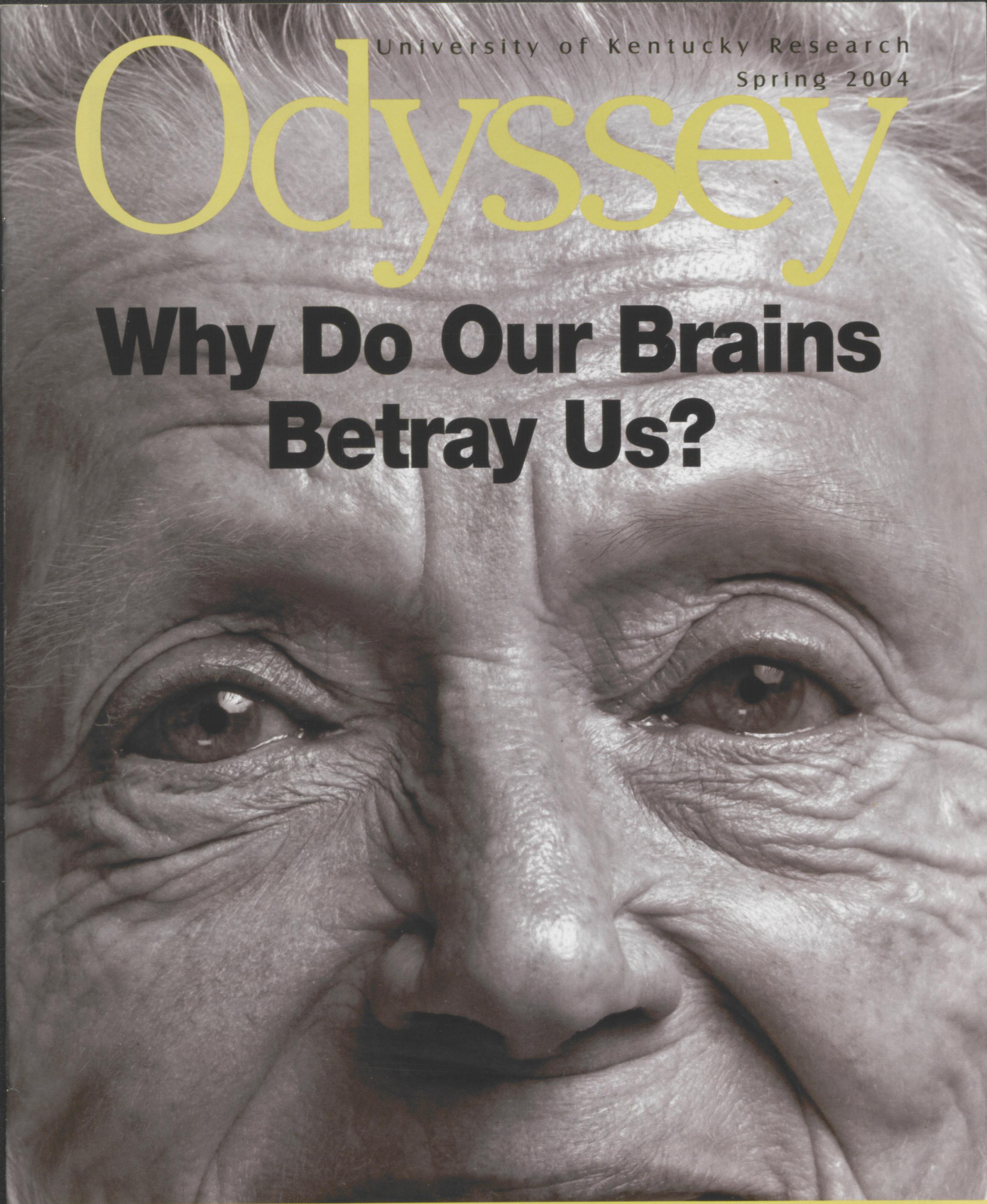




University of Kentucky Research  
Spring 2004

# Odyssey

## **Why Do Our Brains Betray Us?**

**The Fight against  
Alzheimer's Intensifies**

**UK** UNIVERSITY OF KENTUCKY



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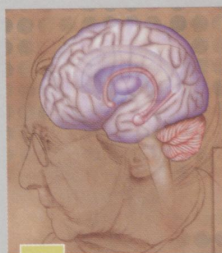
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# University of Kentucky Research Spring 2004 Odyssey



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## Cover Story

### Why Do Our Brains Betray Us?

For over 30 years, UK researchers have been using science to battle Alzheimer's. And the fight has intensified. Current projects explore vitamin E and selenium, incipient Alzheimer's, enzymes A-beta and proteasome, DNA microarray technology, and memantine—the first FDA-approved medication to treat Alzheimer's.

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Correction: In the Fall 2003 Odyssey, we mistakenly referred to Hilary Boone as the late Hilary Boone. We regret the error.





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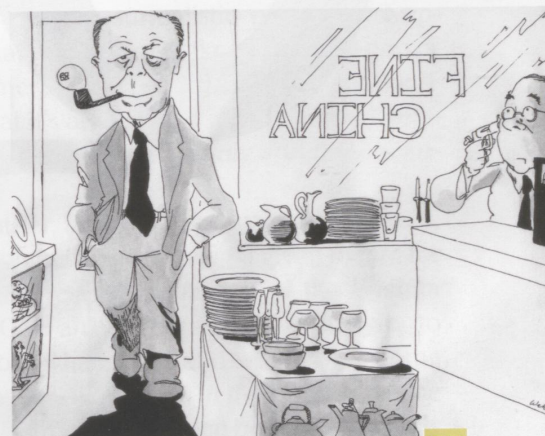
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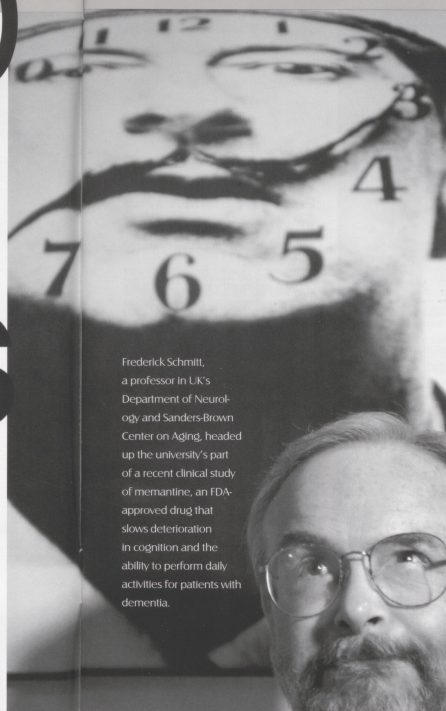
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# Why Do Our Brains Betray Us?

The Fight against Alzheimer's Intensifies

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Frederick Schmitt, a professor in UK's Department of Neurology and Sanders-Brown Center on Aging, headed up the university's part of a recent clinical study of memantine, an FDA-approved drug that slows deterioration in cognition and the ability to perform daily activities for patients with dementia.

WRITTEN BY  
Jeff Worley

**F**rederick Schmitt, a professor of neurology at the University of Kentucky, has two framed photographs on his office walls in UK's Sanders-Brown Center on Aging. One is an M.C. Escher print in which water seems to run uphill, playing tricks on perception; stairways defy spatial sense and lead back only to themselves. Directly across from this, I see the famous Salvadoré Dali self-portrait. Dali's face is a skewed and melting clock, his moustache the two clock-hands.

Both of these surrealist pieces must approximate what it feels like to be in the grip of Alzheimer's disease. The world is suddenly not what it's always been. Time warps. Everyday objects are otherworldly and disconcerting.

My father, late in second-stage Alzheimer's, would pick up a paperweight given to him for his many years as president of the Wichita Stamp Club and turn it over and over, trying to figure out what it was and what it was doing there on his nightstand. In the small house he shared with my mother, he began to regularly see his mother, dead 30 years, drifting through the hallways at night.

By now, almost everyone reading these words has lost a grandfather, a grandmother, a father, a mother, a sibling, or friend to the all-demanding claims of Alzheimer's.

As the baby boomers have aged, the number of people in this country with Alzheimer's disease and related disorders has grown. Newly published research suggests that 4.5 million Americans now have Alzheimer's and that the numbers will swell to as many as 16 million by mid-century unless a cure is found.

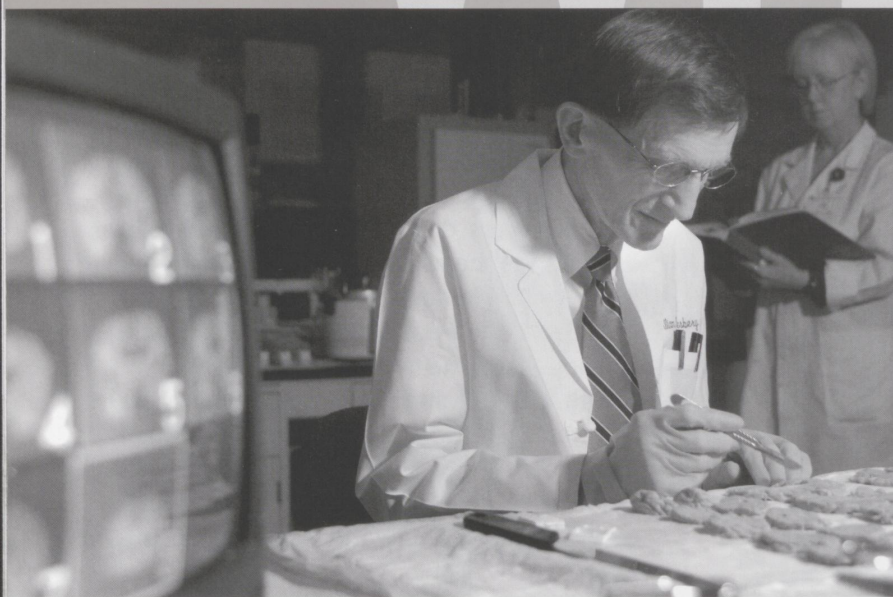
Here are a couple of other facts about Alzheimer's. The disease now strikes more

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# Why

William Markesbery, with help from Ann Tudor in the Sanders-Brown Center on Aging, examines brain tissue from a patient with probable Alzheimer's disease. Markesbery has been researching the causes of dementia for over 30 years at UK.



## Can a Combination of Vitamin E and Selenium Prevent Alzheimer's?

William Markesbery, the University of Kentucky's patriarch of Alzheimer's disease research and director of the UK Alzheimer's Disease Research Center (ADRC), believes the key to Alzheimer's disease is prevention. He also believes that vitamin E is an important part of this key. And though he is an uncommonly soft-spoken man, he wants his E-message to get out loud and clear.

"So far, vitamin E has emerged as one of the weapons we have against dementia," Markesbery says from his office in the Sanders-Brown Center on Aging, where he has served as director since 1979. "There are several other things you can do to lower your risk of getting Alzheimer's, but vitamin E taken in conjunction with vitamin C is important—a previous study showed that vitamin E is one factor that slows, slightly, the progression of the disease. The important thing for individuals at risk is to take vitamin E and vitamin C along with folic acid prior to getting the disease."

So what are these risk factors?

A major factor is age: The risk of developing Alzheimer's increases with age. One out of every 10 persons 65 years and older is a victim of Alzheimer's disease, although some victims may be in their 40s and 50s. Approximately 20

than one in 30 Americans, slowly causing memory loss, confusion, and, ultimately, death. Incidence increases with age—about half the population that lives past 85 gets Alzheimer's. And the disease is the third most costly in the United States, each year draining \$100 billion from the U.S. economy.

How and why do we get Alzheimer's disease? Why do our brains betray us?

For over 30 years the University of Kentucky Sanders-Brown Center on Aging has been working to understand the mechanisms of Alzheimer's, always with an eye toward prevention. Dozens of projects carried out through the Alzheimer's Disease Research Center have made important inroads to our understanding of the disease—who gets Alzheimer's and why—and research in 2004 continues at a vigorous pace.

The projects discussed in the following pages are all concerned with a common goal: prevention and—in the longer run with the pooled knowledge of researchers worldwide—cure of this devastating and dehumanizing disease.



**"You just can't overstate the importance of prevention. Alzheimer's disease starts many years before it ever shows up clinically." —William Markesbery**

percent of Americans between the ages of 75 and 84, and almost half of those 85 years and older suffer from Alzheimer's disease.

Other risk factors under study are traumatic head injury, low education attainment, early low linguistic skills, high-fat and high-caloric intake, and genetics. What scientists are now calling "incipient" Alzheimer's—the earliest onset of the disease regardless of age—has been clearly shown to be genetic in origin. Three genes, Markesbery explains, account for less than 2 percent of cases of those with early-onset Alzheimer's disease.

People in all of these at-risk categories may benefit from a study Markesbery is currently heading up. Funded by a \$5 million grant from the National Institute on Aging, the study will pair vitamin E with selenium, an essential trace element found in all cells and tissues in the body. Selenium is found in water and food—seafood, meats and Brazil nuts, for example. Vitamin E is found in a wide range of foods, especially vegetables, vegetable oils, nuts, and egg yolks.

There is prior evidence that enhanced levels of selenium in the brain might increase antioxidant defense mechanisms against Alzheimer's disease. Taken together, Markesbery says, these two natural antioxidant supplements might work better than alone in fighting

oxidative stress.

"What is oxidative stress?" Markesbery asks rhetorically. "Well, we obviously need oxygen to live, but the reactions that oxygen undergoes in the body have to be carefully controlled or else your body begins to produce oxygen radicals that damage lipids, proteins and DNA in cells, especially neurons."

This current project, which is called PREADVICE (Prevention of Alzheimer's Disease by Vitamin E and Selenium), will link up with SELECT (Selenium and Vitamin E Cancer Prevention Trial), a large National Cancer Institute-sponsored study looking at the effects of these two substances in preventing prostate cancer.

The five-year PREADVICE study will examine a subgroup of about 10,000 of the more than 32,000 men being recruited nationally for SELECT.

"Like prostate cancer, Alzheimer's disease usually occurs later in life, so this study presents a unique opportunity to assess the impact of selenium and vitamin E on the beginnings of dementia," Markesbery says.

So far, more than 400 locations in the United States, Canada and Puerto Rico have enrolled men in SELECT. Study investigators hope to recruit all the participants during the first five years of the trial, so each man can be followed for at least seven years. Five study sites are

located in Kentucky, including Central Baptist Hospital in Lexington and the UK Markey Cancer Center.

Men may qualify to participate in this study if they are age 62 or older (60 or older if of Hispanic or African origin) and in general good health. Participants must also have no history of diagnosed dementia and no major head injury in the last two years.

"Prospective participants take a mental status examination, and they have to score in the normal range on that," Markesbery explains. "And there's an intake assessment where they're asked a lot of questions, especially about their family history." Participants are then placed randomly into one of four groups: They get either vitamin E or selenium, vitamin E and selenium, or a placebo.

"We're in the very early stages of this 12-year-long trial," says Markesbery, "and the key right now is active recruiting. Obviously the assessment of all the data we get won't occur for some time, but we will get updates along the way on how we're doing."

The PREADVICE study is one example, he says, of how basic laboratory data from many Sanders-Brown studies is being translated to preventive studies in Alzheimer's disease. "You just can't overstate the importance of prevention. This disease starts many years before it ever shows up clinically."



# Do



Stephen Scheff, a professor of anatomy and neurobiology at UK, is focusing his work on mild cognitive impairment, the earliest phase of memory decline.

## A New Focus on “Mild Cognitive Impairment”

Detection of the earliest phase of memory decline has become so important that there is now a term used to describe this fairly new research focus: mild cognitive impairment, or MCI.

“This phase is marked by memory complaints that become more pronounced as time goes by,” says Stephen Scheff, a professor of anatomy and neurobiology at the Sanders-Brown Center on Aging. Several Sanders-Brown researchers, Scheff among them, are now working to better understand MCI, work that is made possible by the UK ADRC and its control group of volunteers. These participants, many of whom are spouses or relatives of an Alzheimer’s victim, are neurologically normal and in the interest of science have volunteered to be research subjects. The control group is headed up by David Wekstein, associate director of Sanders-Brown.

In this group of over 400 people, about half are at high risk of developing Alzheimer’s because of their family history—about 30 to 40 percent of cases are thought to be hereditary, according to Markesbery. All of these subjects have agreed to donate their brains after they die (see sidebar on p. 9).

“These participants undergo extensive cognitive testing and represent a



**"The best way to keep your synapses functioning normally is to keep your brain very active—what I call 'low-impact mental aerobics.' In the shower, say your ABCs backwards or do a math problem.**

**Learn a foreign language. Learn to play a musical instrument. And keep as physically healthy as you can." —Stephen Scheff**

unique resource for research into the relation between neuropathologic changes and cognitive performance in aging," Scheff says. He adds that participants in the control group who show significant cognitive changes or who develop dementia continue to be actively followed by the ADRC.

"By studying this normal group of volunteers, we're getting closer to being able to detect the earliest possible onset of the disease, and we believe that with early preventive treatment, we can slow the progression of the disease," he says.

Scheff is among the vanguard of researchers in the country involved in this relatively new NIH initiative. "We can learn a lot from looking at end-stage Alzheimer's, but the focus has shifted somewhat to trying to understand what happens in early stages of the disease." Working with Scheff at Sanders-Brown are Frederick Schmitt and Doug Price, who Scheff characterizes as "an indispensable research tech" who has been with him for 17 years.

Some of these control subjects will begin to show some declines in cognitive ability. "Typically, these are individuals who function normally all day long," Scheff says, "but have a memory problem in one particular area. It's a small loss of memory that might manifest itself in, for example, delayed recall, and we can test this." A standard

way to measure possible memory loss is to give the patient a list of words and ask him, five or 10 minutes later, to recall the list. People with MCI show a deficit in delayed recall, Scheff says, and some researchers believe this might be the beginning of Alzheimer's disease.

In addition to talking to people in the control group who report possible slight memory loss, Scheff also gathers neurological evidence of MCI. An expert in brain anatomy, he has performed brain autopsies for the past 16 years at Sanders-Brown.

"I'm a neuroanatomist," Scheff says. "I've been teaching brain anatomy in the College of Medicine here for over 23 years." He is part of the UK autopsy team, which also includes Markesbery, who collect particular pieces of tissue that researchers need to analyze. These tissues are used by UK researchers as well as scientists at other institutions around the country. "We're a brain bank," Scheff says. "We store lots of tissue, and we share it with other ADRCs doing excellent research since we're all working to solve the Alzheimer's puzzle."

Some of the brain tissue Scheff studies comes from people in the control group who have been followed by Sanders-Brown researchers for as long as 10 years. "We go back and review the clinical charts and then combine this data

with what we see in their brain tissue. We can then determine whether or not the person had MCI."

Scheff closely studies the brains of those who are determined to have had MCI at the time of death, focusing on what he calls "synaptic connectivity."

"You are born with essentially all the neurons you're ever going to have. What develops is the connectivity, through synapses, between different portions of the brain. You have trillions of synapses, and you lose and regain them every day—your brain is constantly remodeling as you learn new things," Scheff explains.

Early on in this work, he focused on several areas in the cortex, association areas that, like tiny assembly plants, put together a lot of information. These areas are where higher-order learning takes place, Scheff says, and Alzheimer's disease especially likes to attack these parts of the cortex.

Using stereology, a mathematical way to estimate the total number of objects using a 3-D model, Scheff can determine the number of synapses in these association areas. "What we've found is that in Alzheimer's disease there is a significant loss of synapses, and the Alzheimer's brain doesn't seem to be capable of replacing these lost connections." Scheff, with several colleagues at Sanders-Brown, has published papers extensively on this work.



# Our

More recently, he has focused on another area of the brain—the hippocampus. This is the curved, elongated ridge of brain tissue located behind the ear that has long been thought of as critical for memory.

"This is the area of the brain used for learning and memory, and it's been in the popular press a lot lately. We've gotten tissue from people in the control group who have died, and some of these individuals were tagged as having mild cognitive impairment. In analyzing their brain tissue, we've found that people with MCI tend to have a significant loss of synapses in the hippocampus."

Being able now to count and measure synapse loss is an important step to understanding the mechanisms of Alzheimer's, but even more important, Scheff says, is to learn why this degradation happens.

"We've been dealing with this research challenge head-on for years here at UK," Scheff says. "We've looked at all kinds of toxins as well as free-radical activity. And a part of my work is to see

if there is a relationship between the levels of free radicals and changes in number of synapses.

Echoing Markesbery, Scheff says that prevention remains the key. What can you do to keep synapse activity normal and strong?

"Even though it's true that the highest risk factor for getting Alzheimer's is aging, we've found that if you are well educated and you take care of yourself, even people in their late 80s and 90s don't show the loss of synapses and, therefore, don't necessarily get Alzheimer's," Scheff says. "Everybody used to think that if you live long enough, you're going to get Alzheimer's. We don't believe that anymore.

"The best way to keep your synapses functioning normally is to keep your brain very active—what I call 'low-impact mental aerobics.' In the shower, say your ABCs backwards or do a math problem. Learn a foreign language. Learn to play a musical instrument. And keep as physically healthy as you can."

## How Do Enzymes Fit into the Alzheimer's Puzzle?

While Scheff is busy studying synaptic connectivity, Louis Hersh is working to better understand another kind of connection: enzyme activity and amyloid beta (A-beta) protein deposits in the brain. In dozens of projects both outside and inside of a living organism, scientists in the past 20 years have found that A-beta protein deposits are a major component of senile plaques in Alzheimer's-diseased brains. These plaques and neurofibrillary tangles (shriveled strands resembling bundles of straw inside damaged neurons) are strong signatures of the disease. Recent data suggests that the A-beta protein may also be toxic to cells before it forms deposits.

So how do you stop A-beta deposits from forming?

Hersh, professor and chairman of the Department of Biochemistry in UK's College of Medicine, believes that two enzymes—neprilysin and insulinisin—might help do exactly that. "These two enzymes have received the most attention as A-beta-clearing proteins," he says.

Like firefighters off at the alarm bell, enzymes marshal their forces when the call comes. Their job is to move to the scene of action as quickly as possible to





### The BRAiNS Program

David Wekstein can't ever count on a good night's sleep.

"My phone might ring at midnight, at 3 a.m., anytime really. And I have to be ready, along with other researchers here in the ADRC (Alzheimer's Disease Research Center), to get moving,"

says Wekstein, associate director of UK's ADRC and Sanders-Brown Center on Aging.

The most recent caller was a close friend of someone in the BRAiNS (Biologically Resilient Adults in Neurological Studies) program who had just died. Within an hour of the call, the body was on its way to the University of Kentucky, where researchers immediately performed an autopsy. Both the caller and his friend were part of a group of older Lexington-Fayette County residents who have agreed to donate their brains after they die to help researchers learn more about Alzheimer's disease.

Most agree to participate in the control group because they have personal knowledge of Alzheimer's. They've lost a relative or a friend to the disease, which afflicts an estimated 4.5 million people in the United States over the age of 65, including an estimated 60,000 Kentuckians.

Jim Geddes, a UK associate professor of anatomy and neurobiology, says that because the brain deteriorates so quickly after death, it's vital that an autopsy be performed as soon as possible. "The support of family and friends has been tremendous. We are often able to do an autopsy within three hours of death," Geddes says. "This does mean coming in at all hours of the night sometimes, but luckily we have a dedicated group of neuropathologists and researchers who do that."

Since it opened its doors in 1985, UK's ADRC has diagnosed and followed hundreds of older people with non-treatable memory disorders—mostly Alzheimer's disease. Wekstein has directed the BRAiNS program since its beginning in 1989.

But studying the brains of Alzheimer's patients alone is not enough, Wekstein says. "We can study Alzheimer's brains for the next 20 years, but if we don't study brains of people who don't have the disease, we can't draw valid conclusions." This is why in 1989 he began recruiting people for a control group. To date the center has recruited over 700 normal older persons, many of whom are at high risk of developing Alzheimer's disease because of their family history and other reasons. All of these subjects have agreed to donate their brains at their death.

"The Sanders-Brown brain bank is one of the most respected and highly regarded in the country," says UK pharmacologist Eric Blalock, whose research is based on brain samples he receives from the ADRC. "Very few Alzheimer's disease research centers have the kind of rapid-response team we have."

For additional information on BRAiNS, contact Wekstein at 859/323-6040 or at [dwekste@email.uky.edu](mailto:dwekste@email.uky.edu).

start chemical reactions the body needs to stay in balance and keep going. Enzymes are enablers.

The most recent and compelling evidence that neprilysin is an A-beta regulator comes from research with "knockout" mice, who have had this enzyme removed. "In these mice, A-beta peptide levels go up," says Hersh, who has studied neprilysin for over 25 years through a variety of projects. "We take this as evidence that neprilysin normally breaks down these A-beta peptides, and when the enzyme isn't there or decreases in amount, the A-beta levels go up, and that's not good." He adds that although mice don't naturally make amyloid deposits as the human brain does (which is probably why mice don't get Alzheimer's), many of the same enzymes, such as neprilysin, are present in both mice and humans.

Insulysin has also shown itself in the past few years to be a mighty A-beta regulator, so Hersh's lab has turned its attention to this first cousin of neprilysin (both have a metal ion and contain some zinc).

"Enzymes work on and break down small molecules, and whatever an enzyme goes to work on is called its substrate," Hersh explains. "For example, digestive enzymes work on many substrates—think about the variety of food you eat in one day." The A-beta

*continued on p. 10*



Louis Hersh in UK's College of Medicine is focusing his work on two enzymes—neprilysin and insulysin—that team up to clear away dangerous amyloid beta deposits in the brain.

# Brains



peptide, it turns out, is a substrate for insulysin, so insulysin and neprilysin have a common enemy.

One very important recent finding in Hersh's lab is that these two enzymes work to stop A-beta in different but complementary ways.

"The reason neprilysin has been so widely studied is because it's one of the few enzymes that work on the surface of the cell, on the cell membrane. A-beta peptides are secreted from the cell. So neprilysin can go to work on A-beta as it's being secreted or as it's beginning to travel into extra-cellular space." Insulysin, on the other hand, works inside the cell, so there's a sort of tag-team approach to stopping A-beta in its tracks.

It used to be thought, Hersh says, that as we age we overproduce A-beta, that it overwhelms the cell. There is evidence now to the contrary.

"We're starting to believe that rather

than an overproduction, what's happening is an 'under-clearance,'" says Hersh. "The activity of the enforcer enzymes is somehow lessened, which allows the damaging effects of A-beta to go relatively unchecked."

This realization has moved Hersh's work into a new direction, he says. With continued funding through the Alzheimer's Association and the National Institute of Aging, he's looking now at various ways to increase the activity in the brain of these two key enzymes.

"We've never lost sight of the potential clinical applications of what we're doing," Hersh says. "We're looking at a number of approaches to utilize these enzymes to break down A-beta both in the brain and elsewhere in the body. We're just starting work with a biotech company to screen chemical libraries to see if we can find drugs that will activate insulysin. That's what I'm most

excited about right now." Hersh hopes this research will lead to clinical trials in about five years.

**Jeffrey Keller** never thought his years of research training would lead to an intense study of garbage, but, he says, that's just what's happened.

"Cells, like people, generate garbage, and all cells have to remove it. In order to keep this clutter at a non-dangerous level, cells rely on one particular intracellular enzyme, called the proteasome," explains Keller, a UK assistant professor of anatomy and neurobiology whose research at Sanders-Brown is focused on understanding the work of this essential enzyme. Think of proteasome as the cell's chief garbage collector.

The garbage under scrutiny is mainly oxidized or mis-folded proteins, and since accumulations of this substance have been implicated in Alzheimer's disease, Huntington's disease and stroke, Keller's research might help provide important clues to the etiology of these diseases.

Scientists think they have a handle on what the enzyme generally does but very little is known about the exact expression of proteasome activity in the normal and diseased brain, and even less is known about the possible role of proteasome inhibition in cell death, says Keller, who spent one year



as a postdoc at Sanders-Brown after earning his doctorate here in molecular and cellular biology in 1998.

"Our lab is trying to understand exactly what the garbage disposal in the brain looks like when it's operating normally and what it looks like when it goes bad. In addition, we're interested in understanding what causes it to stop functioning normally as we age, or in age-related disease."

In his studies Keller uses basic molecular techniques, called the reverse transcriptase polymerase chain reaction (or RT PCR), in cellular, animal and human tissue.

"Using RT PCR, we are able to visualize or quantify the expression of individual proteasome subunits," Keller says. "This is a common way of investigating gene expression. When we couple this with our ability to isolate and purify the proteasome enzyme, we have very powerful techniques for exploring the proteasome in aging and age-related disease."

In this work, he and his co-investigators are utilizing yeast, which, he says, looks a lot like human brain tissue. "Remarkably, the pattern of proteasome expression and the process of oxidative stress are similar in yeast and human tissue. The advantage of using yeast lies in the power of genetics—we can rapidly and directly test the role of specific genes in regulating the proteasome

**"Our lab is trying to understand exactly what the garbage disposal in the brain looks like when it's operating normally and what it looks like when it goes bad. We're also interested in understanding what causes it to stop functioning normally as we age."**

**—Jeffrey Keller**

and its toxicity in a matter of days instead of months. We can then apply this knowledge to the animal models of disease, and even the actual tissue from human disease."

Keller admits that this approach is extremely challenging, not because of their methodology but because of what he calls "the numbers game."

"Proteasome is so complex. At its heart, it's a structure made up of 28 different proteins. There are at least 82 additional proteins that can combine in different ways to comprise this 28-protein complex. Every cell has a smorgasbord of choices to assemble its garbage disposal." The bottom-line goal of this work, he says, is to differentiate the changes that occur with normal aging from the changes that occur with Alzheimer's disease.

Keller says his lab is making good progress in "getting proteasome to give up its secrets," and that any success is due to the various collaborations in the Center on Aging: Allan Butterfield (chemistry and Center of Membrane Sciences), Harry Levine (Center on Aging), Rodney Guttman (gerontology Ph.D. program), and Jim Geddes (anatomy and neurobiology). "They're experts in different areas of neuroscience, and we are able to apply their skills to our project. And of course Dr. Markesbery, who's at the center of all of the work we do here," Keller adds.

Keller is at the halfway point in this work, which is being supported by the National Institute of Aging for \$1 million for four years and by other grants from the National Institutes of Health and private foundations.



**"The most important thing to come out of our recent work is that we have identified hundreds of genes that correlated with the early phase of Alzheimer's. Then we were able to assign identified genes to biological process categories to get an idea of which cellular pathways were being turned on."**

**—Philip Landfield**

### **Microarrays: Chipping Away at the Mysteries of Alzheimer's Disease**

Genes, like enzymes, are also role-players, and molecular biologists continue to spend long hours in the lab working to shed light on these various roles. Traditional methods in molecular biology generally work on a tedious one-gene-in-one-experiment basis, which does not allow for a whole picture of gene function. However, advances in technology are now paving the way for biologists to study genes on a much larger scale.

"In the past several years a new technology, called DNA microarray, has revolutionized how we do gene research," says Philip Landfield, professor and chairman of the Department of Molecular and Biomedical Pharmacology in the UK College of Medicine. An array, he explains, is an orderly arrangement of gene probes on a small chip. "What this new technology allows us to do is measure 20,000 genes simultaneously and to look at entire genetic pathways," he says.

This work starts with what looks like, but isn't, a simple chip. DNA chips such as the human one used in Landfield's current study, which is focused on better understanding incipient Alzheimer's disease, are fabricated using a process called photolithography (the same tech-

nology used in the manufacture of high-performance computer chips like Intel Pentium processors).

In Landfield's project, human brain tissue from UK's ADRC was used to analyze gene activity based on chips made by Affymetrix, a Santa Clara-based company. The UK group analyzed the chips in the university's MicroArray Core Facility, which houses complete gene chip instrumentation. Kuey-Chu Chen, a member of the team involved in this study, directs this facility.

To understand how each of these genes is detected on the chip, we have to dust off some basic terminology from Genetics 101.

Information about protein structure that is encoded into DNA is transcribed into complementary (closely related) RNA structure. These RNA transcripts convey this key information from the nucleus to protein-production sites (ribosomes) in other parts of the cell. This RNA becomes a sort of messenger, and is aptly called messenger RNA (mRNA).

These mRNA molecules bind naturally and specifically to their complementary DNA templates, like a key in a lock. A microarray works by exploiting this union. The probes on the surface of the chip act like a field of thousands of keys, all waiting for the unique locks for which they were specifically made. When a key fits in a lock, binding occurs, and it can be detected using laser

scanning technology.

"When a laser is focused on a highly bound region of the chip, it shines more brightly than on an unbound region, so by measuring the light intensity, we can quantify the amount of binding and, therefore, the amount of mRNA in the tissue," Landfield explains. In this way, the researchers can determine which genes are turned on and to what degree.

"By using an array containing many complementary probes to which a subject's tissue is added," Landfield says, "we can determine in a single experiment the expression levels of thousands of genes."

"This is the wonderful thing about microarrays," he adds. "They provide us new ways of dealing with complexity because they allow overviews of the simultaneous activity of multiple cellular pathways."

**Recently**, Landfield's group has used this technology to better understand incipient Alzheimer's. "Incipient" means the very beginning of the disease regardless of age," Landfield explains. "This earlier time point is extremely vital to study."

And this is where microarrays come in. This technology recently allowed Landfield and his team to analyze the simultaneous activity of multiple cellular pathways in the hippocampus of 31



Utilizing a new technology called DNA microarray, Philip Landfield (left) and his team, which includes Kuey-Chu Chen and Eric Blalock, in the UK College of Medicine are analyzing thousands of genes and genetic pathways to better understand "incipient" Alzheimer's—the earliest stage of the disease.

# Us?

brain samples—22 Alzheimer's subjects of varying severity and nine "controls." All of these brain samples were obtained through the ADRC's BRAiNS program (see sidebar on p. 9).

An article on this work by lead author Eric Blalock (pharmacology) appeared last month in *Proceedings of the National Academy of Science*. In what co-author Landfield calls "a welcome comment" on this article, one reviewer said, "the UK group has convincingly shown us a new model, in what is the largest and best microarray study of Alzheimer's disease; the idea of correlating gene expression with pathology is unprecedented in this kind of study." Article co-authors included Landfield, Jim Geddes (Spinal Cord and Brain Injury Research Center), Chen (pharmacology), Nada Porter (pharmacology), and Markesbery.

Two basic indicators of Alzheimer's disease were initially examined in this study: neurofibrillary tangles (NFTs) in the hippocampus and scores on the standard MiniMental Status Examination (MMSE). All of the brain samples had previously been characterized by Markesbery, Geddes and other collaborators, who routinely do brain autopsies at Sanders-Brown, to determine brain pathology. NFT density was given a "score" in order to quantify the amount and type of brain deterioration.

Second, each subject's record on the



MMSE was examined and used as a cognitive marker of decline. This test represents a brief, standardized method by which to "grade" cognitive mental status. It assesses orientation, attention, immediate and short-term recall, language, and the ability to follow simple verbal and written commands. It also provides a total score that places the individual on a scale of cognitive function. The researchers therefore had two ways to quantify the severity of Alzheimer's-related dysfunction in each subject: mental decline as measured with the MMSE and pathological changes in the brain as measured by NFT.

"The reason we took this strategy instead of initially putting the known Alzheimer's subjects into groups (incipient, moderate or severe) versus the control group is—and I can't emphasize this enough—it's hard to tell when someone has incipient Alzheimer's,"

Landfield says. "It's very easily confused with normal aging."

So the researchers ignored whatever diagnosis the subject might have had and, instead, used a statistical correlation strategy to define what "incipient" meant. "We correlated each gene with how many NFTs there were, and we did the same for the cognitive scores," says Blalock, who did the number crunching in the office next to Landfield's. "We subsequently identified thousands of genes that correlated with one or the other marker in all 31 subjects."

"But the most important thing to come out of this is that we also identified hundreds of genes that correlated with the early phase of Alzheimer's," Landfield says. "We were then able to assign identified genes to biological process categories to get an idea of which cellular pathways were being turned on." One important discovery the group made was that incipient



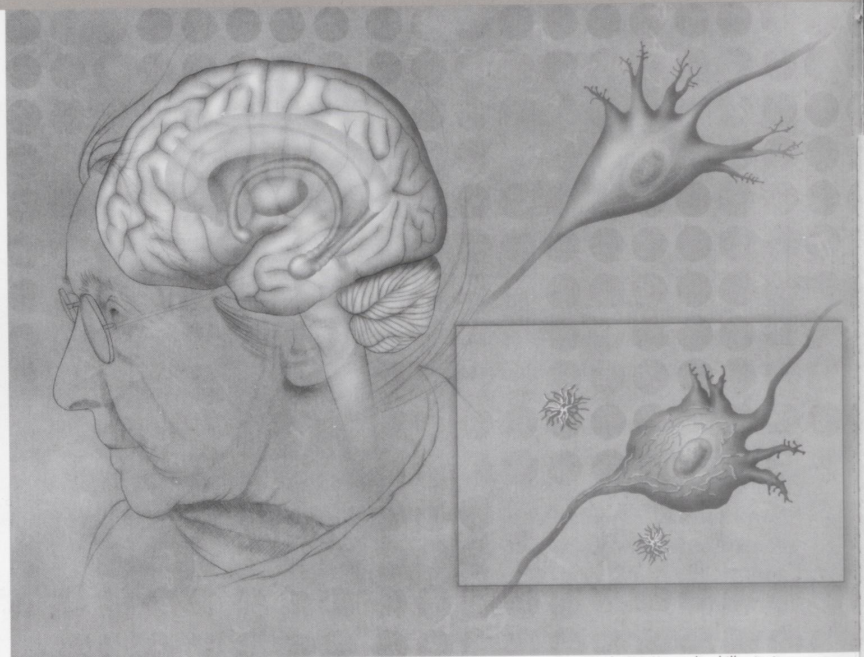
Alzheimer's is what Landfield calls "a genomically orchestrated phenomenon."

"Researchers knew some genes were turned on or off, but this is the first study to find hundreds of these genes that correlated with incipient Alzheimer's."

"We've now defined pathways that are activated or repressed, and this knowledge can become a tool to diagnose—and predict—who's going to develop incipient Alzheimer's disease," Blalock says. Landfield emphasizes the fact that in order to make such a diagnosis, scientists wouldn't need much tissue. "Brain biopsy is a possibility," he says. "It's done in some brain cancer patients."

"Another possibility," Blalock says, "is a blood test. White blood cells and specialized brain cells called microglia have a lot in common. Certainly some of the signals that we are measuring in our study could have originated from microglia. If these signaling pathways are activated in parallel in the brain and blood of Alzheimer's patients, then a diagnosis could be made using microarray-based blood tests."

"Of particular importance, these genes and genetic pathways can now become targets for new drugs," Landfield adds. "We hope that, by using these kinds of genetic markers and patterns, it'll become much easier for pharmaceutical researchers to develop these drugs."



A healthy neuron (top right) contrasted with a damaged neuron (note its shriveled state and the presence around the nucleus of neurofibrillary tangles)

Tom Dolan, UK medical illustrator

"The ultimate goal," says Landfield, "is to intervene earlier so that we can slow the progression of this terrible disease, or possibly stop it in its tracks."

### Now on the Market: The First Drug Shown to Slow Alzheimer's

A new drug on the market may be excellent news for people with mild to severe Alzheimer's disease and their families, says Frederick Schmitt, a professor with the UK Department of Neurology and Sanders-Brown Center on Aging. The drug, memantine (brand name Namenda™), is the first medication approved in the United States to treat moderate to severe Alzheimer's disease. Namenda™ was given the FDA stamp of approval last October and has been available by prescription since

January.

Schmitt and Wes Ashford (now at Stanford University), working through Sanders-Brown and the ADRC, headed up UK's part of a large, multi-center clinical study of memantine, which was shown to suppress the activity of a key brain chemical involved in mental deterioration. The results of the study, which was funded by the drug's German manufacturer, Merz Pharmaceuticals, and the National Institute of Aging, were published in *The New England Journal of Medicine* in April 2003.

The study involved 32 medical centers nationwide and enrolled 252 patients who lived independently. All had difficulty with daily activities, but could still speak and walk. During the 28-week study, patients received either memantine or a placebo twice a day. Neither the patients nor their physicians



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**Memantine (Namenda™) is  
the first medication approved  
in the United States to treat moderate  
to severe Alzheimer's disease. Namenda™  
was given the FDA stamp of approval  
last October and has been available  
by prescription since January.**

knew which pill they received. Behavioral, cognitive and functional tests were used to evaluate patients throughout the study.

Overall, the study found that the patients who were taking memantine showed significantly less deterioration in cognition and ability to perform daily life activities.

"These patients seem to be declining much less, about half as much as ordinarily expected, over a six-month period," says Barry Reisberg, a professor of psychiatry at New York University School of Medicine, who led the study. "This medication will slow down the otherwise inexorable progress of this disease, and it is remarkably free of side effects." A few patients did report dizziness, confusion, headache, and constipation.

"Although this drug stabilizes and slows progression, brain cells are still dying," Schmitt says. "However, memantine may result in delaying nursing home placement by six months to a year or longer. We now are looking at this drug for early Alzheimer's disease." Studies led by Schmitt and Greg Co-

per (UK neurology, Sanders-Brown Center on Aging, and Lexington Clinic) are now under way to determine whether this drug or a similar drug known as neramexane will help these patients.

Memantine blocks the activity of a brain chemical called glutamate, which excites neurons, Schmitt explains. "In the past few years, we've learned that when neurons become over-stimulated because of excess glutamate, the nerve cells can become damaged or they can die. Neurons are literally excited to death." Many brain cells that respond to glutamate are involved in memory and learning.

One reason for doing clinical trials such as this one is obviously to further medical knowledge and hope that it translates into effective drug development, Schmitt says. But he says there is another important motivation.

"It allows you to spend more time with patients than might be possible in a typical busy clinical practice. In these studies, patients get quality care from a whole team—researchers, physicians, a social worker, and a nurse," Schmitt says. [For one patient's personal

memantine story, see sidebar on next page.]

Is memantine the wonder drug everyone's been looking for?

"We need to stress that although this is a wonderful scientific finding, it isn't a cure," Schmitt says. "It's another step in treating a very complex disease." ■

**For more  
information  
about Alzheimer's  
disease clinical trials  
at the UK Sanders-  
Brown Center on Aging,  
call 859/323-6729  
or visit  
[www.mc.uky.edu/coa](http://www.mc.uky.edu/coa)**





Ruth Hobbs (left) with her daughter DeEtta Blackwell was a participant in a national clinical trial of memantine, a drug to treat memory loss. Says Ruth today: "I'm delighted about how I'm doing. I can do anything I want to do really. I'm sure a happier person than before they started giving me this drug."



## Memantine User Says UK Study Has Changed Her Life

This was Ruth Hobbs on Thanksgiving Day 2002. For the first time, she hadn't cooked Thanksgiving dinner for her family or even had a hand in the cooking. For an hour, she sat alone in a corner, speaking to no one. When she finally did say something, it was to her daughter, DeEtta. Ruth, 73, wanted to know, for the fifth time that day, when they were leaving to see the doctor.

"Around this time, Mom would call me six to eight times a day at work. She wanted to go to the doctor every other day. The day after Thanksgiving dinner, she didn't even know it had happened. The quality of her life and well-being was horrible," DeEtta Blackwell says.

Soon after, Ruth was diagnosed with Alzheimer's. "I never felt so hopeless in my life when we got that diagnosis," DeEtta says. "I'm a nurse, and I knew very well what it meant."

Then DeEtta learned about a new UK study of the drug memantine, used in Germany for more than 20 years for general neurological disorders and approved in 2002 for use in Alzheimer's patients throughout Europe. "When Dr. [Greg] Cooper told me about this, I asked Momma if she'd like to join the study. 'Sure,' she said. 'If I do have Alzheimer's, what have I got to lose?'" Cooper is an assistant professor at UK's Sanders-Brown Center on Aging and head of the neurology section of the center's memory disorders outreach clinic.

The first six months of the study were "blind," meaning that neither the pa-

tient nor the physician knew whether patients were getting memantine or a placebo. After six months, all patients enrolled in the study were given memantine.

"We still don't know what Mom was getting the first six months, but after she started taking memantine at the six-month point, she got noticeably better nearly overnight," DeEtta says. "We couldn't believe the difference."

Ruth went back to cooking family dinners and going to church with her son. Now she sews, cleans and arranges silk flowers. And she continues to live independently in a green-roofed cottage surrounded by flower beds she tends regularly.

"The memantine has dramatically changed her life," DeEtta says. "Her sense of well-being is back, she makes notes and keeps a calendar to help her remember upcoming events."

DeEtta was especially impressed when, four months ago, her mother read about a program on KET about Alzheimer's, made a note to see it, and then remembered to watch the program. "I'd forgotten it was on myself, but Mom didn't," DeEtta says. "I had mixed feelings about her seeing it, but it's something she wanted to do."

After watching the program, Ruth called her daughter. "God, DeEtta, I'm so glad they're giving me this pill. Without it, I'd be just like those people on TV."

"This was really touching, I thought," DeEtta says.

Ruth developed severe pneumonia during the 2003 Christmas holidays and

was hospitalized for four days. DeEtta and other family members noticed that Ruth slipped mentally by the time she returned home, and they worried that it was the beginning of another decline.

"It took her four months, but she is almost back to where she was before getting pneumonia," DeEtta says. "I know that without the memantine she wouldn't have come back. She wouldn't be herself any more. She would have lost her independence."

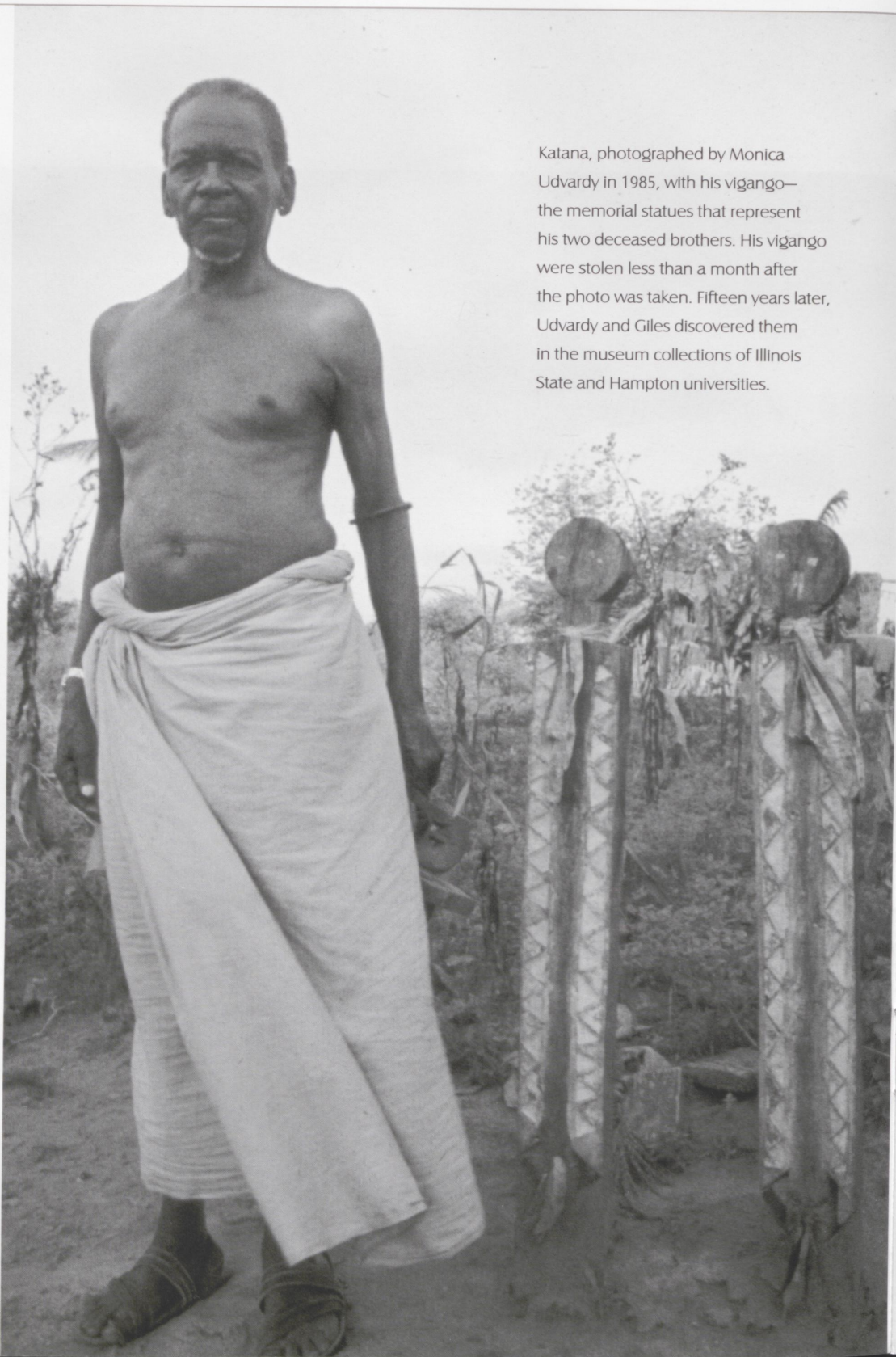
DeEtta gives high marks to the Sanders-Brown team she and her mother have worked with during and after the clinical trial.

"It may sound strange to say this, but I feel like we have our own private care team for Alzheimer's." The team included Frederick Schmitt, UK professor of neurology, Cooper, Ashleigh Lucas, study coordinator at the Lexington Clinic, and Marie Smart, clinical associate, Alzheimer's Disease Research Center. "I can trust Momma in their hands, and now I don't have to stay glued to the Internet looking for every new book out there on Alzheimer's. It's because of them that Momma is in her own house right now."

This is Ruth Hobbs today: "I'm delighted about how I'm doing. I can do anything I want to do really. I'm sure a happier person than before they started giving me this drug. I was starting to get depressed."

"I live by myself and live a happy, normal life."





Katana, photographed by Monica Udvardy in 1985, with his vigango—the memorial statues that represent his two deceased brothers. His vigango were stolen less than a month after the photo was taken. Fifteen years later, Udvardy and Giles discovered them in the museum collections of Illinois State and Hampton universities.



# In Search of Africa's Ancestral Statues

W R I T T E N   B Y  
A l i c i a   P .   G r e g o r y

1985. Kenya. Monica Udvardy follows Katana from his mud-walled house to the outskirts of his homestead. The old man stops in front of two elaborately carved wooden posts that embody the spirits of his dead brothers. Strips of blue, red and white cloth, tied around the neck of the abstract human forms, sway in the wind.

Udvardy lifts the camera to her eye, unaware that this click of the shutter will bring about her transformation from anthropologist to crusader against global traffic in East African "art."

This transformation does not happen overnight. It is a long journey, with stops along the way in Africa, where she conducts firsthand research on gender roles, in University of Kentucky classrooms, where she teaches 400 students each fall, and at professional conferences, where she presents the results of her research. It was at one such conference in 1999 that Udvardy had her eureka moment.



"It's important to leave the tangible manifestations of a living culture with the people who have created those objects and who use them on a daily basis, no matter how 'beautiful' they are," says Monica Udvardy, an associate professor of anthropology at UK. In the background is a replica of a *vigango* made for her by a grad student.



Born in Canada, to Finnish-Swedish and Hungarian parents, Udvardy grew up speaking Swedish. So after getting her master's in anthropology at the University of California at Santa Barbara, a move to Sweden just made sense.

"Sweden gives most of their developmental aid to African nations, so there are strong historical ties," says Udvardy, who was a doctoral student at Uppsala University in Sweden in 1985. "That was the primary reason I chose Africa."

Her interest in gender and aging led her to East Africa and a group of people called the Mijikenda. She zeroed in on the

Giriama, a subgroup of about half-a-million people, because 20 years earlier researchers had compiled baseline data on the Giriama's elderly.

"I was looking at how the elderly gain power and influence, and I was studying women and men separately," she says, adding, "Nobody at the time had done firsthand research on old women." So Udvardy began to explore how old women get power in a society that automatically awards authority to men.

To test her hypothesis that women gain influence through their sons, Udvardy, who says she speaks enough of their language to "get by" but often had the help of an interpreter, spent 14 months interviewing older women in a rural Kenyan community. "Giriama extended families reside in homesteads, or compounds. There are usually three generations—





Udvardy's photo shows a typical mud-walled, thatched-roof house and koma (statues that represent the spirits of people who did not belong to the secret society) erected in a clearing in the middle of the Giriama homestead.

Photo: Monica Udvardy

a father, his wife or wives, all of his sons, the sons' wives, any unmarried children, as well as numerous grandchildren." Homesteads range in size from seven to 70 people.

To conduct her research Udvardy says she relied on what is called "snowball sampling": "I'd start with one woman, and her friends would become curious, you know, 'Why is this white woman in your homestead?' They'd say, 'We want her to come talk to us.'" The women in this community became very comfortable with Udvardy, a fact that opened a door to a supposedly defunct secret society and a first-hand view of the Giriama's reverence of ancestral spirits.

"One day as I was interviewing two or three older women, I needed to go and relieve myself, and you usually do that by just walking into the bush," she says. "There I saw what looked to me like a pit latrine—a little mud-walled, thatched-

roof structure that you find at about every tenth homestead." But when she opened the door, instead of a latrine, Udvardy found a platform with a couple of clay pots.

"Having done my historical reading, I suspected this was the shrine of Kifudu, a female secret society I'd read about in records from the 1910s. I had no idea it was still active. I asked, and the women laughed and said, 'Oh, yes. That's Kifudu.' And that's how I got interested in women's roles in the secret society."

Udvardy's dissertation focused on how post-menopausal women, the custodians of these clay pots, are responsible for the fertility of the entire ethnic group. "The pots stand for the ancestresses," she explains. To honor them, the women take the pots from the shrine, bring them to the





Photo: Monica Udvardy

"This was one of the primary homesteads in my research and also one of the largest, with 64 members," Udvardy says. Pictured are the head of the homestead (man in all white at right), his two wives, his brother and wife, his grown sons and their wives, and numerous grandchildren.

center of the homestead, and "play" them—by putting their mouths in the openings of the pots and blowing. "The sound produced is a signal to all of the people in surrounding homesteads that a party is going on," Udvardy says. There's free food and drink, and people bring other instruments and they play all night.

"Without the women performing rituals centering on these clay pots, the Giriama believe that young fertile women will have problems in childbirth.

"In order to contextualize this female society, I needed to learn about the male societies," says Udvardy, recognizing that this research offshoot is what brought her to Katana's door in 1985 and what inevitably led to her present-day cultural activism.

"The Giriama have five male secret societies, and then Kifudu, the only female secret society," Udvardy says.

She interviewed five members of the all-male Gohu society, including Katana. "The Gohu society, similar to the Lions Club or the Masons, is a fraternal organization for wealthier-than-average men. You have to be elected to membership and pay membership fees, which by local standards are quite expensive. There isn't a lot of wealth stratification among the Giriama, but Gohu membership requires giving a bull, which costs about three months' income."

The key feature of the Gohu society is how they honor their members when they die. "Men in the society are skilled carvers and are paid to create the kigango—a memorial statue—for the dead Gohu member," Udvardy says. She explains that these statues (vigango: the plural form of kigango) are part of an expensive ceremony. "It costs about the equivalent of \$185 for them to pay the carver and sponsor a feast to honor the deceased," she says.

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. Udvardy says, "Photographs from the early 20<sup>th</sup> century show more elaborately carved vigango. The head was more three dimensional than the ones they make today. The carving itself has always been what's called chip carving, but that's become more stylized—more simplified—over time. On the other hand, the painting has increased. You'll find vigango painted bright red these days, and others painted blue or white."

Blue is often equated with black, she explains, in the East African color palette. "Black is the color of god, and white is the color of purity. Red is an accent color. It adds emphasis to whatever other color it's with." Strips of cloth in these colors, representing clothing, adorn the necks of the statues.



Vigango are placed around the edge of the homestead, but they are not the sole monuments. Other uncarved wooden statues, called koma, are raised in honor of non-Gohu members and occupy the middle of the homestead. "These smaller statues are erected in a clear space that is surrounded by homes. People are buried right next to their houses, so these statues do not actually mark the graves," Udvady explains.

Even these ordinary statues play a role in the daily lives of the Giriama. When they drink palm wine ("Something the Giriama drink every day," Udvady says. "It's like beer."), they'll pour a few drops on the ground in front of the statues and say a few words to the ancestors.

She laughs and recalls, "I overheard one elder say to an ancestor, 'You know those tourists that come up from the coast to watch us? Can you make one of those fat wallets the men carry in the back of their jeans fall out on the ground?'"

"There's a strong belief in the power of the ancestors to influence the lives of the living on an everyday basis. The remarkable thing about the Giriama is that, despite the inroads of Islam and Christianity, indigenous religious beliefs continue to be strongly held, and primary among those is veneration for the ancestors and ancestresses."

In the case of vigango, they are believed to embody the spirit of the ancestor. These statues are the tangible link between the living and the dead, and must be honored through animal sacrifice and libations. Failure to perform these rituals or, worse yet, removing a kigango from its site (an act Udvady says 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, drought, diseased livestock, or even children who can't find employment. But, as Udvady points out, "the older generation believes in the power of ancestral spirits to a much greater degree than the younger people."

And that's where trouble comes in. With growing populations, poor economies ("a holdover from colonialism, which was as recent as the early 1960s in most African countries"), and not enough land to farm, young Mijikenda men can't find work. "They're desperate. They need incomes. And some young men resort to stealing vigango, because there's a market for them in the West."

"Vigango are considered the art form of East Africa," says Udvady, who estimates that there are at least 1,000 of these statues in existence, "but most Westerners fail to realize these



Photo: Veronica Lubyansky

Giriama homesteads are scattered around groves of coconut palms, the main cash crop in coastal Kenya.

objects are ritual artifacts of a living culture.

"I'm a cultural anthropologist: I study cultures alive today. It's important to leave the tangible manifestations of a living culture with the people who have created those objects and who use them on a daily basis, no matter how 'beautiful' they are."

But vigango 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," she says.

Katana began to cry as he held the photos of his statues Udvady had taken a month earlier when she first visited his homestead. "I was very surprised to see tears rolling down his cheeks, and that was when he told me his vigango had been stolen," Udvady 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."

In 1999 Udvady, an associate professor of anthropology at the University of Kentucky, was splitting her time between teaching undergrad and graduate courses, acting as the department's director of undergraduate studies, and conducting research. She traveled to Philadelphia to take part in a panel on Mijikenda culture at the African Studies Association annual conference.

"I talked about the Gohu society, and among the images I showed were slides of Katana 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,'" Udvady says. "There was one of Katana's statues! We took my slide, put it in her tray and went back and forth between the two images. Everybody in the room was just astounded."

And in that eureka moment, she clearly saw her future as a cultural activist. "We decided we needed to try to repatriate the statue."

"The dean responsible for the museum at Illinois State immediately indicated he was willing to do the right thing." Not long after that conference, Udvady and Giles took a weekend, poured over exhibit catalogs from all of the African art collections in American museums, and found Katana's other statue. Last summer they wrote to, but have not yet heard back from, the curator of Hampton University Museum in Virginia, which has 99 vigango, including Katana's, in their collection.

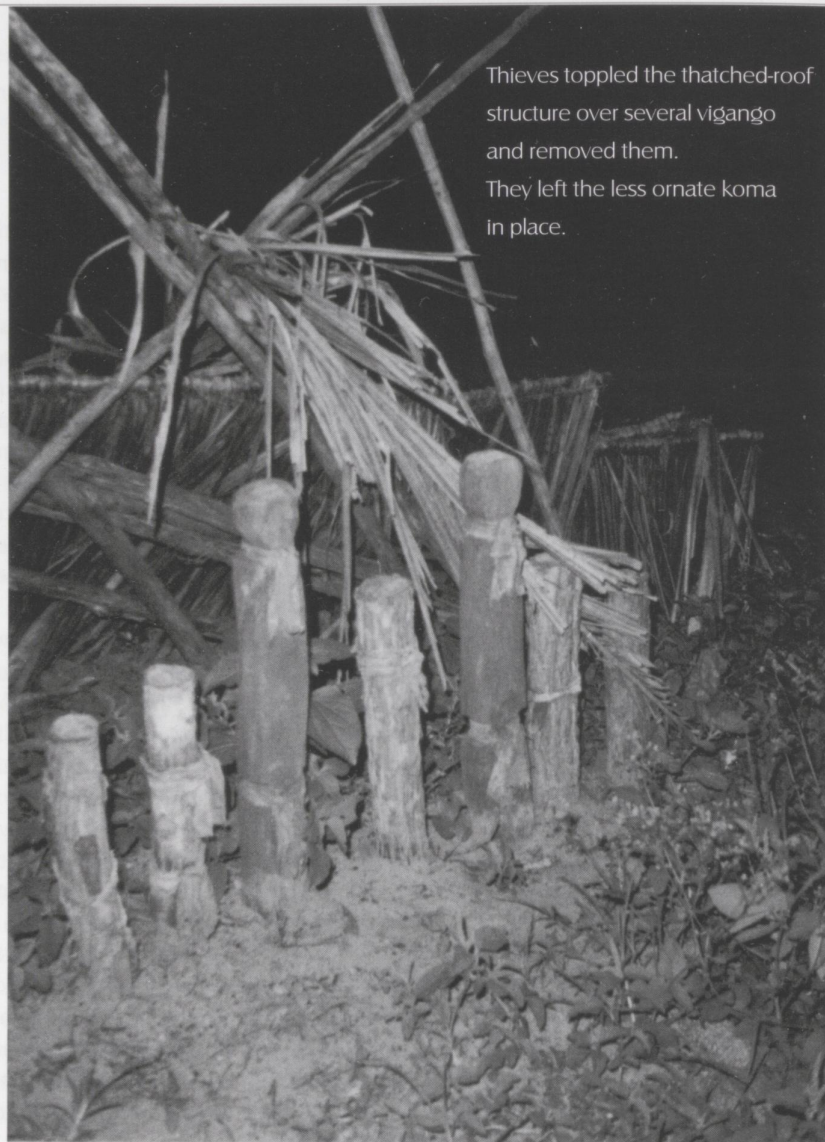


Since 2001, one of Giles's research assistants, a young Giriama man named John Mitsanze, has been playing the role of field detective. "In the course of trying to collect information on the thieves, John was told that sometimes they perform a kind of counter-ritual to offset the curse believed to be triggered by moving a kigango," Udvardy says. Mitsanze is documenting what he hears about stolen vigango and photographing existing statues. "That's our small, grassroots effort to stop the traffic in these particular statues."

Udvardy's next step is to trace the journey of Katana's vigango. "I'll be looking at the different people involved, from Katana and his family, to the thief, to the art dealer who sells vigango in the United States, to the collectors of vigango—many of whom are Hollywood celebrities—to the collector's accountants, to the museum curators who accept them as donations. I'll focus on the transformation in meaning of the objects through the different hands that have had the objects."

Of the roughly 360 vigango in American museums, Giles and Udvardy have traced 90 percent back to one American art dealer. "This particular dealer almost single-handedly created a market for these objects," Udvardy says. "He has done so despite the fact that he has spent time with the Gohu elders and has written a book about vigango, so he knows they should not be removed."

Art dealers are key characters in Udvardy's study: "It's important for an art dealer that the purchaser in the West gets a little bit of knowledge about the object, but not too much. It's also important for the dealer to keep the Western collector separate from the local people because, after all, this in-



Thieves toppled the thatched-roof structure over several vigango and removed them.

They left the less ornate koma in place.

Photo: John Mitsanze

termediary role is how he makes his living."

The Western art dealer is able to make a huge profit because of the economic inequity between the West and the non-Western world. Udvardy lays out the money chain: the thief is paid \$50 by the local shopkeeper, who sells the object to an art dealer for several hundred dollars, who then sells it to art collectors for \$1,000 to \$4,000.

A number of Hollywood celebrities (including Andy Warhol, Linda Evans, Gene Hackman, and Powers Boothe) have collected vigango. Udvardy knows this because the names show up in what's called an accession record. She explains: "When an item comes in, the museum gives it a number and records who it came from, and the date it came in. They also add the biography of the object—called the provenance—that includes what it is, where it came from, and how old it is. This kind of cataloging is a time-consuming process for the museum, but it's crucial."

In fact, such records show that Boothe donated eight vigango to the Illinois State Museum in 1986, including Katana's statue. Udvardy wants to know if these



celebrities are buying vigango for their own home collections or if their accountants are purchasing items in the celebrity's name, getting objects appraised, and then donating them to museums as a tax write-off. "Those are my two competing hypotheses," Udvardy says with a smile, "Do you know how to call up a movie star?"

Public awareness is Udvardy's goal. She uses the forum of the university classroom—she teaches 400 students every fall—to convince the next generation that taking cultural objects out of their context hurts everyone.

"The general public is not aware of how far science has come in studying artifacts. Archeologists can do chemical analysis of the soil surrounding an object, analysis that yields all kinds of valuable information about the people who created and used an object." She also gives practical shopping advice like: "If it looks weathered, recently embedded in dirt, or someone tells you it's 'authentic,' don't buy it."

Authenticity is one of the topics Udvardy looks forward to exploring. "I'm very curious about why people collect African art. I think Western collectors have a fascination with what they consider to be 'exotic' cultures, and their interest in vigango probably has something to do with their notions of authenticity—that these are objects of a pure, natural, uncorrupted culture."

Udvardy is working with Kenya's national museums, and she's even lobbying for international legislation. "We're recommending that a lot of the features of the Native American Graves Protection Act (NAGPRA) be made international," she says. "Enacted in 1995, NAGPRA says objects in U.S. museums that can be traced to a particular cultural group belong to that group, and museums have an obligation to inventory their collections and make that information available to the group."

Udvardy, Giles and Mitsanze have published three articles on the cultural importance of vigango in *American Anthropologist* (September 2003), *Anthropology News* (September 2003) and *Cultural Survival Quarterly* (Winter 2004).

And they've ruffled some feathers along the way. "We've presented these papers in various venues to museum curators, art historians and anthropologists. We did get a couple of curators who bristled when we said that these are stolen objects, and they asked us, 'What proof do you have?'" Udvardy says.

In most cases, even if curators suspect something was stolen, they can't prove it. Udvardy says that's the big dilemma: there's international legislation that prohibits traffic in stolen goods, but you have to be able to document that they were stolen. "That's what's unique about our case," Udvardy says with increased animation. "We can actually trace these statues back to their point of origin—that's extremely rare."

"At conferences when Linda and I try to initiate a group discussion, curators tend to skirt these questions about their involvement in accepting collections and their relationships to art dealers. But many curators have come up to us individually to tell us that they know many things donated to museums are stolen."

"After reading one of our articles, a museum employee sent me an email to bring our attention to one museum's large collection of vigango, of which Linda and I were unaware. But, in doing so, the correspondent requested anonymity," Udvardy says.

The difficulty for museum curators, she explains, is their relationship to art dealers, particularly in the United States where there is less federal funding for museums than in Europe. U.S. museums rely on patrons for donations of money and art. So the art dealer becomes the broker between wealthy collectors and curators, says Udvardy. "From the curator's perspective: they want collections and they need donations, so they need to maintain good relationships with art dealers."

In the case of a university museum, Udvardy recognizes that building a collection is important. "Universities want to have a wide variety of objects because they use them in teaching, but how many are truly needed for educational purposes? No one museum needs 99 vigango—so that becomes one of the ethical questions we pose to curators."

"Linda and I appreciate the awkward position curators are in. We aren't being pulled in as many directions. We have the freedom to raise awareness of these ethical issues, so that's why we've taken it on to lead the charge to return these objects to their rightful owners."

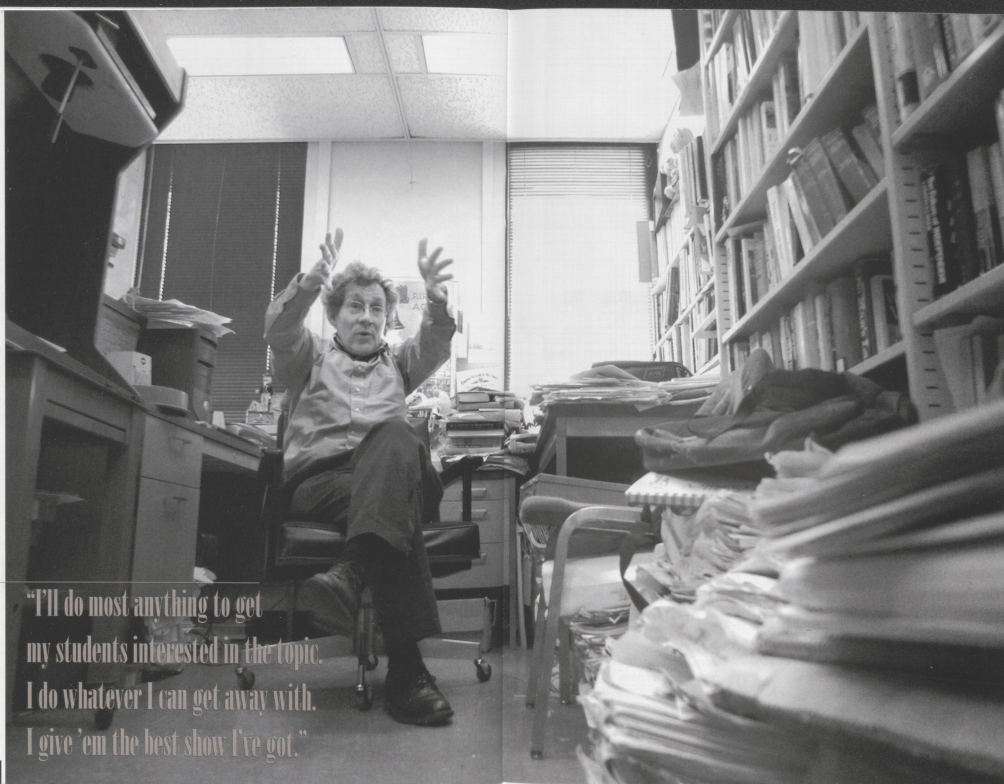
Although Udvardy suspects Katana will not have the chance to see his statues again (he has probably been honored with his own kigango by now), she is dedicated to returning these memorial objects to his descendants. And she looks forward to continuing her work to preserve the cultural heritage of the Giriama. ■



WRITTEN BY  
Jeff Worley

# Mark Summers and the Serious Business of

"I'll do most anything to get  
my students interested in the topic.  
I do whatever I can get away with.  
I give 'em the best show I've got."



**M**ark Summers is never going to receive the Good Housekeeping Seal for Office Tidiness. When you enter his office, you have to pick your way carefully around and through the maze of manila folders that rise an impressive three feet or so from the floor and prop each other up. You realize right off that a careless elbow might touch off an avalanche of precariously balanced stacks—on desktops, tables and shelves.

"Heavens, no—I don't have any idea what's in some of these folders," says Summers, a University of Kentucky professor of history. "Occasionally I'll dislodge one of these folders and what's in there comes as a complete surprise. And there are some things I know are here, but a team of archaeologists would be hard put to come up with them."

Some of the folders contain classroom lectures Summers has given over the past 20 years at UK, some hold notes he's taken on various historical issues from as far back as his grad school days at Berkeley, and others are stuffed with

# Political Cartoons





The caption for Bernhard Gillam's cartoon reads: Phryne Before the Chicago Tribunal. Ardent Advocate.—"Now Gentlemen, don't make any mistake in your decision! Here's Purity and Magnetism for you—can't be beat!"

political cartoons. Lots and lots and lots of political cartoons.

"Here's Fred Morgan of the *Philadelphia Inquirer*, 1905, very nice stuff," says Summers, unwedging a yellowed folder from one of the stacks. "And here's Thomas Nast, 1873. And this one"—he pulls a fat file from the stack that teeters under the watchful eye of a small rubber frog perching atop his computer—"is full of cartoons from 1944, lovely things."

When Summers discusses political cartoons, their artistry and their value, he talks like a man who's just hit the lottery.

"Not only are some of these artistically stunning, but they can also be very, very powerful," says Summers, whose six books on American politics in the 19<sup>th</sup> century include discussions of cartoons that ridiculed civic and political leaders, and that in some cases affected the outcome of elections.

"There are so many good examples of the power of these creations," Summers says. "One that comes to mind is the fate of B. Gratz Brown, a senator and then governor from Missouri and a relatively important character in the 1860s and 1870s." Brown, born in Lexington, Kentucky, in 1826, was Demo-

cratic nominee Horace Greeley's running mate in the 1872 presidential election. When political cartoonist Thomas Nast wanted to draw a caricature of Brown, however, he was stymied because he couldn't find a drawing or photo of him, so Nast drew him as a little tag on the back of Greeley's coat.

"So throughout the campaign, newspaper readers continually saw Brown as nothing more than this little tag, this little insignificance," Summers says. "The effect was that at the end of the campaign, after Greeley and Brown lost to Ulysses Grant, B. Gratz Brown was less known than he'd been before he ran for vice president—he was seen as completely irrelevant and pointless."

Nor was Greeley spared the sharp jab of Nast's pen during the election. "During the campaign, Nast, a Republican, produced a series of cartoons attacking Greeley, who commented that the venom of these cartoons was so bad that he scarcely knew whether he was running for the presidency or the penitentiary," says Summers. Greeley died soon after the election, and one friend claimed that Greeley had been crushed by the unmerciful ridicule Nast had heaped on him.

James G. Blaine is another politician

who was forever branded by a cartoonist's pen. In his third try, in 1884, for the Republican nomination for president, Blaine was portrayed by cartoonist Bernhard Gillam in *Puck* magazine as a man whose scandals and sins were so much a part of him they were tattooed all over his body. "Little Rock RR Bonds," one tattoo announces, alluding to a well-known railroad scandal Blaine was implicated in. "Corrupt Lobby" and "Anti-Chinese Demagogism" read two others.

Gillam's cartoon is a parody of the painting titled "Phryne," by Jean-Leon Gerome, in which the Greek orator Hyperides attempted to defend the courtesan Phryne against charges of prostitution by revealing her breasts to the jurors [the entire story is too complex to go into here]. So in addition to having Blaine's misdeeds tattooed on his body for all to see, he was also alluded to as a prostitute.

"After this cartoon appeared, it wasn't easy for people to ever associate him in any other way," Summers says. Blaine did win the nomination that year but lost to Democrat Grover Cleveland by an extremely slim margin—three-tenths of 1 percent of the popular vote—in the election. "It's impossible to say to what



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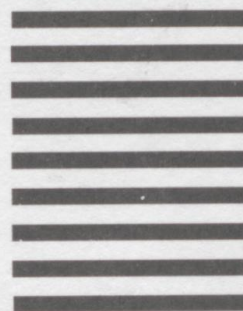
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"If you're doing your job as a political cartoonist, you're offending lots of people day after day after day. It's one of the fastest ways you can imagine to get lots of hate mail."



degree Gillam's portrayal of Blaine translated into votes against him, but it certainly played some part in the election's outcome," Summers says.

Sometimes a cartoonist can turn politicians into such figures of ridicule that they can never be taken seriously again. Former Vice President Dan Quayle is a good, contemporary example, Summers says. "His idiotic remarks [Quayleisms: 'It's wonderful to be here in the great state of Chicago'; 'I love California—I practically grew up in Phoenix'] were easy fodder for cartoonists who depicted him as a bubblehead. He was a perfect foil."

Political cartoons, Summers says, can carry a wallop that even the best editorial can't manage. "For one thing, cartoons are a lot easier to read," he says. "I heard somewhere that the average time a reader spends with a cartoon is eight seconds." Summers adds that cartoonists can put their message in simple story form to hammer home an idea in a plain and obvious way; an editorial might make a lucid and convincing argument, but the form is almost always rhetorical, not narrative.

Summers's interest in political cartoons began when he was 8 or 9 years old, and he started collecting them in scrapbooks. His father, a professor at Yale, would take his son along with him to the university library for four- or five-hour stretches of time, and young Mark would "make a beeline" for the shelf that held Thomas Nast's cartoons. "I was just entranced. All those bright colors from the Gilded Age! All that wonderful art!"

Summers recalls a day about this time when he was home sick from school and found a book about Reconstruction on his father's shelves. His intense interest in this period of 19<sup>th</sup>-century American history, already fueled by Nast's cartoons, was to become a lifelong passion. "Reconstruction had such marvelous villains and wonderful heroes," Summers recalls.

His interest in history, politics and cartooning dovetailed nicely, Summers says, and he began to draw his own political cartoons in seventh and eighth grades. He published cartoons in his high school newspaper and then in the college newspaper at Yale when he was an undergraduate.

"I never really learned to draw in any formal way, and it shows," Summers

admits. "But I kept at it and kept paying close attention to other people's political cartoons—and it was great fun." (For Summers's artistic comment on President Gerald Ford, see above.)

He adds that although his drawing and publishing cartoons was politically motivated, it also served as a way to let off steam.

"It was the '60s and I was upset and angry about a lot of things that were happening. The war in Vietnam was getting worse and worse and stupider and stupider, and there didn't seem to be any way out of it. The administration was digging us in deeper, and everything that was coming out of the White House was a lie."

Underlying all of this discussion of American political cartoons is what Summers says is the most important reason for their existence: political cartoons are serious business. "If you do it just for laughs, you abdicate your responsibility. You become an extension of the funnies page. It's important to have a sense of indignation and anger—a political point of view that's consistent."

Among Summers's favorite cartoonists, besides Nast, are Herb Block (who died in 2001 at the age of 91), Mike



**"If you do political cartoons just for laughs, you abdicate your responsibility. You become an extension of the funnies page. It's important to have a sense of indignation and anger—a political point of view that's consistent."**

Peters, Tom Toles, and Ben Sargent. "Toles is dazzlingly good, very artistic, and Ben Sargent is one of very few who can do a political cartoon that makes me fall on the floor laughing. And Joel Pett [Pulitzer Prize-winning cartoonist for the *Lexington Herald-Leader*] is doing exactly what political cartoonists are supposed to do," Summers adds. "I think his Pulitzer Prize was entirely deserved."

There's nothing easy, Summers says, about being a professional political cartoonist. You have to be politically savvy and insightful, clever, funny, and unique—and you have to understand the power of the image. Cartoonists with major daily newspapers usually have to produce five cartoons a week all year long. And there's the omnipresent "fringe benefit," Summers says wryly, that comes with the territory: lots of people aren't going to like you.

"If you're doing your job as a political cartoonist, you're offending lots of people day after day after day," says Summers. "It's one of the fastest ways you can imagine to get lots of hate mail."

Unpopularity and the pressure of daily production are major reasons, he believes, that many cartoonists are tempted to do a comic strip instead. "A

comic strip means an awful lot more money for one thing. You can get syndicated in many papers, and comic strips can be collected into books and sold in stores. Also," he adds, "it'll cut way down on your hate mail."

Why aren't political cartoons collected into books?

"They're very transitory for the most part," Summers explains. "Their purpose is to speak to present-day issues, and the result of that is after these issues are either resolved or disappear from the public scene, the cartoons don't hold up that well." There are some exceptions, he says. "Doonesbury" comes to mind, and I think it transcends the years primarily because people come to care about the running cast of characters."

Summers makes it clear that his professional life isn't *all* about political cartoons. He loves the collegiality of being a professor and he loves teaching. Among the classes he's taught at UK are frontier history, Civil War and Reconstruction America, the Gilded Age and Progressive Era, the Age of Jackson, and, of course, the History of Political Cartoons.

"I'll do most anything to get my students interested in the topic," he ad-

mits with a shrug. "I've been known to jump on desks, wave my arms around like a crazy man and clamber from desk to desk. I do whatever I can get away with. I give 'em the best show I've got."

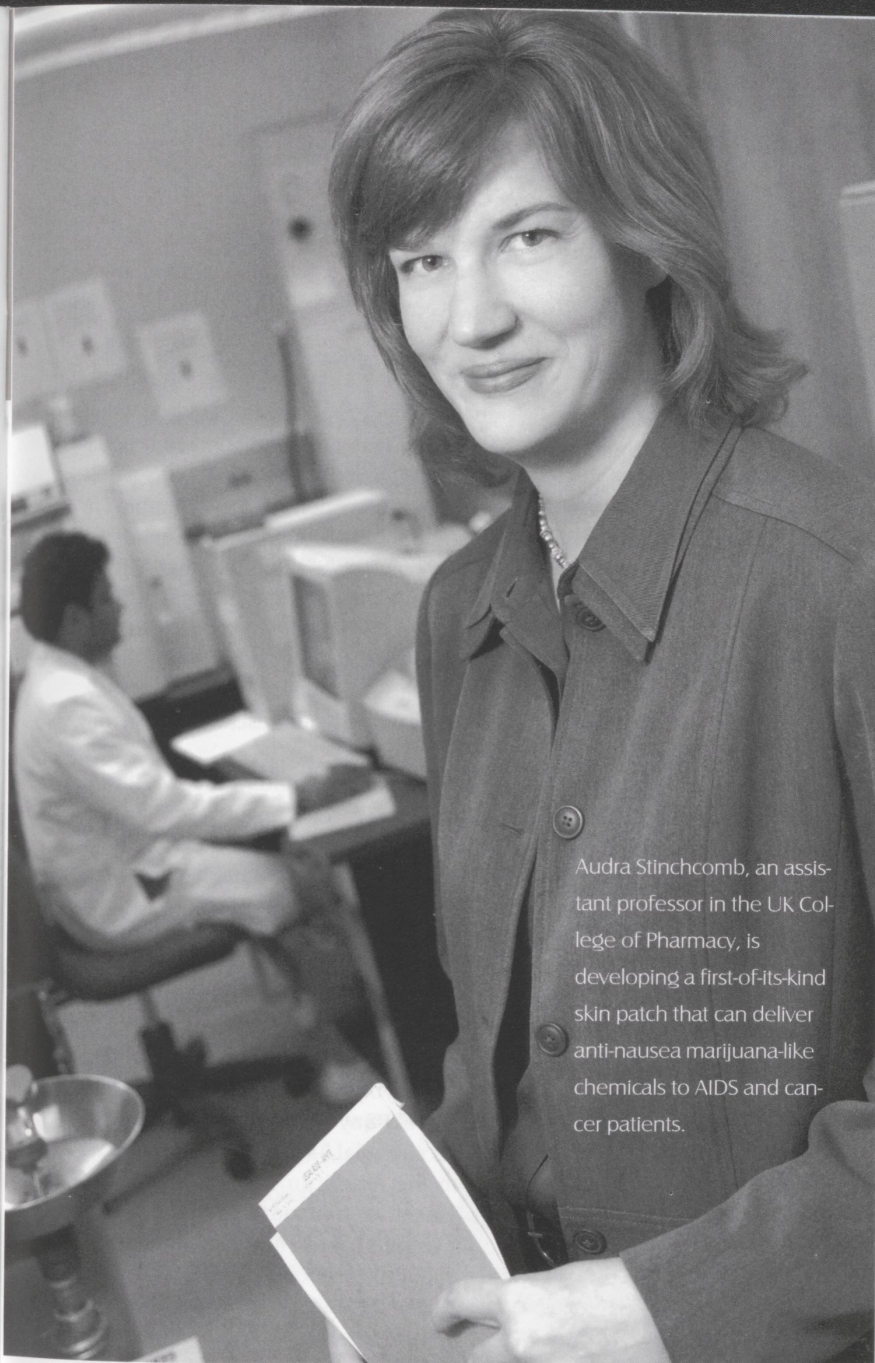
Students might see their professor walk into the classroom dressed in a Colonial outfit, a "very lovely, big broadcloth coat," or maybe a Lincolnesque top hat. Summers also plays characters in class to enact historical moments. He's done Lyndon Baines Johnson (a terrible imitation, Summers admits) rounding up votes, and he's portrayed a Vietnamese interpreter with an American investigator. He's even done dialogues between a Vermont farmer and God—playing both parts.

It was both his teaching and research that earned Summers the first Thomas D. Clark Endowed Professorship in History, according to David Hamilton, history department chairman. The recipient holds this honor until he or she either retires or leaves the university.

"If it weren't for his annoying habit of whistling opera tunes as he walks the halls, Mark Summers would be a perfect colleague," Hamilton says with a grin. "Mark relishes reading the work of his colleagues, and with his superb editorial skills he invariably returns the chapters of a manuscript with page after page of comments and suggestions for revision. And if the department needs an extra class taught, he can't volunteer fast enough. Mark may end up teaching as many students as Tom Clark did."

"I don't do teaching overloads because I have to; I do overloads because I enjoy teaching," Summers says. "Teaching is a thrill. I'm very happy when the school year begins and very depressed when it's over. It's a wonderful complement to doing research. You can't just do research all the time or you turn into a hermit crab—and hermit crabs aren't much fun at all." ■





Audra Stinchcomb, an assistant professor in the UK College of Pharmacy, is developing a first-of-its-kind skin patch that can deliver anti-nausea marijuana-like chemicals to AIDS and cancer patients.

W R I T T E N B Y  
A l i c i a P. G r e g o r y

**S**kin. The human body is covered in 21 square feet of the stuff. Skin weighs in at 7 to 8 pounds per person, and it's composed of around 300 million cells.

Scientists are targeting skin, the largest organ in the human body, in their drug-delivery research with new therapeutic drugs.

And drug-delivery expert Audra Stinchcomb at the University of Kentucky knows what she's up against: "The skin was designed to keep chemicals out of the body, so our challenge is to find exactly the right molecules with the right chemistry to penetrate the skin."

Transdermal (skin) patches, a technology born in the 1980s, are the delivery system of choice. Patches are composed of a drug dissolved or dispersed in a porous material. The patch is backed with paper, plastic or foil, plus adhesive. A special membrane controls the rate at which the drug inside the patch can pass through the skin and into the bloodstream.

Magazine and TV ads tout the convenience of patches for everything from motion sickness and pain relief to smoking cessation, birth control and hormone replacement. But Stinchcomb's targets—cancer and AIDS—are new to patch delivery.

Patches offer many pluses when you compare them to pills, and that's especially true when you're talking about cancer and AIDS.

"Patient compliance is so much better with patches," says Stinchcomb, who was recruited to UK in 2001 from the Albany College of Pharmacy as part of Kentucky's Research Challenge Trust Fund initiative. "Because patches can be worn for up to a week, patients don't

# Skin Patch PROMISED LAND

## UK's Novel Patch to Ease AIDS, Cancer Pain





have to worry about taking tablets multiple times a day.

"Also, we can put less of the drug in a patch for the drug to be effective because it bypasses the liver." She explains, "The liver chews up a lot of drug after you swallow a tablet or capsule. And patches are good because you get a nice steady delivery rate of drugs into the body, rather than peaks of drugs like you would with an immediate-release tablet. A steady trickle can decrease side effects."

But the big plus for patches, Stinchcomb says, is their ability to bypass the stomach. "Because the patch releases drugs directly into the bloodstream, they are less likely to cause stomach side effects like nausea." And that's important for people with AIDS and cancer, people whose very treatment regime makes it difficult to keep food down.

Building on the patch's anti-nausea benefit, Stinchcomb looks for chemicals "born" to cross the skin. "Only a few drugs naturally lend themselves to delivery through the skin," says Stinchcomb, who has been focusing on transdermal drug delivery since she entered grad school at the University of Michigan in 1989. "I look for drugs with penetrating properties that are already in other dosage forms. That's how I got into cannabinoids. They have a pretty good chemistry to go through the skin, and they're very potent."

She's working with synthetic cannabinoids—marijuana-like chemicals—that are created in the laboratory, not taken from the illegal plant. (Smoking marijuana for medical purposes is outlawed in most states.)

Cannabinoids are the only drugs that simultaneously increase appetite and decrease nausea and vomiting, and Stinchcomb says that's vital for AIDS and cancer patients. Marinol, a capsule using a synthetic form of THC (the main intoxicating chemical in marijuana), was approved by the FDA in 1985, but "if people can't keep the pill in their stomach, it can't do its job."

So Stinchcomb formulated a plan: create a first-of-its-kind prescription patch, a safe and legal method to deliver marijuana-like chemicals to ease nausea and stimulate appetite in people with AIDS and cancer.

And in 2000 her idea earned her \$361,000 in research funding—the first grant from the American Cancer Society to fund a marijuana-related research project. "Why did they buy into this? I think they wanted to show they were interested in cancer survivors, as well as treating the disease

itself," Stinchcomb says. Pain and nausea are inevitable byproducts of the chemotherapy and radiation cancer patients face as they go through treatment.

About 60 of the 400 chemicals scientists have identified in marijuana are cannabinoids, and Stinchcomb evaluated a dozen of their synthetic counterparts for use in her patch.

Research with cannabinoids falls under the U.S. Drug Enforcement Administration's Schedule 1 controlled-substance category and requires a permit. "When I applied for my first DEA license at the Albany College of Pharmacy, before I came here, it took nine months just to get the permit to start the project," she says.

So why did she pursue cannabinoids—was she just a glutton for punishment?

Stinchcomb laughs and says the red tape does deter many scientists. "It's definitely part of the problem, because who wants to wait nine months to do a research project?" Things were significantly simpler when she came to UK—the university has a blanket license from the DEA that allows research on controlled substances once the project protocol is approved.

"We keep a very specific inventory of the synthetic chemicals we purchase, and everybody on the project has to get a DEA background check. But any hassles are outweighed by the enormous research potential," says Stinchcomb, who is seeking funding from the American Cancer Society and National Institutes of Health to continue this project. "A lot of people believe cannabinoids are the future of pain relief."

Easing the pain of multiple sclerosis and neuropathy (a common type of nerve damage) are just two of the possible applications of cannabinoid research. And unlike morphine-based drugs, cannabinoids wouldn't have side effects like nausea and dependency. The chemicals could also treat depression, Alzheimer's and Parkinson's disease.

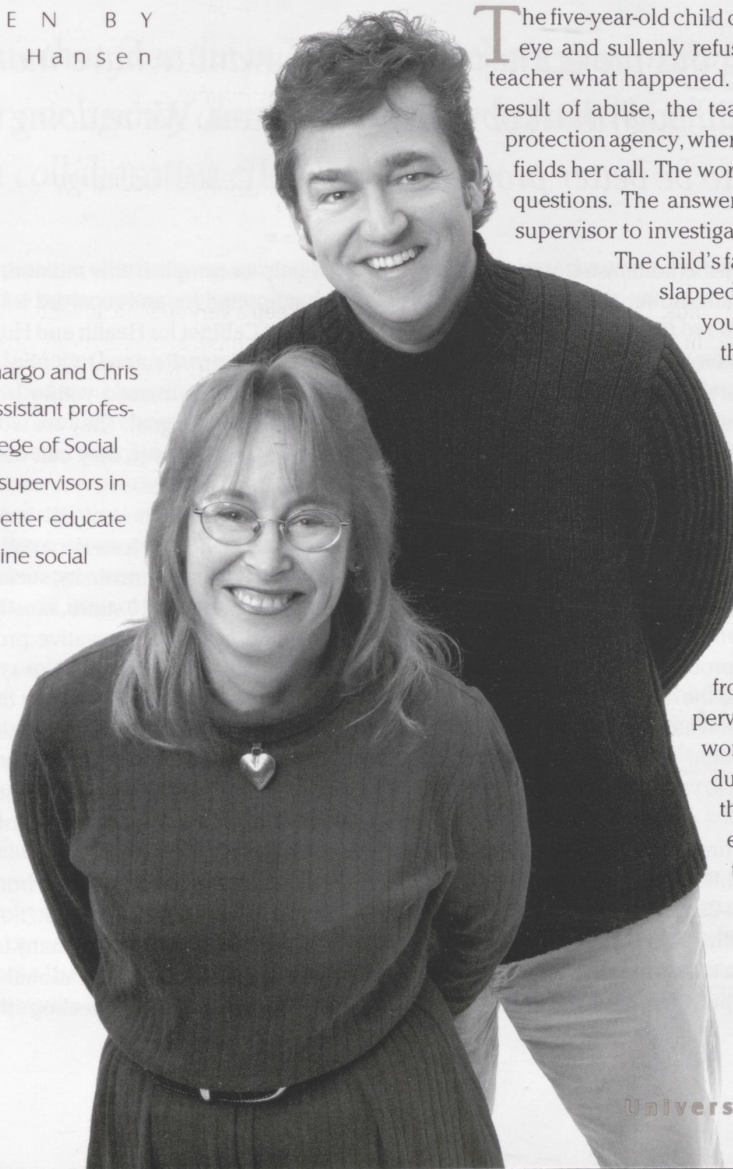
Stinchcomb's cannabinoid studies, which began with lab experiments in 1999, led her to use a special species—hairless guinea pigs—in early 2002. "This is the closest small animal model to human skin. We were excited to see that our cannabinoid patches were successful in getting therapeutic levels of drugs into the animals. That was a really big step for us," she says, noting, "We'll move on to pigs, next year. They're the best match to human skin." ■



# Building a Stronger Safety Net for Children

WRITTEN BY  
Elizabeth Hansen

Crystal Collins-Camargo and Chris Groeber, clinical assistant professors in the UK College of Social Work, are helping supervisors in a 10-state region better educate and support front-line social workers.



The five-year-old child comes to school with a black eye and sullenly refuses to tell her kindergarten teacher what happened. Suspecting the injury is the result of abuse, the teacher calls the state child-protection agency, where a 23-year-old social worker fields her call. The worker asks the teacher several questions. The answers lead the worker and her supervisor to investigate.

The child's father had been drinking and slapped her because she had hit her younger brother. Now the father is furious the child's injury has been reported. "Yes, I hit her and I'll do it again," he tells the worker. "It's my job to parent. You're not a parent. What can you tell me about raising children?"

Unable to break through the man's anger, the worker seeks advice from her supervisor. The supervisor, burdened with paperwork and other administrative duties involved in overseeing the work of a half dozen workers, quickly tells the worker two or three things to do and sends her off to deal with the father, never learning if the suggested actions were appropriate or effective.

This hypothetical case



is typical of what happens in many child-protection agencies, according to Crystal Collins-Camargo, clinical assistant professor in the University of Kentucky's College of Social Work, and Chris Groeber, clinical assistant professor and director of the college's Training Resource Center. The child-protection system is "limping along in terrible shape," Collins-Camargo says. "We don't have very good research on what works so, by and large, people are out there just doing what they think is right." Also, child-protection agencies are bureaucracies where organizational structure dictates that

Workers become confident in their abilities, so everyone benefits—the family, the agency and the community.

Groeber adds that the social worker is also more likely to remain with the agency if she feels efficacious and supported, countering a major problem child-protection agencies have in retaining workers. Many front-line social workers leave the field not because of low pay, but because of the liability they face and the lack of support they get to do their jobs well. "Figuring out how to support workers so they will stay in the job is a mission for both Crystal and me," Groeber says.

*"We're not doing this project just because we want to have more competent social workers, although that's obviously important. We're doing it because we want these kids to be better protected." – Crystal Collins-Camargo*

supervisors focus on their roles as administrators rather than spend time working to educate and support front-line social workers.

How might the scenario involving the five-year-old have played out had the supervisor been more focused on helping the worker deal with the family? It might have gone like this: Before the worker goes out to meet with the family, she and the supervisor meet. She asks the worker a series of questions and role-plays with her to prepare. Together they work out several case plans for the worker to offer and discuss when she meets the family.

One of these plans is agreeable to the father, who signs the case plan and consents to work on what led to the abuse in the first place—his drinking problem. The worker then meets with the supervisor to discuss the details of the meeting. The supervisor asks questions: "What makes you think he is actually going to follow through?" "What did you say that got him to back down and listen to you?" "What is your next step with this family?"

With this approach, over time the worker becomes more competent in using lots of different approaches with different types of families, Collins-Camargo says. "And the family realizes that this worker really cares about them and wants to make a difference; she isn't there merely to offer criticism or to look for reasons to put their child in foster care."

To help accomplish this mission, Collins-Camargo and Groeber applied for and received a \$2.5 million grant from the federal Cabinet for Health and Human Services to establish the Southern Regional Quality Improvement Center (SRQIC), which is housed within UK's Training Resource Center. Bottom-line goal: They are working to change child-welfare organizations so they can better serve abused children and their families.

The SRQIC established at UK is one of only four such centers nationwide. It fosters partnerships between child-protection agencies, university social work programs and community groups in 10 states, mostly in the rural South, to support and evaluate innovative projects designed to improve the child-protective services system.

Spearheading this project during the first year of this five-year grant, the University of Kentucky was funded to conduct a "needs assessment" in the 10-state Southern region to determine how the project could best improve child-protection systems and to build a collaborative network among these states.

"That's how the need for better front-line supervision was identified," Collins-Camargo says. "Solid, thoughtful supervision is a crucial issue because many front-line workers don't have the experience or educational background to do the extremely difficult work of dealing effectively with families."



"The stakes are incredibly high," Groeber adds. "It's life or death in some cases."

After determining front-line supervision was a major issue, the UK center sought applications from institutions in the region for projects designed to improve practice. The four most compelling projects were funded in October 2002 for three and a half years. They are administered by the University of Missouri at Columbia, the Arkansas Division of Children and Family Services, the Tennessee Department of Children's Services, and the University of Mississippi. All of

by 2006, the final year of the grant when representatives from all 10 states in the region, the federal government and national child-welfare leaders will convene in Lexington at a national conference to analyze and respond to the project's findings, and plan strategies for improving the well-being of children.

Like many of the social workers and supervisors they want to help, Collins-Camargo and Groeber both felt called to social work. Adopted as an infant, along with her sister, Collins-Camargo says she knew from the time she was in

*"The problems that face the public child-welfare system cannot be solved by one person or one agency alone. We need our best and brightest at the table—it has to be a collaborative effort." — Chris Groeber*

these projects are cooperative efforts among university faculty, public child-welfare agencies and community organizations.

Collins-Camargo and Groeber have heard recently that the program has already reaped some benefits, that through one-on-one interaction with carefully chosen mentors, supervisors are learning how to better educate and support workers. And while the researchers are pleased to hear such anecdotal evidence, they want statistical evidence as well and are testing hypotheses in three areas: preventing worker turnover, improving worker practice and measuring how changes in these areas will impact outcomes for families and children.

"We're not doing this project just because we want to have more competent social workers, although that's obviously important," says Collins-Camargo. "We're doing it because we want these kids to be better protected." To determine the impact of this project, the researchers will measure three outcomes the federal government requires child-welfare agencies to track, including recurrence of maltreatment within a certain time period.

In a sense, the researchers say, the SRQIC is a "field test" for other such projects to come. "We'll be looking for ways to 'bring this work back home,' back to Kentucky," says Groeber, who points out that the results of this project will be known

middle school she wanted to be involved in social work, and a summer internship with a child-welfare agency while she was in high school fueled her interest in child protection.

For Groeber the call came when he spent a month working in a hospice operated by Mother Teresa in Calcutta, India, in 1986. At the time, he was planning to go to medical school, but his experience at the hospice changed his plans. "Mother Teresa was such an amazing presence. Her genuineness and her dedication to making other people's lives better was a life-changing example to me." Groeber returned to the United States and took a job as a houseparent at a children's home in Hope, Kentucky. He also began work on a master's degree in social work, which he received in 1993, at the University of Kentucky.

"Improving the lives of children and their families involves many very complicated challenges," Collins-Camargo says. "By learning how universities, public agencies and the community can be strong partners in solving child-welfare problems, the field of social work will be better prepared to face those challenges head on."

"The problems that face the public child-welfare system cannot be solved by one person or one agency alone. We need our best and brightest at the table—it has to be a collaborative effort," Groeber says. "And facilitating this problem-solving interaction is truly an honor for us." ■



# UNIVERSITY RESEARCH PROFESSORS

CAROL BASKIN:  
LAYING THE GROUNDWORK  
FOR TROPICAL REFORESTATION



When Carol Baskin wrote a text on seed germination throughout the world's various climate zones, she was no expert on the montane rainforests at such a high altitude that the cool temperatures give rise to a much different type of flora than that found in rainforests at lower altitudes. Tropical montane forests are found in Central and South America, Africa, southeast Asia, and the Pacific Islands.

Baskin, a UK professor of biology and agronomy, and past president of the Botanical Society of America, included only 30 montane species in *Seeds: Ecology, Biogeography, and Evolution of Dormancy and Germination* (1998), a book she co-wrote with her husband, UK professor Jerry Baskin. Since then, she has been adding new species from the tropical montane to her list, primarily because of seed samples provided by various researchers in Hawaii.

"I now have germination data for 317 species, but this is just a drop in the bucket. There are over 2,000 species in the Pacific montane alone."

Learning more about seed germination in the tropical montane could prove important for a region threatened by logging and by local farmers, who typically cut down all the trees to create grazing land. The tropical montane has been nibbled away, and scientists recognize a need to restore it to improve erosion control, water catchment for cities below, and habitat for rare animals and plants.

"If you're going to restore a forest, you've got to know how to germinate the major species," Baskin says.

She is using money from the University Research Professorship to make her information on seed germination in the montane more complete. Baskin is currently traveling throughout the tropics, visiting colleges and agricultural stations, and seeking collaborators for her work.



WRITTEN BY  
Doug Tattershall

# 2003-2004

## JEREMY POPKIN: TAKING A NEW TURN INTO AUTOBIOGRAPHY

Jeremy Popkin's soon-to-be-published book, *History, Historians and Autobiography*, took the UK history professor in a new direction.

"Even though I've been writing and publishing for over 25 years, this is my first venture into studying autobiography," says Popkin, who used his research professorship, in part, to work for two months in France earlier this year. "The truth is, I wanted to do something different, and I enjoy reading that is as much literature as it is history." This shift of interest is particularly appropriate for a professor who has written extensively on 18<sup>th</sup>-century France, since Jean Jacques Rousseau's *Confessions* is considered one of the founding texts of modern autobiography.

Popkin, who has taught at UK since 1978, focused his research this year on examples of autobiography from the first half of the 19th century in France, because that is when it became common for French authors to publish autobiographies while they were still alive. His sources included declarations of candidacy for the first elections held in France after the French Revolution (1848).

"The revolution made it possible for any man to run for office," Popkin explains, "and most candidates issued statements that often were mini-autobiographies."

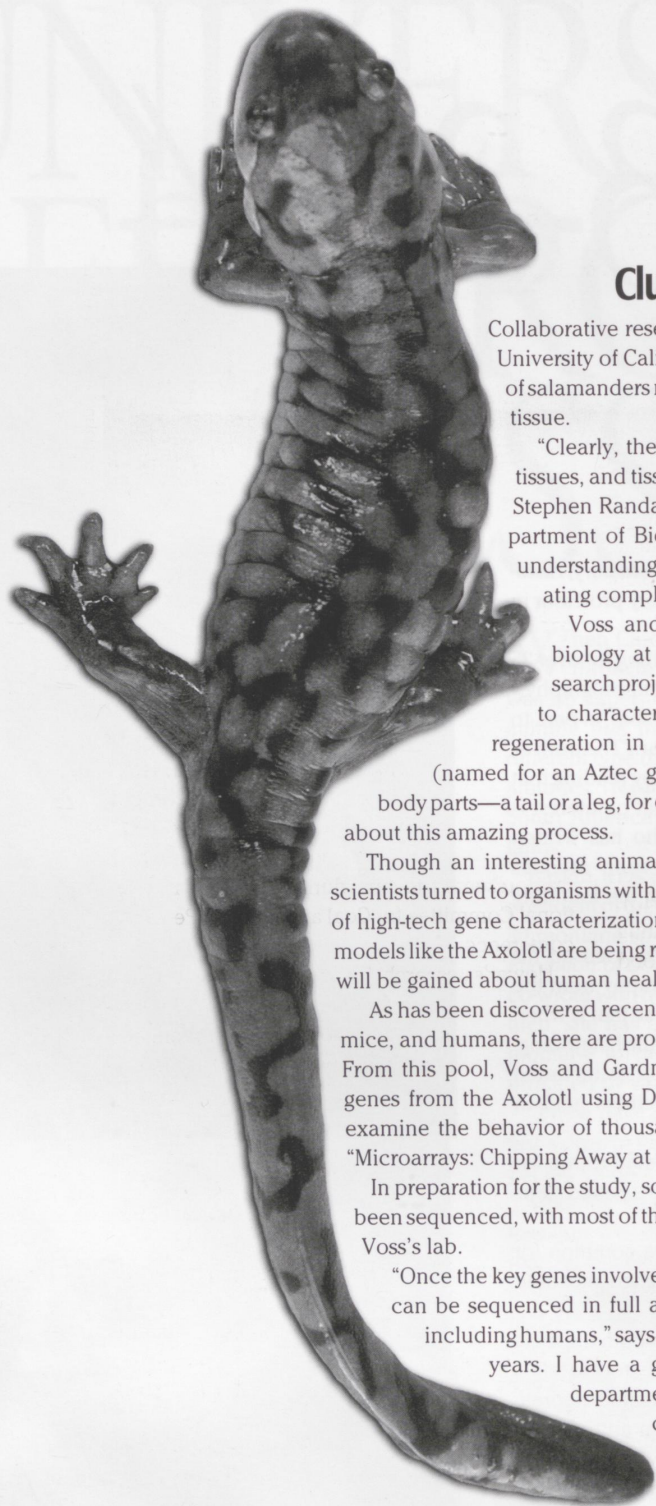
Up to that time, Popkin adds, it was more common for authors to leave their manuscripts to be published after their death.

"Autobiography fascinates me because it is both the most accessible form of writing—everyone has a life story to tell—and because it poses some of the most complicated theoretical problems about the relationship between authors and their texts. This is especially true in France, where the great classic of autobiographical literatures, Rousseau's *Confessions*, is the story of a man obsessed with telling the truth about his life, but acutely aware of the obstacles to doing so. His example has haunted French life-writing for more than 200 years."



The University of Kentucky Board of Trustees first awarded University Research Professorships in 1977. The goal is to enhance scholarly research and awareness of UK's research function by recognizing outstanding achievement by members of the university's faculty. Faculty receive professorships of \$35,000 each to advance their research.





## Clues to Organ Regeneration

Collaborative research at the University of Kentucky and the University of California-Irvine involving the genetic structure of salamanders might offer clues about regeneration of living tissue.

"Clearly, there is a lot of interest in the regeneration of tissues, and tissue repair in organisms is within reach," says Stephen Randal Voss, an assistant professor in the UK Department of Biology. "However, we are a long way from understanding how to coax the human body into regenerating complex body parts after injury or disease."

Voss and David Gardiner, a research professor of biology at UC-Irvine, are engaged in an extensive research project funded by the National Institutes of Health to characterize genes that are expressed during limb regeneration in a Mexican salamander called the Axolotl (named for an Aztec god). Salamanders can regenerate complex body parts—a tail or a leg, for example—but scientists know relatively little about this amazing process.

Though an interesting animal to study, Axolotls fell out of favor when scientists turned to organisms with fast generation times. With the recent advent of high-tech gene characterization tools, however, many traditional research models like the Axolotl are being reexamined, with the hope that novel insights will be gained about human health and disease.

As has been discovered recently in other vertebrates such as fish, chicken, mice, and humans, there are probably around 30,000 genes in a salamander. From this pool, Voss and Gardner plan to identify important regeneration genes from the Axolotl using DNA microchip analysis, a method that can examine the behavior of thousands of genes at the same time. [see also, "Microarrays: Chipping Away at the Mysteries of Alzheimer's Disease," p. 12]

In preparation for the study, some 60,000 salamander gene fragments have been sequenced, with most of the work performed at a robotic workstation in Voss's lab.

"Once the key genes involved in regeneration have been identified, they can be sequenced in full and compared with those in other animals, including humans," says Voss. "We are very excited about the next few years. I have a great group of people in my lab, and our department has some of the finest equipment in the country for pursuing questions of this nature."

In 2001, Voss was awarded a \$500,000 NSF CAREER Research grant and a \$1.4 million grant from the National Institutes of Health.

This past December he received a \$300,000 grant from the Kentucky Spinal Cord Head Injury Research Trust for research on spinal cord regeneration.

—Ralph Derickson, UK Public Relations



## Good Cholesterol, Estrogen & Heart Disease

Does "good" cholesterol lower the risk of heart disease? Does estrogen play a role in lowering the risk of heart attacks? Should postmenopausal women go on hormone replacement therapy (HRT) to prevent heart disease?

A UK study sheds light on these questions by presenting a new picture of the roles of estrogen, estradiol (a form of estrogen used in HRT) and good cholesterol (high-density lipoproteins, or HDL) in heart disease.

Previous studies by other scientists showed that HDL and estrogen stimulate the production of nitric oxide. A UK team, led by Eric Smart, associate professor in the Department of Pediatrics and Barnstable-Brown Chair in Diabetes Research, found that estrogen, as well as estradiol, and HDL act together to protect the heart by stimulating production of nitric oxide, which lowers blood pressure and acts as an anti-inflammatory agent.

In cell culture and animal studies, the researchers found male HDL and female HDL are different. In human studies, HDL from premenopausal women or postmenopausal women receiving estradiol stimulated the production of nitric oxide, whereas HDL from postmenopausal women did not.

The study, published last year in the *Journal of Clinical Investigation*, gives a new model for examining the cardiovascular effects of HDL and estrogen, and may have future implications in women's health, particularly the use of HRT for cardio-protection. This project is part of the \$8.3 million National Institutes of Health Center for Biomedical Research Excellence grant, the largest single grant ever awarded in the area of women's health at UK.

—UK Public Relations



Tom Dolan, UK medical illustrator

## CAER's Jim Hower Wins Thiessen Medal

Jim Hower, a 25-year veteran of the University of Kentucky Center for Applied Energy Research, has won the prestigious Reinhardt Thiessen Medal, awarded annually to one outstanding petrologist. Hower is the 27th recipient of the medal and only the fifth American to receive the award, which was presented to him during the 2003 International Committee for Coal and Organic Petrology conference.

Hower's research focuses on the history and chemical composition of coals, and the interaction between coal burned at a power plant and the mineral's combustion by-products. "I'm particularly interested in the quality of Kentucky coals," says Hower.

"We maintain active ties with the coal-burning utilities in the state and regularly conduct a survey on the amount of combustion by-products produced, the utilization of these products, the quality of the coal burned, and the quality of the by-products produced."

In addition to his research, Hower has served as editor-in-chief of the *International Journal of Coal Geology* and as associate editor of *Organic Geochemistry*.

"It is an honor to get a career award when I feel that I still have much of my career ahead of me," Hower says, "and to have my work recognized as having had an impact beyond the borders of Kentucky."

—Marybeth McAlister, CAER



## A Case of the "Baghdad Boil"

When Staff Sergeant Eric DiVona, from Ft. Campbell, Kentucky, returned from serving nine months in Iraq, he brought along with him an unwelcome souvenir. In an interview in mid-April with AP reporter Stephen Manning, DiVona described how the small bumps on his left earlobe and face kept swelling, one bump growing to the size of a silver dollar.

The condition is common enough in Iraq that soldiers have given it a name: the "Baghdad boil"; its scientific name is leishmaniasis. Doctors at Walter Reed Army Medical Center, where DiVona was treated, reported 653 cases of leishmaniasis by April 19.

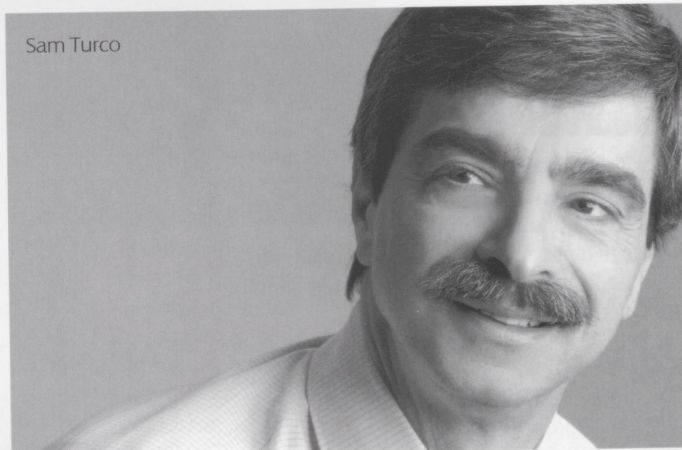
"I'm not surprised, really, by these numbers," says Sam Turco, a UK professor of biochemistry who has spent 20 years studying the unique characteristics of this rugged and potentially deadly parasite. "This is the peak season for sand fly breeding, and I understand that many soldiers sleep outside at night, which is the sand fly's favorite mealtime."

Leishmania is a survivor. It lives—and thrives—in the gut of a sand fly. When a host sand fly bites a human, and macrophages rush to the site of the bite to fight off the invader, leishmania doesn't care. Engulfed by the mighty macrophages, leishmania makes itself at home and calmly goes about its business of replicating.

"One of the intriguing things about this parasite is its ability to live in the most hostile of environments," Turco says. Leishmaniasis that remains on the skin causes open, slow-healing and sometimes disfiguring skin sores. If the bug works itself inwards, it can spread to several organs and can cause death if left untreated. About 2 million new cases of leishmaniasis occur each year, primarily in India, Sudan and Afghanistan.

Turco and his colleagues at UK, along with collaborators at Washington University in St. Louis, have recently made some important inroads to understanding how this parasite functions.

"We've been looking at various parasite-molecules in this single-cell organism that allow it to survive so well, and



Sam Turco

we found likely candidates—sugar-coated lipids and sugar-coated proteins," Turco says. In lab tests, when the researchers genetically engineered leishmania to prevent it from making these lipids and proteins, the parasite didn't survive in sand flies or in macrophages. "So we found that these lipids and proteins are essential for the parasite to survive and likely important in enabling disease in humans."

But because of a second discovery about this crafty parasite, this wasn't the end of the road for leishmania.

"We were on the right track, but, unfortunately, we've also discovered 20 different leishmania species," Turco explains, "and our magic sugar-coated lipid and protein bullets appear to work in only some of these. In other species of leishmania, if we knock out these lipids and proteins, the parasite still survives." The research team is currently working to understand the biochemical makeup of these non-affected species, which may be making other specialized molecules to protect themselves.

Turco has given lectures around the world on his parasitic infectious disease research. His current work is being supported through two grants from the National Institute of Allergy and Infectious Diseases, one of which was a prestigious MERIT award.

—Jeff Worley



## Rockefeller Humanities Fellows at UK

The Rockefeller Humanities Fellowships, hosted by the Appalachian Center and UK's Committee on Social Theory, bring scholars and Appalachian activists to UK's campus to interact with faculty and students interested in issues of globalization, democracy and environmental sustainability. This is the second year of the program.

"The combination of elements the grant supports makes this program unique, not only on UK's campus but nationally and internationally," says Wolfgang Natter, co-principal investigator of this four-year project. Natter is an associate professor in UK's Department of Geography.

Tom Hansell, a documentary filmmaker from Appalshop in Whitesburg, Kentucky, will research the connection between coal mining and electricity generation—and the hidden costs of exporting coal and electricity—for a film to increase public awareness of these costs. Kentucky exports twice the electricity it consumes, according to a 2000 Department of Energy study. The Kentucky Coal Association reports that Kentucky exports coal to 26 states and 11 foreign countries.

Susan Williams, who is education coordinator at Highlander Center in Morristown, Tennessee, has worked extensively with immigrant laborers. She hopes to further understanding of the impact of globalization on the flow of migrant workers and why people come to the United States to work. During her fellowship she has spoken about immigrant labor to graduate and undergraduate classes at UK, and conducted research at the Lexington-based Democracy Resource Center.

Jenkeri Okwori, an English and drama professor from Nigeria, is using theatre to educate Nigerians about democracy and citizenship. During his fellowship in Kentucky, he will be studying how groups such as Appalshop and Kentuckians for the Commonwealth have used arts programming to strengthen democratic processes. "I come from a country that only recently emerged from

## Working toward a Healthier Environment

A cleaner and safer environment is the goal of researchers working in a new facility at the University of Kentucky. The Environmental Research and Training Laboratory (ERTL) is a shared-use, core facility funded for \$2.3 million by the National Science Foundation. ERTL includes renovated laboratories in the Raymond Building and Anderson Hall for a variety of organic, inorganic, microbial, and stable isotopic analyses.

"ERTL's mission is to improve environmentally related research by providing researchers and students access to, and training on, state-of-the-art laboratory equipment and techniques," says Gail Brion, a UK associate professor of civil engineering, who is director of the facility. Her research interests include water treatment, water reuse and pathogens in water environments.

Since it opened, ERTL has been a magnet for both graduate and undergraduate students. The facility has supported research for 37 graduate students in eight disciplines, ranging from agronomy to engineering to geology, and nine undergraduate students.

"Right now, faculty are involved in about a dozen studies," Brion says, "including an EPA-funded project to define sources of fecal pollution in the Kentucky River, an NIH-funded project to determine effects of PCB on selenium uptake, and identification of toxic contaminants deposited on firefighters' clothing."

"One of the goals of this award was to enhance the visibility of UK research by supporting faculty and students with access to not only state-of-the-art equipment, but computer facilities where they can analyze their data and produce presentations," says Brion. Both students and faculty have access to computers loaded with statistical analysis software and graphic presentation programs purchased for use in ERTL, she adds.

decades of military dictatorship," he says, "so I have a compelling interest in this work."

"The Rockefeller Fellows have brought a deeper understanding to the UK community of how our struggles as citizens are the same, whether in the coal fields of Kentucky, in Tennessee or in Nigeria," Natter says. "What these activists also bring to Kentucky is a renewed sense of hope that we can overcome our problems through the sharing of information and ideas."

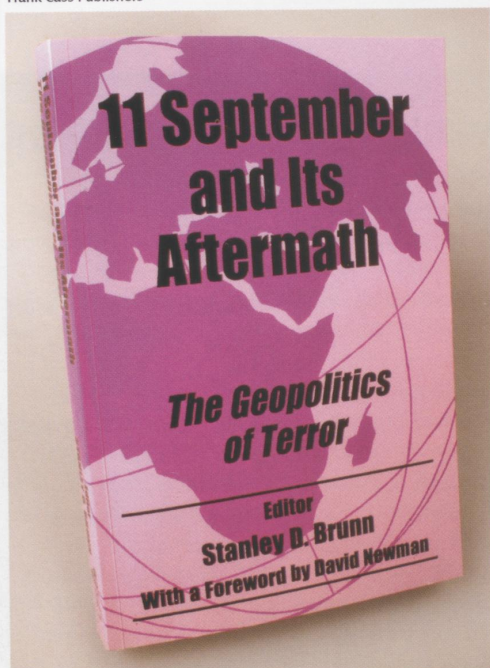
—Jeff Spradling, Appalachian Center



## Book End

# The Shifting Geopolitical World

11 September and Its Aftermath: The Geopolitics of Terror,  
edited by Stanley D. Brunn,  
Frank Cass Publishers



**9/11** will forever be branded into the American consciousness. A just-released book of essays edited by Stanley Brunn, a UK professor of geography, discusses the changes in the geopolitical makeup of the world brought about by the destruction of the World Trade Center twin towers on September 11, 2001.

"When such a catastrophic world-changing event like this happens, academicians and writers tend to think, 'Let's just leave this to the historians or the political scientists or the politicians to sort out.' But the international geography community has something to say about interpreting what happened and why—the geopolitical impact—and this collection of essays helps us understand some of the ramifications."

In assessing the impact of short-term events such as 9/11, Brunn believes it's important to quickly seize the opportunity to study them.

"The first time I did an impact study was right after the Three Mile Island disaster in 1979. I was teaching at Michigan State at the time, and within one month of the event a couple of doctoral students and I sent a survey to people who lived in

and around Three Mile Island. We asked them the impact of that event on their lives, on the economy, on the environment."

A few days after 9/11, Brunn contacted David Newman, the editor of the journal *Geopolitics*, and Newman immediately agreed to publish this book as a special issue. "I wanted the collection to represent different disciplines, both men and women scholars, younger and more experienced academicians," Brunn explains in discussing the people he contacted and invited to submit an essay.

In the book the authors discuss, from a variety of perspectives, America and emerging world orders, terrorism, environmental security, civil society, and the visual and print media. Brunn wrote the book's introduction.

Among the essay titles are "Calling 911: Geopolitics, Security and America's New War," "The Naming of 'Terrorism' and Evil 'Outlaws': Geopolitical Place-Making after 11 September," and "Tabloid Realism and the Revival of American Security Culture."

Four of the essays were written or co-written by UK geography doctoral recipients or graduates. Those writers are Margo Kleinfeld, a current geography doctoral student; Carl Dahlman, who is on the faculty of the University of South Carolina; Chris Jasparo, a member of the faculty of the Military College of Hanover; and Jon Taylor, who is on the faculty at California State University.

What would Brunn like readers to take away from this book?

"Everybody knows we live in an interdependent world, which means we need to know a lot more than we do about other cultures. We really don't know much about Islamic culture, for example, and how it plays out in foreign policy. It's embarrassing that we have so few people trained in other cultures and languages.

"I think if you are going to try to prevent something like 9/11 from happening again, you're going to have to take a look at the root causes of terrorism and people mixing faith with foreign policy."

Brunn also believes that the United States squandered a wealth of worldwide empathy and sympathy after 9/11.

"One of my greatest disappointments from the impact of this event is that our own political administration has not used this as an opportunity for understanding and for healing," Brunn says.

"This book is an important contribution to the geopolitics literature and, in particular, the understanding of some of the wider implications of the events of September 11," says Newman. "Professor Brunn has brought together a group of scholars whose take on this event is not the normal analysis offered to us by the politicians and governments. We are offered an insight into the way 9/11 has affected communities around the world."

—Jeff Worley



Odyssey  
Spring 2004

# Parting Shots

**"To me, old age is always  
15 years older than I am."**

—BERNARD M. BARUCH

**"Death is just a distant  
rumor to the young."**

—ANDY ROONEY

**"You're never too old to become  
younger."**

—MAE WEST

**"He has a profound  
respect for old age.  
Especially when it's  
bottled."**

—ATTRIBUTED TO W. C. FIELDS

**"How old would  
you be if you didn't  
know how old you are?"**

—SACHELL PAIGE

**"The secret of staying young is to live  
honestly, eat slowly, and lie about your age."**

—LUCILLE BALL

**"After age 70 it's patch, patch, patch."**

—JIMMY STEWART

***"How to live to be  
100? Get to be 99.  
Then be very  
careful."***

—ATTRIBUTED TO GEORGE BURNS

**"Old age is like a plane  
flying through a storm.  
Once you are aboard  
there is nothing you  
can do."**

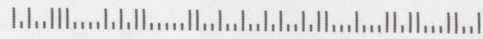
—GOLDA MEIR



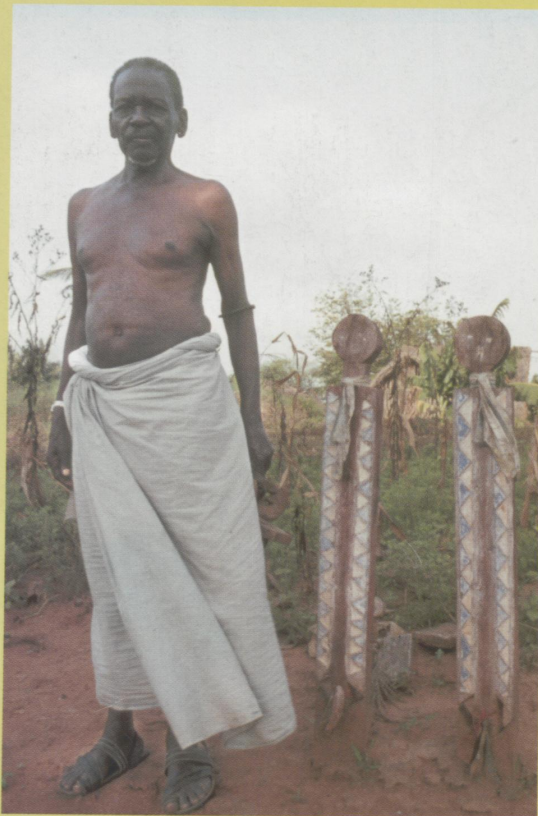
## Odyssey

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## In Search of East Africa's Ancestral Statues

p.18

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*Mark Summers and the Serious Business of Political Cartoons*, p. 28

*Skin Patch Promised Land*, p. 33

*Building a Stronger Safety Net for Children*, p. 35

**UK** UNIVERSITY OF KENTUCKY