

Odyssey

University of Kentucky Research
Summer 2009



Can **Fat Mice**
Teach Us How
Obesity Kills?



THE UNIVERSITY OF
KENTUCKY

Lee T. Todd Jr., President
Kumble Subbaswamy, Provost
James W. Tracy,
Vice President for Research

Agriculture

M. Scott Smith, Dean

Arts and Sciences

Mark Kornbluh, Dean

Business and Economics

Devanathan Sudharshan,
Dean

Communications
and Information Studies
H. Dan O'Hair, Dean

Dentistry

Sharon P. Turner, Dean

Design

Michael A. Speaks, Dean

Education

Mary John O'Hair, Dean

Engineering

Thomas W. Lester, Dean

Fine Arts

Robert Shay, Dean

Graduate School

Jeannine Blackwell, Dean

Health Sciences

Lori Gonzalez, Dean

Law

David A. Brennen, Dean

Medicine

Jay A. Perman, Dean

Nursing

Jane Kirschling, Dean

Pharmacy

Patrick McNamara,
Interim Dean

Public Health

Stephen W. Wyatt, Dean

Social Work

Kay Hoffman, Dean

Odyssey

Editor

Jeff Worley, jworley@uky.edu

Associate Editor, Art Director

& Web Designer

Alicia P. Gregory, apgreg@uky.edu

Designer

Shear & Shear

Photographer

Lee P. Thomas Photography

Printer

Gateway Press

Odyssey is published twice a year by the Office of the Vice President for Research and covers the latest research advances, innovative scholarship, and outstanding people that are part of the University of Kentucky's \$336-million-a-year research enterprise.

To receive a free subscription, contact
UK Research Communications/Odyssey
213 Bowman Hall
University of Kentucky
Lexington, KY 40506-0059
859/257-8297

Member of the University
Research Magazine Association
www.urma.org

An Equal Opportunity University

©2009 University of Kentucky

University of Kentucky Research
Summer 2009

Odyssey



COVER STORY

Can Fat Mice Teach Us How Obesity Kills?

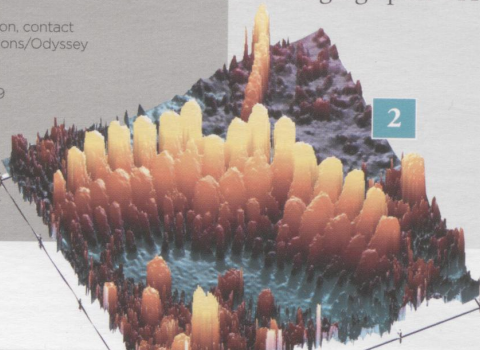
21

What started as a landmark discovery in 1988—fat makes the precursor to a protein that drives up blood pressure—has led Lisa Cassis, who chairs the UK Graduate Center for Nutritional Sciences, to 25 years of research on the hormone-based renin-angiotensin system. Using fat mice, Cassis is learning how obesity kills and finding mechanisms to stop it.

IN BRIEF

2

Imaging live cells on a nanoscale • reducing our carbon footprint • battery research in Lexington • Norman named poet laureate • Raitz appointed state geographer • Herring publishes foreign relations epic



Copy 1

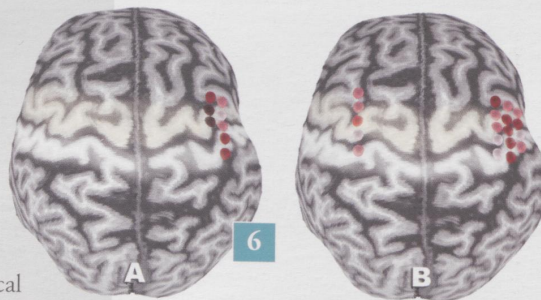
visit us online

www.research.uky.edu/odyssey

FEATURES

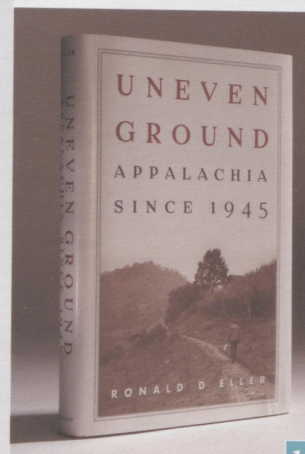
Taking Good Care 6

Based on the latest research about the brain's ability to form new neural connections, UK's Lumy Sawaki is helping patients regain the use of stroke-damaged hands, legs or arms. Her approach, which combines therapy with the latest technology, is central to the research program in physical medicine and rehabilitation at UK and Cardinal Hill Rehabilitation Hospital.



A Walk across Uneven Ground 12

UK history professor Ron Eller was a consultant for Diane Sawyer's 20/20 program "A Hidden America: The Children of Appalachia." He talks about that experience, stereotyping, his new book, and the consequences of "modernizing" Appalachia.



Kentucky Speeds into the Future with Internet 2 16

A federal appropriation will equip UK to install a state-of-the-art network connection to Internet 2. Ten times faster than the current 1 gigabit access, this network will benefit doctors, patients, medical students, teachers, and scientists across Kentucky.

UK Attracts 33 New Cancer-Fighters 18

"Shining star" B. Mark Evers, an accomplished surgeon from the University of Texas Medical Branch in Galveston, and 32 other recruits are helping to shape the future of the UK Markey Cancer Center. Evers' goals: achieve national cancer center designation and attract more top scientists to target Kentucky's deadliest cancers: lung and colorectal cancer.

Burgers Make Me Happy 31

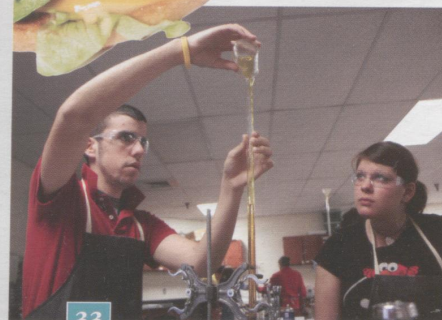
Three UK professors have recently conducted research on emotional intelligence—the ability to understand and manage our emotions when making decisions—and its role in consumer decision making. Their objective: to help people learn to make better decisions about what to eat and drink.



RESEARCH OUTREACH

Math and Science Partnership Scoring High Grades 33

An Appalachian program is helping students in 56 school districts boost their math and science IQ, and supporting teachers with the latest technology.



Hopping Probe to Study Nanostructures at the Surface of Live Cells

An international team of scientists, co-led by University of Kentucky physiologist Gregory Frolenkov, has developed a technique for imaging nanostructures on the surface of living cells. The team developed "hopping probe ion conductance microscopy," in which a nanoscale probe "hops" over the surface of a cell. This hopping probe, similar to a sewing machine needle, never touches the surface of the cell, unlike previous "sliding" probes that can damage cells.

The technique, which was published in the journal *Nature Methods* in April, allows researchers to get high-resolution, three-dimensional images of the surface of complex living cells.

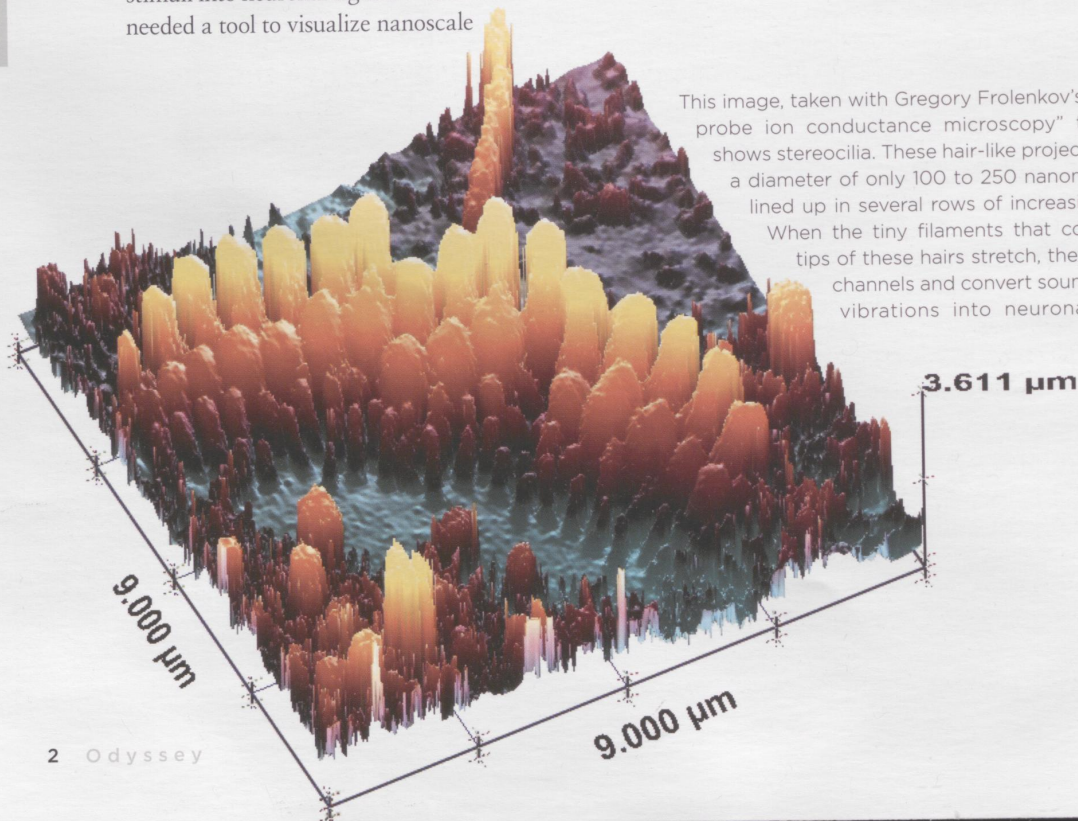
"Until now, we had no idea what the surface of most live cells looked like at nanoscale resolution," says Frolenkov, who came to UK in 2005 from the NIH's National Institute on Deafness and Other Communication Disorders.

Frolenkov and his research team are studying the mechanosensation—the conversion of mechanical stimuli into neuronal signals—in the inner ear and needed a tool to visualize nanoscale

objects on the surface of live inner ear cells. "Many diseases affect the cell surface, and abnormal mechanosensitivity of the cell is involved in deafness, pain, cardiac arrhythmia, and even cancer.

"Now we can see nanostructures such as individual protein or protein complexes in a living cell and probe their function. We expect that our technique, together with emerging high-resolution imaging techniques looking inside the cell, will clarify the mechanisms of a number of diseases, just as optical microscopes revolutionized medicine centuries ago," Frolenkov says.

Co-principal investigators on the project were Yuri Korchev of the Imperial College London Division of Medicine and David Klenerman of Cambridge University's Department of Chemistry. Ruben Stepanyan of the UK Department of Physiology was also part of the research team.—JW



This image, taken with Gregory Frolenkov's "hopping probe ion conductance microscopy" technique, shows stereocilia. These hair-like projections, with a diameter of only 100 to 250 nanometers, are lined up in several rows of increasing height.

When the tiny filaments that connect the tips of these hairs stretch, they open ion channels and convert sound-induced vibrations into neuronal signals.



Reducing Our Carbon Footprint

The University of Kentucky Center for Applied Energy Research (CAER) has created a consortium with government agencies, electric utilities and their research organizations to seek cost-effective technologies to reduce and manage carbon dioxide emissions from coal-fired power plants. Kentucky state government and the industrial partners will provide \$24 million over 10 years to support the research.

The consortium will pursue three major carbon management research projects:

1. Post-combustion carbon dioxide capture, using a pilot plant at CAER that was funded by E.ON US;
2. Large-scale carbon dioxide capture, in a portable unit to be constructed and operated at the power plants of consortium industry members; and
3. Development of a new combustion technology process for solid fuels like coal and biomass that could provide a more efficient power production technology for next-generation power plants.

The consortium is designed to split the cost of research on large-scale carbon dioxide capture systems, work which has often been too expensive and risky for a single utility or government agency to undertake.

"This consortium is an ideal example of the public and private sector partnering to solve one of Kentucky's—and the nation's—major problems," says UK

President Lee T. Todd Jr. "In creating this partnership, Kentucky is asserting itself as a national leader in developing technologies that will help reduce America's carbon footprint. This is an important step for the future of Kentucky's energy industry."

New Partnership to Build Battery Industry in Kentucky

The University of Kentucky and the University of Louisville are partnering with Argonne National Laboratory and the Commonwealth of Kentucky to establish a national Battery Manufacturing Research and Development Center to advance battery technology. This partnership is a move toward securing U.S. energy independence, reducing greenhouse gas emissions and strengthening the economy. The battery center will be built at Spindletop Park next door to UK's Center for Applied Energy Research on Ironworks Pike.

"This center has the potential to transform Kentucky's economy," says UK President Lee T. Todd Jr. "With UK's Coldstream Campus just two miles from the center and with the nation's automobile manufacturing base located in Kentucky and surrounding states, there will be great potential to attract and develop new companies. With this center in Kentucky, our state is uniquely positioned to become a national leader in next-generation automobile technology."



From the *Odyssey* archives: Gurney Norman (left), filmmaker Andy Garrison, and actor Ned Beatty take a break from filming Norman's short story "Fat Monroe" in 1989. In his new role as Kentucky's poet laureate, Norman will be the state's official arts ambassador, promoting Kentucky arts and artists across the state.

Gurney Norman Named Kentucky Poet Laureate

Gurney Norman, director of the University of Kentucky Creative Writing Program, has been named Kentucky Poet Laureate for a two-year term.

For over 30 years, Norman has been a driving force in the literature of Appalachia and the South. He was instrumental in the founding of the Appalachian Poetry Project and the Southern Appalachian Writers Cooperative. He is also known as a stellar and life-changing teacher, and his students include Kentucky writers Frank X Walker, Chris Holbrook and Rebecca Howell.

His first novel, *Divine Right's Trip*, was originally published in the margins of the *Last Whole Earth Catalog*, which sold two million copies worldwide. Norman has also published *Book One From Crazy Quilt: A Novel in Progress* and *Kinfolks: The Wilgus Stories*. Norman's short story "Fat Monroe" was made into a film starring Ned Beatty in 1990, and the film was shown at the New York Film Festival.

Norman was born in Grundy, Virginia, in 1937 and attended the University of Kentucky from 1955 to 1960, majoring in journalism and English. He then studied writing at Stanford University as a Stegner Creative Writing Fellow. Norman will soon complete his 30th year teaching at UK.

The word "poet" in the position's title is interpreted in its broadest sense to include writers whose accomplishments are in any literary form, including the novel and

short fiction. Norman succeeds 2007-2009 Kentucky Poet Laureate Jane Gentry Vance, who is also a professor in the UK Department of English.

Karl Raitz Appointed State Geographer

Karl Raitz, a professor of geography at UK, has been named the next Kentucky state geographer. In this post appointed by the governor, Raitz will assist state and local officials with boundary studies, mapping, cartographic programs, planning and zoning, and land-use studies, serve as a resource for teachers and publishers of geography textbooks, and work with geographers in other states to analyze and disseminate geographic information.

"Along with these other activities, I have a particular interest in working with researchers who are developing digital data sets for use in Geographic Information Systems analysis of mapping and environmental problems," adds Raitz, who will serve a one-year term beginning January 1.

A former chair of his department at UK and a long-time student of culture and its material artifacts, Raitz has spent the past 35 years examining American landscapes, an interest which began during his undergraduate days. As a student traveling through Kentucky on the way back to his native Minnesota, Raitz says he was swept off his feet by the Bluegrass. He took a visiting professorship in geography at the University of Kentucky in 1970 and never left.

His early interest in this region focused on how the most extensive collection of quarried rock fences still standing in the United States came to be built. His investigation traced the origins of the fences to the work of Irish stonemasons who came to the Bluegrass in the mid-19th century. The detective work of Raitz and his co-researcher, Carolyn Murray-Wooley, an architectural historian, led to the publication of *Rock Fences of the Bluegrass*.

Raitz says he is particularly proud of another publication, *The Atlas of Kentucky* (University Press of Kentucky), which he co-authored with UK colleagues Richard Ulack and Gyula Pauer. "This was a major undertaking. More than 20 researchers working in collaboration over a period of eight years contributed to this effort," Raitz says.

Currently, he is working on several projects relating to the role of roads as a shaping influence on landscapes. His research in this area has led to publication of two books: *The National Road* and *A Guide to the National Road*.—JW

Former Head of UK History Department Publishes an Epic on Foreign Relations

George Herring, UK alumni professor emeritus of history, retired from the university in 2005 after a 36-year teaching career, but he continues to be an influential and respected scholar of U.S. history. Herring recently published *From Colony to Superpower: U.S. Foreign Relations Since 1776* (Oxford University Press, 2008), a thousand-page volume that is part of the Oxford History of the United States series.

A November signing at the Washington, D.C., bookstore Politics and Prose—part of Herring's nationwide book tour—was televised by C-SPAN, and the book has been named an "Editor's Choice" by *The New York Times Book Review*. Kudos for Herring's book have kept coming: *From Colony to Superpower* was one of five finalists for the 2008 National Book Critics Circle award in the nonfiction category and received the 2008 Robert Fer-

rell Prize given by the Society for Historians of American Foreign Relations for the best book in the field.

How long does it take a scholar to write a 1,035-page, scholarly book?

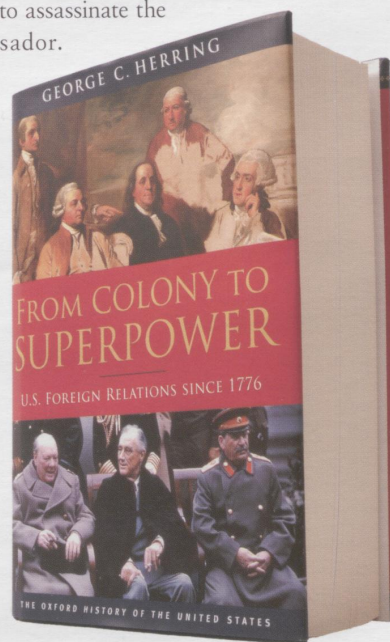
"I began serious work in the summer of 1997 and finished in early 2008," says Herring. "Of course, I was doing other things, too, during most of those years. Only after I retired was I able to devote full attention to the book."

Herring rates two U.S. diplomats as standouts: John Quincy Adams and Franklin D. Roosevelt. "Both had an instinctive understanding of how the world works, what diplomats is all about, and what could and could not be done in dealings with other nations. Their appreciation of the limits of power sets them apart from many diplomats and helps explain their success."

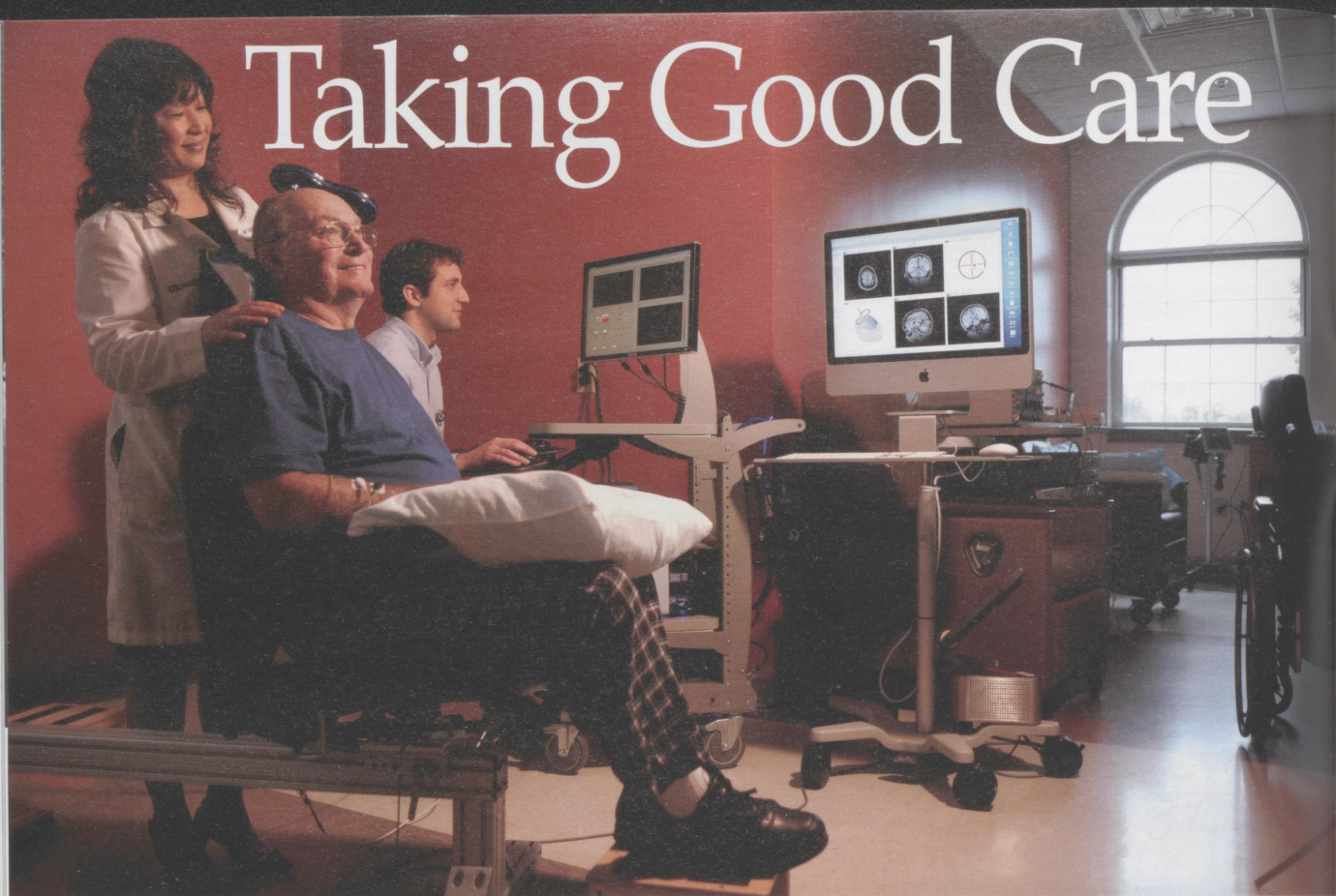
The worst U.S. diplomat of all time?

Herring laughs. "Oh, he's easy to identify, and, I am sorry to say, was a Kentuckian—Edward Rumsey Wing of Muhlenberg County. As Minister to Ecuador in the 1860s, he tried, first, to annex that country to the United States and then to assassinate the British ambassador.

Fortunately, he drank himself to death before he could further damage U.S. interests."



Taking Good Care



By Jeff Worley

Hi-tech Approach Helps Stroke Patients Regain Their Lives

David Rader knew something was very wrong. He suddenly felt dizzy and weak. He'd been working for more than an hour in his sweltering attic in late August 2007, putting in an air-conditioning system, and thought he was suffering from heat exhaustion. His wife, Jean, drove him to the VA hospital, 10 miles away in Lexington, where he was examined and released. But the next day he felt worse. He went back to the VA, where he had a massive stroke.

"His doctor told us he wasn't going to make it," Jean recalls. "They said to call our daughter in Florida and call the chaplain. But I know my husband—he's tough—so I told the doctor, 'Not so fast,'" she says, spacing out the three words for emphasis.

Jean knew David, 75, was a fighter and that with proper rehab care he could make a comeback. She did call her daughter, Kate, in Florida, because she remembered that Kate knew someone at Cardinal Hill Rehabilitation Hospital in Lexington and that the hospital had a good reputation. So she took David there. This

Working with biomedical engineer Kenneth Chelette, Lumy Sawaki uses transcranial magnetic stimulation (TMS) to induce electric currents in the brain tissue of stroke patient David Rader. When TMS stimulates an area of the brain that controls movement of a particular muscle, that muscle will move. After stimulating multiple brain areas and monitoring muscle response, Sawaki maps the brain area that controls a particular muscle. These maps confirm the reorganization of neurons in the brain. Sawaki is an associate professor in UK's Department of Physical Medicine and Rehabilitation.

turned out, Jean says, to be an excellent choice. The rehabilitation programs at Cardinal Hill have played a pivotal role in ongoing clinical studies originating from the University of Kentucky.

At Cardinal Hill, David (who we'll return to shortly) was put into the care of Lumy Sawaki, an associate professor in the Department of Physical Medicine and Rehabilitation at the University of Kentucky, who immediately strikes you as a confident, affable and approachable woman. She included David in one of her four ongoing research projects that she brought with her from Wake Forest University when she came to UK last year as the Cardinal Hill Endowed Research Scholar in Stroke and Spinal Cord Injury Rehabilitation.

"The common ground of all these studies is measuring the effects of intensive, task-oriented therapy that uses the latest technology to help stroke patients, some of whom have suffered major, life-changing damage," says Sawaki, her English tinged with the flavor of her native language—Portuguese. (She was born and grew up in Brazil.) The titles of three of her projects include the word "neuroplasticity," which refers to the brain's ability to reorganize itself by forming new neural connections to compensate for injury and disease.

The Brain Can Find a Way

In conventional stroke treatment, therapists frequently focus on teaching patients how to compensate for loss of function on one side of the body by making greater use of the unaffected side. However, this compensatory approach does not address the potential for the affected side to recover some function.

During the last two decades, scientists have learned that the brain is able to relearn and redirect more activity after a stroke injury than previously thought possible. Neuroimaging techniques, like fMRI, which shows the functional activity of the brain, have revealed that remarkable changes can occur after constraint-induced movement therapy (CIMT). This approach involves constraining the use of a stroke patient's non-affected arm with a mitten for 90 percent of his waking hours for two weeks so that the weaker arm will have to do more of the work in daily activities. In this way, use of the weaker arm triggers new neuronal brain activity. The really good news is, brain rewiring can occur even for patients who had a stroke 10 or 20 years ago.

Sawaki was the lead author on a CIMT study published last year in the journal *Neurorehabilitation and Neural Repair*. In this multicenter study, 30 subjects between three and nine months after their stroke were randomly assigned to the experimental group (who received CIMT immediately after initial evaluation) or the control group (receiving CIMT after four months). Each subject was evaluated using transcranial magnetic stimulation (TMS), a noninvasive method to excite neurons in the primary motor cortex, located toward the back of the frontal lobe. The job of the motor cortex is to plan and execute movements.

Here's how TMS works. By positioning a handheld, wand-like device on a patient's head, a therapist induces weak electric currents in the patient's brain tissue to trigger brain activity. When TMS is used to stimulate an area of the brain that controls movement of a particular muscle, that muscle will move. By stimulating multiple brain areas and monitoring muscle response, the therapist can map the brain area that controls a particular muscle and compare this map to previous patterns of activity. As the patient's ability to perform a certain movement improves, these brain maps confirm the reorganization of the associated area of the brain.

"Both groups in this study demonstrated improved hand-motor function two weeks after baseline," says Sawaki, "but the experimental group showed significantly greater improvement in grip force after the intervention and at follow-up." In the experimental group, CIMT produced significant improvements in damaged arm motor function, she explains as she demonstrates, moving her right arm side-to-side. This group also had an increase in the TMS motor map area compared with the control group over a four-month period, which provided evidence that the constraint-induced approach led to new and functionally significant neuronal reorganization.

In discussing the importance of TMS in mapping areas of new neuron activity, Sawaki cites a breakthrough study by Harvard neuroscientist Alvaro Pascual-Leone. Volunteers with no neurological disorders were brought into a Harvard lab to learn a five-finger exercise on a piano keyboard connected to a computer. The subjects did a two-hour practice session for five consecutive days, and each day's practice was followed by a test that measured their progress. Before the first practice session and every day afterwards, Pascual-Leone and his team used TMS

to map the motor cortical areas that target finger flexor and extensor muscles. As the subjects' performance improved, the size of the cortical representation in the brain for both muscle groups increased significantly.

"But he didn't stop there," Sawaki continues. "He had a second group of subjects merely *think* about practicing the piano exercise." They played the simple piece of music in their head, holding their hands still while imagining how they would move their fingers. Then the volunteers sat beneath the TMS coil. Pascual-Leone saw that the cortex region that controls the piano-playing fingers also expanded in the brains of volunteers who simply imagined playing the music—just as it had in those who actually played it. This discovery did nothing less than show that mental training had the power to change the physical structure of the brain. That finding is the basis for Sawaki's work with severely affected patients like David Rader to guide them to move stroke-affected areas that previous therapists had given up for dead.

Reading a Patient's Brain Map

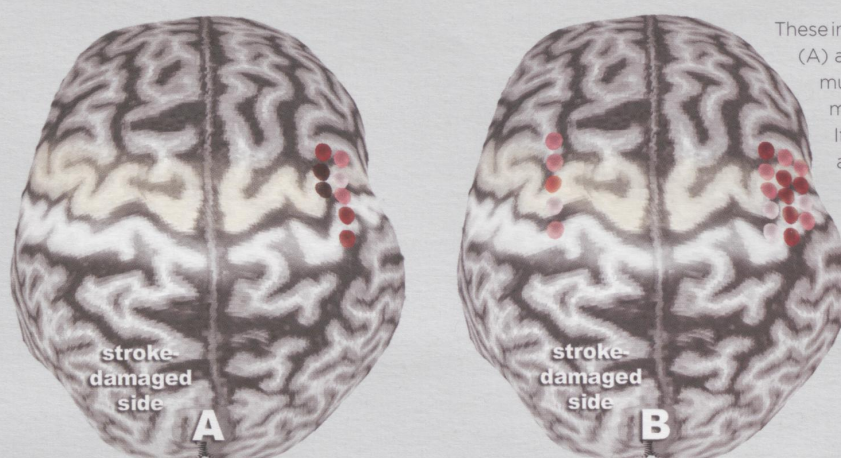
Scientists have long known which parts of the brain control which parts of the body. Humans spend a lot of time talking and manipulating objects with their hands, so we have large amounts of cortex devoted to mouth, tongue and hands. (Different species have different patterns. Rats get a lot of information from their whiskers, so a large amount of sensory cortex is devoted to the whiskers.)

"It's this 'cortical priority' that, early on, inspired some therapies for brain-damaged patients," Sawaki notes, "and it's the basis for our CIMT work."

In one of Sawaki's current studies, she is pinpointing clusters of new neurons and, through some trial and error, figuring out which parts of a patient's damaged tissue are triggered by activating these neurons. This work is made possible through the development of a futuristic offshoot of TMS called transcranial direct current stimulation (tDCS), which involves applying weak electrical currents to the head to generate an electromagnetic field to excite and fire neurons. Sawaki uses this technology in conjunction with TMS.

In several of her studies, she is also using peripheral nerve stimulation (PNS) to increase the brain's ability to reorganize. "In each PNS session, three nerves in the subject's affected arm are stimulated by mild electrical pulses," Sawaki explains. "These pulses travel to the brain and excite areas in the motor cortex." Each session lasts two hours and is followed by intense, task-oriented occupational therapy.

The new technology is wonderful, Sawaki says, exuberantly, but any success—movement in the damaged area of the body—is highly dependent on the patience and perseverance of the stroke victim. "I think of myself as a guide in this process. Once I find the area of the brain where I believe new neurons are taking over a movement function, I tell the patient to *envision* moving that area."



These images show a stroke patient's brain before (A) and after (B) therapy. The dots represent muscle activation; the lighter the dot, the more activation in that area of the brain. If the motor cortex (highlighted yellow area) is damaged by a stroke, neuron regeneration often happens next door in the sensory cortex (highlighted white area). Brain map B shows significant improvement in muscle activation in the motor and sensory cortex on both the stroke-damaged and non-stroke sides of the brain. These 3D renderings were created using software called Brainsight.

This is analogous to the work of Pasqual-Leone, who asked volunteers to envision practicing a piano exercise.

But how can someone imagine moving, say, a stroke-damaged finger? How can we think about something the body has always done automatically?

"This is actually very common," Sawaki says. "In people who have lost a limb, for example, there is still the perception of sensations, usually including pain, in the missing arm or leg. The brain still gets messages from the nerves that originally carried impulses from that limb. Amputees often talk about being able to 'move' their missing limb." And more to the point, Sawaki knows that when patients envision the process of movement, this mental picture facilitates the brain's rewiring.

Two Recent Successes

When David Rader became Sawaki's patient, he wasn't optimistic about his chances of recovering any movement in his damaged arm or leg. His wife, Jean, placing a hand on her husband's shoulder (David is still unable to speak), sadly states that his whole left side was still without feeling a year and a half after the stroke. After he completed traditional therapy through home health and outpatient services, his daughter, Kate, convinced him to try working with the UK neurorehabilitation research team at Cardinal Hill. There, Sawaki placed David in one of her studies, which lasted two weeks.

"Two weeks might seem like a short time," Sawaki says, anticipating the question of the study's brevity, "but this is very intense work."

She used TMS to determine which parts of David's brain controlled his arm and hand. Based on that evaluation, Sawaki gave him experimental treatment for two hours a day, followed by four hours of intensive, task-oriented occupational therapy. This training often involved work with a robotic arm (see p. 10). His progress was slow, but then came the breakthrough.

"Toward the end of the second week," Sawaki says, "we were continuing to focus on Mr. Rader's damaged arm in daily PNS sessions. After stimulation during one of these sessions, I told him to envision moving the muscle in his arm that we had targeted; and suddenly his arm moved."



Joe Springer, a professor of anatomy and neurobiology, is heading up the research program in physical medicine and rehabilitation at UK and Cardinal Hill Rehabilitation Hospital in Lexington. Springer, who also serves as a research associate in UK's Spinal Cord and Brain Injury Research Center, is one of several UK faculty members located at Cardinal Hill.

"David was both surprised and thrilled," his wife exclaims, recalling the moment. "Now he can move his arm, which he thought he would never do. And because he knows now he can move it, he's more motivated to work at home to move it even more. It's wonderful."

In October 2004, stroke attacked Wendall Trent, 33, in his sleep. When he went to bed, he felt fine, he said, maybe just a bit sore from a tough workout instructing his martial arts class. He'd been thrown by another instructor and "landed wrong." But he didn't think much about it until he woke up at 2:30 a.m. next to his bed on the floor, the whole left side of his body without feeling. His wife drove him to St. Claire Regional Medical Center in Morehead, Kentucky, close to where they live, and the prognosis was bleak: "The doctors said my carotid artery had been torn, that I'd never be able to use my arm or hand again, or walk again," Wendall states, solemnly.

He was taken by helicopter to the UK Hospital, where a stent was put in his neck. After four days in critical care, Wendall was taken to Cardinal Hill, where he had inpatient therapy for two months. By February 2005, he was able to stand up and take a few steps, but his left arm and hand failed to respond to traditional rehab exercises.

Four years passed, and still he had no feeling in his disabled arm and hand. Then he decided to return to Cardinal Hill and see if he could be helped through the new rehabilitation research program he'd heard about there. "I was paired up with Lumy and was impressed

with her from the beginning. She has a great can-do attitude—no negativity is allowed in. The therapy was strenuous, but I stuck with it.”

In March of this year, working with Sawaki’s team and their neurorehabilitation techniques, Wendall envisioned his left pinkie finger moving—and it moved. “I thought, ‘Wow! *There’s* some progress!’ Her expertise on this high-tech equipment has given me new hope. The whole process reminds me of hot-wiring a car,” he laughs. “It’s another step on the road to recovery.”

Sawaki is pleased by the progress these two patients—and others—have made, but she re-directs any praise aimed at her to the patients themselves. “Yes, I have the tools here to ‘facilitate’ the rewiring process, but it’s the effort and desire of the patient that ultimately determines the outcome. I’m simply helping these people help themselves.

“Everybody who comes here improves. My mission here is beyond that,” Sawaki says. “I want every patient to be able to go back to their jobs or their lives and be physically able to do things again. That’s the big goal.”

“Lumy’s work is the perfect match for the type of research program we are building here,” states her colleague Joe Springer, professor of physical medicine and rehabilitation at UK and research associate in UK’s Spinal Cord and Brain Injury Research Center. Springer is one of several UK faculty members located at Cardinal Hill. “Following our growing understanding of the brain’s potential for neuroplasticity, her focus on identifying novel neurorehabilitation strategies is moving us into important, uncharted territory.” ■

Rehab Robots—Partners in Recovery

The latest robotic technology is helping patients like David Rader and Wendall Trent regain movement and balance. In January 2008 the Lokomat robotic system debuted at Cardinal Hill Rehabilitation Hospital in Lexington, which has a close affiliation with the UK College of Medicine. The Lokomat’s harness and lift system raises patients from a wheelchair and places them in a standing position on the treadmill. Robotic devices attached at the patient’s thighs and knees provide support to properly “unweight” the patient. The Lokomat then operates at an appropriate speed, creating a walking rhythm.

Cardinal Hill is the only facility in the state to offer Lokomat treatment to the public and one of only 25 in the country used for therapy, says Kara Lee, a doctor of physical therapy and coordinator of the Lokomat program in the Center for Outpatient Services at Cardinal Hill. An anonymous donation made in honor of Dusty Hicks, a Central Kentucky teenager injured in a diving accident in 2006, made the Lokomat purchase possible.

This equipment simulates natural walking patterns, actual pace and gait, Lee explains. When she talks about working with patients who use the Lokomat, she charges the air with enthusiasm and makes you think she is a perfect fit for the job she’s chosen. The latest virtual reality software is an important part of this, she continues, gesturing to a large screen that faces the patient. As he walks in the harness, his avatar chases various animals and tries at the same time to avoid enemy dogs. “Software registers different amounts of force on each leg. Lokomat teaches people to walk at a faster pace, go around objects, and regain balance.”

A physical therapist and a student intern can change three parameters as needed: body weight support, speed, and the percentage of work the robot does. A typical intervention program involves working with the Lokomat for six to eight weeks, twice a week, doing 45-minute sessions. “We’ve had more than 200 people use this so far,” notes Lee, “and it’s booked solid from 9 to 5, five days a week. We would love to have a second one, honestly—it would likely be booked solid, too. It’s amazing how much progress someone can make using this equipment.”

See the Lokomat in action: www.youtube.com/watch?v=CWGJUQJqb-Q

Sawaki enlists the aid of another robot in her comprehensive approach to helping stroke victims. This device, an upper extremity robotic therapy system, is able to mimic a fluid, natural extension of the patient’s arm using pneumatic “muscles” and can be programmed for repetitive exercises specific to the user that improve arm and hand flexibility and strength. “Our goal with this device is to help stroke survivors regain the ability to perform

basic tasks, such as reaching for objects or feeding themselves,” Sawaki says, pushing a button that stirs the robotic arm to life.

Here’s how one of the exercises works. The patient is buckled into a swivel chair—imagine being strapped into a barber chair—and the stroke-affected arm is placed in a large cuff. The patient’s hand wraps around a joy stick to control movement of a large dot on a video screen. The patient is asked to move the dot from the center of the screen and place it in various outer circles, moving it up and back as directly as possible.

“It’s like a video game,” Sawaki says, “with one major difference. If you go too far astray on any given task, the robot takes over and moves your arm in the right direction. Repetition and intensity are the two main elements of this exercise. The robot does 960 repetitions per session, which would totally wear out any therapist!”

The robot in this way helps the patient reestablish the brain-arm connection, as does all training, she adds, emphasizing that this is intense therapy: it demands up to four hours of active participation daily and up to two hours of experimental treatment beforehand for two consecutive weeks. The UK Healthcare Stroke and Spinal Cord Neurorehabilitation Research Program at Cardinal Hill has the only robotic arm in Kentucky. ■



Physical therapists Dana Lykins and Matt Kudron help stroke patient David Rader on the treadmill of the Lokomat, which simulates natural walking patterns. This system uses a harness and lift system to place patients in a standing position, and robotic devices attached at the thighs and knees provide support to properly “unweight” the patient. The Lokomat is located at Cardinal Hill Rehabilitation Hospital in Lexington, which has a close affiliation with the UK College of Medicine.

A Walk across Uneven Ground

A Conversation with Appalachian Historian Ron Eller

A child's teeth riddled with cavities.
Tumbledown shacks.
Hopeless poverty.

These were some of the images that flashed across the TV screens of nearly 11 million viewers when Diane Sawyer's 20/20 program, "A Hidden America: The Children of Appalachia," aired last February. This documentary focused on the lives of four young Appalachians and the challenges they face as they chase after their dreams. The program elicited a broad range of responses, and there was a near-consensus that Appalachia had, once again, been stereotyped.

Ron Eller, a UK history professor and former director of the University of Kentucky Appalachian Center, was brought in by 20/20 as a consultant for this special report. Eller, who has spent the last 30 years teaching and writing about the Appalachian region—his latest book is titled *Uneven Ground: Appalachia Since 1945*—has always been in demand as a speaker on Appalachian issues at colleges, conferences, and community forums throughout the nation. But his life got even busier immediately after this program aired. Eller was bombarded with emails and public requests to respond to the documentary. He spoke at Union College in southeastern Kentucky and found himself in a packed auditorium talking to several hundred students. He was interviewed on talk radio, spoke at Kentucky's Berea College, did interviews for three newspapers, and was interviewed at length by the local ABC TV affiliate—all in one week.

A few weeks after 20/20 aired, after he finally had time to breathe, I sat down with Eller in his history department office. Surrounded by books and journals, and with the frequent beep from his computer signaling, perhaps, another email request, Eller talked about his part in the 20/20 program, stereotyping, his new book, and the consequences of "modernizing" Appalachia. And in this exclusive interview for *Odyssey*, he also suggests some possible solutions to bridge the inequality gap in Appalachia.—Jeff Worley

You've spent your entire career writing about and studying the people of Appalachia and the social and political policies of the region. Where did this intense interest come from?

I came by it naturally. I'm a descendent of eight generations of families from Appalachia and was born in southern West Virginia. I've always been in love with the mountains.

But you moved away from the mountains.

Yes. Because my father couldn't find a job, we moved to Ohio in the early '50s. Years later, in college, I took a southern history class, and all the stories about Appalachia were about people who were poor and lived in log cabins up on the hillside and played the banjo and drank moonshine and shot everybody as they walked by [laughs]. We were living in Ohio, but our family would travel back to West Virginia every other weekend, so I knew these depictions were simple stereotypes. It made me angry. So I decided I would rewrite Appalachian history from the perspective of the people in the region. And the rest, as they say, is history.

The 20/20 program. How did you become involved in this? Did one of Diane Sawyer's "people" call you up?

I was first contacted by ABC a couple of weeks before the program was to air. The producers had finished all of their filming but were having difficulty providing the "context" for their story, and they felt they needed more information about the history of the region. Diane Sawyer decided they needed to do a taped interview with me, so they flew me to New York the weekend before the program was to air, and I was interviewed for about two hours by Diane. They ended up using only a few seconds of that interview because, I think, they were more interested in constructing an emotional story about the conditions endured by these children than in describing the context, causes and solutions to the region's problems. But I did get the last word in the program. They quoted me saying that what Appalachia needed as much as anything else was the ability to dream about an alternative future free of the inequalities of the past.

What was your impression of the 20/20 program?

Well, I had certain expectations based on previous coverage of Appalachia by the national media. Over the past few decades Charles Kuralt, Dan Rather, Rory Kennedy, and dozens of other journalists decided to

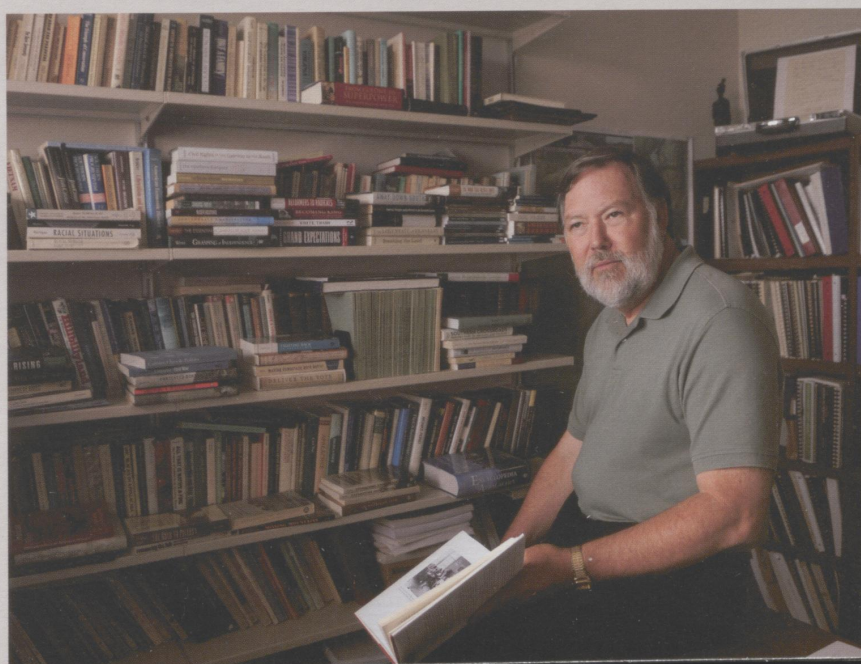
take us on a little shock walk through Appalachia, so I didn't expect anything different from Diane Sawyer. Shock journalism, of course, often utilizes stereotypes and paints entire regions and communities of people with unfair and inaccurate generalizations. In this most recent treatment, you have shots of trash-filled yards, ramshackle shacks, toothless men and women, small children whose teeth are dotted with cavities, a young man sleeping in his truck. And mostly I was disappointed because the program didn't delve more deeply into the causes or the problems of Appa-

lachia, or illuminate some of the programs working to address them.

But if such images aren't in some sense "true," why do they still persist in national media coverage?

Stereotypes persist because they are useful, not because they are accurate. They have political power and always mask some self-interest. They are used by those in power to justify some action, some exploitation, toward those who have little power. Stereotypes in Appalachia have helped to justify exploitation of the land and the people for profit by those who don't live in the region. These same images that we

Ron Eller, a UK history professor and former director of the University of Kentucky Appalachian Center, served as a consultant for Diane Sawyer's 20/20 program, "A Hidden America: The Children of Appalachia," which aired last February. His impression of the program? "Mostly I was disappointed because it didn't delve more deeply into the causes or the problems of Appalachia, or illuminate some of the programs working to address them."



saw in 20/20 have been used to blame the persistent poverty of Appalachia on the culture of the people rather than on basic social injustices and structural inequalities handed out by the economic and political systems. Stereotypes allow us to blame the victim.

Clearly the program dealt us some stereotypes, but didn't it also result in some viewer sympathy and care. I read that someone sent the 12-year-old girl featured on this report the Hannah Montana-style boots she wished for. The 18-year-old football phenom who slept in his truck was offered scholarships to several Kentucky colleges, and ended up accept-

ing one. And Pepsi has promised to send a fully equipped mobile dental clinic to supplement the Appalachian dentist who talked about "Mountain Dew mouth" and childhood tooth decay caused by constant soda drinking from toddlerhood.

I would be last person to argue that charity is not a good thing. But if we stop at charity, we never get to the point where we address the underlying issues that generated the problems that exist. We never get to the "justice" side of the social equation. And there's a very significant difference between charity and justice. One of the points I make in *Uneven Ground* is that in Appalachia we have chosen paths to development that have benefited some at the expense of others, and we continue to define development in ways that bring opportunity and resources to some, but leave others with poor health care, poor access to education, and less opportunity for decent-paying jobs.

What "underlying issues" are we talking about? Why have the poorest communities in Appalachia remained so poor?

One of the inequalities that has occurred in the region is that when programs like the War on Poverty focused on Appalachia, a disproportionate amount of money and resources flowed into the higher population centers. There's been a significant leveling of ground in Appalachian areas of northern Georgia, western New York state and western Maryland, based upon socioeconomic measures we tend to use; but in central Appalachia, no. In terms of income, poverty

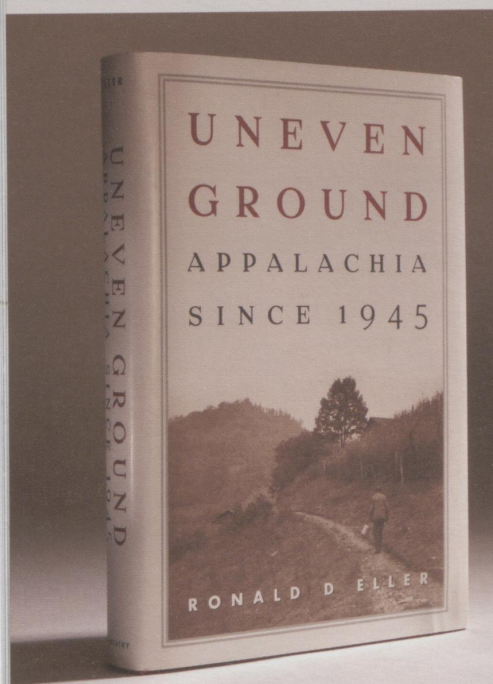
rates, educational levels, and general health, we've made much less progress there.

Is it a matter of these people being literally harder to reach? Is it because of the barrier of the mountains?

This is a common belief, that the land itself is to blame, its daunting geography. When in reality, the issues facing the region and the inequalities there are not a result of the landscape. I've traveled throughout Western Europe, Germany and Switzerland, as well as mountainous areas of the Northwest and Northeast in this country, areas that are just as mountainous as Appalachia. But the people who live there haven't suffered from the types of disadvantages as people in central Appalachia have. The bottom line is, we can design strategies for equal economic opportunities no matter what the landscape is.

So then, what accounts for the inequality?

This is a major point I make in *Uneven Ground*. Our approach to helping Appalachia has been to take national assumptions about how we define progress and superimpose those ideas on local communities in Appalachia, a top-down approach that has created inequalities there. The remodeling of the education system is one example among many. The idea took hold in the 1960s that consolidating schools, as cities all over the country had been doing, would clearly lead to a better education for students in the



"Stereotypes persist because they are useful, not because they are accurate. Stereotypes in Appalachia have helped to justify exploitation of the land and the people for profit by those who don't live in the region."

mountains. The problem was thought to be that there were too many small schools, two- and three-room schoolhouses, isolated all over the place. The new equation was that consolidated schools equal a quality education—obviously we couldn't put science labs in every one of the small schools. So we built consolidated high schools that looked just like consolidated high schools anywhere else in the country.

But didn't the model of the consolidated high school work pretty well in the rest of the country?

Some worked very well, but we aren't talking about the rest of the country. What the new model did throughout the Appalachian region was take schools out of communities and relocate them primarily next to the growth centers of county seat communities. Then we began to transport rural kids from their homes, three hours one way sometimes. What we did is take a very important social institution away from community. We put these kids in what, in many cases, was an alien environment. And as an added "bonus" to these students, because of the distances they had to travel, they had less opportunity to participate in extracurricular activities.

Didn't some of the students do well, despite the travel time?

Yes, and it's not surprising which ones succeed: kids who come from middle-class backgrounds. They generally don't have as far to travel because middle-class families tend to live

closer to these schools rather than in far-flung rural areas. So their kids can participate in extracurricular activities more easily after school. Middle-class parents are more likely to be engaged in the school because of proximity and culture. Consolidated schools are often culturally alien to working-class and poorer students who have little experience with highly structured learning environments and competitive learning strategies. Working-class and poorer students tend to experience learning from a more oral, less formal, usually family-based and peer-group set of relations. What we've found through the years is, kids from more rural, more remote, communities are the first to drop out and are less likely than middle-class students to go on to any level of college. So what the consolidated schools approach did is design an educational system modeled after an urban environment that has created unequal ground, that has reenforced the inequality that has existed in the region.

If you were in the position to make specific changes in Appalachia to solve some of the problems you've been discussing, what would those changes be?

First, there are no easy solutions to the challenges facing our communities. If there were, we would have already addressed them. But my immediate response to that question is, we must look beyond an extractive-based economy to one that values and enhances the landscape and the resources that it holds, one that connects

our own sustainability and future to that of the mountains themselves. We must begin by abolishing surface mining, including the radically destructive practice of mountaintop removal. Mountaintop removal isn't necessary to the regional or the national economy; it's just cheaper. We can continue to mine coal, gas, and other mineral resources but the impact of extraction on the land, on water, on forests, and other sensitive ecosystems must be strictly regulated and enforced.

Second, I'd like to see the decentralization of education and health care, putting schools and health providers back into smaller communities, especially rural communities where they provide not only jobs but community cohesion, collaboration, identity, and responsibility. It is much easier for a parent to be involved in a child's education if the school is down the road instead of across the county.

What would it take to achieve these goals? Nothing less than a new generation of leaders for Eastern Kentucky who dream and think creatively. Appalachia, and especially East Kentucky, is one of the most creative places on Earth. Our musicians, artists, writers, and storytellers make magic out of nothing but dreams. This same culture can surely create new and innovative ways of thinking about what makes a good life and how to achieve it. ■

Kentucky *Speeds into the Future* with Internet 2

By Alicia P. Gregory

Tomorrow's Internet is happening now and happening fast, thanks to \$1.4 million in federal funding for the University of Kentucky. And across Kentucky, doctors, patients, medical students, teachers, and scientists will all benefit.

This direct appropriation from the Health Resources and Services Administration, secured by U.S. Senator Mitch McConnell, will allow UK to install a state-of-the-art network connection to Internet 2—a 10-gigabit network. This connection is 10 times faster than the current 1 gigabit access available across Kentucky.

What does this mean? Kentuckians will be able to share information at the fastest speed available, explains Doyle Friskney, who has served as UK's associate vice president for information technology for half of the 24 years he's worked at the university. Speed has big implications for the future of health care. "This money will allow UK to partner with health-care professionals in rural hospitals and clinics to share electronic patient records, including digital X-rays and CT scans, and do video teleconferencing to get consultations on treatment options. Right now only doctors in big cities have these capabilities."

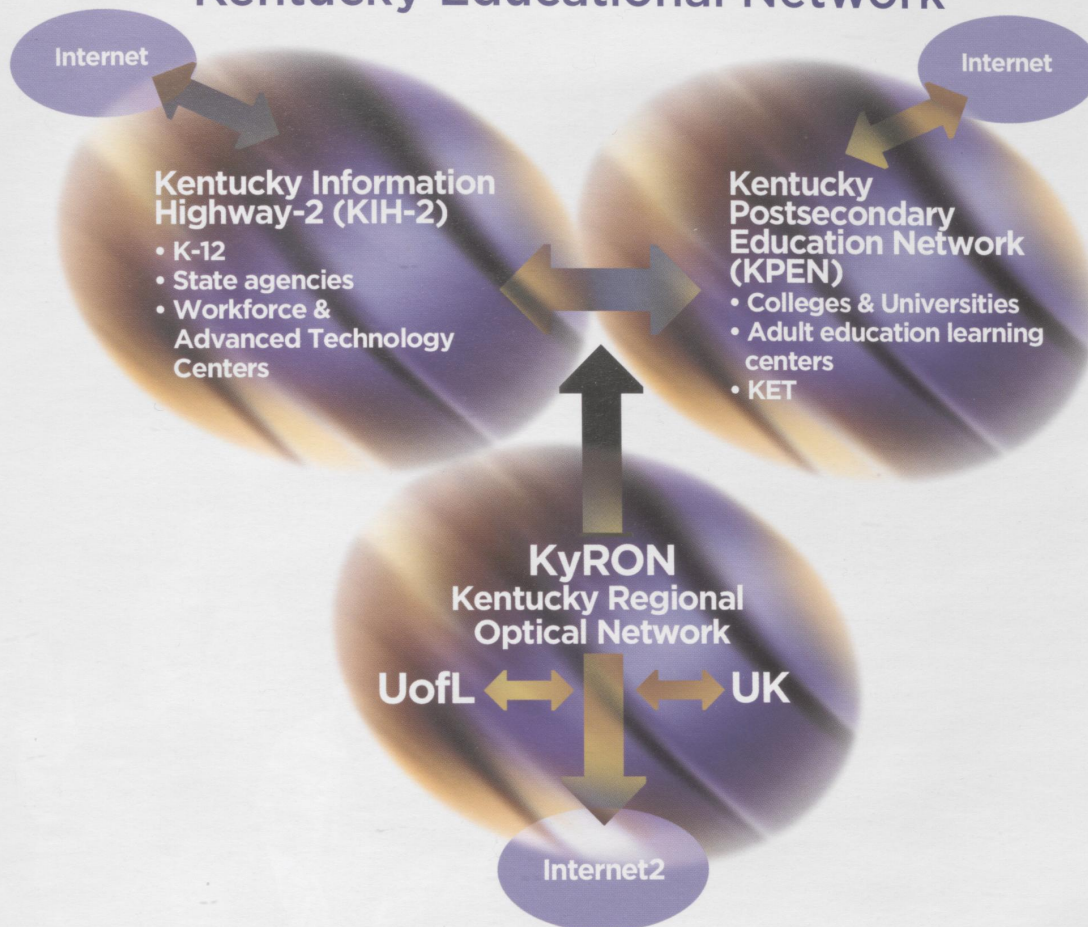
The Internet 2 network also will enable UK's medical colleges—Medicine, Nursing, Dentistry, Public Health, Health Sciences, and Pharmacy—to deliver online education programs to meet, in part, the growing need for health professionals in Appalachia.

James W. Tracy, vice president for research, who leads UK's \$336-million-dollar-a-year research enterprise and serves as principal investigator for the appropriation, emphasizes that this funding will boost the university's efforts in translational medicine. "The network will make it possible for UK researchers to more quickly move their health-care discoveries from the lab to the doctor's office. New technologies to diagnose and treat illnesses will get to patients faster."

But the benefits aren't limited to health care. "The enhanced connections provided by Internet 2 will increase our faculty's eligibility for advanced research grants from NIH and NSF, and will allow our scientists to participate in and contribute to national collaborative projects," says Tracy.

Friskney points out, "This will ripple over into other areas, like education and agriculture." For instance, a third-grade teacher in Harlan County could consult with a special education expert at UK, or a College of Education class on campus could watch a teacher in Letcher County lead a math lesson. "This could give teachers, and medicine or pharmacy students on rotation across the state, a way to collaborate with their mentors at UK and open access to all of the online resources at the university," says Friskney. He emphasizes that the physical infrastructure to do this is already in place, thanks to Kentucky's current \$20 million annual commitment to high-speed networks. "Kentucky

Kentucky Educational Network



hasn't taken a back seat to other states in terms of networking."

Friskney describes the three current statewide networks: KIH-2, KPEN and KyRON. The Kentucky Information Highway-2 (KIH-2) connects all of the state's K-12 schools. The Kentucky Postsecondary Education Network (KPEN) links colleges and universities, adult-education learning centers and KET. And the Kentucky Regional Optical Network (KyRON) unites UK and the University of Louisville to the main Internet connector in Louisville that links Kentucky to the rest of the world.

"This new funding means we can join these three networks together, ramp up the speed from 1 to 10 gigabits,

and put in a dedicated, future-focused research line," says Friskney.

He explains that the Internet 2 network will have two parts: a production line and a research line. The production line, a connection that will always be "live" (think of the dial tone you get when you pick up the phone) and is currently 1 gigabit, will be upgraded to 10 gigabits. "This line will work like the Internet works today—you link together a series of servers, and the speed of that connection determines how fast you can go."

The research line is something new. "Our researchers will be able to use it and study it," Friskney says, setting up an example. A UK researcher modeling air flow over a turbine blade is working

with an engineer at Vanderbilt. He needs 5 gigabits to transfer a large set of data. That UK scientist would simply dial up a dedicated, "point-to-point" connection between himself and the researcher at Vanderbilt to transfer the information. And because this is a point-to-point connection, Friskney explains, the research line wouldn't be tied up by the activity of everyone else on campus.

"In anticipation of the Internet moving toward point-to-point connections, computer scientists at UK like Jim Griffioen and Ken Calvert will be doing research on this network to prove that this type of network is what we need for the future." ■

A “shining star,” a “top-tier director,” an “accomplished surgeon and prolific researcher.” These were some of the accolades used to describe B. Mark Evers at the April 2009 press conference announcing his appointment as the new director of the Markey Cancer Center.

But what stood out most was his modesty. “There’s been a lot of talk about me,” Evers told the audience. “And I’m very embarrassed about that, because I normally like to fly under the radar.”

It seems counter-intuitive, but could this self-deprecating attitude be the secret to his success? Maybe his preference to shift the focus from himself to his laboratory full of talented colleagues (15 of whom followed Evers from the University of Texas to the University of Kentucky), as well as six other outstanding cancer investigators who have come with their own independently funded lab teams, is his most telling trait. Evers is a mentor, primarily interested in helping others in the shared quest to cure cancer.

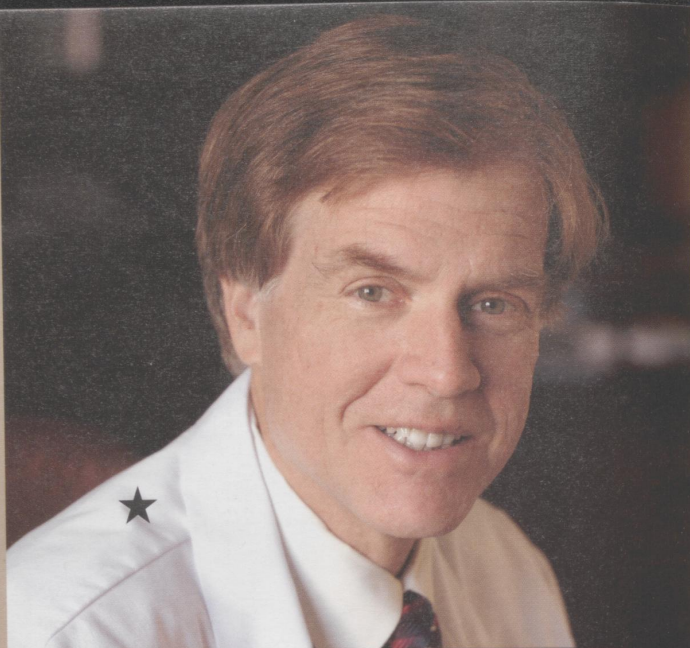
In his new UK office, brimming with oversized orange crates—“I’m still in the process of getting settled,” Evers says by way of apology—he describes his two families, his “spicy” research, and his vision for targeting lung and colorectal cancers, the cancers that kill the most Kentuckians each year.

Let’s start at the beginning

“I was the first person in my family to go to college. My dad never went to high school, and my mom went no further than high school, but they both instilled in me a really strong work ethic,” Evers says.

But what is the connection between a strong work ethic and his choice to become a surgeon? He explains that in the small farming community in southern Tennessee where he grew up, there was “beloved and revered” Dr. Thomas. “There was God and then there was Dr. Thomas,” Evers states with a broad smile. “He was the quintessential surgeon. He’d do a diverse array of surgeries in the morning, go to the ER and fix a broken leg, then see patients in the clinic all afternoon and sometimes all evening. He treated everybody. In high school I saw that and thought, ‘Gee, that’s really what I’d like to do.’”

Evers earned his medical degree, *summa cum laude*, at the University of Tennessee in Memphis and completed his residency training at the University of Louisville in 1988. “I was a general surgeon with a gastrointestinal (GI) focus. I wanted to be an academic surgeon—do research and perform surgeries—so I went to arguably one of the best GI



Who are these people? Find out at the *Odyssey* website.



UK Attracts 33 New Cancer-Fighters

Led by “Shining Star” B. Mark Evers

By Alicia P. Gregory



physiology laboratories in the country in Galveston, Texas.”

The University of Texas Medical Branch (UTMB) in Galveston became his home. Over the next 21 years, he created a second family: his 15-member lab team as well as the more than 40 junior faculty, residents, postdocs, and grad students he mentored along the way.

Evers explains that his lab team focused on a hormone called neurotensin, which is generated in response to fat consumption and found in the small intestine. Neurotensin plays a critical role in colorectal cancer, the country’s second-leading cancer killer, causing nearly 60,000 deaths each year. Evers’ team linked neurotensin to the production of IL-8, a potent inflammatory protein that accelerates the growth and spread of colorectal cancer.

Based on findings by other scientists that turmeric, a curry spice used for centuries in traditional Indian medicine, could fight skin and breast cancer, in 2006 Evers’ team discovered that turmeric could also knock out neurotensin. Turmeric’s active ingredient, curcumin, blocked the signals inside colon cancer cells, reducing the production of IL-8 and suppressing the growth and the migration of the cells. “Our findings suggested that curcumin may be useful for colon cancer treatment and suppression in cells that respond to this gut hormone neurotensin,” Evers says. “About a third of all colorectal cancer cells have the receptor for neurotensin. So just like hormonally responsive breast and prostate tumors, the therapy for colorectal cancer would block hormones.”

Jay A. Perman, dean of the UK College of Medicine and vice president for clinical affairs, underscores the importance of Evers' finding: "Curing cancer relies on being able to stop the spread of cancer from one part of the body to another. If blocking a hormone sequesters cancer cells, we've made a huge leap in treatment."

Evers' success at UTMB brought him a slew of titles: professor of surgery, director of the UTMB Comprehensive Cancer Center and the Sealy Center for Cancer Cell Biology, and the Robertson-Poth Distinguished Chair of General Surgery. He has amassed hundreds of publication credits, for both clinical studies and basic science projects, and he has been continuously funded by the National Institutes of Health for the past 17 years—an impressive feat considering the aggressive competition for NIH dollars, especially recently. Evers brought nearly \$14 million in grant funding to UK.

Perman says, "As important as the research is, one of the first things he asked me when we met was, 'What are you doing here to create, to develop, to stimulate more physician-scientists to conquer the scourge of cancer?' That was his concern, and I particularly value that, because that's how the impact of bringing Dr. Evers here is multiplied."

A new Kentucky home

But why did he pick up and move to Lexington? Was it a tough sell for his wife Karen, a pharmacist, and son Benjamin? His daughter Lauren, 19, is a student at Washington University in St. Louis, so the closer proximity of Lexington was a draw.

"I just caught the excitement. Everybody did." While Evers toured the

campus and cancer center, his son Ben enjoyed a UK football game and birthday cake (he turned 13 during the family's first visit to Lexington) at Commonwealth Stadium, courtesy of Michael Karpf, UK's executive vice president for health affairs, and his wife. And Evers' colleagues came to Lexington, too, to see what it had to offer. Evers says, "And what we saw—a huge emphasis on building, on growth, on people, on care—was impressive to the entire group."

Evers adds that in his experience the cooperation he witnessed between the College of Medicine and the UK Hospital is a rare commodity. "In the academic medical world there's often infighting between the hospital and medical school. It's so counterproductive. Here, to Dr. Karpf and Dr. Perman's credit, the enterprise system has everybody working together. You've got shared visions and goals, and that really excited me."

He says that the Top 20 business plan was the icing on the cake. "You sort of go, 'Yeah, yeah, yeah,' because a lot of institutions say, 'We want to be in the Top 20.' But you come to UK, and President Lee Todd and Dr. Karpf have a *plan*. They're sticking to it in terms of growth, and so you know it's going to happen. And you just want to come and be part of that excitement."

Evers stresses that because the colleagues who allowed him to succeed have joined him in Lexington, he's confident he can "hit the ground running. When you can transplant an environment that is working well, you can keep up the level of productivity." And he says he's looking forward to working with the excellent clinicians and scientists at UK. "The Markey Cancer Center is extremely strong

clinically and in basic science." His goal is to foster translational teams. "By going after multi-disciplinary grants that team up researchers with physicians, we can succeed in translational science—taking cancer discoveries from the lab to patients faster."

He adds that in the next five years he wants to earn National Cancer Institute designation, a distinction from the National Institutes of Health held by only 64 institutes in the country. "It's a symbol that you're the best of the best," Evers says emphatically. "It's more than prestige—it puts you in the running for the most cutting-edge clinical drug trials. It's a huge boost for the university."

And in a region crippled by cancer—Kentucky ranks first in lung cancer, second in colorectal cancer—Evers says his focus will be recruiting top researchers and clinicians to UK's lung and colorectal cancer programs. "Building up areas where Kentucky has significant problems in terms of cancer is the fastest way to make a difference."

But what is the biggest difference for Evers in his new Kentucky home? "I hate to admit it, but I was probably more of a football guy. But even I've been caught up in the Coach Cal excitement. I've missed SEC sports. I can't promise I'll always stay quiet if Tennessee scores, but I promise I won't wear any orange." The corners of his mouth ease into a grin as he says, "I have a whole closet full of orange clothes, but they never went with my hair anyway." ■

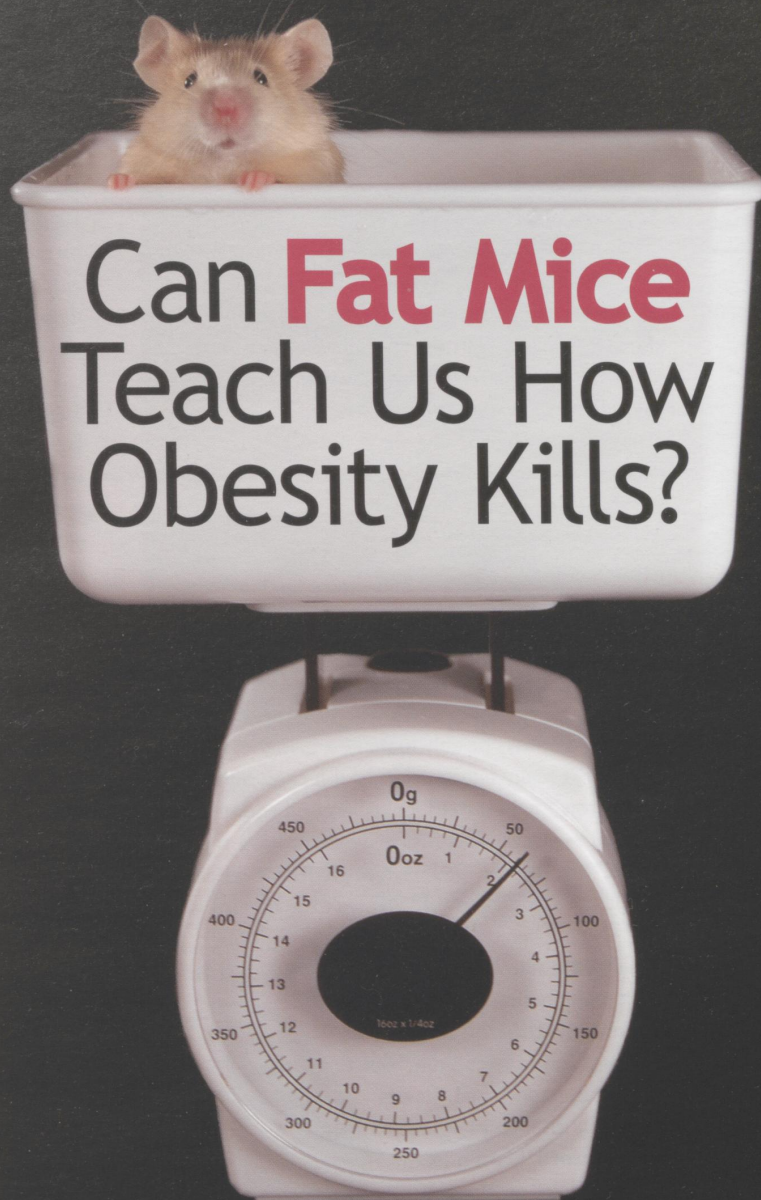
By Alicia P. Gregory

Lisa Cassis has been studying fat since before it was “big.” Back when kids still played outside, and restaurant portions weren’t the size of your head. Before two-thirds of American adults were labeled overweight or obese. “Back in the ’80s scientists didn’t really care about fat. It was boring,” she says, drumming her fingers on the table.

And even after Cassis made a landmark discovery about fat cells in 1988, she says it was difficult to get funding for her research. “My scientific peers thought I’d made a mistake—surely fat couldn’t be *doing* anything,” Cassis says with a wry smile.

Her discovery, which she describes as a “pure accident,” happened while she was looking for a protein that makes angiotensin, a component of the renin-angiotensin system. This hormone system regulates blood pressure. “I was trying to find out if blood vessels could make this stuff themselves, so I was looking for the precursor protein, angiotensinogen.” But because she hadn’t thoroughly cleaned the bit of vessel she was examining under the microscope, she accidentally found heaps of angiotensinogen in the fatty tissue clinging to the vessel.

If a fat cell could make this protein, she reasoned, that meant it could make angiotensin and drive up blood pressure. And suddenly the “boring” fat cell was brimming with activity, and dangerous potential.



This discovery led Cassis, now chair of the University of Kentucky's Graduate Center for Nutritional Sciences, to 25 years of research to answer new questions: why would a fat cell make angiotensinogen? Does it automatically make angiotensin? What regulates a fat cell's ability to produce these things? And then, says Cassis, the ultimate question: is this the link between obesity and cardiovascular disease?

To find out if angiotensin is a mediator of obesity's cardiovascular complications—hypertension (high blood pressure), atherosclerosis (hardening of arteries) and abdominal aortic aneurysms (ruptured bulges in the aorta that cause massive internal bleeding)—Cassis started feeding mice a high-fat, “Americanized” diet. She admits that mice aren't a perfect model for human obesity: “There's always a disconnect between species. Mice aren't men or women.” But she's convinced that fat mice can teach us how obesity kills and can reveal mechanisms by which we can stop it.

Big Fat Deal

It wasn't Cassis's dream to make mice fat. Chuckling at the thought, the West Virginia native says, “My parents didn't go to college. They grew up during the Depression. They told my brothers and I that if they were going to send us to college, we were going into health care, because we'd always be able to make a living.

“I wasn't really interested in health care; my favorite subject was English. But I looked around and settled on pharmacy—mostly because I wouldn't have to touch people,” she laughs. “So I went to pharmacy school and liked it, but I didn't know if I wanted to do that my whole life.” One of her professors asked Cassis if she'd ever considered research, and she ended up working in his lab on “a really boring project.” Her blue eyes roll, and then she admits, “It's amazing I stayed in research.” But with that experience Cassis caught the discovery bug.

She earned her Ph.D. in pharmacology at West Virginia University, went to Germany for a year and a half on a prestigious Alexander von Humboldt postdoctoral fellowship, and spent three years as a

postdoc at the University of Virginia with mentor Michael Peach, the biggest name in the renin-angiotensin game at the time.

In 1988, Cassis got her first faculty position in the UK College of Pharmacy. And that position brought success and marriage—her future husband, Rob Lodder, started in the college just three months after Cassis, and their professional collaboration led to a new medical device and research on a sugar substitute that may be a therapy for diabetics. (For more, see “Love, Patents and Sugar” on p. 28.)

It was in her first year at UK that Cassis made her discovery that a lot more is going on inside fat than meets the eye.

Fat, a.k.a. “adipose,” is connective tissue composed of adipocytes—fat cells. These cells have one big vacuole, a large compartment that stores lipid droplets. Lipids are naturally occurring molecules (like oils, waxes and cholesterol) that can dissolve into fat tissue. Adipose tissue stores energy in the form of fat, and it cushions and insulates the body.

The angiotensinogen Cassis first found was in a specialized type of fat called brown adipose tissue, the so-called good fat that generates heat. “But there are other types of fat that even I combat in my daily life,” she says begrudgingly, with a downward glance at her mid-section. White adipose tissue—to blame for the telltale “spare tire”—harbors vast stores of angiotensinogen. Cassis adds, “I looked in virtually every fat deposit in rats I could find, and the protein was everywhere.”

This is the finding she presented at a conference in 1988, and one that skeptics questioned until years later when, she says, “a number of high-powered scientists found fat was pumping out all kinds of things.” At least 50 known substances are made by fat cells.

Scientists labeled these substances adipokines, and Cassis's protein angiotensinogen became one of them. “Many adipokines regulate inflammation. Angiotensin promotes inflammation in blood vessels, and that's important because inflammation underlies a lot of diseases.”

Cassis points out that where fat ends up is critical to the development of disease.



"If fat is deposited subcutaneously—under the skin—many studies have shown it's not as dangerous as when it's deposited viscally—in the abdomen around the organs. When we make mice obese, the biggest changes to the renin-angiotensin system are in the abdomen. The mouse's fat tissue makes more of the precursor protein and more angiotensin specifically in the belly." She says other scientists are transplanting fat from the abdomen to other parts of the body to see if fat retains its bad effects, but for now nobody knows why abdominal fat is so life-threatening.

"We do know there is a connection between obesity and type 2 diabetes, and there are well-established connections between both of these conditions and cardiovascular disease."

In fact, in 1998 the World Health Organization defined an entirely new disorder—Metabolic Syndrome—to draw attention to these connections. The American Heart Association estimates that more than 50 million Americans have Metabolic Syndrome. Risk factors include excessive abdominal fat, low HDL and high LDL cholesterol, elevated blood pressure, and insulin resistance.

"Obesity seems to be the common denominator in diabetes and cardiovascular disease. What we don't know is exactly how those connections are mapped out on the cellular, biochemical level. If we knew those mechanisms, we'd be able to develop new treatments. That's why I've used mouse genetics to manipulate the renin-angiotensin system specifically in fat cells," Cassis says, gesturing toward her lab space on the fifth floor of the Wethington Building. The roar of a helicopter, taking off from the roof of the UK Hospital next door, is a temporary distraction from her description of how she makes mice fat.

"We feed them commercially available diets high in saturated fat. We have a 45 percent fat diet and 60 percent fat diet." Cassis notes that "the 45 percent fat diet is more analogous to what most Americans are eating. We feed the mice this diet and they become very obese little butterballs. They get all the different parts of the Metabolic Syndrome and some develop atherosclerosis."

A Systematic Approach

"I want to learn how obesity kills, so that's the angle I take in looking at the renin-angiotensin system. People have been studying this system since the late 1800s, and, believe it or not, just this year we published a paper on a new component: ACE 2."



The chair of the UK Graduate Center for Nutritional Sciences, Lisa Cassis leads a team of 10 who are studying the mechanisms of the renin-angiotensin system in fat cells. Pictured with Cassis is her nephew Paul Cassis (center), from Charleston, West Virginia, who came to work in her lab for a month last summer, and Sean Thatcher, a postdoc with a Ph.D. in physiology from Marshall University, who has worked with Cassis for two years.

But, Cassis says, "Let's start with the basics. This is a hormonal system. It has proteins and enzymes that come together to make a peptide family called angiotensins." (Peptides are short molecules formed from the linking of amino acids, the building blocks of life.)

The system starts with the protein. "*Angiotensinogen*: my daughter loves that word," Cassis says, overemphasizing each syllable in a squeaky kid voice. She adds that her daughter Laura, now 14, can't wait to spend a summer working in a UK lab like her 17-year-old brother Andy. Both of Cassis's children are interested in science. Her son will probably follow in his father's engineering footsteps, while her daughter has expressed an interest in health care. "I'm not pushing them in this direction. To me, the important thing is that you like what you do, because if you're spending all this time at it and you're miserable, that's no way to live."

Clearly, for Cassis, studying angiotensinogen has been the right choice. "This big protein is fascinating. In humans it's 452 amino acids long," she explains. "Forgive me, but it makes you wonder why God would create this huge protein and in the 100 years people have been studying it the only thing they've found it does is give rise to this puny eight amino acid peptide. Such biological inefficiency!"

Angiotensinogen is made predominantly by the liver, "but we found it is also made in fat cells. It's basically spit out from the cells into the bloodstream. There it encounters the enzyme renin, secreted by the kidneys, that converts this big ol' protein by clipping off 10 amino acids at one end to make angiotensin I." Cassis explains that the only purpose for angiotensin I is to lead to angiotensin II.

"As angiotensin I floats by in the blood, a second enzyme, angiotensin-converting enzyme (ACE), clips it to eight amino acids to create angiotensin II. This is the biologically active peptide that causes blood vessels to constrict and drives up blood pressure." She adds that angiotensin II has a very short half-life: about 12 seconds. "It's not around long, but it does a lot in a very short time."

Two ACEs in the Hole

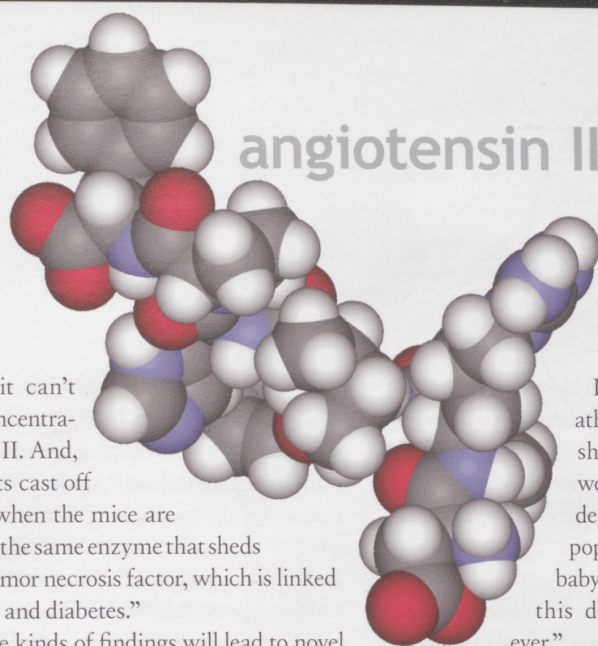
Scientists had figured out that overproduction of angiotensin II was dangerous, but what component of the system was the first target for therapeutic drugs? ACE.

First discovered in the mid-1950s, ACE could produce angiotensin II, a way to raise blood pressure, as well as break down bradykinin, a peptide that lowers blood pressure. Cassis explains, "Drug companies went after it because you get two for the price of one. You take out this enzyme and you have two mechanisms to control blood pressure. It was the most-studied component of the system. They knew a whole lot about its chemical structure, so they knew how to keep it from doing its job."

Developed in the '70s, ACE inhibitors are widely used today to treat high blood pressure and congestive heart failure. And Cassis says her research confirms that these drugs should be the number-one choice of physicians—"anything that controls the overproduction of angiotensin II in the obese, at-risk population is going to benefit cardiovascular health."

Just last year Cassis began working on a new enzyme produced by fat cells, ACE 2. "It has a similar structure to ACE, but what this enzyme does is break down angiotensin II—it converts it to a different form of angiotensin." She explains, "We found that this enzyme doesn't work well in fat cells from obese mice. Why? It's being shed





from the cell, so it can't control the local concentrations of angiotensin II. And, as it turns out, it gets cast off to a greater extent when the mice are obese. Interestingly, the same enzyme that sheds ACE 2 also sheds tumor necrosis factor, which is linked to insulin resistance and diabetes."

Cassis hopes these kinds of findings will lead to novel ways to regulate the renin-angiotensin system in fat tissue. And now she's looking at fatty acids as a prime regulator. "The diets we feed mice are enriched with fatty acids. We're looking at the effects of specific types—the bad, saturated fatty acids versus the Omega 3, heart-healthy fatty acids." Cassis's goal is to answer the question: Could diet modification alone regulate this overactive system and save lives?

The Trash Collector Controls Angiotensin

"Drug companies looked at ACE first, because renin differs from species to species and this makes it hard to develop a drug that effectively inhibits the enzyme," Cassis explains. "Basic scientists like me discovered pretty early on that if we developed a drug that targeted renin in a rodent, it didn't work in humans. It was simply harder to figure out." But eventually the drug company Novartis did and, because of a chance encounter in a hotel lobby, Cassis and her main UK collaborator Alan Daugherty were chosen to test this renin inhibitor.

Daugherty, the Gill Foundation Chair in Preventive Cardiology, has spent almost all of his 12 years at UK working with Cassis. Born in Liverpool, England, Daugherty earned his Ph.D. and D.Sc. (an even higher tier of research doctorate) in pharmacology at the University of Bath and then spent 15 years at the Washington University School of Medicine in St. Louis. He now serves as senior associate dean for research in the UK College of Medicine. This past spring Daugherty, director of the UK Cardiovascular Research Center, was named American Heart Association Scientist Advocate of the Year for his work in promoting the importance of cardiovascular research.

Daugherty is emphatic as he says atherosclerosis is something everyone should care about: "all men and women in their 40s and 50s have a degree of atherosclerosis. With the population bubble coming up—the baby boomers in their 60s—studying this disease is more important than ever."

Cassis and Daugherty are perhaps most widely known for accidentally creating a mouse model of aortic abdominal aneurysms (AAA), a disease that predominantly affects males over 55. "In 2000 Lisa and I were doing studies in which we infused angiotensin into this specific strain of mice. And we began to notice these big bulges in their abdomens." The bulges turned out to be AAA. When Daugherty and Cassis published their finding, the scientific community adopted their animal model as a way to study the mechanisms of the disease, and their work has been cited in medical journals close to 300 times. (For more on AAA, see www.research.uky.edu/odyssey/winter07/research_profs.html.)

Of their professional collaboration, Daugherty laughs and says, "We're quite often described as scientific brother and sister. We have some discussions that are not so cordial at times. Lisa and I feel fairly secure with each other to express our opinions. That's what you need in science: a colleague who will tell you exactly what they think because there's not much point beating around the bush, frankly. I would have never gotten into angiotensin without her."

Daugherty points out that high blood pressure on its own increases a person's risk for atherosclerosis, so utilizing a drug to control the renin-angiotensin system has a lot of potential to curb this disease. "The way we started working with Novartis was one of those strange, small-world experiences," he says.

Cassis explains, "I was at a conference, and I was standing in line to get my hotel room. This man in front of me said something funny, so I laughed. He turned around and we started talking. He worked for Novartis and told me they were making this compound, aliskiren, a renin

inhibitor, to treat patients with high blood pressure. So I told him about our work with mice models of atherosclerosis."

"It turns out I'd known this guy, David Feldman, for 20 years!" Daugherty says, explaining that he met him when Feldman worked at the Cleveland Clinic but hadn't seen him in years. "We started to discuss whether we could do studies with their drug." Now, Daugherty is the principal investigator, and Cassis co-investigator, on two contracts with Novartis. Last year the UK team published findings that Novartis's renin inhibitor successfully reduced the size of atherosclerotic lesions in mice. And these findings led to a worldwide clinical trial. "Novartis is recruiting 700 people. They'll have two groups: one will take 300 milligrams of this new renin inhibitor, and the other will take a placebo. Each group will undergo something called an intravascular ultrasound to look at the size of their lesions. Two years later, they'll come back for another ultrasound to see if the inhibitor has altered the lesion size."

Daugherty explains that atherosclerosis is a chronic inflammatory response in the walls of arteries due to accumulation of macrophages ("the professional trash collectors of the body") and cholesterol-carrying proteins. Macrophages are born from monocytes, white blood cells that speed to the site of inflammation and change into macrophages to elicit an immune response. "Macrophages are our first line of defense," he states. "They attack and ingest foreign substances in an indiscriminate way."

Cassis says, "In studying Novartis's compound, we took renin away from bone marrow-derived cells in mice that develop atherosclerosis in response to a high-fat diet. And we found that even though the rest of the renin-angiotensin system was present in the mouse, taking away renin from these cells effectively reduced atherosclerosis."

Daugherty mentions that other scientists had suspected renin could be made in other places than the kidneys, but nobody thought enough of it was produced to be of any importance. "We were the first to show that targeting renin in bone marrow-derived cells, such as macrophages, can dramatically reduce atherosclerosis."

Cassis adds, "We think macrophages are little syn-

thetic factories that make angiotensin, and they deliver it to wherever they go. If they travel to a forming atherosclerotic lesion, they take it with them. If they go to fat cells, they take it there."

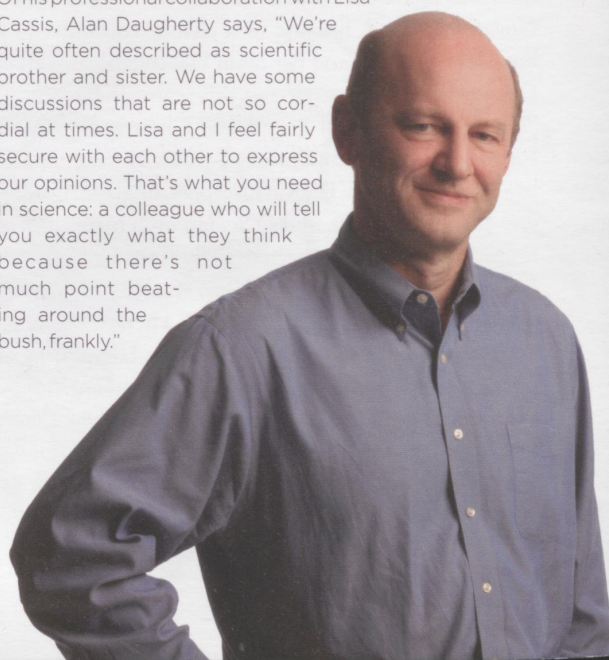
But Daugherty quickly points out, "Macrophages are a very diverse cell type, so our next question is: 'Why are some macrophages generating angiotensin and probably causing disease while others are inert?'"

"We've just found the tip of the iceberg," says Cassis.

COBRE: A Training Tool to Tackle Obesity

For Cassis, making new discoveries in the laboratory wasn't enough. She wanted to promote the importance of obesity in cardiovascular disease, and she found two big ways to do it. In 2003 she became the director of the Graduate Center for Nutritional Sciences (a center started by faculty because nutritional sciences training was scattered across campus), and in 2008, after three grueling rounds of competition for NIH funding, she became principal investigator of the UK COBRE in Obesity and Cardiovascular Disease. Center of Biomedical Research Excellence (COBRE) grants are focused on training junior research faculty to compete successfully for NIH funding.

Of his professional collaboration with Lisa Cassis, Alan Daugherty says, "We're quite often described as scientific brother and sister. We have some discussions that are not so cordial at times. Lisa and I feel fairly secure with each other to express our opinions. That's what you need in science: a colleague who will tell you exactly what they think because there's not much point beating around the bush, frankly."



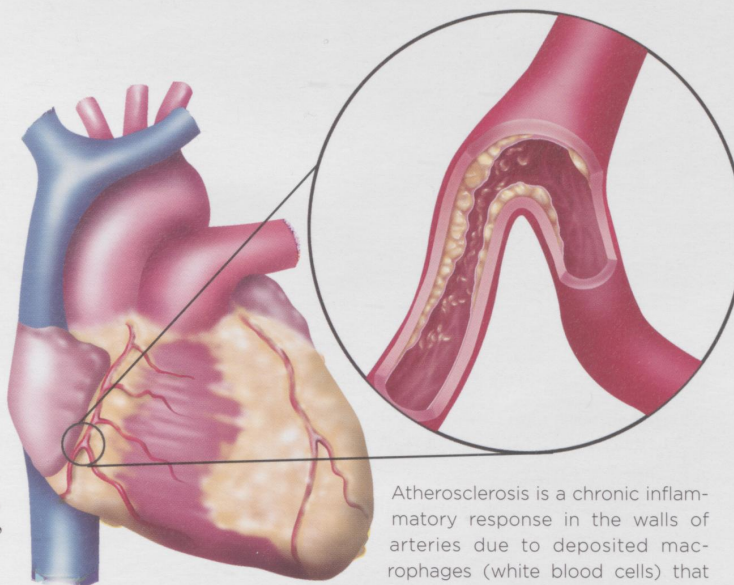
"In 2003-2004, when I went to professional meetings, there was just a void," Cassis says. "There were researchers studying why people become obese, but there were very few scientists with cardiovascular expertise asking, 'Why do people who are obese die from cardiovascular disease?'" Cassis's voice underlines the word "die."

"So Fred DeBeer [chair of internal medicine] and I championed the idea here on campus that we should have a center dedicated to obesity and cardiovascular disease, and we submitted our proposal to the NIH COBRE program." Because of the highly competitive nature of COBREs, it took UK three tries to secure the \$10.5 million, five-year grant. But even without the money, Cassis's brainchild thrived—five of the junior scientists on the proposal had already "graduated" (secured grants) by the time UK received the COBRE funds in fall 2008.

"We have a whole new batch of junior investigators—Jianhua Shao and Shuxia Wang in nutritional sciences, and Eric Eckhardt, Zhenyu Li and Victoria King in internal medicine—doing very novel research, all using our diet-induced mouse model of obesity. Because they're all using the same mechanism to induce obesity, and all of our mice end up diabetic, they can crosstalk. By sharing their findings, our researchers can get at the complexity of how fat cells change with obesity."

The COBRE team is bolstered by a new initiative to fight diabetes. Last fall Patricia Barnstable Brown and her family pledged funding to develop the Barnstable Brown Kentucky Diabetes and Obesity Center at UK. Funds will come specifically from the internationally known Barnstable Brown Gala in Louisville, whose proceeds allow the family's foundation to support diabetes research, education and patient care in Kentucky.

"Kentucky needs few things more urgently," says Michael Karpf, UK executive vice president for health affairs. "This gift will catapult UK into national prominence as a diabetes center and help address the health needs of Kentucky."



Tom Dolan and Matt Hazzard

Atherosclerosis is a chronic inflammatory response in the walls of arteries due to deposited macrophages (white blood cells) that contain lipids (cholesterol and fatty acids). These deposits, a.k.a. plaque (the yellow buildup), narrow the artery, raising blood pressure. Robert Lodder explains: "The theory with 'vulnerable plaques'—the ones most likely to rupture and kill you—is that they have a large lipid pool that can leak, and a thin fibrous cap that can tear. When the contents ooze out, a large clot forms and you fall over dead from a heart attack or stroke."

According to the CDC, Kentucky has the fourth-highest rate of death from heart disease among the 50 states. The state comes in at No. 7 for the prevalence of both obesity and diabetes, and it ranks high in other primary risk factors for cardiovascular disease, such as hypertension and inactivity, according to the most recent Robert Wood Johnson Foundation statistics.

"These stats show just how important it is that we tackle these problems at UK," Cassis emphasizes. The university recently recruited Philip Kern to lead this center, which will serve as a nexus for faculty efforts in diabetes and obesity care, and research. "Dr. Kern is a physician-scientist with an internationally known research program in type 2 diabetes," Cassis says, introducing the man now in the office next to hers. "Working with him, we'll be able to take the mechanisms I identify in mice—say Omega 3 as a regulator for the renin-angiotensin system—and apply them in the clinic to humans. Dr. Kern will help basic scientists studying obesity and diabetes bridge the gap between mice and men." ■

Love, Patents and Sugar

Rob Lodder, who earned his Ph.D. in analytical chemistry from Indiana University in 1988, came to the University of Kentucky just three months after Lisa Cassis, and they began working together. Why? "Because she had rats," Lodder deadpans. "I needed rats with atherosclerotic plaques."

The calling card of atherosclerosis is plaque. "The theory with 'vulnerable plaques'—the ones most likely to rupture and kill you—is that they have a large lipid pool that can leak, and a thin fibrous cap that can tear," Lodder puts it simply: "When the contents ooze out, a large clot forms and you fall over dead from a heart attack or stroke. But if the plaque has a small lipid pool and is covered with a lot of collagen, then maybe it will never cause a problem."

In 1988 Lodder was trying to do something no one had done before: use near-infrared spectroscopy—a technique that uses laser light to measure the absorption of light by different molecules—to peek inside human arteries. He wrote an algorithm that could digitally reconstruct a blood vessel wall, with the ultimate goal of predicting where a heart attack was going to occur up to a year before it happened.

"We took some of Lisa's mice, removed the artery, suspended it by its ends in a solution, and pumped a solution containing excessive LDL cholesterol through it," Lodder explains. "We think atherosclerosis can develop at the site of a previously existing injury, so we were causing that injury, then using the spectrometer to see how the artery tried to repair the damage using the cholesterol."

His technique looked so promising that in 1988 Lodder and three other UK faculty members formed a start-up company, InfraReDx. His relationship with Cassis, which began as a convenient way to get rats, became something more, and this project essentially secured their future: "In 1990 I entered the paper based on this research in the IBM Supercomputing competition. I won first prize—\$25,000—in the life sciences division. We took the money, got married and made a down payment on a house."

In 1995, Lodder's infrared spectrometer was patented, and InfraReDx took the technology, developed a commercial catheter and secured FDA approval. In May 2008 the new catheter was used in the first patient. Lodder, who's only a shareholder in the

company now, says, "The catheters are relatively inexpensive—around \$1,000. You use it once and throw it away. The clinical studies still under way are showing that approximately one in five patients, assigned to a therapy based on conventional catheterization, is assigned to the wrong one." He explains that once physicians see the data from his infrared catheter, they better know what length of stent (a tiny mesh "scaffold") to use and where to place it inside the artery to maximize blood flow. "Based on this alone, we think Medicare will approve our device this year."

Lodder, who holds joint appointments as a professor in pharmacy, engineering and chemistry, says his interests have always veered toward the sci-fi. In fact, he serves as editor in chief of the journal *Contact in Context*, a scientific forum for research in astrobiology and the search for intelligent life in the universe. And as far as TV preferences in their household: "Lisa hates when I watch sci-fi at home. She always switches to Law & Order."

In fact, his sci-fi bent led him to work with Spherix. Lodder serves as president of this scientific research company that is developing a sweetener, Naturlose™ (D-tagatose USP), as a therapy for Metabolic Syndrome. "Spherix went public back in the '60s. Their big claim to fame was the Mars Viking Mission," he says, adding that the company's founder, Gilbert Levin, examined a large number of sugars because of the Viking project.

"Viking took three life-detection tests to Mars. One of those was Gil's labeled-release experiment," Lodder describes how the test worked: "Viking would take some Martian soil, add radioactive sugars (like tagatose), some

Kentucky has the fourth-highest rate of death from heart disease among the 50 states. The state comes in at No. 7 for the prevalence of both obesity and diabetes, and it ranks high in other primary risk factors for cardiovascular disease, such as hypertension and inactivity.

water, and mix them up. Viking would heat it up so the water didn't freeze and then wait. If there were any microbes or spores, they would "hatch" and release radioactive carbon dioxide gas that they made from the sugar.

"And it worked. The test resulted in carbon dioxide, but then the other two life-detection tests showed zip." So everyone assumed something was wrong with Levin's test. "It took NASA 20 years to figure out that there was something wrong with the other two tests!" In fact, Lodder says his friend Levin has always maintained that had the probe dug 5 or 6 more centimeters into the Martian dirt, they would have hit the ice scientists now know is there.

"Viking was why I got involved with Spherix. I began working on a proposed Mars mission with them in 2004. But when tagatose started looking like a therapy for disease—when it looked like we could really do something with it—I was the only one on the board of directors with pharmaceutical experience, so I switched over to tagatose."

Tagatose is a natural sweetener. It's very similar in texture to table sugar and is 92 percent as sweet, but has only 38 percent of the calories. "If you heat up milk on the stove, you'll make tagatose," Lodder says. Spherix had been trying for a number of years to market tagatose as a replacement for artificial sweeteners, but they just couldn't produce it cheaply enough to compete.

However, Lodder says, during food-safety testing, Spherix scientists discovered tagatose had hidden potential as a therapy for diabetes. "Things that aren't economical as foods can be economical as drugs. Tagatose has the same number of atoms as fructose, only rear-

ranged. Because of the way it's arranged, your body doesn't really recognize it, and 75 percent of the tagatose you eat passes through unchanged." You don't metabolize it, so you don't gain calories. "The sugar goes down the same pathways, hitting the same enzymes, as glucose and fructose. So if you're diabetic, glucose and fructose end up being stored in the liver until the tagatose is gone. It has an effect like insulin, even though it's not."

But this wasn't what Lodder, Cassis and her graduate student Sara Police were looking for; they had set out to find out if tagatose promoted atherosclerosis. In 2007, the FDA issued a warning that the diabetes drug Avandia had the potential of significantly increasing the risk of heart attack and heart-related deaths. The FDA is making roughly 50 companies go back and retest their diabetes drugs for cardiovascular effects because of the Avandia scare.

Cassis says, "Rob wanted to test tagatose in mice models of obesity and atherosclerosis, so we did a series of studies comparing diets containing sucrose to diets enriched in tagatose. The sucrose diet made the mice very obese, and they had all the symptoms of Metabolic Syndrome, including much worse atherosclerosis. The tagatose diet did next to nothing."

The UK team's findings, published in the journal *Obesity* in 2008, revealed tagatose lowered "bad" LDL cholesterol, which meant less atherosclerosis, stabilized plaques, and lowered blood sugar levels. Recent preliminary results from a phase 2 human trial also show that tagatose lowered glycosylated hemoglobin, triglycerides and LDL. (The glycosylated hemoglobin percentage corresponds to the average glucose level over the previous two to three months, unlike routine diabetic blood-sugar measurements, which reflect food intake over the previous 12 hours.) And in some human trials tagatose has even caused weight loss. "A treatment for diabetes that causes weight loss and improves atherosclerosis? I think we're going to make some money," Lodder muses.

He's so sold on tagatose, he's been making sweets. "We went to a conference last week, made peanut brittle out of tagatose, and passed it out to people. When we told them it was made from our drug, of course they asked 'Can you do that?' Yes." In 2001 tagatose was classified



Fat mice brought Lisa Cassis and Rob Lodder together shortly after they both became assistant professors in the UK College of Pharmacy in 1988. The professional collaboration of this husband and wife team led to a new medical device that allows doctors to peek inside arteries and identify dangerous plaques before a heart attack happens, and research on a sugar substitute that may be a therapy for diabetes.

as a Generally Recognized as Safe product by the FDA. Today tagatose is used in some diet sodas, light ice creams and hard candies, and the University of Kentucky and Spherix are in the process of patenting tagatose as a therapy for Metabolic Syndrome.

Lodder asserts, "Nobody had any ill effects. Compare that to some other diabetes drugs. You can have a heart attack or you can have peanut brittle." ■

Burgers Make Me Happy

The Link between How We Feel and What We Eat

By Robin Roenker

Blair Kidwell, an affable, young assistant professor of marketing at UK, shows a group of undergraduates a picture of a Big Mac and asks, "How does this make you feel?"

Hungry, some say. But others, as he would predict, say it makes them feel happy.

The latter response gets at the emotional connections we all have to food, and how those emotions play a role—often without our being aware of it—in the types of foods we choose each day.

If losing weight or maintaining a healthy lifestyle is your goal, then feeling happy at the sight of McDonald's signature sandwich is "perhaps the worst thing you can feel," says Kidwell, who earned a Ph.D. at Virginia Tech in 2004 and came to UK in 2005 after a short stint at Kansas State University. It's a sign that, consciously or not, you desire that Big Mac not just for its nutritional content but for the emotional high you think it will serve up.





Kidwell, along with colleagues Terry Childers and David Hardesty, is conducting research on emotional intelligence and its role in consumer decision making. The idea of “emotional intelligence”—the ability to understand and manage your emotions when making decisions—caught fire among psychology researchers doing relationship studies in the late 1990s. The UK research team is among the first to apply the idea to consumers.

“We need to understand that sometimes those emotions can help us in terms of avoiding things that are dangerous, but sometimes they can propel us toward behaviors that we regret later,” says Childers, the Gatton Endowed Chair in Electronic Marketing and an expert in how consumers process information. “Our main focus in this work is helping people learn to make better decisions about what to eat and drink.”

As a starting point in accomplishing this goal, the team has spent three years refining a measurement tool—an 18-question survey called the Consumer Emotional Intelligence Scale (CEIS)—that aims to assess a consumer’s ability to perceive, use, understand, and manage emotions. Their current work, following two publications in the *Journal of Consumer Research*, will establish connections between emotion and food choice.

But in our food-happy, health-conscious society, why haven’t these connections already been determined?

Part of the reason, Kidwell says, is the difficulty of measuring something as abstract and shifting as emotional ability. But since the team has used this scale, the preliminary results have been revealing.

In 2008 respondents, mostly UK undergrads, were asked to identify on a computer-generated menu the foods they might typically eat in an average day. The menu included an array of healthy and not-so-healthy food choices, from salads and wraps to pizza and beer. Those

who scored low on the CEIS scale, meaning that they had below-average emotional intelligence, reported consuming nearly 3,500 calories in an average day, while those who showed above-average emotional intelligence consumed 1,800 calories on average.

“The premise of the approach,” Kidwell says, “is this: people who tend to be less aware of their emotions when making a decision rely more on implicit assumptions when selecting a product, in this case food. They’re more swayed by the attractiveness of the foods in pictures. Rather than rationally thinking through that food choice—how good it is for them—they’re driven by impulses, emotion, and a tendency to unconsciously associate unhealthy food with tasty food. That’s particularly the case with people who are obese.” The result is a diet that’s chock full of feel-good comfort foods high in fat.

But perhaps the best news, Childers emphasizes, is that emotional intelligence is not innate—it can be learned. The team is currently conducting a study in which the respondents who had a low CEIS score participate in a one-day training session that involves learning how to better perceive and identify emotional responses.

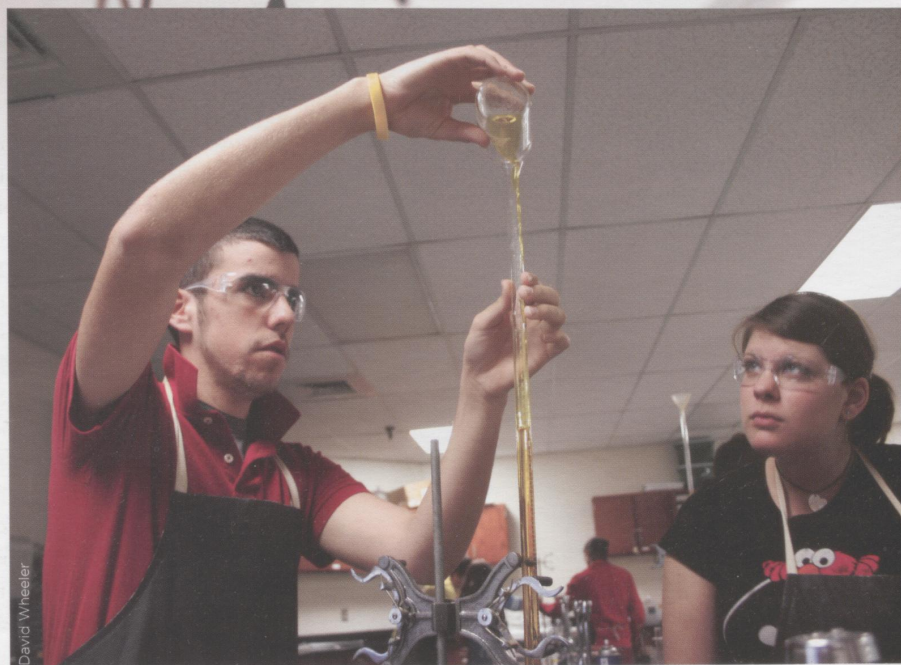
Hardesty, an associate professor of marketing, explains that by teaching people to be more aware of the emotions at play in their decision making, you can equip people to make better choices. Instead of an emotional response to a Twinkie, based on memories of childhood fun, the consumer will think: “If I eat this Twinkie now, how will I feel about it later?”

After the training session, the respondents kept a food diary, detailing everything they ate for three days. The goal, of course, was to show that their caloric intake after the training dropped.

Significantly, the research team has also shown that it’s not just how in tune you are to your emotions, it’s equally as important that you have confidence in your ability to respond appropriately to those emotions. In each study, the respondents who report the most healthy food choices are those who not only score highly on the CEIS, but who also self-report a high estimation of their emotional ability.

The team has shown that boosting respondents’ confidence through training in turn leads them to make better choices. “There are people who have the emotional ability to make good choices, but they just aren’t sure they can make the right choice. If you boost their confidence, then they’re more apt to use that ability,” Childers contends. “Ultimately, that’s our goal: finding ways to enhance consumers’ decision-making skills so that they can make the best possible choices.” ■

Math and Science Partnership Scoring High Grades



By David Wheeler

It's 10:40 a.m. at Lewis County High School in northeastern Kentucky, and that means it's time for Shawna Voiers' Chemistry II class to begin. "We've been balancing redox reactions for a few days now," says Voiers, an energetic teacher with curly blond hair and glasses. "Today we're going to perform what we call a redox titration," she adds, tossing the scientific phrase off as if it's commonplace. After Voiers explains the assignment, the students put on their goggles, find a partner and head to their chemistry stations. At first glance, it looks like an activity from a typical high school chemistry book. But what's different about this experiment is the follow-up assignment, which Voiers calls "Making Meaning." The students conduct a college-level analysis of the experiment—what went right, what went wrong and why it matters. You won't find this assignment in a textbook because it was developed by Voiers herself at a professional development session.

As a testament to the effectiveness of this advanced curriculum, Morehead State University offers college chemistry credit to students who make a high

Lewis County High School senior Cory Collins and foreign-exchange student Sarah Straub mix two solutions together to determine the endpoint of a redox reaction—oxidation, in which electrons are lost or transferred, and reduction, in which electrons are gained.

enough score on the final exam in Voiers' Chemistry II class. Voiers attributes the higher-level classroom experience to resources and innovations made possible by the Appalachian Math and Science Partnership (AMSP). [To find out how this project began, go to www.research.uky.edu/odyssey/spring03/primenumber.html.]

A \$24 million program funded by the National Science Foundation, AMSP was developed to address the stubborn problem of academic underperformance in central Appalachia, where students consistently score below state averages in math and science. With UK as the lead institution, AMSP created a partnership among 56 central Appalachian school districts, 10 higher education institutions, and the Kentucky Science and Technology Corporation. The program, launched in 2003, emphasizes professional development as one of its main components.

More than 400 schools from four states participate in AMSP. Ask a science or math teacher at any one of these schools for an assessment of the program, and you'll hear lengthy success stories, peppered with examples of eureka moments for students in the classroom. You'll also get positive reviews from Inverness Research Associates, an independent educational research organization hired by the National Science Foundation to evaluate AMSP. But those reviews deal with qualitative data—primarily verbal evidence. Meanwhile, quantitative data on AMSP has been

"AMSP is a true partnership, and the testimonies we hear are just glowing. Good things are happening in Appalachian classrooms."

—John Yopp, AMSP project director

more difficult to find, because the hard-and-fast numbers that show an improvement in student test scores have been elusive. That is, until now.

Numbers Tell the Story

You won't see any test tubes in Genia Toma's office in Patterson Office Tower, but there's a lot of science going on in there—social science, specifically. "I've been studying the economics of education my entire career," says Toma, a Kentucky native and professor in UK's Martin School of Public Policy and Administration, "and this is a project where I'm bringing those tools to Kentucky schools—and that's fun."

Toma explains that it has become clear to academics and policymakers that certain approaches to solving the problem of underperformance in schools—such as across-the-board increases in school expenditures and teachers salaries—simply weren't working. "We spent a lot of time thinking that we should just change expenditure levels, but this approach hasn't panned out," says Toma, who holds a Ph.D. in economics from Virginia Tech. "There is a lot of quantitative evidence, however, showing that teacher quality affects student achievement."

Thus, two of AMSP's components address teacher training: pre-service training (before teachers enter the classroom) and professional development (for teachers already in the classroom). But it will be a long time before the effects of such training are known; after all, it might take decades before the teachers undergoing AMSP's pre-service training constitute a majority of the teaching workforce in Appalachia. In the meantime, Toma's pilot project looked at the effectiveness of AMSP-sponsored professional development.

How can you tell if professional development works? For the layman, it might seem that the answer could be found simply by looking at school test scores before and after those teachers participated in the AMSP-sponsored training. If scores went up, the professional development succeeded—right?

Well, test scores certainly have improved, but because so many human variables are involved it's difficult to be sure what actually made the difference. Therefore, Toma used a technique inspired by economics in order to control for variables that tend to increase or decrease student per-

formance. Her preliminary research showed that, when other factors were accounted for, Kentucky schools with teachers participating in AMSP programs exhibited statistically significant improvements in math and science scores.

"The proof is in the stats," Toma says, burrowing into one of the half dozen or so stacks of paper in her office and pulling up a chart. "We found improvement for seventh-grade science scores, eighth-grade math scores, and 11th-grade math and science scores." Among the more specific findings: "We found that after controlling for other factors, if the percentage of teachers participating in AMSP professional development within a school is increased by 1 percent, math scores of 11th-graders rise by .29 points."

With such promising preliminary research, Toma received an additional \$1.5 million NSF grant to further substantiate these gains. The new study will conclude in September 2011.

The "Nanotechnology" of Educational Research

Toma's study did indeed find a correlation between professional development and higher math and science scores. One question she hopes to answer by continuing to research the effects of AMSP is, which professional development activities work best? The answer requires more specific data, Toma says adjusting her black-framed glasses. The pilot project used school-level data, showing information such as the percentage of teachers participating in AMSP



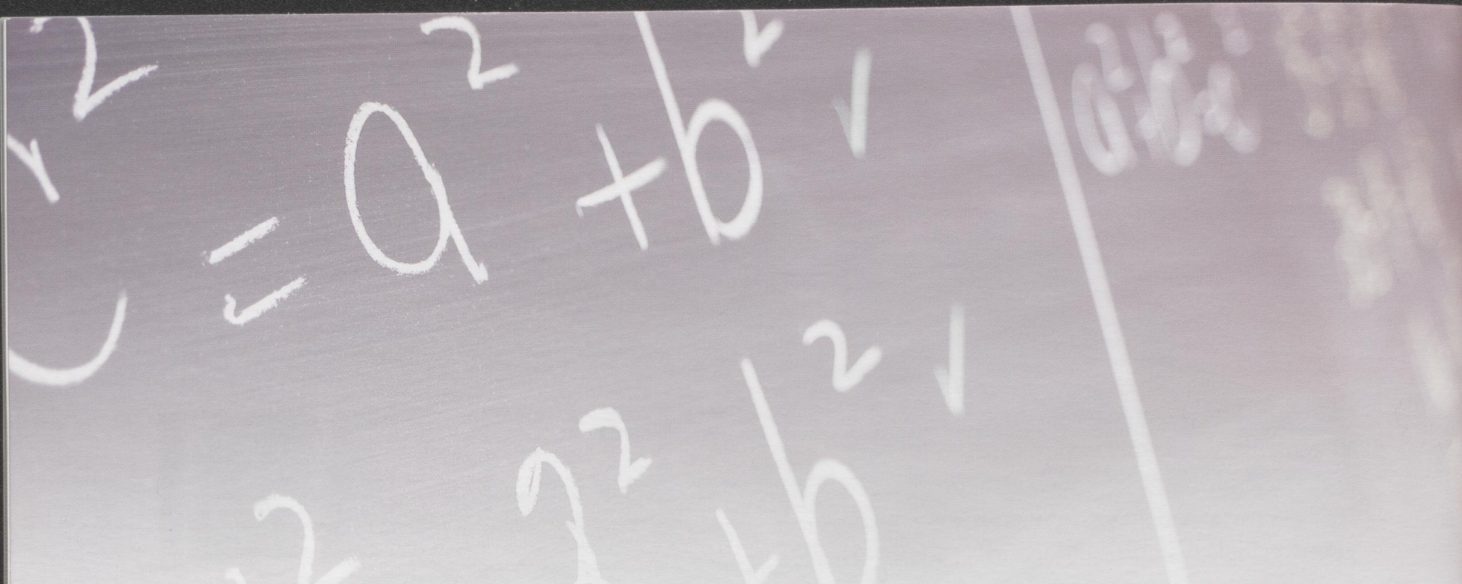
Genia Toma, a professor in UK's Martin School of Public Policy and Administration, has focused her career on studying the economics of education. "This is a project where I'm bringing those tools to Kentucky schools," she says.

professional development and the average test scores for certain grade levels. The new study will provide data on which professional development workshops specific teachers attended, which students were in which classes, and how those individual student test scores changed after the student took a class from that teacher. To protect privacy, teacher and student data is coded, and names are removed.

"With the new study, we will know specifically which types of the AMSP

activities were more effective than others. We're actually going to be able to delineate those by going down to a very micro level." She pauses, smiling. "It's kind of like nanotechnology. We're going down to the smallest unit possible.

"We'll be able to match students enrolled in a class to the teacher who taught the class. So if there is an effect of AMSP on the participating teacher, we should see it directly from those students in the classrooms of the teach-



ers who participated in AMSP.”

While the techniques Toma uses are known in economics, they are much less used in education research. Toma explains that in this work she treats AMSP as an intervention, “kind of like a medical treatment,” she adds. “We realized that the intervention was not done randomly. You don’t put heart stents in both healthy people and unhealthy people. So one of the things we have hypothesized in this study is that there is a selection bias, or non-randomness, that describes which teachers choose to participate in these professional development programs.” Some teachers might feel they need the extra help, others might be self-motivated to try these specific sessions, and still others might be encouraged to attend by the principals at their schools.

Toma also focused on another variable: changes at the schools from year to year. “Test scores may have changed because the socioeconomic composition of the classrooms changed,” she explains. “So we control for those sorts of things. And now that we’re going down to the student level, we’ll actually be able to identify these students’ particular characteristics, and we’ll know certain characteristics of the teacher.” For example, as you would hope, most teachers with five years of experience in the classroom are more

effective than teachers who are brand new. “So we’ll be able to control for those other things that may influence the effectiveness of a specific teacher.”

“A True Partnership”

The AMSP project participants and coordinators were thrilled with Toma’s innovative method and preliminary results. Several are hoping that her method will be used to study the effectiveness of AMSP in other states and nationwide.

When AMSP began six years ago, the UK team included Wimberly Royster, Stephen Henderson, Ron Atwood, Paul Eakin, and Carl Lee. Royster, the original AMSP project director, says he is pleased with the rising test scores, but points to another significant result of the program. “We have developed relationships and a better understanding of what partnering is,” says Royster, referring to the collaboration among teachers, professional development leaders and AMSP project leaders.

John Yopp, the current AMSP project director, echoes Royster’s sentiments. “What satisfies me the most about AMSP is that it is a true partnership; it’s not a top-down model,” says Yopp, who is also UK’s associate provost for educational partnerships and international affairs. “The testimonies

that we hear are just glowing. It is the antithesis of the stereotypical image of Appalachia. Good things are happening in Appalachian classrooms.”

Anyone unconvinced of the teachers’ enthusiasm need only talk to Voiers at Lewis County High School. At the first mention of the initials AMSP, she lights up.

“Oh, my gosh,” Voiers says. “AMSP has been absolutely wonderful. They have given us so much training and help with technology. For example, in our redox probe reactions experiments, where the students analyze a solution, the AMSP folks provided us with a logger pro. This computer-like device allows an interface with a laptop where data from the experiment can be collected and analyzed. The big picture is, you’re able to improve the curriculum. It’s a huge step forward—for teachers and students.” ■

Odyssey
Summer 2009

Parting Shots

I like rice. Rice is great if you're hungry and want 2,000 of something.

—Mitch Hedberg

I went into a McDonald's yesterday and said, 'I'd like some fries.' The girl at the counter said, 'Would you like some fries with that?'

—Jay Leno

Part of the secret of success in life is to eat what you like and let the food fight it out inside.

—Mark Twain

The most remarkable thing about my mother is that for thirty years she served the family nothing but leftovers. The original meal has never been found.

—Calvin Trillin

We are indeed much more than what we eat, but what we eat can nevertheless help us to be much more than what we are.

—Adelle Davis

Preach not to others what they should eat, but eat as becomes you, and be silent.

—Epictetus

Never eat more than you can lift.

—Miss Piggy

As a child my family's menu consisted of two choices: take it or leave it.

—Buddy Hackett

I don't want to live in a world where I have to eat sugar-free sugar cookies.

—Takayuki Ikkaku,
Arisa Hosaka and
Toshihiro Kawabata

My doctor told me to stop having intimate dinners for four. Unless there are three other people.

—Orson Welles

Food is an important part of a balanced diet.

—Fran Lebowitz

I've been on a diet for two weeks and all I've lost is two weeks.

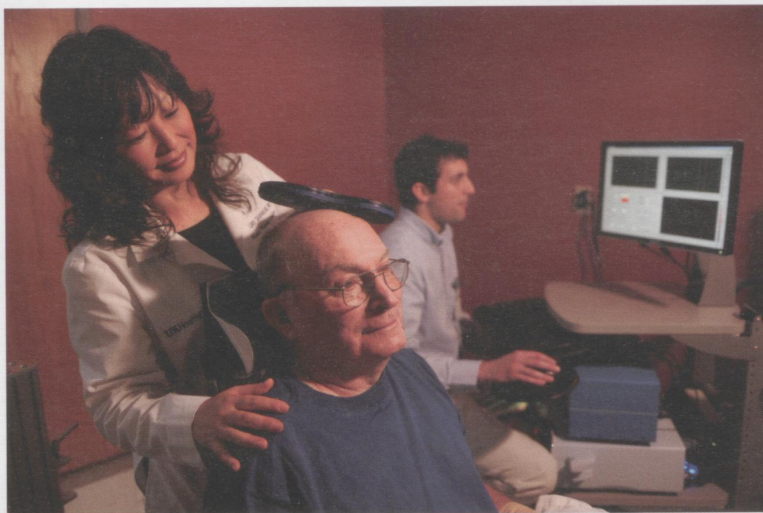
—Totie Fields

Odyssey

213 Bowman Hall
University of Kentucky
Lexington, Kentucky 40506-0059

0039

NANCY DEMARCUS
SPECIAL COLLECTIONS & DIGITAL PROGRAMS
204 M.I. KING BUILDING



Taking Good Care, p. 5

Also in this issue:

A Walk across Uneven Ground, p. 12

UK Attracts 33 New Cancer-Fighters, p. 18

Math and Science Partnership Scoring High Grades, p. 33

www.research.uky.edu/odyssey

THE UNIVERSITY OF
KENTUCKY