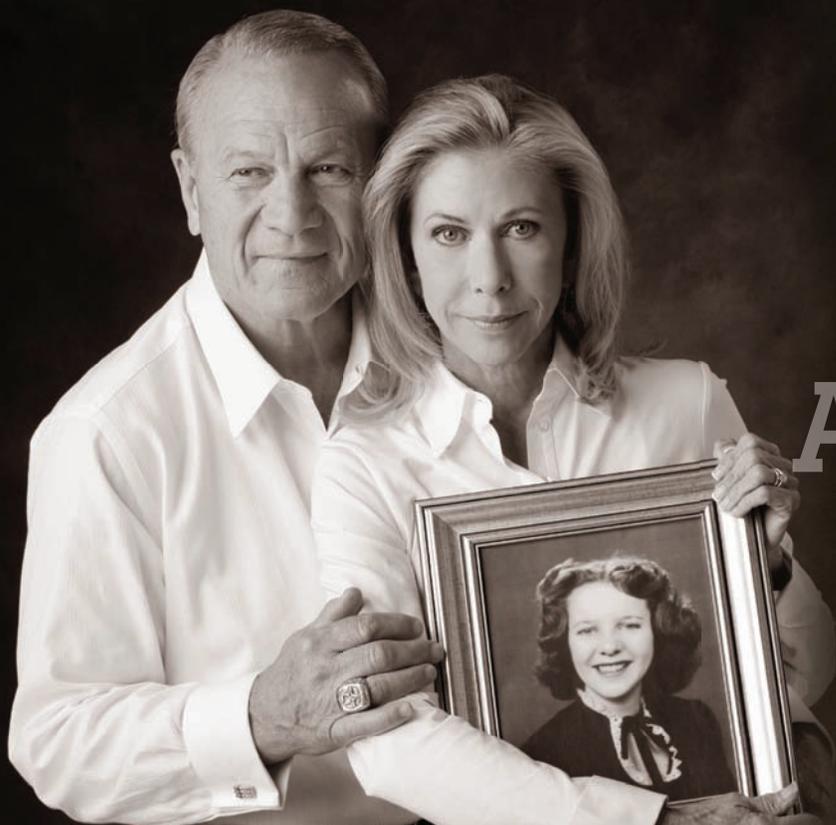


FINDINGS

Winter 2011 • omrf.org

NO WALKING AWAY





Don't let Alzheimer's steal someone you love

I never imagined my mother would lose her laughter. Or that she'd one day forget how to swallow and, finally, to draw a breath.

Alzheimer's disease robs more than 5 million Americans of their memories and, eventually, their minds. Here in Oklahoma, we have one of the top medical investigators in the world, Dr. Jordan Tang, leading a team that is working each day to solve this mystery of human health. An experimental drug based on this research is currently undergoing human clinical trials.

Your gift to the Oklahoma Medical Research Foundation ensures that this progress will continue. And that all those who've lost their lives to Alzheimer's will not be forgotten.

Becky Switzer

Becky Switzer



825 N.E. 13th Street, Oklahoma City, OK 73104

405-271-7400

omrf.org

FINDINGS

Winter 2011 • omrf.org



CHAIRMAN OF THE BOARD Len Cason, Esq.
PRESIDENT Stephen Prescott, M.D.

EDITOR Adam Cohen
ART DIRECTOR Jenny Lee
WRITERS Greg Elwell
Shari Hawkins

PRODUCTION ASSOCIATE Lisa Tullier
PHOTOGRAPHERS John Jernigan
Steve Sisney

405-271-8537
800-522-0211
findings@omrf.org

© 2010 Oklahoma Medical Research Foundation. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

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.



10

WHEN A DOOR CLOSSES, A WINDOW OPENS A farm accident robbed John Enns of the life he knew. But sometimes hope grows in the most unlikely fields. How one Oklahoman turned his personal tragedy into a way to help others suffering from spinal-cord injuries.

PRESIDENT'S LETTER

04 A Bumper Crop

DIALOGUE

05 Lessons in Living

DISPATCHES

06 An Alzheimer's Advance

07 Run, Toby, Run

08 One Man's Legacy

09 Ask Dr. P
Grants

FEATURES

10 No Walking Away

16 Dr. Moser's Opus

COVER STORY



WEB BONUS

AUDIO SLIDESHOW

John Enns, moving forward

>>interactive.omrf.org

A BUMPER CROP

Farming is part of the fabric of our state. For generations, it has represented much more than the backbone of our economy; it has defined a way of life for many rural Oklahomans.

The job requires hard work. Perseverance in the face of adversity. The faith that the seed you plant today will sprout in the future. Indeed, in each of these ways, farmers are like medical researchers.

In this issue, you will read about how one Oklahoma farmer—John Enns—faced down personal misfortune and transformed it into an opportunity for medical research in Oklahoma. By spearheading the creation of the Oklahoma Center for Adult Stem Cell Research, he has sowed seeds that we hope will be reaped by future generations of sick and injured Oklahomans. Indeed, he is but the latest in a long line of state farmers who have labored to help OMRF deliver healthier tomorrows.

From 1961 through the mid-1970s, 450 wheat producers from 34 counties pledged a percentage of the profits from their crops to OMRF. At the outset of the season, they'd sign a pledge promising to deliver a certain number of bushels—the amount was up to them—"to a public grain elevator for the account of the Oklahoma Medical Research Foundation." The form, which was created by a group of farmers who dreamed up the OMRF wheat campaign, carried an illustration of a single grain of wheat, along with the words: "This grain of wheat reminds me of the endeavor of all of us who grow wheat to provide for this year's harvest, to give as many bushels as we possibly can for the Oklahoma Medical Research Foundation."

Those who participated in the drive were people of modest means, men and women who coaxed their living from Oklahoma's dry, cracked soil. They gave by plowing. Watering. Threshing and harvesting. In one year alone, they dedicated more than 9,000 bushels of wheat to OMRF.

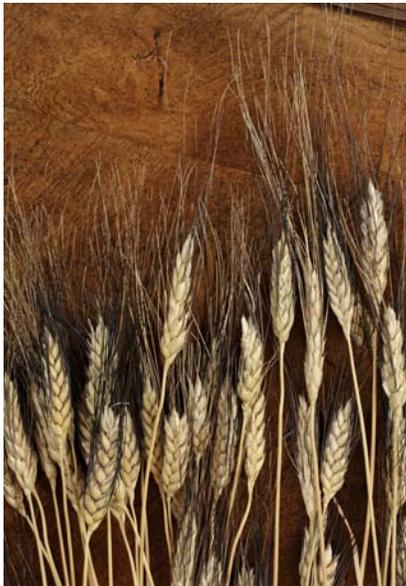
The wheat campaign not only funded life-changing research, but it helped connect OMRF to rural Oklahoma. That bond is one that continues to this day.

OMRF physicians conduct clinical research throughout Oklahoma, which gives rural patients access to the latest advances. In our labs, we train high school, college and graduate students from small communities. Today, Dr. Judith James, a Pond Creek native who first began learning about medical research at OMRF while still in her teens, now leads our Arthritis and Clinical Immunology Research Program.

Throughout OMRF's history, rural Oklahomans have also been some of our most generous supporters. Just one of those many stories appears on page 8, where you can read about a retired Enid man who left OMRF a surprising gift to help fight heart disease.

Perhaps it's the sweeping plains. Or the faith that grows from overcoming stiff challenges. Because when it comes to medical research, rural Oklahomans have always had remarkable vision. They've always seen the possibilities the future holds.

Stephen M. Buscott



HER MESSAGE LIVES ON

Your article about my colleague Debbie Ocker brought me to tears. It reminded me of a similar reaction I had simply watching her walk across the stage at the teacher of the year ceremony in February. How often does inspiration walk right in front of us? She was an inspiration to students and friends for years—not just now, but her whole career. In that one walk across the stage—her last at Putnam City—I felt her courage and strength and then a sudden surge of energy, respect, awe, appreciation, love. I felt it that night and in every interaction I've had with Debbie or her story. Thank you for writing about her.

Steve Lindley
Putnam City Schools

Your article "The Last Lesson" was upsetting but, at the same time, uplifting to know you are doing all you can to find a cure. My son had a kidney removed due to cancer in March 2009. Since then, the disease has reappeared in his lung, his spine and his hip, but treatment has enabled him to continue working. His last checkup revealed all things were holding. I am sure he would agree with Debbie Ocker's statement, "My message has always been about living with cancer, not dying from it." Even his oncologist has said as much. Please continue your good work!

Margaret A. Riggs
Winterville, NC

As a former OMRF employee and long-time supporter, it's easy to look forward to all publications that tell us what's going on in research. The most recent issue of *Findings* had all the traits of an award-winning publication: a magazine about real people with real issues. "The Last Lesson" was a moving and information-filled picture of one woman's life with cancer. And "The Griffin Game of Life" was a clever way to show a glimpse of two OMRF's researchers' personal lives. Thanks for educating us all in such a palatable way.

Suzy Morgan
Oklahoma City

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!  



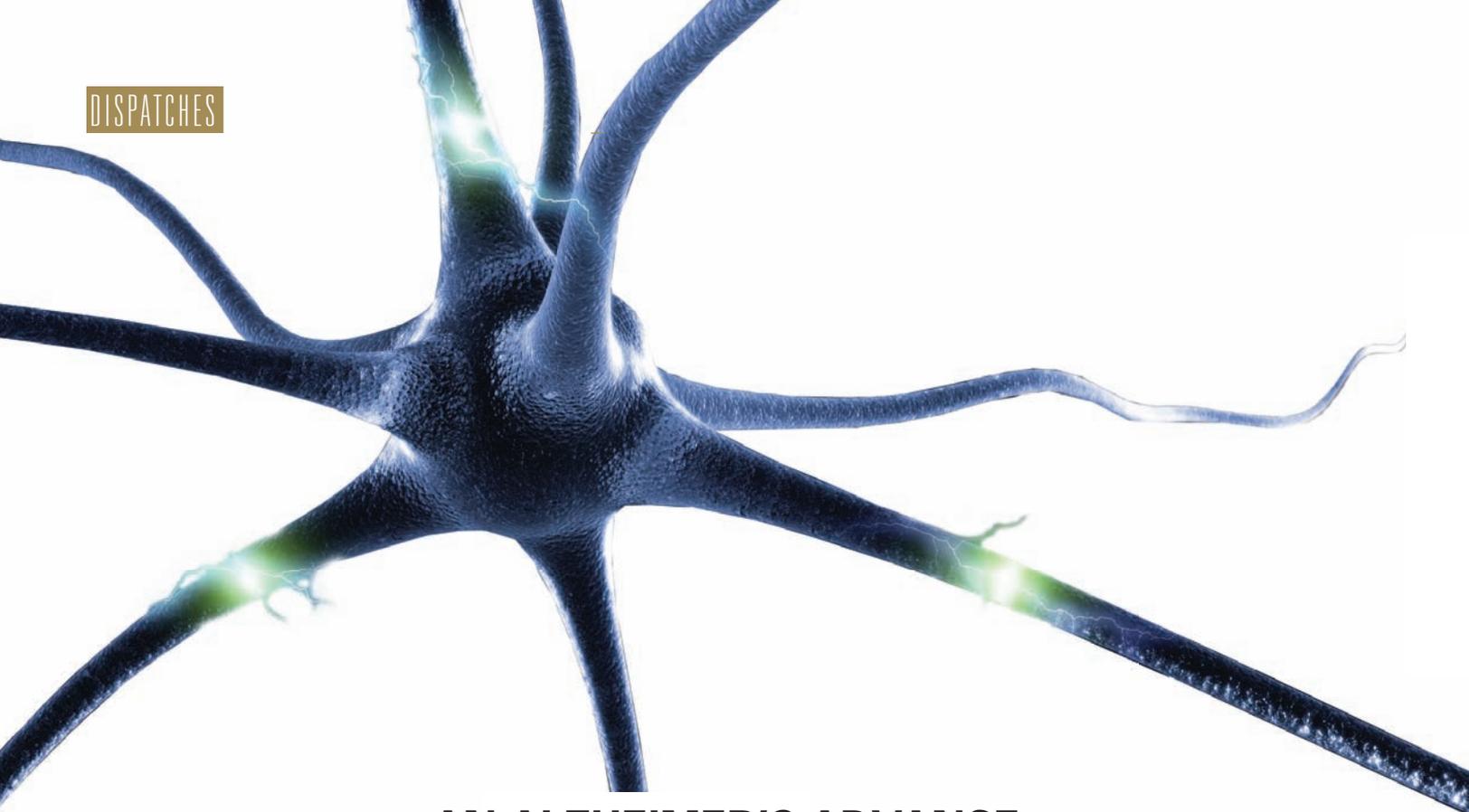
I want to tell you how much my son enjoyed his summer as a Fleming Scholar. He has regaled us all with stories of challenges and new friendships. As a commercial might declare, "A summer as an OMRF Fleming Scholar? Priceless."



J. Brent Clark
Norman

Clark's son Peter spent eight weeks at OMRF as a 2010 Sir Alexander Fleming Scholar. He's now a junior at the University of Texas pursuing a degree in neurobiology, with plans to enter an M.D./Ph.D. program. But his first look at research came during an OMRF tour with his high school biology class. "To me, OMRF was a strange and wondrous place with bizarre tools and equipment," says Peter. "It seemed like the perfect environment where I could let my curiosity run wild. I almost felt like I was in Willie Wonka's chocolate factory. In OMRF's labs, the only limit is your imagination."

You can also read about one of Peter's Fleming classmates on page 7.



AN ALZHEIMER'S ADVANCE

IN NEW RESEARCH, scientists from OMRF and Purdue University have created an experimental compound that reduces memory loss and Alzheimer's disease-causing plaques in mice genetically engineered to develop the illness.

When technicians treated the animals with a new compound developed by OMRF's Dr. Jordan Tang and Purdue's Dr. Arun Ghosh, they found a 75 percent reduction in disease-causing plaques. "And the mice performed almost as well in memory tests as mice without the Alzheimer's gene," says Tang. Based on these results, the researchers will continue to study and develop the compound as a possible treatment for Alzheimer's in humans.

An experimental drug based on Tang and Ghosh's previous work is already undergoing trials in humans, but the latest research involves a new and different compound formulated by the OMRF team. "Alzheimer's is a complicated, multi-faceted disease, so it's important to press forward on as many fronts as possible," says Tang, who holds the J.G. Puterbaugh Chair in Medical Research at OMRF. "We cannot rely on a 'one-treatment-fits-all' strategy, because what works in one patient will not necessarily work in another."

The new compound inhibits an enzyme known as memapsin 2. "Memapsin 2 is like a pair of biological scissors in the brain, snipping off sections of a chain of amino acids," says Tang. "As we get older, those snipped strands

become tangled together and form plaques that cause Alzheimer's disease."

OMRF technicians gave regular doses of the new inhibiting compound to laboratory mice genetically engineered to develop a condition similar to Alzheimer's. They then compared the brains of the mice to genetically altered mice that did not receive the inhibitor. By the age of 10 months, the brains of untreated mice showed the same plaques found in humans with Alzheimer's, but mice given the inhibitor showed only a fraction of those plaques.

The researchers also administered a memory test for the mice by submerging a platform beneath a pool of opaque liquid and allowing the mice to swim around to find it. They then repeated the test several times to assess the animals' ability to remember the platform's location. The better a mouse's memory, the faster the animal was able to find the platform.

The mice that received the inhibitor remembered the location of the platform almost as well as normal mice. In contrast, mice with the Alzheimer's genes that did not receive the inhibitor began having difficulty finding the platform at around 6 months, and their performance kept declining as they aged.

"These are impressive results," says OMRF President Stephen Prescott. "With his new findings, Dr. Tang has made another important advance in the search for a way to stop Alzheimer's."

“Alzheimer's is a complicated, multi-faceted disease, so we cannot rely on a 'one-treatment-fits-all' strategy.”

OFF AND RUNNING

“AN EXPERIMENT,” says Toby Bothwell, “is a lot like running. Some things work, and some don’t. You have to try different approaches to optimize your results.”



Bothwell should know. In 2009, his senior year at Westmoore High School, he was named the Gatorade Oklahoma Boys Cross Country Runner of the Year for a season that included titles at several statewide invitational meets and a runner-up finish at the Class 6A state meet. Meanwhile, with a perfect 36 on his ACT and a stellar academic record, he also emerged from a field of nearly 100 applicants to earn 1 of 12 spots in OMRF’s 2010 class of Sir Alexander Fleming Scholars.

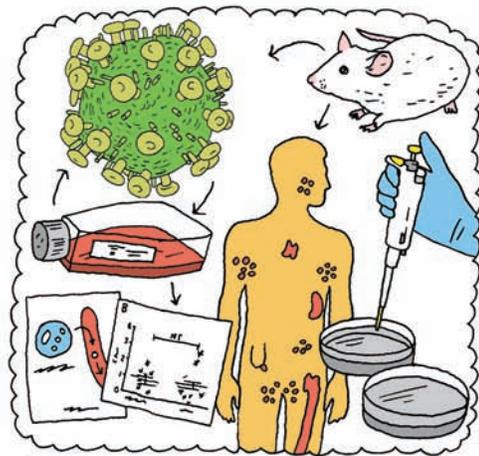
As a Fleming Scholar, he spent the summer working under the guidance of Dr. Susan Kovats. Accustomed to front-running both as an athlete and a student (he graduated first in his high school class), Bothwell found himself in an unfamiliar position at OMRF: struggling to keep up. “There were no immunology classes in high school, so the lab was like a whole other world. I’d never been pushed mentally like that before.”

Bothwell’s Fleming project was a far cry from the biology classes he’d aced at Westmoore. At OMRF, his work involved studying why autoimmune diseases are more prevalent in women than men. In particular, he examined whether certain sex-linked hormones might contribute to the development of illnesses such as rheumatoid arthritis, where the body mistakenly turns the weapons of the immune system against itself.

The science was dizzying, and at first it overwhelmed Bothwell. But, he told himself, “I can do this.” His laboratory colleagues gave him a crash course in immunology that, he says, he “absorbed like a sponge.” Soon, he was culturing cells, working with genetically modified mice and tossing around phrases like “increased cell survivability” and “upregulation of langerin.” He concluded his summer at OMRF by producing a research abstract that analyzed the effect a pair of chemicals had on the development of certain cells crucial to the body’s immune response.

Now attending the University of Arkansas on a full academic scholarship, the 19-year-old freshman remains as competitive as ever. He’s double majoring in physics and mathematics, and he’s running for a cross country program that has won 11 NCAA team titles. On a Razorback team filled with national-caliber talent, Bothwell often finds himself “in the back, hanging on. It’s a challenge just to keep up.”

He hopes one day to make the varsity. But Bothwell’s experience as a Fleming Scholar helped him set a longer-term goal. “I’d like to become a scientist and have a lab of my own one day,” he says. Of course, he’ll bring his racing mentality to research. “I’m super-competitive. So you know I’ll want to have the best lab in the building.”



A QUIET GIFT

JOHNNIE FISHER WAS A SHY MAN. But when the retired Vance Air Force Base sergeant died in 2009 at the age of 77, the gift he left to the Oklahoma Medical Research Foundation proved quite an attention-getter.

This past summer, OMRF received a check for \$600,000 from Enid attorney Clark McKeever, who represents the executors of Fisher's estate, Annette Lillie and Sue Smith. The check represents the first installment of a bequest to support heart disease research at OMRF.

"Johnnie specified that his money be used for research in diseases of the heart, and he knew OMRF was doing important work in that area," McKeever says. When distributions from the estate are complete later this year, McKeever expects that OMRF will receive a total of approximately \$900,000.

"Mr. Fisher's generosity follows a long tradition of rural Oklahomans who have chosen to support medical research through estate gifts," says OMRF President Stephen Prescott. "Thanks to donations like this one, our cardiovascular researchers can continue to search for new and better ways to treat heart disease."

To commemorate the gift, OMRF will name a laboratory after Fisher in its Cardiovascular Center, part of its new research tower. The Center, which will open in 2011, will focus on understanding the processes that lead to heart and blood diseases.

Fisher was born in Wisconsin in 1932. He joined the Air Force as a teen and served in the Korean and Vietnam conflicts, retiring as a staff sergeant in 1968. His last military assignment landed him at Enid's Vance Air Force Base. After his retirement, he took a job as a firefighter.

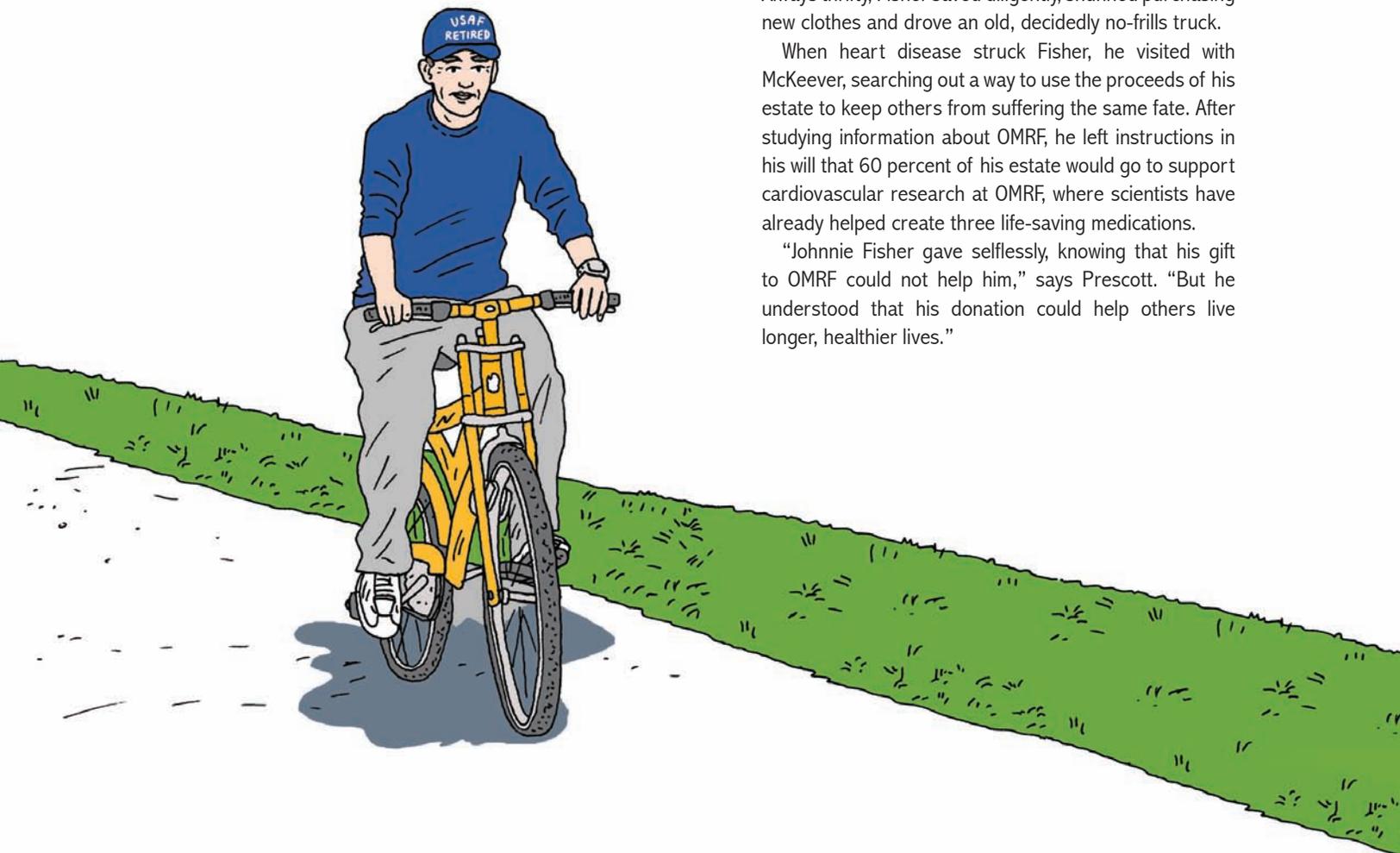
A lifelong bachelor, Fisher retired to Enid's Golden Oaks Retirement Village in 2002. "He was happy there and enjoyed riding his bicycle around the village's lake," said Annette Lillie, trustee of Fisher's estate.

At Golden Oaks, says Lillie, he largely kept to himself, quietly going about his business. "But Johnnie was kind and considerate and always ready to lend a helping hand."

According to Lillie, years of military life left Fisher an early riser, and each day he was the first one in the kitchen to prepare breakfast for his fellow residents. Always thrifty, Fisher saved diligently, shunned purchasing new clothes and drove an old, decidedly no-frills truck.

When heart disease struck Fisher, he visited with McKeever, searching out a way to use the proceeds of his estate to keep others from suffering the same fate. After studying information about OMRF, he left instructions in his will that 60 percent of his estate would go to support cardiovascular research at OMRF, where scientists have already helped create three life-saving medications.

"Johnnie Fisher gave selflessly, knowing that his gift to OMRF could not help him," says Prescott. "But he understood that his donation could help others live longer, healthier lives."





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

Ask Dr. P

I've been told many times—most often by my mother—that the more I exercise, the more easily I'll fall asleep at night. Is there any research to back this up?

Adam Cohen, Norman

In 2009, researchers asked children to wear devices that measured their movements all day. When the scientists examined the kids' sleep patterns, they found that those who were most active during the day fell asleep fastest. For every hour children were sedentary during the day, it took them an average of three minutes longer to nod off at night. Plus, the kids who fell asleep quickly ended up sleeping longer. Studies of adults have yielded similar outcomes, with the results being most pronounced in people who have trouble sleeping.

There are great reasons to get ample shut-eye. Your immune system functions better when you don't skimp on sleep. Research has also shown that sleep deficits are associated with weight gain.

THE LAST WORD The more you exercise, the better you'll sleep. As usual, mother knows best.



Z Z Z

Z Z Z

GRANTS AWARDED (January - June 2010)

Dr. José Alberola-Ila, *Regulation of NKT Cell Development and Function by c-Myb*, National Institute of Allergy and Infectious Diseases; *Hematopoietic Stem Cell Senescence*, National Heart, Lung and Blood Institute

Dr. Dean Dawson, *Segregation of Error-Prone Chromosomes in Meiosis*, National Institute of General Medical Sciences; *Meiotic Functions of Mps1*, National Science Foundation

Dr. Michael Dresser, *Mechanics and Regulation of Chromosome Dynamics in Meiotic Prophase*, National Institute of General Medical Sciences

Dr. Darise Farris, *T Cell Tolerance and Autoimmunity to Nuclear Antigen La*, National Institute of Allergy and Infectious Diseases

Dr. Patrick Gaffney, *Molecular Mechanisms and Genetics of Autoimmunity*, National Center for Research Resources

Dr. Tim Griffin, *Biomechanical Stimulation of Cartilage Antioxidant Function*, Arthritis National Research Foundation

Dr. Judith James, *Oklahoma High-Throughput Serum Analyte System*, National Center for Research Resources

Dr. Paul Kincade, *Hematopoietic Stem Cell Senescence*, National Heart, Lung and Blood Institute; *Early Events of Mammalian B-Cell Differentiation*, National Institute of Allergy and Infectious Diseases

Dr. Florea Lupu, *Intravital Multiphoton Microscope*, National Center for Research Resources

Dr. Rodger McEver, *Cellular Regulation of Selectin-Ligand Interactions*, National Heart, Lung and Blood Institute; *Mechanisms for Blood Cell Adhesion Under Flow*, National Heart, Lung and Blood Institute

Dr. Kenneth Miller, *Signaling Pathways that Regulate Synaptic Transmission*, National Institute of General Medical Sciences

Dr. Kathy Moser, *Gene Mapping in Women with Systemic Lupus Erythematosus*, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Dr. Stephen Prescott, *OMRF Clinical Research Construction*, National Center for Research Resources

Dr. Dario Ramirez, *Free Radicals and Redox Signaling Triggered by Lipopolysaccharide in Macrophages*, National Institute of Environmental Health Sciences

Dr. Xiao-Hong Sun, *Notch-Induced Protein Degradation in Lymphopoiesis*, National Institute of Allergy and Infectious Diseases

Dr. Jordan Tang, *Beta Secretase Inhibition for Treating Alzheimer's Disease*, National Institute on Aging

Dr. Rheal Towner, *Therapeutic Evaluation of Magnetic Nanoprobes Specific for Malignant Tumor Marker*, National Cancer Institute

Dr. Carol Webb, *Role of Transcription Factor ARID3a in Lupus*, National Institute of Allergy and Infectious Diseases

NO WALKING AWAY

BY ADAM COHEN
PHOTOS BY JOHN JERNIGAN





**A DEVASTATING ACCIDENT
ROBBED AN OKLAHOMA
FARMER OF THE LIFE HE KNEW.
BUT SOMETIMES HOPE GROWS IN
THE MOST UNLIKELY FIELDS.**

A TOOTH UNDER A DRILL. SKIN TORN BY A SHARD OF GLASS. A FINGER SMASHED BENEATH THE BLOW OF A HAMMER.

John Enns would gladly have traded any of these for the pain he felt. A half-ton tractor lay on top of him. He was folded beneath the vehicle like the letter U. With his chest crushed, the air could scarcely enter his lungs.

As luck would have it, a friend had seen what had happened. He rushed across the field where John had been spraying his wheat crop and saw the ditch where John was pinned against the earth.

Tales of superhuman strength in such moments of crisis are the stuff of cinema. But this was no movie. John's friend couldn't budge the tractor.

A pick-up raced by. It must have been going 80. Its windows were up, but the thump of heavy metal music leaked from the cab. Help! John's friend bellowed. The truck didn't slow.

Yet a minute or so later, it returned. Two men hopped out. They'd driven about a half-mile past on the farm road in Waukomis, a no-stoptlight town in western Oklahoma, then one had turned to the other and said, Did you hear someone call for help?

The pair grabbed the tractor, pushed it skyward as best they could. John's friend wriggled underneath, unfastened John's seatbelt. Then he dragged John free of the tractor.

John lay on his stomach. He drank in the air in short gulps. His back felt like someone had detonated a bomb in his spine. But he was alive. He couldn't move his legs. They felt kind of strange. Tingly. His friend would call an ambulance, get him to a hospital. He'd be all right. Until then, all he needed to do was keep focused.

Come on, John, he thought, push the pain out of your mind. Push the pins and needles out of your legs.

CRUSHED SPINES, however, do not heal by force of will. The tractor—which would eventually require seven firefighters and a winch to right—had broken John's back in three different places. The most severe damage occurred in his T-12, a vertebra located about two-thirds of the way down his spine from the base of his skull to his tailbone. The half-ton tractor had caused a so-called shotgun blast fracture, shooting bone fragments into his spinal column.

When paramedics arrived, they asked John to describe his level of discomfort on a scale of one (minimal) to 10 (unbearable). Twelve, he said. The paramedics started a morphine drip. It did little to quiet the pain. As the ambulance sped to Enid, John agonized through every bump, every rut, every pothole. The seconds passed like hours.

At St. Mary's Hospital, they placed him facedown on a gurney. They wheeled him past a floor-to-ceiling window, and John caught a glimpse of his reflection. Where his back had once been flat, golf-ball-sized bumps now bulged. I'm in real trouble, he thought. He shut his eyes.

You've got to help me, he begged the ER doctor. She'd known John for years. She understood how important it was for him to get better.

When John was 32, his father died. John's brothers and sister had already moved out of state. That left John to run the farm and to take care of his mother. So for the last five years, it had been just the two of them taking care of the farm.

Please, John told his doctor, I need you to give me a chance.

We're doing all we can, she said. But your injuries are very serious. Then she told him one of the few things he remembers clearly from that day. She said, John, you will never walk again.

SURGEONS MADE AN INCISION in John's back and vacuumed out the bone fragments that had sprayed into his spinal column. They shaved the bony projections from several of his vertebrae. They set two titanium rods in his spine and performed a surgical fusion and bone graft that would help stabilize his back. After implanting ports—soft, plastic tubes—to allow the surgical site to drain properly, they closed everything back up.

Once John's condition stabilized, he moved to the Jim Thorpe Rehabilitation Hospital in Oklahoma City. Doctors had encased his midsection in a body cast to immobilize his spine, and the turtle-shell-like contraption kept him in constant discomfort.

With his injuries, John had lost not only the ability to walk, but also to shower, dress himself, go to the bathroom and even to roll over. All his life, John's physicality had defined him. He'd farmed, fished, hunted, rode horses. Now all that was gone.

So a battery of therapists—physical, occupational and psychological—began the long, hard process of helping him prepare for his new life.

They hooked circulatory pumps to his legs to increase blood flow. Every morning and every afternoon, they stretched his muscles to prevent them from contracting and losing function. They played games with John—Ping Pong, grab the Frisbee—to improve his upper-body strength and dexterity. They brought him to a greenhouse, where he tended plants to refine his small-muscle skills and soak in the peaceful garden environment.

For hours each day, he worked to build strength in his upper body and to restore function to his legs. Expect a miracle, said a big sign that John and his family hung at Jim Thorpe. And John did, even though he couldn't wiggle his toes.

When he was finally ready to leave Jim Thorpe, his uncle built a ramp on the exterior of his home. A friend in the construction business remodeled his bathroom to make it handicap-accessible. John moved from the second-floor master bedroom into a guestroom on the ground floor. He hired a nurse.

The first day John arrived at home, his physical therapist said, yes, you will walk again. Then she stood him up. The strapping farmer, who towered over the five-foot-one therapist, was scared. She supported all the weight his legs once had. She can't possibly hold me, he thought, as she struggled to keep his six-foot-one frame vertical. She's going to drop me. But she didn't. In the months that followed, she kept pushing him, daring his legs to remember what it felt like to put one foot in front of the other.



John Enns on his farm in Waukomis, Okla., on Sept. 8, 2010

John sold some cattle to pay for the new expenses and to hire two part-time farm workers. He started getting around in a manual wheelchair and, eventually, a powered scooter. He fitted his tractor and pick-up trucks with lifts. Now he could drive, plow the fields, plant and harvest crops. He was starting to feel, well, normal.

For years, he'd dated Charla, an Enid schoolteacher. They'd been preparing to get married when John had his accident. For a long while after that, the time just hadn't seemed right. Then one evening, right as they were supposed to go out on a date, John wiggled his toes. Forget dinner and a movie; instead, they spent that whole night gazing at John's right foot.

Not long after that, John and Charla decided it was time to move forward. But you have to be patient, he told her, because I don't want to push myself down the aisle. I want to walk. In July 2006, following two grueling years of rehabilitation—four hours a day, seven days a week—he did.

YET THIS STORY IS NOT A FAIRY TALE.

Today, more than six years after his accident, John is still largely confined to a wheelchair. With the help of a walker and a pair of leg braces that stretch from his feet to his knees, he has been able to walk up to 700 feet. But his rehabilitative progress stopped four years ago, and he now must work constantly to fight the loss of muscle and function in his legs.

He lives with constant pain. And accident-related health problems dog him. This summer, blood clots developed in one of his legs, then broke loose and traveled to his lungs, causing a pulmonary embolism. Doctors told him the thrown clot likely would have killed him but for the strong condition of his cardiovascular system, a product of the vigorous physical therapy regimen he continues to follow. John spent the better part of a week in intensive care, where physicians put him on blood thinners and surgically inserted a filter in his veins to guard against future embolisms.

Still, just days after leaving the hospital, John was back out in the field, planting his winter wheat crop. He's now farming 640 acres of his family's land, and he hopes one day to return to a full 1,000-acre operation.

Since his accident, he's also taken on a second job. In 2006, he was elected to the Oklahoma Legislature. As Representative John Enns, he's had a chance to advocate for issues close to his heart: agriculture, rural development, social services. But perhaps the most profound mark he's made as a legislator will be in the realm of adult stem-cell research.

ADULT STEM CELLS ARE LIKE RAW MATERIALS

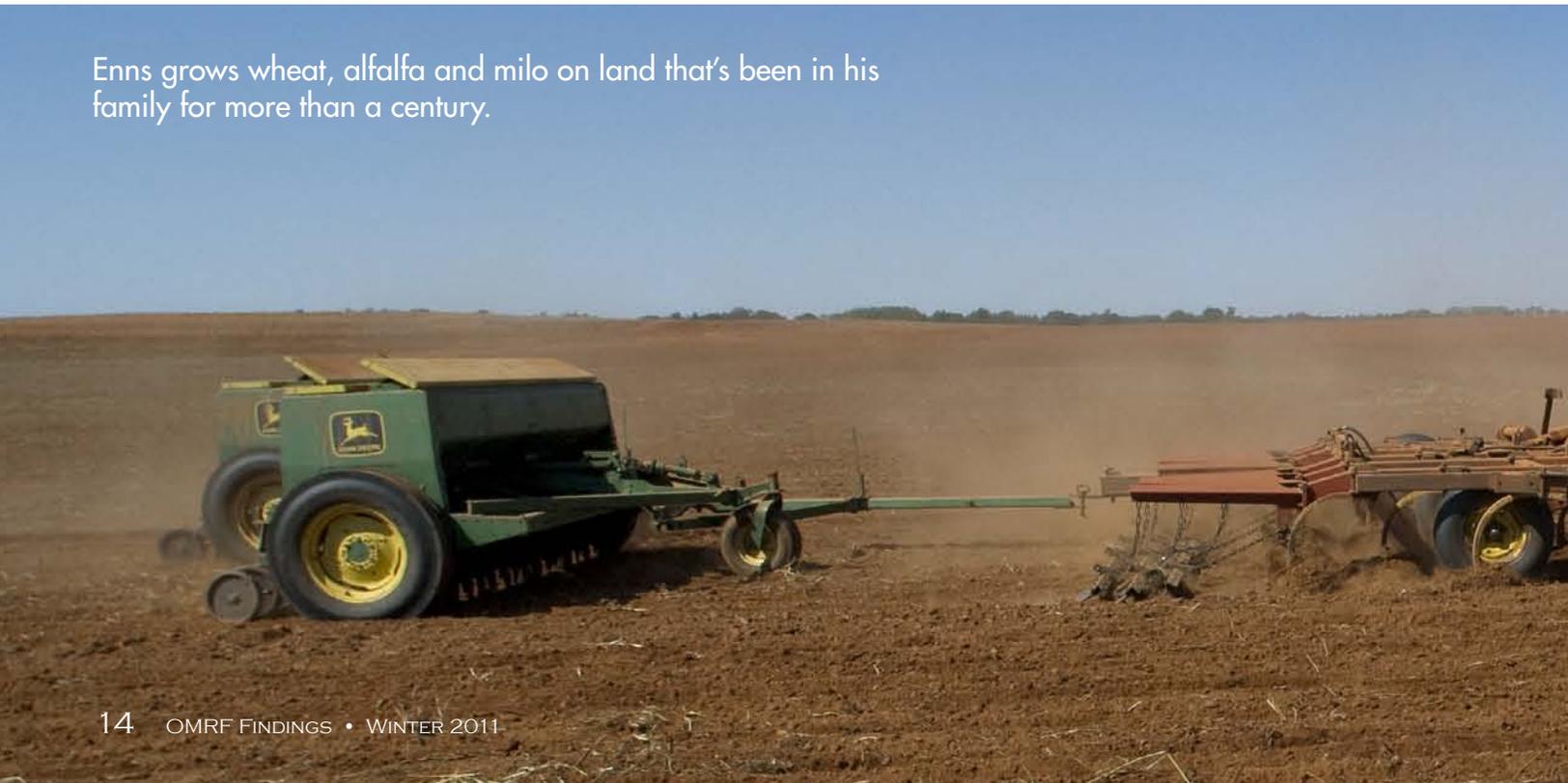
that the body keeps around in case it needs to repair itself. At any point, it may call these cells into action to replenish dying cells and regenerate damaged tissues. The stem cells then "mature" into specialized cells the body needs at that moment.

As a biology major and, later, a microbiology instructor at Northern Oklahoma College, John learned a great deal about these cells. He was intrigued by research suggesting they might have therapeutic uses in treating a wide range of health conditions. And while so-called embryonic stem cells have generated considerable controversy in the research world, adult stem cells have not. That's because work with adult stem cells does not involve the destruction of any embryos.

After his accident, John's interest in this field of research revived. In particular, he learned about how researchers were exploring the use of stem cells to treat spinal-cord injuries. When he became a legislator, he saw an opportunity to help Oklahoma researchers move ahead in this emerging field.

In early 2010, working with the Oklahoma Tobacco Settlement Endowment Trust, John helped establish the Oklahoma Center for Adult Stem Cell Research. With \$5.5 million over an initial five-year period, OCASCR will fund researchers throughout the state as they work on projects using adult stem cells. Dr. Paul Kincade, who heads the Immunobiology and Cancer Research Program at OMRF and has spent more than three decades studying adult stem cells found in bone marrow, was named OCASCR's scientific director. With the help of OMRF administrators and support staff, Kincade established OCASCR's headquarters at OMRF, then set to work on his main goal: giving grants to support adult stem-cell research in the state.

Enns grows wheat, alfalfa and milo on land that's been in his family for more than a century.



Within months, OCASCR awarded \$700,000 in grants to seven scientists at OMRF, the University of Oklahoma Health Sciences Center and Oklahoma State University. The researchers' projects focused on different targets, from lung disease to osteoporosis. But all of them were built upon using adult stem cells as potential treatments. This past summer, one of those researchers made a major breakthrough.

EACH DAY, OMRF'S DR. CAROL WEBB had watched as a group of cells she'd cultured refused to die. By all accounts, they should have been dead months ago. But every morning when she'd peer through her microscope, there they'd be. Alive and kicking.

She puzzled and puzzled over what was happening. Then, one day, it struck her. She dashed down the hall to Kincade's office. Come and look at this, she said. Tell me what you see.

Kincade looked. Yes, he agreed, something very strange was going on. The cells had changed. What once had been adult bone marrow cells now resembled nerve cells and cells lining blood vessels.

Webb had—inadvertently—reprogrammed adult cells taken from throughout the body into different types of cells. She had done it by adding a substance to inhibit the action of a protein in the cells. That process had essentially turned back the clock on the cells, causing them to revert to a stem-cell like condition. The cells then “re-matured” into adult cells that looked quite different from the original cells.

The discovery, published in the prestigious scientific journal *Stem Cells*, could give rise to a method for transforming a person's own cells into whatever special cell is needed. Indeed, doctors recently injected the first patient in the U.S. with human embryonic stem cells as a part of a clinical trial exploring the use of these cells to treat spinal-cord injuries. Webb's method, though, does not use embryonic stem cells. And because it would utilize cells taken from a person's own body, it would not carry with it the risk of the body rejecting the cells.

The work is still at an early stage. Webb has not determined whether the reprogrammed cells are fully capable of changing into all types of cells. She has not figured how to tell the cells

to become whatever kind of cell she wants to make. Even if she figures out these riddles, the reprogrammed cells still could become tumorous.

Despite these uncertainties, Webb's findings represent a significant step ahead. She and her OMRF colleagues are now concentrating on how to make the reprogrammed adult cells become whatever cells the body needs to heal itself. She hopes that years from now, this basic research will lead to new therapies for diabetes or heart disease. For neurodegenerative conditions such as Parkinson's disease and Lou Gehrig's disease. Or for spinal-cord injuries like the one John Enns suffered.

NOT LONG AGO, JOHN WAS LOOKING OUT OVER the plot of land his family had farmed for generations. John had worked this red dirt his entire life. At the age of six, he'd calved his first cow there. As he grew, this was where he'd learned to drive a tractor, to sow crops. After graduating from college, he'd come back to farm alongside his father. Now it was just him.

John sat in the cab of his tractor, an immense machine that dwarfed the scooter he'd used to travel from his pick-up to the tractor. Then a power lift had hoisted him, legs dangling, into the driver's seat.

The adult stem-cell research that's taking place in Oklahoma, he said, it's a source of great promise. One day, that work is going to pay off. And when it does, it's going to mean the world for lots of sick and injured folks.

He's visited OMRF's labs, seen the work that OCASCR is making possible. He's a realist, and he understands that whatever is happening now likely won't come to fruition in time to help him. Still, he holds out hope.

But, he said, supporting medical research has never been about him. It's about helping people who might someday find themselves in his situation.

The engine roared to life. John had 80 acres of winter wheat to sow that day, and it was already noon. He threw the tractor in gear and began to roll out of sight. To move forward. It was the only way John had ever known. ■



poco decresc.
by Greg Elwell
photos by Steve Sisney

Dr. Moser's Opus



She'd felt like this before. At scientific conferences, before giving a presentation, her stomach would begin twisting and turning and jumping and spinning, like Cirque du Soleil was putting on an impromptu show in her gut.

DR. KATHY MOSER COULD HEAR the audience file into their seats at the Oklahoma City Museum of Art. From behind the curtain, she looked at the other half-dozen scientists who were participating in the OMRF Creativity Project and wondered if they were feeling it, too.

This night would be the culmination of a remarkable experience. Pathways in her brain that had lain fallow for many years had not only been reopened but tested and strained under the weight of a brand new pursuit: composing music for a string quartet in a mere 10 days. No matter that she'd never played a stringed instrument nor composed music. That was all part of the experiment. And as a medical researcher, she knew a thing or two about experiments. Except, usually, she was the one doing the experimenting.

The curtain drew back, and with it went her breath. An audience of hundreds sat waiting as a quartet from the Oklahoma City Philharmonic picked at their strings.

Moser knew her composition inside and out. She'd pieced it together note by note, heard its passages play in her head countless times. She'd even listened to the musicians rehearse the finished product. But opening night—the bright lights, the cameras, the crowd—had washed all that away. Now only her anxieties remained, and they dogged her with questions.

“Will my piece be any good?”

“Will the crowd like it?”

“Will I even be able to hear it over my heart thumping?”

Soon enough, she'd have her answers.

MONTHS EARLIER, at a conference on creativity, OMRF President Stephen Prescott was pushing food around his plate, not terribly interested in the meal before him. Instead, his attention was focused on the man at the podium, Jerod Tate. An accomplished composer, Tate was telling how he taught his craft—to children.

The Oklahoma native and member of the Chickasaw Nation explained how he took the raw emotions and untuned ears of students and gave them the tools to compose beautiful music. The wheels in Prescott's head began turning. The scientists at OMRF were some of the most imaginative people he'd ever encountered. But was their creativity transferable? If a mind could dream up a way to stop Alzheimer's disease, could it also conjure up a sonata?

When Tate finished his presentation, Prescott took him aside. “Do you think you could do the same thing with scientists?”

“I don't know,” said Tate. “But I'd love to find out.” And so was born the OMRF Creativity Project.

Tate signed on to lead the effort, and OMRF received a grant to fund the initiative from the Kirkpatrick Foundation. The Oklahoma Educational Television Authority also joined in, agreeing to film the project as an episode of its “State of Creativity” series. All that was left was to find a group of OMRF scientists willing to serve as musical guinea pigs.

Prescott issued a lunch invitation to a group of OMRF scientists he knew had at least a rudimentary background in music. But none had ever played a stringed instrument. And none knew about the experiment their boss was about to propose.

When the researchers entered the room, it was set for lunch, tables circled like wagons. At the front was a stranger with a long braid: Tate. Prescott introduced him and told the story of their meeting. Then he unveiled the plan: Anyone who chose to participate would take part in a 10-day musical “boot camp.” While continuing to run their scientific labs, the researchers would, under Tate's tutelage, compose a piece for a string quartet. The project would culminate with a professional string quartet performing their compositions in front of a live audience.

“Okay,” Prescott asked the 10 researchers, “who's in?”

“This experience, scary as it sounded, was so unique and so new, I didn't want to pass it up,” Moser says. “So I told them I'd be thrilled and terrified to try.”

Moser was not the only one to say yes; six other OMRF researchers agreed to participate. Dr. Courtney Griffin had spent her formative years as a competitive pianist. Her husband, Dr. Tim Griffin, played the clarinet—until eighth grade. Dr. Jordan Tang had taught himself to play the piano. Dr. Courtney Montgomery had been a voice major in college until she opted for the sciences. Dr. Yasvir Tesiram noodles a bit on the guitar. And Dr. Luke Szveda tickled the ivories in his youth.

“There was a wide range of experience in the group,” says Tate. “But even after I'd only spent an hour with them, I could see that everyone who signed on was ready to embrace this challenge.”

Tate had taught scores of composition classes in his two-decade career. Orchestras across the land—including the National Symphony at the Kennedy Center in Washington, D.C.—had performed his work. He'd received numerous accolades for his musical achievements.



Yet as the researchers shook his hand and said how much they were looking forward to the project, he could feel his pulse quickening, his mouth drying. “I’m used to teaching kids. But now I was going to be working with incredibly intelligent, high-achieving scientists. They were going to attack this project with the same intensity they use to try to understand cancer and heart disease.” Tate realized he was nervous. “I wondered if I was up to the task.”

But as he prepared for the OMRF project, Tate decided his nerves were a good sign. “You get a little jittery when you’re pushing yourself into new horizons. That’s good, though. Because new horizons are where the biggest discoveries lie.”

FOR DR. KATHY MOSER, the project offered a reprise of sorts. She’d begun playing the piano at the age of 4, and she quickly became a competitive performer. By the time she attended Bartlesville High School, she was not only performing but also teaching the instrument to others. As college approached, she had to decide whether she wanted to major in music and make a career out of teaching piano.

“I had to think long and hard about whether I could dedicate literally three or four years of my life to learning a 32-page piece of music, spending four or five hours a day at the keyboard,” says Moser. “And in the end, I just couldn’t do it. I just couldn’t see myself sitting on the bench for the rest of my life.”

After earning her undergraduate degree in microbiology, she took a job as a laboratory technician at OMRF. The hands-on experience of working with DNA gels, cell cultures and running experiments in the lab sparked a fire in Moser that never went out. She returned to school and received her Ph.D. from the University of Oklahoma Health Sciences Center. In time, she found her way back to OMRF, where she now studies lupus and Sjögren’s syndrome, “autoimmune” diseases in which the body turns its own defenses against itself.

Moser loves her work. But when Tate opened the door to her musical past, she decided to leap through. “Yes, I was scared. But when I thought about it, I asked myself, ‘When will I ever get an opportunity like this again?’”

ON A GRAY SATURDAY MORNING this past spring, the seven scientists drove to the Post Oak Lodge in Tulsa to begin the project. Tate would lead an intensive two-day musical retreat. After stashing their bags, they found themselves in a rustic classroom with some very modern equipment. Tate was waiting for them with his keyboard and a stereo system.

Everyone was nervous for the beginning of the “master class,” as Tate called it. Fingers rapped expectantly on the wooden tables. Small talk ceased when the composer approached the front of the room and pressed play.

“AhWoooooo!”

The students looked at each other after hearing the tell-tale wolf’s howl from Michael Jackson’s “Thriller.” Closing his eyes, Tate swayed to the thumping bass line, then turned and began rocking out on air guitar.



Showtime Dr. Kathy Moser (in red) was “thrilled and terrified” to compose a piece of music for a professional string quartet.



“I want you to know, your compositions can be anything,” he said. “The only rule is that you have to write for a viola, two violins and a cello. Everything else is up to you.”

By the end of the first day, Moser’s head was spinning. Reality had sunk in. She would have to write a composition. Every note of it. Some of the other scientists had already begun writing. One had basically finished. Yet Moser had nothing. That night, she sat alone in her room and made a decision.

“A blank sheet of paper would not do,” she says. “I needed to get something down. That night. A melody or an idea or something. I could not go into the second day with nothing.”

It’s the kind of panic researchers get when a grant application is due, she says. The need to produce something is vital. No matter if it changes later. You have to start with a kernel, because that kernel will eventually grow into a full-fledged grant application. Without the grant, there’s no money to pay for supplies, equipment or salaries for technicians—and no science.

Moser paced around her room. She got out her laptop and went to YouTube to watch videos of different musical performances.



Outside her door, she could hear the other scientists. They were talking, laughing, playing pool. Moser downloaded a keyboard simulator for her iPhone and started tinkering around. The voices of her fellow researchers quieted and then silenced as the clock passed midnight.

In those wee hours, Moser kept searching the Internet. Reacquainting her fingers with her makeshift keyboard. She needed to find her own voice. Finally, she heard a note in her head. Then another. And she began to write.

By the following afternoon, she'd settled on a theme for her composition: a day in the life of her family. She'd start with the alarm going off, getting the children ready for school. There'd be music to represent each "movement" in the day—the coffee brewing, the kids scrambling to get out the door.

As she made this concoction, she'd slip in treats for each of them. For her daughter, Brianna, it would be a few bars of "You Are My Sunshine." For her husband, Todd, it would be a Motley Crue song. There'd also be musical winks to her boys, Brandon and Blake.

By inserting slivers of their favorite songs, they'd understand the music belonged to them, too. This wouldn't just be her song. It would be all of theirs.

THE NEXT DAY, Monday, Moser began her week of one-on-one classes with Tate. But OMRF is no musical sanctuary, and her days were still filled with science—running her laboratory, OMRF's Sjögren's Syndrome Clinic and Lupus Family Registry and Repository. That left scant time to work on her composition.

"The workload was incredible," she says. "Every night I was up past 2 or 3 a.m. writing, because I couldn't walk into my meetings with Jerod empty-handed."

Each day after lunch, she'd sit in a tiny alcove outside the OMRF cafeteria, headphones in her ears, fingering the keys on her keyboard simulator. She'd tap out tunes until she was satisfied, then transcribe her notes onto the page to bring to Tate, who'd set up shop in a conference room at OMRF. He'd spend an hour a day with each of his seven pupils, and the 1:00 slot belonged to Moser.

"What have you got?" he'd ask each afternoon when she'd arrive. He'd study what she'd penned in her notebook, then start peppering her with questions: Do you like this tempo? What are you trying to do with this passage? Before long, he'd scoot over to his keyboard, or begin decorating his dry erase board with her notes. As the week progressed, they sewed a rich tapestry from the scraps she brought him each day.

By Saturday morning, it was time to give the compositions to the string quartet. They would sight-read the pieces that, on Monday, they would perform for a live audience at the Oklahoma City Museum of Art. Moser invited her family to the rehearsal. Her two boys, ages 5 and 7, would be too young to sit through an entire concert, but she wanted all of them to hear what she'd written. She wanted them to hear their song.

As Todd, Brianna, Brandon and Blake listened to the string quartet play Kathy's work, smiles crept across their faces. Except for Todd, whose mouth hung open—in awe, he'd later tell Kathy. That she'd created something so beautiful and complex had stunned him. It was, he says, like discovering his wife had a superpower.

Yet as Kathy sat by Tate, listening to the four musicians perform, she realized she still had work to do. The piece needed fine-tuning. Change a note here. Fix a rhythm there. Only two days remained to make it sound in her ears the way it sounded her head.

ON THE NIGHT OF THE CONCERT, Kathy took a deep breath when it came time for the quartet to play her piece. The cello mimicked the rumble of her husband's voice. The chattering of the violins arrived like her children awakening each morning. And there was Kathy, the viola in the middle of it all, keeping order.

When the music ended, applause filled the theater.

She'd done it. She'd taken a song that had played only in her mind and given it to the world. And in the process, she'd awakened something inside herself. "I thought I'd left music behind years ago, but when I jumped back into it, I felt that same deep connection like it was yesterday," she says.

When the music ended, when the clapping gave way to silence, Kathy put her lab coat back on and returned to her work. There were autoimmune diseases that hadn't seen new treatments in a half-century. And patients who desperately needed those treatments.

But when a spark rekindles, it doesn't go out with the first breeze. For a long time, Kathy had been toying with purchasing a piano. After the concert, she went out and bought one. She's now reworking her composition, so that she can play it with her own two hands.

In the meantime, every once in a while, when she needs a bit of inspiration, she'll find the CD of the performance and pop it into her computer. Sometimes she'll close her eyes, let the music wash over her. It only takes a few violin notes, and she's back at the concert. To that night when she learned that some of the best experiments have nothing to do with laboratories. ■

Watch the OETA documentary and listen to music from the OMRF Creativity Project at omrf.org/oeta.



825 N.E. 13th Street
Oklahoma City, OK 73104

Non-Profit Org
U.S. Postage
PAID
Permit No 639
Oklahoma City, OK



A LOOK BACK

Scientists and thinkers as far back as Aristotle have also excelled in music. To the scientific mind, is music simply another formula to follow? Or could the link be mathematical? Whatever the reasons, hands that reach for test tubes often comfortably fit on a piano or other musical instruments. Can you name this famous scientist who also was a “relatively” talented violinist? Send your answers to findings@omrf.org or call (405) 271-7213 for a chance to win an OMRF t-shirt.