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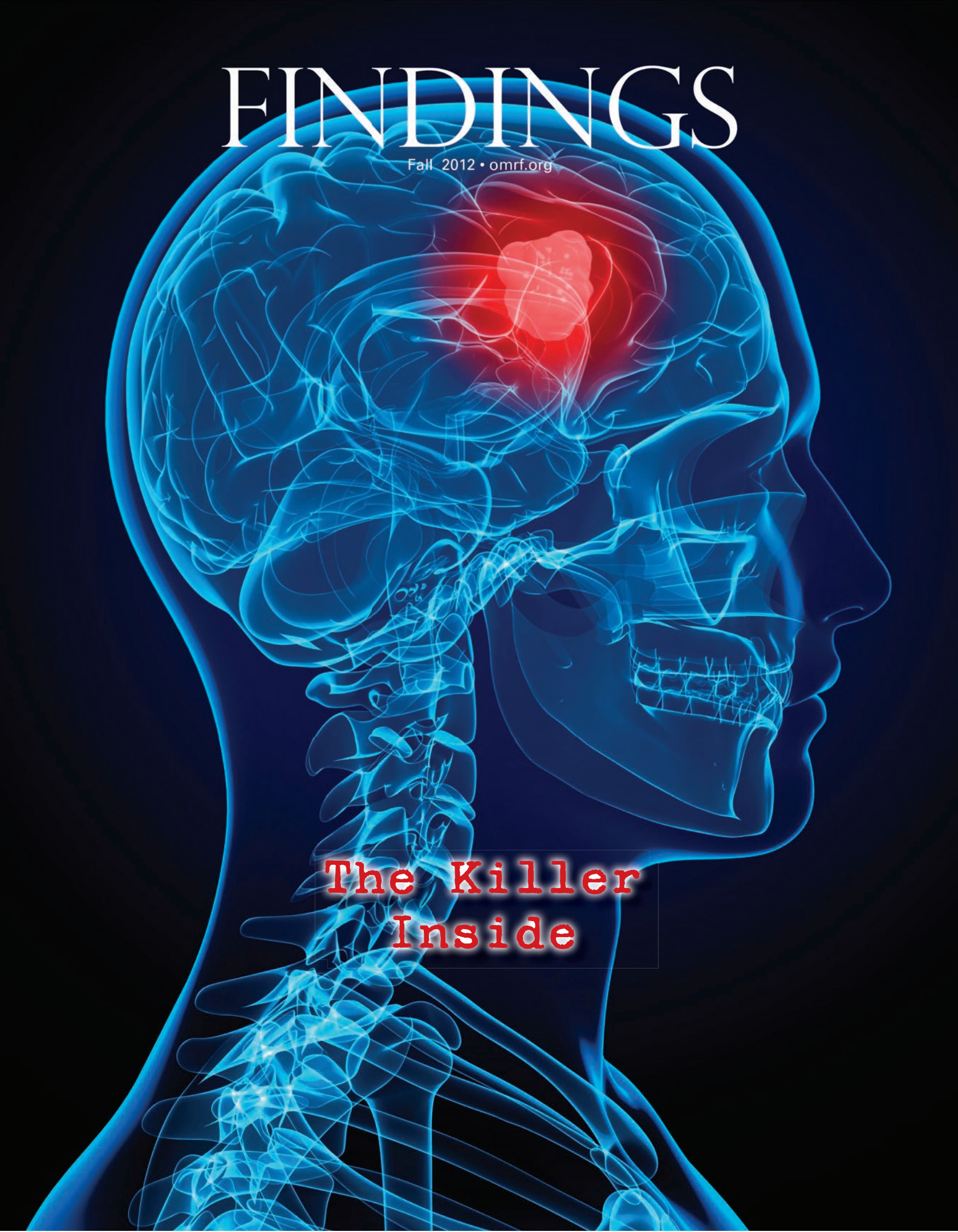

The Killer Inside

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Chartered in 1946, OMRF is an independent, nonprofit biomedical research institute dedicated to understanding and developing more effective treatments for human disease. Its scientists focus on such critical research areas as Alzheimer's disease, cancer, lupus and cardiovascular disease.

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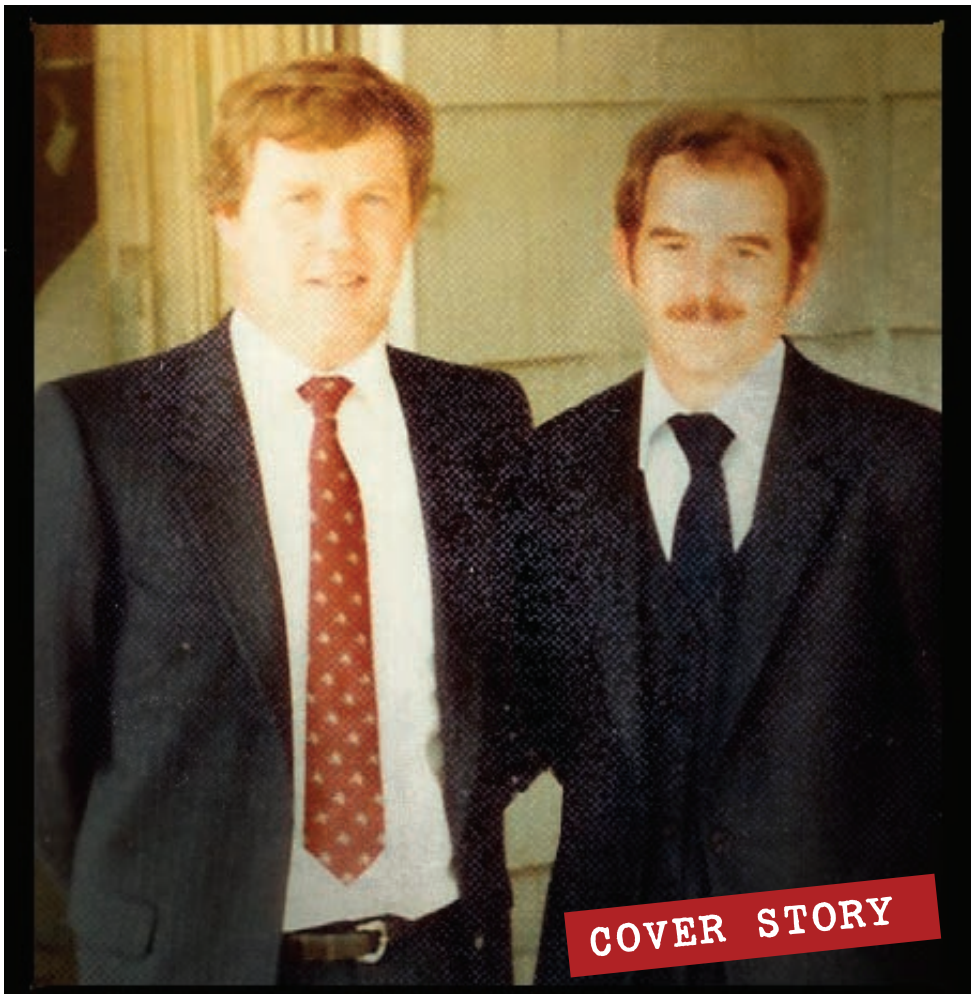

10 **STAND BY ME.** When John Kennedy succumbed to a fatal brain cancer, his older brother could only watch from his bedside. But now, as director of a clinical trial targeted at the same form of cancer, OMRF's Larry Kennedy has transformed John's death into a personal mission of hope.

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Feedback

I am a patient in OMRF's **Multiple Sclerosis Center of Excellence** and would like to say thank you to all the staff members who have helped and are currently helping me. All the doctors and nurses are amazing, and through them I have learned there is time needed to deal with my MS. They have also helped my family and me feel very comfortable and more understanding of MS. I always brag about how wonderful the staff is and will always remember my time at and my special friends from OMRF. Thank you for showing me I can have a life in spite of my MS. It may not be the same, but it will be a life with new goals, decisions and choices!

Krys Greenlee
Comanche

The article "Tower of Power" in the winter/spring issue of *Findings* gave a good glimpse into the new OMRF research tower. It cannot be stressed enough the importance of this world-class facility in attracting quality research talent from all over the nation. This is just another example of OMRF setting the proper climate to effectively recruit top scientists. OMRF's new research tower is an example of another investment in the future that will pay dividends for generations to come. Successful completion of this project should be a source of pride for all of us as Oklahomans.

Paul Schulte
Kingfisher

I recently had the privilege of visiting Dr. Jordan Tang's lab at OMRF and learning more about his research. It was an awesome honor for me to hand over a check for $1 million from the Masonic Fraternity of Oklahoma to help fund his work.

Richard Massad
Oklahoma City

I'm always glad to do my very little part when I send a check to OMRF. You are a worthy recipient.

Deann Owen Lewis
Crescent

Marguerite French as a Fleming Scholar in 1957 and today

I just read "Pioneer Woman" about Dr. Marguerite French, OMRF's first African-American Fleming Scholar, in the Fall 2011 issue of *Findings*. Every summer, we OMRF employees look forward to the arrival of the scholars. Their enthusiasm is infectious. Stories like these give me a real sense of camaraderie at OMRF, especially as an African American. And it's a bit of OMRF history that I didn't know. I especially liked her comment, "When I got to OMRF, I can't recall any segregation. We scholars did everything together."

Marsha Lewis
Midwest City

Fleming Scholars Class of 2012

WRITE TO US!

Send us an email at findings@omrf.org or mail your letters to *Findings*, 825 Northeast 13th Street, Oklahoma City, OK 73104. Please include your name and address, and you'll receive an OMRF T-shirt if we publish your letter.

FOLLOW US ONLINE!

Rockin' for Research

"School's out for summer!" sang the guy with long, black hair into the microphone. "School's out forever!" responded the crowd of hundreds who'd gathered on the patio of OMRF's new research tower to hear him. "School's been blown to pieces!" chanted the crowd and singer together.

In other words, it wasn't your typical OMRF fundraiser.

Rock legend Alice Cooper visited the foundation in June to help raise funds for clinical trials of an experimental drug to treat brain cancer (go to page 10 for the full story on the trials). The events began with a wine festival and concert at the foundation, where guests enjoyed musical performances by Cooper, the Red Dirt Rangers, the Okie Stompers, Jessi Colter and Shooter Jennings. The following day, Cooper joined 143 others on the links for a tournament at Oak Tree Country Club.

Cooper, an avid golfer with a two handicap, met OMRF President Stephen Prescott at a charity golf tournament years ago, and the two became friends. So when Prescott asked Cooper to appear at the OMRF fundraiser, the man behind hits like "School's Out" and "Eighteen" jumped at the chance.

"The Doc"—Prescott—"explained the clinical trials to me," says Cooper, "so I said, 'Let's go raise the money.'"

The two-day effort, which also included a live auction, raised $690,000 for the trials. Going forward, OMRF plans to make the "241" (two events for one great cause) an annual tradition.

Cooper sees the clinical trials as a potential source of great pride for Oklahoma. "If this drug works," he says, "I think the whole state can be proud of that. You can say, 'We're the ones who beat brain cancer.'" And that, says the rocker, would be "pretty good bragging rights."

Alice Cooper helped OMRF raise $690,000 for brain cancer research

Ask Dr. P

OMRF President Stephen Prescott answers your health questions

A Gridiron Gamble?

This is my 10-year-old son's first season playing full-contact football. It seems like every day I read about the dangers of concussions and hear horror stories of athletes who've suffered long-term damage from them. My son can't hit like a pro, but kids can really wallop each other on the field. Should I be worried?

Tim Hassen, Norman

While I don't want to crush a young boy's dreams of playing football, there are many studies that point to repeated concussions having deleterious effects later in life. That doesn't mean everybody should stop playing football, hockey or other contact sports. But we should be conscientious about how those sports affect our bodies, especially young bodies like your son's.

First of all, let's talk about what a concussion really is: a brain injury, often caused by a blow to the head. The brain gets bruised and swollen because the skull restricts its ability to expand.

Like an injury to any other part of the body, concussions vary in severity and long-term effects. If you break a leg enough times, after a while, that leg doesn't work exactly right again. The same goes for our brains. Too many concussions, especially ones that occur before the brain has time to heal from a previous blow, can cause damage that restricts language, motor functions and cognitive abilities.

But there's good news. For one thing, we're learning more about concussions all the time, and because of heightened awareness of the risks, coaches and parents pay closer attention to hits sustained in athletic competition. New products like padded helmet covers can add an extra layer of protection to those little noggins. Still, it pays to take some precautions of your own.

Consider having a neurologist take a baseline reading of your son's brain. That will provide a comparison point should he sustain an injury later. And familiarize yourself with the symptoms of concussion. Difficulty thinking or concentrating, headache, dizziness, nausea, blurred vision, emotional shifts or interruptions in sleep patterns may point to a possible concussion and should prompt an immediate visit to the doctor.

Ultimately, the responsibility lies with the parents of any young athlete to make the best choice about future participation. It's not an easy line to toe, but (to use a metaphor from a sport that's usually concussion-free) that's par for the course when it comes to parenting.

Send your health questions to Dr. Stephen Prescott at askDrP@omrf.org.

A Coal King's Green Legacy

Clean coal: A gift from the foundation created by McAlester fossil fuel magnate J.G. Puterbaugh (shown left at OMRF's 1947 groundbreaking) helped OMRF flip the switch on 18 new wind turbines, creating what is believed to be the world's largest rooftop wind farm.

When OMRF unveiled its new rooftop wind farm in June, it not only became the first medical research facility anywhere to harness the wind to help power its labs. It also added another chapter in a remarkable story that began more than a century ago with a 14-year-old boy sweeping up coal dust.

J.G. Puterbaugh learned the coal business from the bottom up. In his autobiography, he cites "debts and drought and hard times" for sending him to work for a coal company to help support his mother and siblings. He swept the company office, built fires, shoveled mountains of coal and even served as the company's bill collector—all for $20 a month.

A year later, he left his job to return to high school, which he completed in two years' time. With diploma in hand, he returned to the coal business, working his way up the corporate ladder as a traveling salesman. When Puterbaugh's paycheck rose to $85 a month, he "felt like a millionaire," he later wrote. By 1907, he actually became one through his ownership of the McAlester Fuel Company, one of the largest distributors and producers of Oklahoma coal.

With rail travel expanding and the advent of coal-powered electricity, Puterbaugh found himself on the cutting edge of energy production. And it made him a fortune.

Puterbaugh always looked ahead, trying to anticipate the next wave in energy sources and consumer needs. So it seems fitting that the foundation bearing his name provided funds that made OMRF's new wind turbines possible. "Even a hundred years ago, Mr. Puterbaugh understood the value of sustainable energy," says Oklahoma Supreme Court Chief Justice Steven Taylor, who serves as chairman of The Puterbaugh Foundation.

"When we heard about OMRF's plan to employ the wind to power its new research building, we pledged our support for it." The foundation ultimately donated $500,000 toward the turbines, which cost OMRF a total of $819,000 to acquire and install. According to various news sources, the 18 turbines make OMRF's the largest rooftop wind farm anywhere.

"Mr. Puterbaugh would have loved the idea of using his coal money to purchase wind turbines," says Taylor. "Especially for a groundbreaking project like this one." Puterbaugh was also one of the first to give significant financial support to OMRF. He joined the board of directors when OMRF existed only on paper and served as its second volunteer president from 1947 until 1950.

"Mr. Puterbaugh helped OMRF open its doors more than 60 years ago," Taylor says. "It's a partnership that we hope keeps powering discoveries for decades to come."

Dr. Courtney Griffin

Web Wonder

In this summer's hit movie "The Amazing Spider-Man," an insect bite changes a teen into a superhero. An OMRF scientist discusses whether there's any scientific basis for this Hollywood fantasy.

In the comic series that spawned the film, a spider bite transforms puny Peter Parker from a nerd to a wall-climbing, web-spinning crime fighter. While Stan Lee wrote the original story way back in 1962, the idea that Spider-Man's DNA—deoxyribonucleic acid—was altered by a spider's bite came in later issues. Still, it got us wondering: Could it really happen?

"The short answer is no," says OMRF scientist Dr. Courtney Griffin. "The long answer is yes, but with a lot of luck and a lot of spider bites." Griffin should know. In the lab, she studies genetics and how it affects the formation of blood vessels. She also examines certain enzymes that turn gene functions on or off and how those actions might lead to disease.

Radiation can absolutely alter DNA, she says. Will it give you the power to climb walls and sense danger? Probably not. For one thing, mutating DNA in one cell doesn't mean it will mutate the same bit of DNA in the other cells. "Radiation mutates randomly and could affect any of your 20,000 genes, so instead of super powers, you might end up with cancer," says Griffin. "Mutations are unpredictable, and altered DNA might turn on, or turn off, some mechanism that is important to how your body functions. It all depends on where and when the mutation occurs. In this case, it would take multiple bites, and every cell would have to mutate in exactly the same way."

Wall-climbing, though, is just one of Spider-Man's powers. You want super strength? Get ready to have all of your muscles bitten several times. To acquire "spider sense," you'd need to have your head bitten—from the inside. Even then, all of the painful nastiness might go to waste without the proper amounts of spider venom and radioactivity.

All that doesn't mean that DNA can't be changed. Researchers are looking for ways to treat genetic diseases, including a process called "gene therapy." So while Peter Parker's DNA was overwritten with code giving him the proportional strength of a spider, allowing him to walk up walls and even sense danger, gene therapy seeks to correct mutations so cells can behave normally.

"Gene therapy only needs to be applied to the portion of the body where the DNA needs correcting," Griffin says. "Conditions like Parkinson's disease, where the problem originates in the brain, could someday be treated with gene therapy that targets a specific area to alter the DNA. It wouldn't really matter if the DNA in muscle cells in your arms or legs stays the same, because they're not creating the kinds of proteins that cause the disease."

So your chances of becoming a web-spinning wonder and hero to millions through DNA mutations are slim to none. And gene therapy is still in experimental stages. But don't let that stop you from grabbing your popcorn and enjoying the show.

Grants Awarded

January - June, 2012

Dr. José Alberola-Ila
Hematopoietic stem cell senescence

Dr. Yunzhou Dong
Role of epsins in atherosclerosis; Drug development for prostate cancer

Dr. Michael Dresser
Zeiss LSM710 confocal fluorescence microscope for live stem-cell imaging; Mechanics and regulation of chromosome dynamics in meiotic prophase

Dr. Taishan Hu
RAS/MAPK cascade controls iNKT cell development and function

Dr. Kenneth Humphries
Mitochondrial dysfunction in amyotrophic lateral sclerosis

Dr. Judith A. James
Oklahoma Autoimmunity Center for Excellence

Dr. Paul W. Kincade
Hematopoietic stem cell senescence; Early events in mammalian B-cell differentiation

Dr. Hui-Ying Lim
A fluorescence stereomicroscope for characterization of adult stem cells in intact tissues of various model systems

Dr. Florea Lupu
Spinning disk confocal microscope for intravital imaging; Complement inhibition as sepsis therapy

Dr. Rodger P. McEver
Interdisciplinary research in vascular biology; Cellular regulation of selectin-ligand interactions; Mechanisms for blood cell adhesion under flow; Protein-glycan interactions in the vascular system

Dr. Joan Merrill
Clinical outcomes and quality of life of lupus nephritis patients in a prospective international inception cohort

Dr. Kenneth G. Miller
Signaling pathways that regulate synaptic transmission

Dr. Courtney Montgomery
Comprehensive genome interrogation of African-American sarcoidosis families

Dr. Swapan K. Nath
SLE susceptibility and clinical significance at 2q22-24 across multiple ethnicities; Identification of lupus predisposing variants by comparing multiple populations

Dr. Xiao-Hong Sun
Notch-induced protein degradation in lymphopoiesis

Dr. Linda Thompson
Fluorescence activated cell sorters upgrade

Dr. Weidong Wang
An automated high-throughput microscope for adult stem cell research in Oklahoma

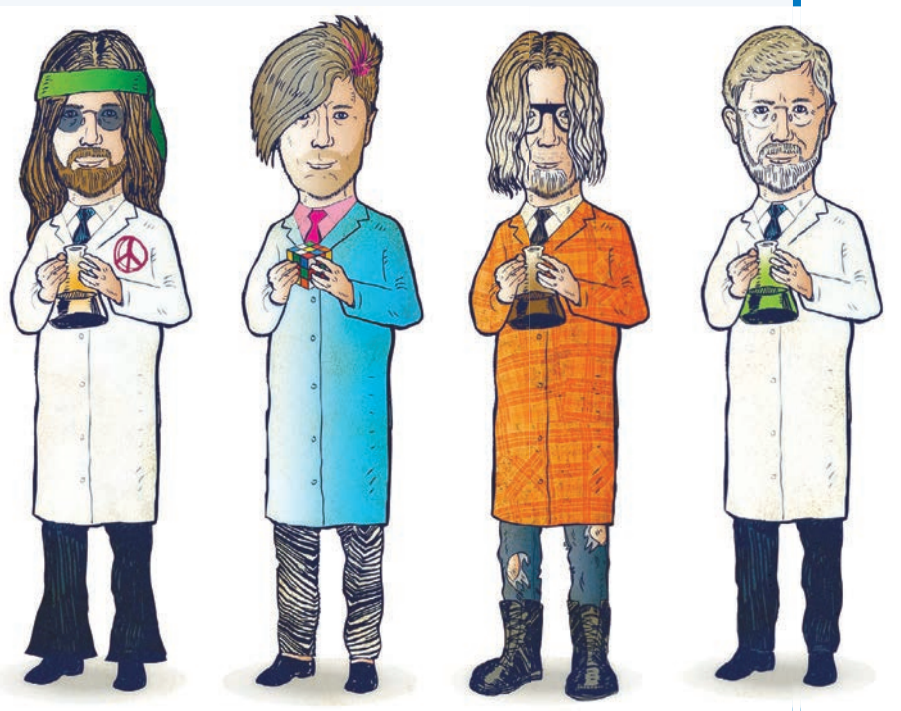
Dr. Lijun Xia
Role of mucin-type O-glycans in intestinal inflammation; Microtome for histological analysis of adult stem cell based therapies

Long Live the Grant!

When a scientist receives a grant, that's great news. The funding provides the means for a scientist to explore a hypothesis and run his or her lab. But those grants are not unlimited; they provide funding only for a set period of time, typically three to five years. But for OMRF's Dr. Paul Kincade, one grant has proven the medical research equivalent of the Energizer Bunny.

First awarded to Kincade when Richard Nixon was President and bell bottoms were the rage, *Early events in mammalian B-cell differentiation* has remained funded for a whopping 38 years. Kincade attributes this success, which includes seven separate renewals of the grant, to hard work, a steady stream of new findings and, of course, a little bit of luck. Still, after almost 40 years, does anything remain to be learned about this particular topic?

"The human immune system is an incredibly intricate machine, and every day we learn something new about how it develops and functions," says Kincade, who holds the William H. and Rita Bell Chair in Biomedical Research at OMRF. "That knowledge continues to help us better understand and treat diseases like lupus, leukemias and lymphomas."



HIS BROTHER'S KEEPER

BY SHARI HAWKINS • ILLUSTRATION BY BRIAN TAYLOR

This fall, OMRF will begin clinical trials of an experimental drug for a deadly form of brain cancer. For the trials' director, finding a new treatment for a fatal cancer is not just a moral imperative. It's personal.

Every evening at 6:00 sharp, the bells sang out atop St. Joseph's. Their booming chorus filled the five square blocks that made up Andale, Kansas, reminding its 400 or so residents that another day was drawing to a close.

When the Kennedy children heard that pealing, they dropped everything and tore out for their old two-story frame house with the wraparound porch. Because they knew the rules. Rule number one: Dress for dinner. Number two: Bring a vocabulary word and a debate topic, both of which you should be prepared to discuss. And number three …

Be inside by the sixth chime. Because if you weren't in the house by the time those bells went silent, you'd be in big trouble.

The older Kennedy boys were forever sprinting across the threshold in the nick of time. As they caught their breath—chests heaving, hands on knees—they'd look at the massive dining room table. And there, amidst the fresh-cut flowers and plates of piping hot meat and vegetables, would sit their little brother, plaid shirt tucked in, napkin in lap.

It wasn't that John Kennedy tried to make his brothers look bad. It was simply that, even as a boy, John was careful. Careful to arrive at the dinner table on time. Careful to complete his chores. Careful to do all of his schoolwork.

John grew up in post-World War II middle America, not far from where America's most celebrated general, President Dwight Eisenhower, had spent his formative years. But while other boys devoted countless hours to the re-enactment of epic battles against the Nazis, John preferred more bookish pursuits. When he didn't have his nose buried in a text, he'd opt for a game of chess or the company of his fellow members of the math club.

A talented student, John earned stellar grades in high school. He secured a coveted spot in a five-year engineering program at the University of Kansas, then completed his coursework in four years. During summer breaks, he worked odd jobs and scraped together enough to pay for most of his education. After graduation, he married his college sweetheart and landed a position as a bridge designer with the Kansas Department of Transportation, where he'd spend his entire career.

The pair built a home and adopted two children. When he wasn't busy being a father, husband or engineer, John loved to putter in the garden, cook, make wine and build wood furniture.

Through it all, he took care of things. He saved enough money to pay off the mortgage in five years. He squirreled away funds for his children's education, for retirement, for the needs and emergencies that might one day arise. He worried and planned so that his loved ones didn't have to.

A devout Catholic, John began each day by attending mass. It gave him strength, he said, helped to sustain him. Like the bells of St. Joseph's in his youth, this daily rite provided the mooring for a life that seemed picture perfect.

The Kennedy children: John, second from left and Larry, far right

Larry and John in the 1980s

In 1992, as he drove to a family reunion, John detected a distinctive odor. Thinking it must be coming from the car, he pulled to the shoulder to give the vehicle a look. Everything checked out. Odd, he thought as he drove away, still smelling what he could have sworn was sauerkraut.

A few weeks later, he headed home from work by his usual route. But a few minutes later he found himself miles off his intended path. He knew the route so well—he'd been driving it for 25 years. How could he have gotten so lost? He decided he'd better call a doctor.

Tests revealed a brain tumor, a massive growth that his physicians diagnosed as a glioblastoma. This cancer, even when caught early, offered a dismal prognosis. And John's doctors said his tumor had been growing for some time. As it had spread, it had wrapped itself around a major artery in John's brain.

With his diagnosis confirmed, John picked up the phone and dialed a familiar number. Surely his big brother Larry would know what to do next.

In the Kennedy family, Larry was the logical first source for those seeking medical advice. A microbiologist by training, he'd worked in labs studying pathogens, vaccines and even food systems for space flights. After transitioning to management, he remained in the pharmaceutical and chemical industry, serving in a variety of different roles at Burroughs Wellcome, Mallinckrodt and Schering Plough.

Still, three decades in the pharmaceutical industry could not have prepared Larry for the news. Glioblastoma, John said. Larry didn't need to hear more. He knew the grim future awaiting his little brother.

The most common form of primary brain tumor, glioblastomas spread aggressively in and around the brain. As the tumors grow, they cause a range of symptoms: headache, nausea, vomiting, seizures, neurological deficits, and, as John had already experienced, memory loss. Ultimately, the tumors become so large that they cause cerebral edemas—excessive accumulations of water on the brain—or massive amounts of pressure within the skull. Either condition can be fatal. Without medical intervention, glioblastoma patients can expect to live three months from diagnosis. Even with treatment, most live little more than a year.

When John's call came, Larry was working for a pharmaceutical company in Chicago. He had close ties with researchers and physicians at the University of Chicago and Northwestern University, people who would know the cutting-edge techniques that must be emerging to treat this deadly cancer. But when he talked to them, searching for some novel approach to save his brother, each essentially said the same thing: The standard course of treatment is your only option.

That treatment typically entailed removing as much of the tumor as possible, then administering radiation and chemotherapy to whatever remained of the growth, hoping to shrink it further. But by the time doctors found John's tumor, it had firmly affixed itself to his cerebral artery, making surgery impossible. So his physicians began John's treatment by implanting radioactive pellets in his brain. The radiation slowed the tumor's growth, but it also crippled his immune system.

John soon developed a severe yeast infection in his throat. With his airway almost completely blocked, he couldn't talk and could scarcely breathe. Fearing he would choke to death, doctors inserted a breathing tube to keep him alive. To treat the infection, they administered powerful antibiotics. The drugs succeeded, but at a stiff price: They also destroyed the lining of John's throat and stomach, leaving him unable to eat without nausea and extreme gastric distress.

For 2½ years, John lived like this, the disease's growing toll on him compounded by the harsh treatments and accompanying side effects. Finally, the tumor throttled his cerebral artery. With blood no longer able to flow to his brain, John died. He was 47 years old.

To the end, he wanted to ensure that everything was taken care of. "The last time I talked to John, I promised to look after his kids," Larry remembers. "I told him everything would be okay."

But what Larry really meant was, I wish I could have saved you. I wish I could have done something to stop this terrible disease.

In 1998, Larry Kennedy left Chicago and came to work at OMRF. With 30 years of experience working for pharmaceutical and biotechnology companies, he had the tools and know-how to lead the foundation's technology transfer efforts. "Technology transfer is a fancy term for a simple idea," he says. "Our job is to transform discoveries that OMRF scientists make in the lab into therapies that can help patients."

At OMRF, he became the person responsible for sniffing out the projects with the greatest clinical potential. He visited labs, attended seminars and set scores of meetings with OMRF researchers, all in an effort to find those compounds that might, with the proper development, become life-saving drugs.

When Larry identified a promising candidate, he'd use the business skills he'd honed in the pharmaceutical industry to find a commercial partner to help move the discovery from OMRF's labs to pharmacy shelves. This process involved many layers—patenting, marketing, negotiating research funding and licensing agreements—but all of them focused on a simple goal. "Every time scientists knock on my door, I know they may bring news of a discovery that will eventually save lives," he says. "I always keep that in mind, because I know families out there are holding out hope for some new drug that will help save someone they love."

One of the projects that offered a great deal of hope for patients and their families involved a compound known as NXY-059. In experiments involving mice, OMRF's Dr. Robert Floyd found that the compound prevented brain injury in rodents that had suffered certain types of strokes. It even worked when researchers gave it to the rodents up to an hour after a stroke. OMRF had licensed the compound to a pharmaceutical company, which had transformed the laboratory compound into an experimental drug that it wanted to test in humans. Larry negotiated agreements that enabled those human clinical trials to take place.

By making it this far in the process, NXY-059 had already beaten long odds. "For every 5,000 potential new drugs tested in animals, only about five make it all the way to the clinical trial stage," Larry says. But success was far from guaranteed. "Of those five drugs that begin clinical trials, only one will actually make it to market."

Clinical trials progress through a series of phases outlined by the U.S. Food and Drug Administration. Success in early stages, which study dosage and safety, allows doctors to enlist additional participants and examine whether the drug effectively treats disease. Yet as doctors administer the drug to more and more patients, they are more likely to find it has previously unseen side effects—or fails to alleviate patients' illness.

Doctors initiated the trials of NXY-059 by administering small quantities of the drug intravenously to a group of healthy subjects, then slowly increased the dose. When the drug showed no toxicity or side effects, they initiated another trial in healthy older subjects. Again, the drug passed.

A trio of slightly larger trials looked at the drug's safety and efficacy when given to patients who'd suffered strokes in the last 24 hours. The stroke victims tolerated the drug well, and the compound showed indications that it offered protection against some types of brain injury that accompanied stroke. So the pharmaceutical company running the trial made a major decision: It opted to proceed to the stage known as phase III.

Phase III trials comprise the most comprehensive and expensive portion of the process. For NXY-059, doctors tested the drug in 4,700 stroke patients at more than 100 clinical centers in Europe, Asia, Africa, Australia and North America. This stage alone took two years and cost tens of millions of dollars to complete. But when biostatisticians compiled the clinical data, they came to a sobering conclusion: Patients who received the drug fared no better than those who didn't.

The drug company announced that it was abandoning any further efforts to develop NXY-059. Stroke victims would have to look elsewhere for new treatments.

Larry had spent eight years at OMRF working to get the drug to patients. He'd negotiated and renegotiated licensing agreements and financing deals. He'd participated in countless conference calls and meetings, pored over results and strategic plans. And now all of this work seemed for naught.

A few months later, in early 2007, Floyd knocked on Larry's door. The scientist once again wanted to talk about NXY-059.

In the wake of the failed trial, Floyd had studied the data and decided to conduct some experiments that led in a different direction. He had tried variations of the compound to treat mice with liver cancer, and the results proved to be a mixed bag; while the compound showed some promise, they fell short of convincing Floyd that he should continue.

What, he asked Larry, do you think I should do?

Not long before, another OMRF researcher, Dr. Rheal Towner, had sat in Larry's office discussing a new "rat model" he'd developed. By altering rodents' biological make-up so that the animals develop a particular medical condition, scientists can study the illness and find new potential avenues for treating it.

In this case, Towner had developed a model for glioblastoma, the same brain tumor that had killed Larry's brother John. Using a powerful magnetic resonance imager that OMRF had installed, Towner could capture images of the tumors inside living animals. When Towner showed Larry the MRI images of the rat tumors, memories of a decade before came rushing back. "They looked," says Larry, "nearly identical to John's MRIs."

If Floyd's compound showed some promise for treating one form of cancer, Larry realized, it might prove more effective against a slightly different manifestation of the disease. Go see Towner, he told Floyd. Talk to him about trying NXY-059 in his rats with brain cancer.

Towner was familiar with these compounds from his earlier work and agreed to try NXY-059 in his rats. When he administered a dose of Floyd's stroke compound to a rat with glioblastoma, 90 percent of its tumor shrank. "We were amazed," Towner says. "We tried it in several different rodent glioblastoma models, and in every case the tumors decreased and survival increased. It was working, and we wanted to know how."

Again and again, the compound attacked the tumors, inflicting no perceptible damage to surrounding tissues or negative side effects on the mice. Even three months later, after administering the compound to the rats whose brains had once been riddled with cancer, the scientists found no evidence of regrowth or recurrence. The tumors had disappeared completely.

Further tests showed the compound dramatically decreased cell proliferation (spread) and angiogenesis (formation of new blood vessels), and it turned on apoptosis, the process of removing damaged cells so they can't become cancerous. "Those are three major factors needed for a cancer drug," Towner says. "This compound seemed to do all of them."

Every subsequent report from Towner and Floyd fueled Larry's hope that this compound, once pronounced a failure, could still help patients. But Larry wanted some perspective. So he went to visit with OMRF President Stephen Prescott.

Before he came to OMRF in 2006, Prescott had led the University of Utah's Huntsman Cancer Institute. He'd worked alongside the neurosurgeons and oncologists there and seen countless cancer patients come to Huntsman for treatment. He'd also spent years studying the disease's biological mechanisms in his lab.

Prescott listened as Larry outlined the success the OMRF team had when they'd treated the glioblastoma mice with Floyd's compound, which they'd renamed OKN-007. Prescott examined the study data that Larry brought him. I think we really have something here, he told Larry. But to find out for sure, let's ask an expert in human glioblastoma.

Prescott put the team in touch with Dr. Randy Jensen, a cancer specialist and professor of neurosurgery at Huntsman. When Jensen examined the data, he not only agreed with Prescott's assessment—he invited Towner to come work with him in Utah for three months to more closely examine the compound and its capabilities. There the two tested OKN-007 in increasingly aggressive models of the disease Jensen had created. Again, the compound passed with flying colors. And it was in Utah that Towner first encountered people suffering from brain cancer.

"I had talked to patients on the phone, but I'd never come face-to-face with someone battling glioblastoma," he says. "After observing them in Dr. Jensen's clinic and watching some of the surgical procedures, it really sank in that perhaps we could provide some hope to human glioblastoma patients."

The drug development business is risky and expensive. A small research institute like OMRF lacks the resources to bring a discovery all the way from the laboratory to the clinic. So when OMRF scientists make a promising discovery, Larry seeks out a corporate partner to take a compound to market. But when Larry contacted several pharmaceutical companies about the OMRF compound, they declined.

Glioblastoma is considered a rare disease, striking fewer than 1 in 2,000 people. With such a limited population of patients, even with the promising pre-clinical results OMRF had generated, the potential return on investment simply wasn't enough to intrigue drug companies. "It's hard to interest a large corporation in a project that may require a huge financial outlay but produce small profits," Larry says. "But for the families of the 13,000 who die from glioblastoma every year, profit doesn't matter." Larry knew precisely how they felt. "So I couldn't give up."

He spent weeks reviewing the data from other clinical trials and successful drug development projects, looking for ways to make this one more appealing to investors. Then one afternoon, an idea dawned on him. It's our discovery. Why not cut out the middleman and do it ourselves?

OMRF had never before conducted a clinical trial of its own. With every other drug born in the foundation's labs, OMRF had handed the baton to drug companies at this stage, allowing them to assume the costs and responsibilities of coordinating the trials. But this situation offered OMRF a

unique opportunity. The company that ran the failed stroke trial had returned the trial data and remaining experimental drug to OMRF. That data, which showed no significant side effects when given to 4,700 stroke patients, could form the basis of an application to the FDA—prepared at a fraction of the cost it would normally require to put together such a proposal. If the agency approved OMRF's application, the foundation could use the drugs remaining from the stroke trial for a significant number of the cancer patients. Again, this would cut costs significantly.

"With the safety data and drug supply, we were already two steps ahead of the game," Larry says. "If we could iron out the details, there was a good chance we could afford to do this ourselves."

Working with Jensen and doctors at the University of Oklahoma's Charles and Peggy Stephenson Cancer Center, Larry designed a plan for the trials. The two-year trial would start with nine glioblastoma patients at Huntsman in Salt Lake City. Clinicians would administer the compound three times a week for the first month, then follow up with an MRI to monitor changes, if any, in the tumors. If the doctors found acceptable dosage levels and safety data from the initial patients, they'd expand the trial to include patients at Oklahoma's Stephenson Center.

Larry organized a meeting with FDA officials to discuss the data and determine the odds of trying the compound in people. Armed with laboratory results and existing data from the stroke trials, he, Towner and Jensen presented their case to an FDA panel. Submit an application for clinical trials, the FDA reps urged. We'll watch for it.

Larry's staff prepared the Investigational New Drug application for FDA consideration. After weeks of sorting, collating and double-checking, a small parade of dollies left Larry's office loaded with eight boxes of documents—7,232 pages in all—headed for the FDA.

The agency maintains a 40-day window to review applications like OMRF's. Regulators use the time to comb through the documents and request additional information, if needed. If an applicant hears nothing from the FDA, it may proceed with trials.

With only minor modifications to the application, OMRF's 40 days came and went.

Late this fall, more than five years after Floyd first knocked on Larry's door with an idea about using his failed stroke drug to treat cancer, OMRF expects to begin testing Towner and Floyd's experimental compound in patients with glioblastoma. Dr. Gabriel Pardo, a neurologist and director of OMRF's Multiple Sclerosis Center of Excellence, will serve as medical director, and Larry Kennedy will coordinate the project.

OMRF has raised approximately $750,000, enough to fund a portion of the initiative. But the foundation must still raise more funds to complete even the early stages of the trials.

"It's a huge effort and requires real dedication to launch a trial like this," says Floyd. "You can't just say, 'Let's try this.' It takes people believing in it and working hard to make it happen. Luckily, at OMRF, our team believes in this project."

Still, the trial could fail. What then?

"This compound has worked well in animals, but that's no guarantee it will work in people," says Towner. Yet the OMRF researcher remains hopeful. "Even if we only increase a person's survival by three to six months, that's success. With a survival rate of just over a year, if we can add anything more to that, it's worth the effort."

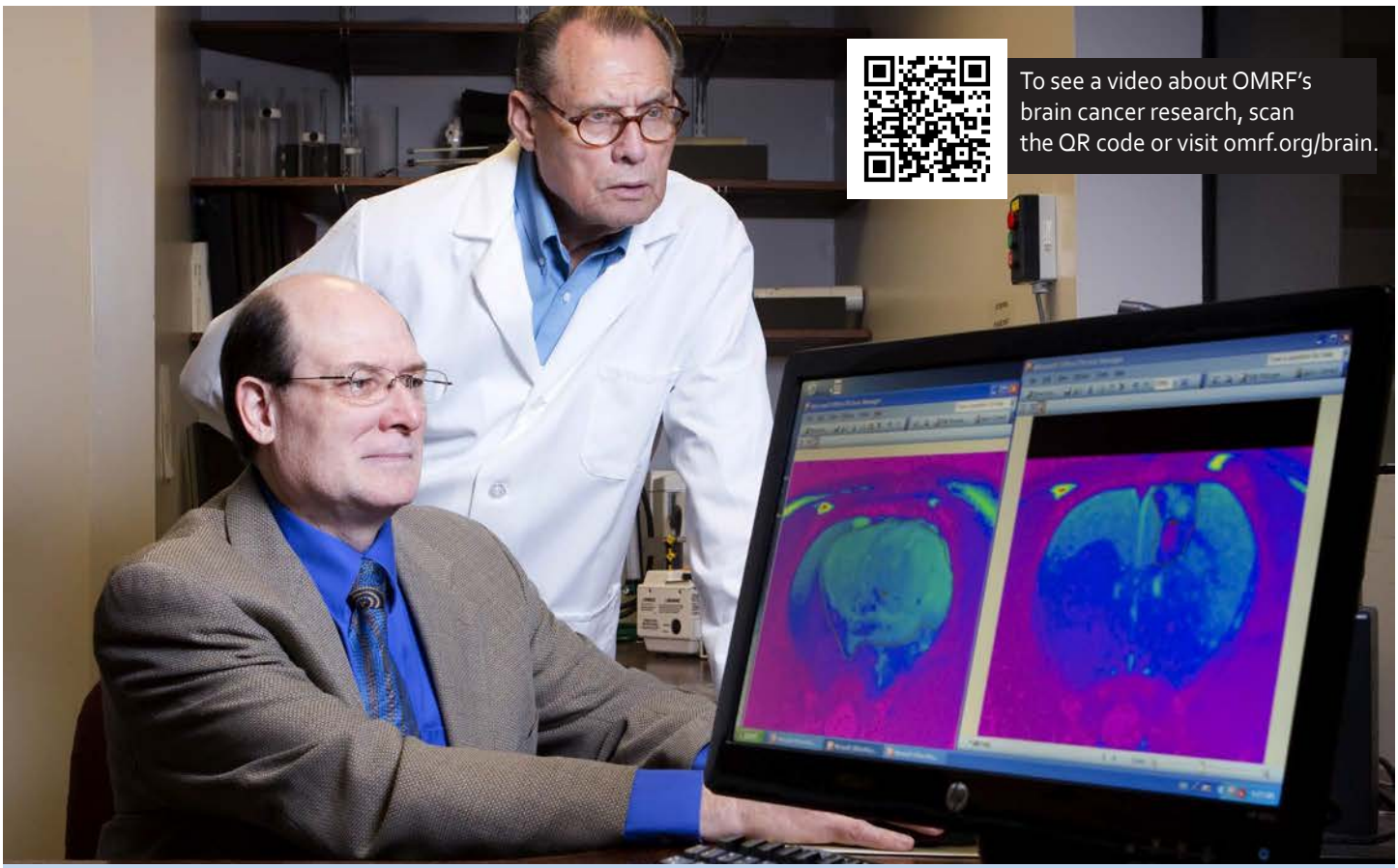
Soon, the first glioblastoma patients will enter Huntsman's doors looking for a miracle or, at least, a little more time on this earth. They'll roll up a sleeve and offer an arm to the needle that will administer the first human doses of the OMRF compound. But the test for this compound will be "severe," Larry says. "Only those individuals who've failed all other standard treatment will qualify for participation." With wrecked immune systems, physical and often cognitive complications, they'll be the sickest of the sick.

Larry thinks of his brother often as he works through the details of the project. He wonders whether John would have agreed to participate in a trial like this. After all he endured at the end, would he have taken a chance on yet one more therapy? And might it have helped him?

"I ponder those questions every time I consider the patients who'll enter these trials," Larry says. "They've already been through so much. I know, because I've seen it firsthand. I know the anger, the frustration, the helplessness."

It's been 17 years since glioblastoma took John's life. His brother's death still haunts Larry, but that loss has taken him down an unexpected path. Only time will tell where that roads leads. Still, for Larry, just making it this far has made all the difference.

"It's immensely gratifying to know that I've been instrumental in this process." It's too late for Larry to save John. But when a door closes, a window opens. And perhaps John's struggles opened the window that led his brother to this clinical trial. To the chance to help other Johns. And maybe, just maybe, to save them. "It feels good to have hope," says Larry. "At last, it feels good."



In experiments using OMRF 's compound, Drs. Rheal Towner and Robert Floyd saw rodent glioblastoma tumors disappear—for good. Doctors expect to begin testing the investigational new drug in human patients this fall.

7 Things You Didn't Know about

Dr. Courtney Montgomery

A self-described health and fitness fanatic, Dr. Courtney Montgomery always looks for ways to keep her body and mind in top shape. In the lab, she studies the genetics of sarcoidosis, a rare immune disease, in hopes of helping others live healthier lives too. Earlier this year, she was awarded a five-year grant from the National Institutes of Health to help her learn more about this mysterious condition. She came to OMRF in 2008, landing her not too far from her hometown of Duncan, Oklahoma.

1. I figure skated as a kid. I wore those sparkly sequined costumes and even made it to U.S. Midwest regional competition. It was a huge deal! But I never got to skate to cool stuff like "Eye of the Tiger." It was all classical music for me.

2. Over the years, I've sung in commercials, a couple of recorded albums, a spot for a hospital and even a music video for a local rock band.

3. Now I just sing my two youngest boys to sleep every night.

4. My husband and I grow a lot of our food—apples, pears, plums, pecans, berries, grapes and vegetables. We trade our produce with neighbors for fresh eggs. If we just had a cow, we'd be set.

5. I'm a total adrenaline junkie. I love extreme workouts like obstacle courses, bungee jumping and parasailing.

6. If I'm desperate to get something done, I often escape to work in my car. It sounds crazy, but it's quiet, full of windows and there are no distractions.

7. I am the IT department at my house, but my six-year-old is catching up quickly.

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