood and bone marrow.

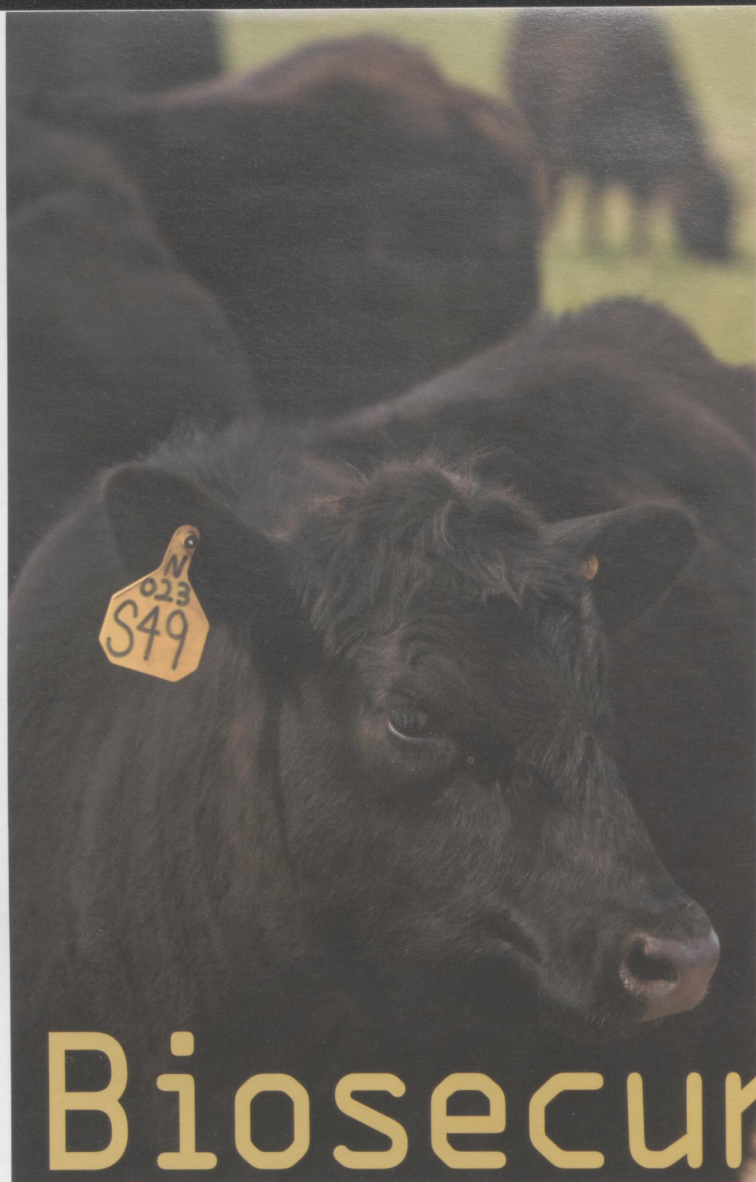
"When we got the diagnosis, I was in disbelief," Howard says. "How do you make sense out of something like this? I came around to the realization that there's no purpose in asking why—things don't happen for reasons, they just happen. This is something my patients through the years have taught me. Reason is what evolves as you respond to what happens. Looking ahead, we wanted Will to walk away from this experience acknowledging that it didn't make sense but that if he could endure this, he could endure anything."

Will's endurance has been tested. He's had three years and three months of chemotherapy, and physical therapy is still a part of most days. But the news is good: He has been in remission for over four years now. "Will achieved a rapid and complete remission early with therapy—the best possible outcome. The longer he stays in remission, the more likely he is cured," says Howard.

And she feels lucky that she has had such a strong support system throughout this ordeal. "My colleagues at UK went beyond themselves to support me personally and professionally. I'm surrounded by some of the most remarkable people anyone could ask for."

Howard also got "amazing support," she says, from the Leukemia and Lymphoma Society. She is now a participant in a group called Team In Training (TNT), the world's largest endurance sports training program. The program provides training to run or walk marathons and half marathons, or participate in triathlons and 100-mile bike rides. This program raises nearly half the national budget for the Leukemia and Lymphoma Society.

"TNT has given me a venue to connect to other moms, professionals and patients on a very personal level," Howard says. "Through this small test of my endurance, I can honor my son and so many others like him—my patients—who really know what endurance means. I'd walk to the other side of the world if it moves us one step closer to a cure for leukemia." ■



Matt Barton

Getting an earful of information. Eric Vanzant, animal and food sciences, is using battery-powered ear tags on cattle to track information such as body temperature and head position, which can tell him if cattle are eating or drinking. That information is valuable because it can indicate if a cow is healthy or sick. This animal health monitoring system is a critical link in Homeland Security-funded biosurveillance research at UK.

Biosecurity

Down on the Farm

by Holly Wiemers

Jared Wright, manager of a small horse farm in southern Kentucky, wakes at 6 a.m., drinks his one quick mug of coffee, and heads off to the barn. There, he moves from stall to stall with morning grain for his five mares. Since they are all pregnant and due to foal within days or weeks, he is especially attentive to their behavior. Do any of them appear to be in distress? Are they eating with their usual enthusiasm? When he gets to the last stall, he realizes one of a broodmare manager's worst fears: the mare has aborted.

The manager checks the condition of the mare, who is contentedly eating her grain. He removes the fetus and placenta from the stall, calls the veterinarian, and finishes the morning chores. Then there's one last thing he needs to do.

He goes back to his office, clicks on to a computer program and enters his observations, highlighting the sad news of the aborted foal.

He also looks over an interactive map of Kentucky that shows the state's current animal health conditions to see if there are any common illnesses or odd behavior among horses at other farms. Then he logs off and continues his day.

The computer program has been developed by the University of Kentucky Livestock Disease Diagnostic Center (LDDC), and the daily information-sharing process was part of a pilot project conducted by the LDDC in August 2007. Dur-

Craig Carter, director of the UK Livestock Disease Diagnostic Center, led the development of a computer program for horse farm managers and others to record and share animal health data.



Steve Patton

ing the study, which was funded by the Department of Homeland Security, UK researchers partnered with 13 Central Kentucky horse farms to capture 30 continuous days of animal health data. Information was fed into a web-based program, and data was statistically analyzed daily by the LDDC to identify possible clusters of illness or disease.

"It's like a neighborhood watch," says LDDC director Craig Carter. "Infectious diseases can insidiously creep in. *Rhodococcus* and *Salmonella* raise their ugly heads every year, but with this computer program in place, we can get a good jump on fighting these diseases."

Since coming to Kentucky three years ago, Carter, a colonel in the U.S. Army Reserves with a military career spanning four decades, has led the development of this computer program—Kentucky's first fully integrated animal health information and surveillance system chronicling animal health. When it's fully operational and in wider use, Carter says, this system will become the information hub for the health of Kentucky's animals.

The software being used has been customized for our state's unique needs, and it will link Kentucky's two state labs with the state veterinarian's office for the first time. This information nexus will get the word out—fast—if there are clusters of similar observations that exceed a statistical threshold. The network will generate automated alerts to farm managers, veterinarians and others. In addition, the new system will generate maps, charts and disease-trend data on the web to help veterinarians and farmers around the state stay current regarding the prevalence of animal disease around the commonwealth.

"If farmers, for example, went to our website and saw the overview map showing cases of blackleg all over their county, they would be alerted to vaccinate their animals right away to head off this disease," says Carter. The system won't only collect and statistically analyze animal health data in the field, but also will offer near real-time information on the weather, soil, toxic plants, and insect populations, Carter adds.



Roberta Dwyer, a researcher at UK's Maxwell H. Gluck Equine Research Center, is working to improve equine disease surveillance and animal disaster plans for veterinarians and animal owners in Kentucky.

The Cost of Animal Disease

The economic impact of a widespread disease among animals can be devastating. During the 2001-2002 breeding season, Mare Reproductive Loss Syndrome (MRLS) hit Central Kentucky particularly hard: an estimated 30 percent of thoroughbred fetuses and foals died, and the state suffered close to \$340 million from losses in all horse breeds. This was a tough blow to Kentucky's horse industry, which has an estimated economic impact of \$4 billion annually and generates approximately 80,000 to 100,000 jobs directly or indirectly, according to U.S. Department of Agriculture figures.

"We ran all the health events surrounding MRLS into our current cluster detection engine. It generated alerts about the problem seven to 10 days earlier than it was recognized in the field at that time," Carter says. "How many foals would have been saved if action had been taken 10 days earlier?"

Equine influenza is another potentially devastating disease in Kentucky. Roberta Dwyer, a researcher at UK's Maxwell H. Gluck Equine Research Center, says that the LDDC surveillance program will also closely monitor any outbreaks of horse flu.

"If a new subtype of the virus was introduced to the United States, it may be possible that equine influenza could begin making the rounds here as it did in Australia in 2007," says Dwyer, who has studied equine infectious diseases for 20 years. "In Australia, equine influenza shut down breeding and racing altogether." Although most horses recuperated from the illness, it severely impacted Australia's economy, she adds. Thomas Chambers, a scientist who also works at the equine center, estimates the direct cost of controlling Australia's equine influenza outbreak to be around \$100 million, which is about \$2,000

for each infected horse. "And the indirect cost to the economy was estimated at \$150 million for the first week alone," he says.

Two of Dwyer's primary responsibilities are equine disease surveillance in Kentucky and the development of animal disaster plans for veterinarians and animal owners. Part of the reason this focus is so important, she says, is that animal disease surveillance is directly tied to human disease surveillance.

Beyond the devastating economic impact, a bigger concern to many of the scientists who monitor and respond to disease outbreaks is emerging diseases that are zoonotic, that leap from animals into humans and succeed there in making trouble. Examples of this animal-to-human contagion are West Nile Virus, *Salmonella* and rabies.

"The risk of human disease is the basis of the avian influenza surveillance program we're conducting," Carter says. "We want to detect diseases such as avian flu in animals as soon as we can—before that disease can begin infecting people."

Why Does Homeland Security Care about These Issues?

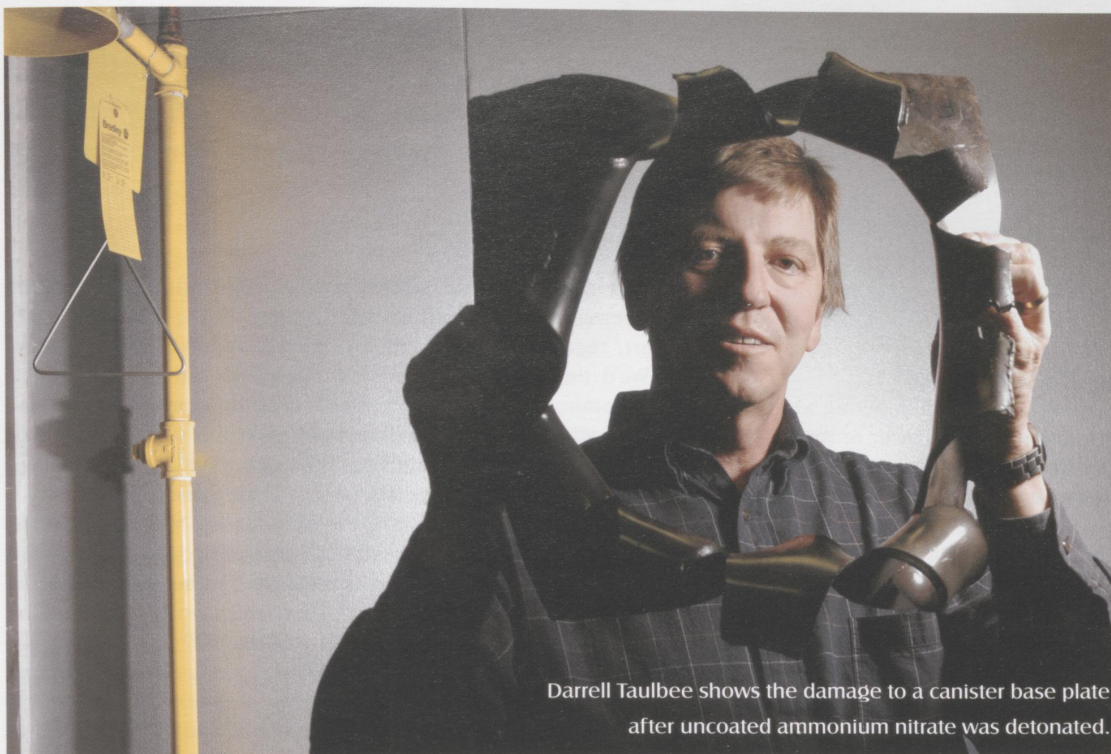
"Homeland Security is interested in our system because they want to preserve what they call the critical infrastructure in the United States," says Carter. "Agriculture is one piece of that critical infrastructure, and a huge part of our economy would crumble if animal agriculture was sabotaged."

And then there is agroterrorism, what keeps researchers who study all the possibilities of an attack on our agricultural industry working in overdrive.

The threat is real. According to a Congressional agroterrorism threats and preparedness report, evidence that agriculture and food in this country are potential al Qaeda targets was uncovered in 2002. Terrorist hideouts in Afghanistan contained agricultural documents and manuals describing ways to make animal and plant poisons.

And it's no secret that agricultural businesses in the United States are soft targets for such plans. Farms are mostly isolated. People can often enter or exit unnoticed. Farms and farmland are usually not guarded. Barns often store chemicals used on crops that could be used with malice elsewhere, such as the ammonium nitrate/fuel mixture Timothy McVeigh used in the Oklahoma City bombing.

"This means that data like that received directly from farmers in the August 2007 pilot project is all the more crucial to keeping Kentucky's animals and agriculture healthy," says Carter, who is now co-writing a grant proposal for a second round of Homeland Security funding. "I feel optimistic about our chances." ■



Darrell Taulbee shows the damage to a canister base plate after uncoated ammonium nitrate was detonated.

by Jeff Worley

On the morning of April 19, 1995, Timothy McVeigh pulled a yellow Ryder rental truck into a parking area outside the Alfred P. Murrah Federal Building in Oklahoma City then casually walked away. A few minutes later, the truck's deadly 4,000-pound cargo blasted the government building with enough force to shatter one third of the seven-story structure to bits. Glass, concrete, and steel rained down. Indiscriminately mixed in the smoldering rubble were adults and children, alive and dead. Gone in one cataclysmic blast were 168 lives. More than 500 others were wounded. Homegrown terrorism had hit.

The explosive McVeigh used was simple ammonium nitrate (AN), packed in 20 plastic barrels and ignited by a slow-burning fuse. AN is commonly used in agriculture as a high-nitrogen fertilizer, but when mixed with hate and fuel oil, it becomes lethal. The same type of home-brewed fertilizer explosive was used in the 1993 bombing of the World Trade Center by Middle Eastern terrorists.

Preventing another Oklahoma City-like blast is exactly what University of Kentucky scientist Darrell Taulbee aims to do through an ongoing research project to create a fer-

tilizer that, if used by terrorists, won't have nearly the explosive impact of AN. And the idea for this project, says Taulbee, who has worked at the Center for Applied Energy Research (CAER) since 1980, was set into motion by the 1995 bombing.

DEFUZZING

TERRORISM

"The night of Oklahoma City, I was coming back from a coal ash meeting in Memphis, watching the coverage of this horrible event on TV in the Atlanta airport," recalls Taulbee, in his deep, mellifluous baritone. "We'd been talking a lot at this meeting about using coal combustion byproducts to alter or remove various materials, so I started thinking about this in connection with defusing the potential explosive power of ammonium nitrate."

But wait. If AN can be an unwitting participant in a bomb blast, why not just ban its use?

Taulbee, who grew up on a farm 20 miles north of Jackson in Eastern Kentucky, explains that there are two possible alternates to AN, both of which have been used with mixed results. Anhydrous ammonia, a compound formed by combining hydrogen and nitrogen, requires more costly equipment to apply and generates toxic fumes. In addition—and this is no small consideration in Kentucky—the compound, unlike AN, is often used in meth labs.

Another alternative to AN is urea, a white crystalline solid produced when anhydrous ammonia chemically reacts with carbon dioxide, is cost competitive with AN but, like anhydrous ammonia, it is susceptible to costly

volatile loss of its nitrogen and its application must be carefully timed during the growing season. Urea can also be used in the manufacture of explosives though not quite as easily as AN. "Ammonium nitrate is the number one choice of farmers overall," Taulbee says. "Our central question from the beginning was, can we keep ammonium nitrate from exploding?"

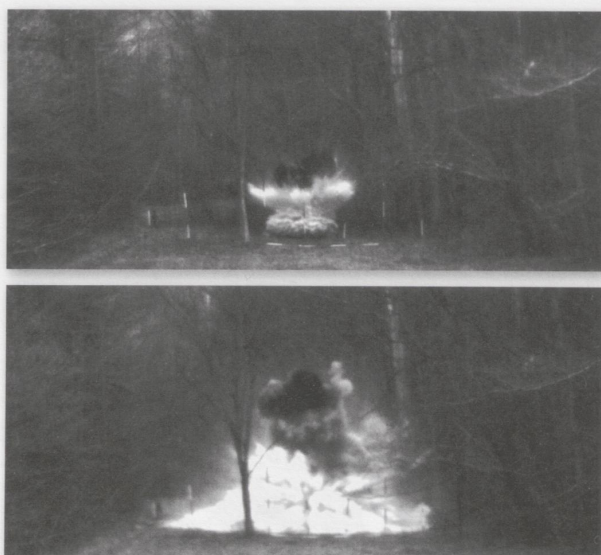
Taulbee's research, initially funded by the Department of Homeland Security, involves blowing up canisters of ammonium nitrate. His field work is focused on carefully tracking the stages of an explosion.

He explains. "When most people think of an explosion, they think it's instantaneous, that it happens all at once, but that's not really true. Explosions happen in stages, or thresholds, one millisecond to the next. Our goal is to drop the energy level so that the explosion won't self-propagate—it will lose its potency. Basically, we want to decrease the energy flux in this chain so that the explosion will extinguish."

Taulbee thought that what might stop this chain reaction is the application of an energy-absorbing, fire-impeding coating to the ammonium nitrate. So he set to work.

Taulbee started with the simplest possible solution, using Kentucky's plentiful supply of byproducts from power plants and other coal-burning utilities, which include fly ash and a lime-based residue produced during the removal of sulfur gases. The coating technique he used is called drum pelletization. Ammonium nitrate particles are put in a five-gallon, steel drum on a roller mill. Cold fly ash is sprayed with a small amount of water, and the drum is rolled rapidly for about five minutes. This gives AN a uniform coating.

To see if this process would lessen the impact of an explosion, Taulbee took this idea to the field or, to put it another way, he took his research back home. "I still have the family farm in Breathitt County, and I also lease about 2,000 acres nearby, which includes an old abandoned log yard. That's where we did most of our tests."



Ammonium nitrate (AN) with a 20 percent coating (top) and uncoated AN (bottom) 10 milliseconds after detonation. Darrell Taulbee found that even a 15 percent coating of fly ash halts the explosion.

“Explosions happen in stages, or thresholds, one millisecond to the next. Our goal is to drop the energy level so that the explosion won’t self-propagate—it will lose its potency.”
—Darrell Taulbee

Working with Tom Thurman, a retired FBI licensed explosions expert and current instructor in Eastern Kentucky University’s College of Law Enforcement, Taulbee added fuel oil to 10-pound charges of AN that had been coated with different concentrations of ash and placed each charge into a steel canister. Thurman then detonated the cylinders with plastic explosives. A high-speed camera recorded the results, and Taulbee was then able to chart the relative effectiveness of the various densities of coating by charting the expansion of the resulting explosion cloud for 10 milliseconds after detonation.

“We wanted to see two things: the difference between the coated samples and the uncoated, and the relative impact of the coating thickness.” Even at a 15 percent coating, the explosion was halted. Predictably, the thicker the coating, the shorter the distance the explosion traveled.

To determine the impact of each blast, Taulbee also noted the relative damage to the cylinder and its square support stand, called a witness plate, which is welded onto the bottom of each cylinder. In his lab in the basement of CAER, he lifts one of these detonated cylinders.

“You can see that the witness plate has been deformed and that the top of the cylinder has been ripped apart pretty well. However, after this one was detonated, some of the AN material spilled out onto the ground, which is exactly what we wanted to see. This means that after detonation, the energy level fell to the point that it could no longer self-sustain. The explosion died.” Taulbee adds that if a McVeigh copycat were to use this coated AN, the explosion would be much less deadly and damaging.

A major challenge in this work is to determine what concentrations of the fly ash coatings are necessary to reduce the power of the explosion while still allowing the AN to be useful as a field fertilizer. After the Oklahoma City bombing, scientists at the National Research Council (NRC) worked to make AN non-explosive not by coating it, but by diluting the ammonium nitrate with various additives, Taulbee believes. (Their tests were not made public, so he’s uncertain exactly how they were conducted.) The NRC concluded that a concentration of around 20 percent was necessary to make AN non-detonable.

“What we found was that a 15 percent coating is effective in stopping the explosion. This is good news,” Taulbee says jubilantly, “because the lower the coating



percentage, the less expensive this will be to manufacture. And in our pilot field tests, we’ve determined that the nitrogen release rate of the coated particles indicates that coated AN appears to be suitable for its intended use as a fertilizer.” He imagines that if such a coating is accepted by farmers, it would simply be an additional step in the established AN manufacturing process.

Taulbee says that this project has attracted national attention. The National Institute for Hometown Security recently awarded continuation funding for the project. “We’ve actually been identified as their top project,” he says. “It’s been showcased in Washington a couple of times, and they’ve fast-tracked our continued work on this.” Thurman and Paul Rydlund, president of El Dorado Chemical, one of two remaining AN manufacturers in the country, make up the research team for the initial project.

In the next few months, Taulbee will work with the Bureau of Alcohol, Tobacco and Firearms, scientists at the New Mexico Institute of Technology, and the FBI at Quantico, Marine Corps headquarters outside of Washington D.C., to get independent confirmation of his detonation results. Closer to home, he’ll also partner with Greg Schwab and John Grove in the UK Department of Plant & Soil Sciences, who will conduct plant growth studies, leaching tests, and soil migration studies to get a more extensive evaluation of the impact of coated AN on agricultural use and the environment.

“If Darrell Taulbee can eliminate much of the ‘McVeigh factor’ in ammonium nitrate, he’ll go a long way in helping contain the threat of these homegrown fertilizer bombs,” says Mike Matthews, one of Taulbee’s main contacts in the Office of Homeland Security.

Braden Lusk is studying the properties of aluminum mesh to lessen the impact of an explosion, work funded by the U.S. Navy.

Making Protective Mesh Stronger

Darrell Taulbee isn't the only University of Kentucky researcher working with high-impact explosives. Braden Lusk has been developing a mining research program at UK focused on the use of explosives, and he admits that this research interest began a long time ago—when he was 10 years old.

"As a kid growing up in Hutchinson, Kansas, I liked to blow up my toys," he says, chuckling at the memory. "I would horde all kinds of fireworks, but I didn't use them on the Fourth of July. I had 'greater uses' for them. My parents had a lot of trouble understanding this hobby," adds Lusk, an assistant professor of mining engineering.

He describes his current research focus as a two-sided coin. "We're looking both at how to make explosives more effective and also how to design materials to lessen the effects of a blast," says Lusk, a robust and effusive man who came to UK from the University of Missouri-Rolla in 2005. His main focus over the last year has been on an aluminum mesh product for blast mitigation. This product development work is being funded for \$433,000 by the U.S. Navy through a company called Innovative Productivity Inc. in Louisville.

Lusk explains that this aluminum mesh could be attached to the windows of buildings near blasting sites, ship holds or as protective layers on mine-resistant, ambush-protected trucks, referred to as MRAPs. Large numbers of MRAPs have been shipped to Iraq. "And it's possible that soldiers in the field could use this mesh for protection," Lusk adds.



And in his work there is a direct tie to the mining industry. Lusk talks about the Sego Mine disaster in January 2006 in Tallmansville, West Virginia, where an explosion trapped 13 miners beneath the surface, leaving only one survivor: "At the heart of that disaster was a seal failure that followed a methane explosion. The seals that failed at Sago had been tested and approved for a methane blast that was much less powerful than the blast that caused them to fail," Lusk explains. "Even before this tragedy happened, there was a big push for the development of more blast-resistant mine seals, and I've thought about this material I'm working on and others like it as a good solution to protect mine seals."

With the help of Kyle Perry, who has a degree in civil engineering (and also happens to be Lusk's brother-in-law), Lusk has been testing the mesh product in the field—an underground quarry in Georgetown, Kentucky. For "donating this space" to his work, he says he's indebted to Frank Hamilton, who owns the property, and his son Richard, both UK alums.

Perry and Lusk set up different thicknesses of mesh around an explosive charge with sensors directly behind the mesh, stand back a safe distance, and then detonate the charge. A sensor, with

no mesh in front of it, collects a reference pressure measurement from each blast to see how much the pressure is reduced with various layers of mesh.

"We're doing some numerical simulations using Autodyn," Lusk explains, "a software program that models blast events, in conjunction with physical testing to validate the mitigating strengths of this mesh." So far the researchers have shot over 150 tests, using a total of around 75 pounds of desensitized RDX, an explosive related to nitroglycerine and used by the military.

In corollary testing, Lusk is simulating blasts using a shock tube, a 120-foot-long reinforced steel tube with a 3/8" steel plate at the end and sensor mounts at different spots along the tube. Using less than a pound of explosives, he can send a shock wave down the tube and collect data that tell him the pressure time history of the wave.

"Field testing involves thousands of pounds of expensive explosives. Using this simulation testing is a lot less expensive and allows us to compare results between the field and tube tests."

After he crunches the data from the tests he's done, Lusk hopes to draw up some guidelines for the use of this mesh, focused on the size and location of the blast. ■

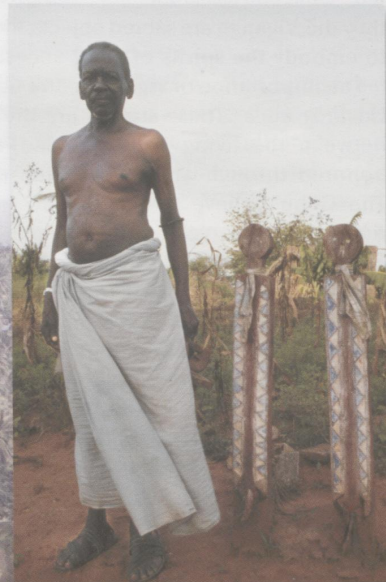
by Jeff Worley

This complex story involves art theft, smuggling, greed, and the curses of African ancestral spirits. And at the center of it all in 1999 was Monica Udvardy, an associate professor of anthropology at UK.

Her journey into the world of the illegal art trade was triggered by a snapshot she had taken 14 years earlier of a memorial statue that belonged to an elderly tribesman named Kalume Mwakiru, a member of an East African group of people in Kenya called the Giriama. Within this group is the all-male Gohu society. "Some men in the society are skilled carvers and are paid to create vigango—memorial statues—for the dead Gohu member," Udvardy explains, whose interest in gender and aging led her to study this group.

The posts, which range from four to nine feet tall, are created from indigenous termite-resistant hardwood. They consist of a circle for the head and rectangle for the body, and vary in decoration. "The key feature of the Gohu society is how they honor their members when

Kalume, photographed by Monica Udvardy in 1985, with his vigango, the memorial statues that represent his two deceased brothers. His vigango were stolen less than month after this photo was taken.



On the Trail of Stolen Statues



they die. Vigango are sacred objects; they are thought to embody the spirits of dead ancestors."

The importance of vigango can't be understated, Udvardy adds. "These statues are the tangible link between the living and the dead, and must be honored through animal sacrifice and libations. The Gohu believe that failure to perform these rituals or, worse yet, removing vigango from their erection sites—an act the Giriama have an explicit prohibition against—will trigger the curse of the ancestral spirit." This curse can take the form of bodily illness or death of the descendants, as well as drought and diseased livestock.

"Vigango are considered *the* art form of East Africa," says Udvardy, who likes to emphasize particularly important points by punctuating the air with a forefinger. "But most Westerners fail to realize these objects are ritual artifacts that are part of a living culture."

And here's where the problem starts. Because of their value to Westerners as art, there's a market for vigango, especially in the United States. These statues are part of a global \$4.5 billion-a-year industry. "Traffic in cultural artifacts is the third-largest illegal industry, after the drug trade and arms smuggling," Udvardy says.

She discovered that Kalume's vigango were among the missing when she visited him again. "Tears were rolling down his cheeks when he told me his vigango had been stolen," Udvardy says, visibly moved by the memory. "He asked me to help him locate them, which I did sporadically whenever I was down on the coast, looking in hotel lobbies and tourist shops, where you sometimes see them. But I never found his statues—until 15 years later."

Serendipity and eureka share a moment

In 1999 Udvardy traveled to Philadelphia to take part in a panel on Mijikenda culture at the African

UK's Monica Udvardy (left), Gohu secret society elders and anthropologist Linda Giles stand in front of the metal enclosure designed to protect the now famous statues from theft.

Studies Association annual conference. "I talked about the Gohu society, and among the images I showed were slides of Kalume with his two statues." It just so happened that fellow anthropologist Linda Giles from Illinois State University was the next presenter. She showed slides of her university museum's large collection of African artifacts, including 38 vigango.

"I yelled, 'Stop! Go back one.' There was one of Kalume's statues!" And in that eureka moment, Udvardy clearly saw her future as a cultural activist. "Linda and I decided right there that we needed to try to repatriate the statue."

Four months later, Udvardy and Giles met up at Illinois State University, where they spent hours pouring over U.S. African Art museum catalogs. And this is where they found Kalume's second stolen statue in the museum collection at Hampton University in Virginia. "This propelled us into a massive search into the extent of vigango theft, and though Linda and I had done research for years, this was foreign territory for us. I was a specialist in gender theory, not stolen cultural property, museums, and international laws prohibiting traffic in stolen property!" The two began a broad-based correspondence with museum curators and directors all over the United States to learn which museums had vigango, how many they had, who had donated them, and when, where and how they were originally collected and brought to the United States.

As energized as Udvardy was to continue to follow these various threads, her research was confined to summers since she usually teaches five courses a year at UK and is director of Undergraduate Studies in anthropology.

The next five summers saw a whirlwind of activity as Udvardy and Giles continued their vigango research in the United States and in Kenya. They wrote formal letters to the two museums that had Kalume's statues, informing the curators about the discovery of the statues and requesting that the museums repatriate them to the Mwakiru family, worked with the National Museums of Kenya to get them actively involved, gave papers at national conferences about the statues, wrote and published

articles in anthropological journals, traveled to museums that had substantial collections of vigango, and interviewed curators and gallery owners about the process of acquisition of the stolen artwork and the desire in the West for African art.

Then during Udvardy's sabbatical in Kenya in 2005 to 2006, the plot of the missing vigango began to heat up.

She went back to Kenya in the winter of 2006 with Giles to locate the family from whom the statues had been stolen. "We found the family and learned that the man who had erected those two statues in 1983—I interviewed him in 1985—Mr. Kalume Mwakiru, had died in 1987," Udvardy recalls. "Now his homestead belonged to one of Kalume's former wives and his nephew Festus William Tinga. We sat down with them and with John Mitsanze, our Kenyan collaborator, who explained that we knew where the statues were. Their jaws literally dropped."

Kalume's widow and Tinga then told the three about all the misfortune that had befallen them since the theft of the vigango. There had been a severe drought in Kenya for several years, which they believed was caused by the loss of the statues, and Kalume's widow attributed the death of her husband to the theft.

"So we asked them if they wanted the statues back, and they said, 'Of course.'"

Udvardy and Giles then compiled a summary of all the misfortunes that Kalume's widow and Tinga attributed to the loss of the statues as the basis for a letter. "Sort of a 'to whom this may concern' kind of appeal," Udvardy says.

The anthropologists included this letter in an up-to-the-minute PowerPoint presentation they gave a few weeks later to the director and staff at the Mombasa branch of the National Museums of Kenya. This group was familiar with Udvardy and Giles's research, so they knew about the continuing problem of the stolen statues. What they didn't know was the extent of the thievery.

"We had documented more than 360 vigango in American museum collections at this point, which both surprised and upset the museum staff. After a heated discussion focused on demanding all of them back, they realized that they didn't have the museum facilities to curate all of these because

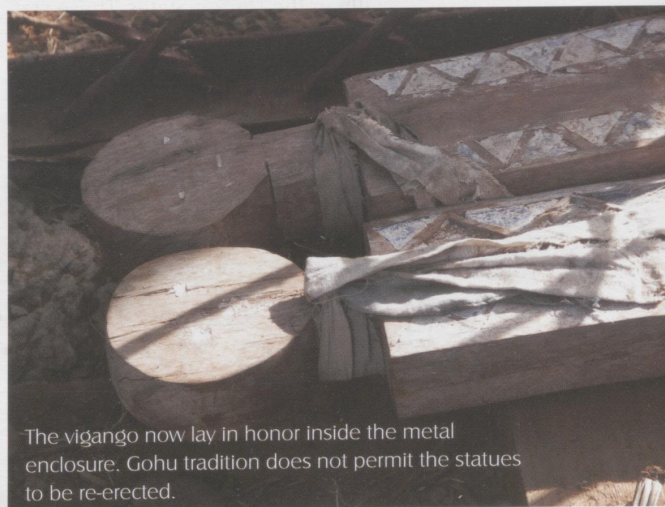
they are so tall and heavy. So instead, they came around to the idea of focusing on the two statues that Linda and I had documented so thoroughly as a way to highlight the theft of cultural property from Africa."

The director of the coastal branches of the National Museums of Kenya, Phillip Jimbi Katana, then wrote letters to the two U.S. museums that had the statues.

Meanwhile, Udvardy and Giles wanted to do what they could to raise public awareness about these art thefts. And as if on some serendipitous cue, Udvardy crossed paths with someone who could do just that.

In their hotel in Mombasa, the researchers met a man named Mike Pflantz, an international newspaper correspondent. He asked them why they were in Mombasa, so they told him their story. Pflantz was intrigued and wrote a piece about this for the *Christian Science Monitor*. The article immediately attracted major international attention.

"This article set off a deluge of interviews," Udvardy says, her voice still registering the surprise of this turn of events in March 2006. Over 30 newspapers covered this story, including *The New York Times*, which gave it two-thirds of a page in their Easter Sunday edition. The BBC and NPR also jumped on the story.



The vigango now lay in honor inside the metal enclosure. Gohu tradition does not permit the statues to be re-erected.



The next major turn of the wheel happened in September when Kenya sent a prestigious delegation to the Illinois State Museum, which had immediately agreed to return the statue after receiving the letter sent from the head of the Mombasa museum. Both Illinois senators sent representatives to this event. "The museum did a terrific job in hosting this event. They built a special crate for the vigango and hosted a daylong series of events for the delegation and for us in Springfield. It was a hugely successful PR event," says Udvardy. This was the first time that a stolen artifact had been returned to Kenya from the United States.

But things, surprisingly, didn't go nearly so well at Hampton University, a historically black university.

"The museum officials there simply refused. Their press release said that they had legally acquired the statue and, therefore, they were not going to return it." But a few weeks after the return event in Springfield, Udvardy says, Hampton University Museum suddenly relented. By February 2007, both vigango were back in Kenya in the custody of the National Museums of Kenya.

The Handover Ceremony

Katana, principal curator of museums, began to make arrangements for what Udvardy calls the "handover" ceremony—the return of the statues to their original site. He drew up a list of regional and national dignitaries to invite to this ceremony and

The men of the tribe dance as part of the handover celebration. The dancers, wearing sashes with mirrors that represent medals, parody marching British soldiers.

returned the statues in a cage-like metal enclosure to help assure their safety.

By now, Udvardy explains, these vigango were famous, and the museum staff wanted to make sure the statues wouldn't be stolen again.

At the June 20 event, framed by coconut palms, baobab trees, and the villagers' mud-walled huts, Udvardy and Giles were welcomed back with open arms. The Kenyan museum board chairman was there. The senior deputy secretary for national heritage was there. The 100 dignitaries who ringed the speaker's platform were a who's who of regional and national politicians and arts administrators.

"The National Museums of Kenya did an incredible job of providing the temporary infrastructure needed for this event, which drew hundreds of people locally," says Udvardy, setting the scene. "They had to bring up a generator from Mombasa to run the microphones, they had to truck in plastic chairs, and they brought their cooks from the museum restaurant. The people from the village had never seen anything like this—they're still reeling from it all."

The ceremony itself included speeches, dance troupe performances and feasting. The keynote speech was given by the minister of Tourism and Wildlife, Morris Dzoro. And Udvardy and Giles were asked to speak to the group, too.

"We wanted to congratulate everybody in the village for their part in this success story—the incredible interest and effort they displayed," Udvardy says, adding that their words were translated by their Kenyan colleague, John Mitsanze, into KiGiriami. "And we stressed the importance of maintaining their local culture."

From the beginning, Udvardy's goal was to raise public awareness about the devastating impact on local communities of the widespread global marketing of the statues, and by anybody's reckoning, she and Giles were hugely successful at doing this. One measure of this success is that other galleries in the United States have begun to follow Udvardy's lead. The owner of the Insiders/Outsiders Art Gallery in Cornwall Bridge, Connecticut, for example, recently returned nine vigango to a museum in Kenya.

What's next?

"I'm working on a book right now," Udvardy says. And I'm also in the beginning stages of putting together a film on this entire adventure." ■

How did this story begin? Visit www.research.uky.edu/odyssey/spring04/africa.

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P a r t i n g S h o t s

"The true mystery of the world is the visible, not the invisible."

—OSCAR WILDE

"We must not allow the clock and the calendar to blind us to the fact that each moment of life is a miracle and mystery."

—H. G. WELLS

"Any genuine philosophy leads to action and from action back again to wonder, to enduring fact of mystery."

—HENRY MILLER

"It began in mystery, and it will end in mystery, but what a savage and beautiful country lies in between."

—DIANE ACKERMAN

"Mystery is underrated, and understanding is overrated."

—LARRY MCMURTRY

"One cannot help but be in awe when he contemplates the mysteries of eternity, of life, of the marvelous structure of reality."

—ALBERT EINSTEIN

"The larger the island of knowledge, the longer the shoreline of mystery."

—MARY B. YATES

"Faith is not the knowledge of what the mystery of the universe is, but the conviction that there is a mystery, and that it is greater than us."

—RABBI DAVID WOLPE

"The mystery of life isn't a problem to solve, but a reality to experience."

—FRANK HERBERT

"The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them."

—SIR WILLIAM BRAGG

"Science cannot solve the ultimate mystery of nature. And that is because we ourselves are a part of the mystery that we are trying to solve."

—MAX PLANCK

"I think one of the most exciting things [about science] is this feeling of mystery, feeling of awe, the feeling of looking at a little live thing and being amazed . . . at how it's emerged through these hundreds of years of evolution."

—JANE GOODALL

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UK anthropologist Monica Udvardy with Kalume Mwakiru's oldest widow and his nephew. Udvardy returned the family's memorial statues in June 2007. These statues were stolen in 1985, likely sold on the black market, and ended up in two U.S. museums.

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