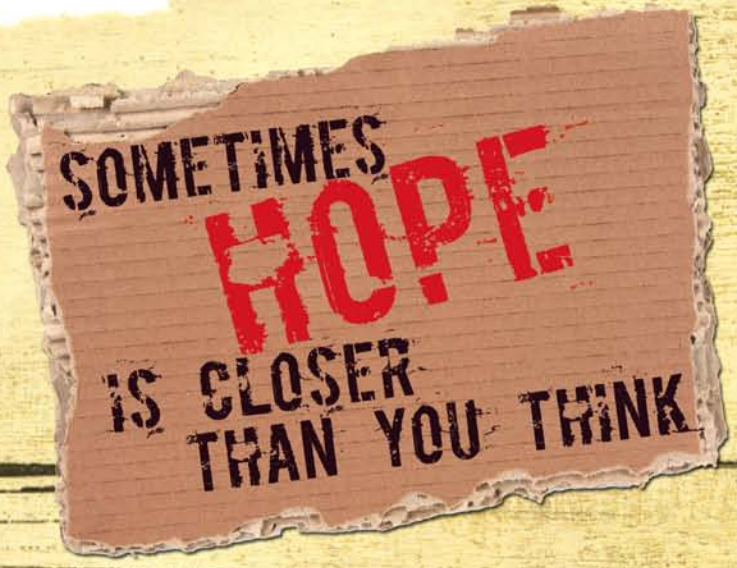
FINDINGS

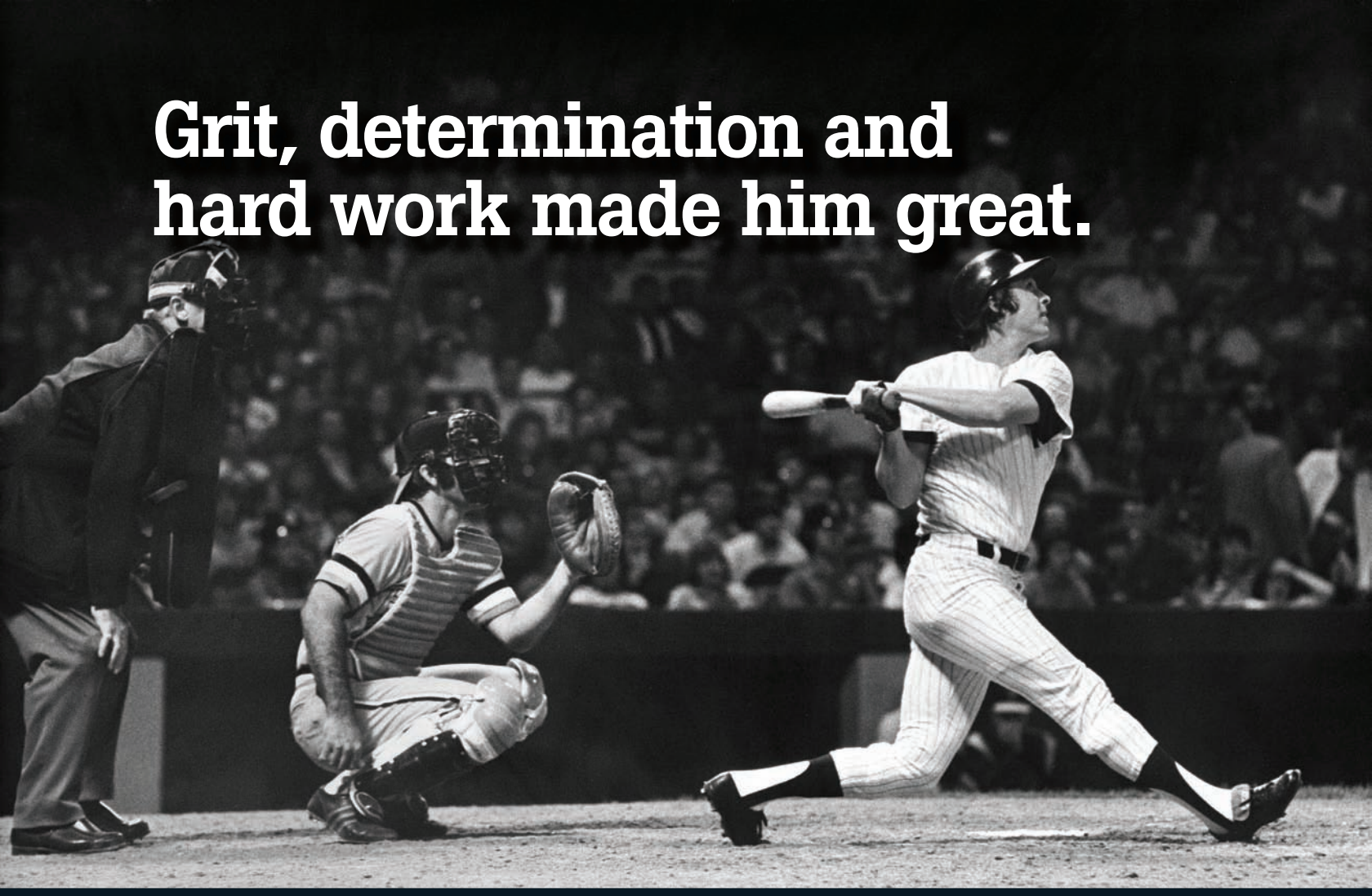
Fall 2008 • omrf.org

SECOND CHANCES



OMRF

Grit, determination and hard work made him great.



But cancer was an opponent Bobby Murcer just couldn't beat.

For 17 years, Oklahoma native **Bobby Murcer** patrolled the outfields of Yankee Stadium, Candlestick Park and Wrigley Field. Dubbed "the next Mickey Mantle," Murcer enjoyed a stellar major league baseball career. But glioblastoma—a **brain cancer**—became the one opponent he could not conquer. Murcer succumbed to the cancer on July 12, 2008, at the age of 62. • At OMRF, scientists are now exploring a **promising new therapy** for patients suffering from this type of brain cancer. In pre-clinical experiments, they have found that the drug significantly shrinks the tumors. The next step will be to begin testing the compound in humans. • **Please help** Bobby Murcer's legacy live on by helping OMRF's scientists in their quest to stop glioblastoma and other deadly cancers.

Bobby was always proud of his Oklahoma roots. He'd be even prouder that some of the world's most promising brain cancer research is happening right here at the Oklahoma Medical Research Foundation. Please support the efforts of OMRF—together we can beat cancer.

Kay Murcer

OMRF

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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.

A United Way Partner Agency

10 **Two Oklahomans suffering from a rare, life-threatening disease. A pair of OMRF scientists bent on solving a medical mystery. Sometimes hope is much closer than you think.**

WEB BONUS

AUDIO SLIDESHOWS

Sandy Roark and Greg Watkins tell their inspiring stories

Get to know two dedicated OMRF volunteers

>>interactive.omrf.org

True Believers

It can be easy to lose the forest for the trees.

Like most scientists, I went into medical research for what I consider to be a "good" reason: to help make our world a better place. More specifically, I wanted to use my skills to develop a better understanding of the processes that lead to human disease. Ultimately, I hoped my work would lead to new ways to treat life-threatening conditions like cancer and heart disease.

In pursuit of those goals, I spent the lion's share of my adult life in the laboratory. Yet as I dug deeper and deeper into the minutiae of research—looking at the processes that lead to inflammation or how blood supply controls tumor growth—I sometimes lost sight of the big picture.

When that happened, something inevitably brought me back into focus. Maybe it was meeting a person who had survived a bout with a deadly disease. Or the widow of someone who hadn't. Inevitably, that human interaction sparked my research, providing an emotional catalyst by reminding me of what was truly at stake when I put on my lab coat.

As an administrator, my job is now to oversee the work of dozens of scientists who are exploring the root causes of human disease. My job is to keep my finger on the pulse of the institution, minding the work of every scientist and every line item on our balance sheet. Of course, it's vital for me to focus on the what and how of our operations. In other words, what are we doing and how can we do it better? Still, the heart of this institution is the why—to help Oklahomans and people everywhere live longer, healthier lives. Without this core mission, OMRF would never have come into being. And it would not still be thriving 62 years later.

This fall, I was lucky enough to meet two people who are living embodiments of OMRF's mission. I was in Ponca City, attending a small gathering, when I was introduced to Helen Bloxsom and Phyllis Moriarty. Tragically, both lost their husbands to Alzheimer's disease. Despite the tremendous devastation that comes with such a loss, Helen and Phyllis refused to give up any more to the disease that had robbed them of so much. So they organized a chicken-and-noodle dinner to raise money for Alzheimer's research.

What began as a small effort grew quickly, to the point that this year's dinner—now an annual event in Ponca City—had to be stretched over two nights and served 500 people. All of the proceeds go to support Alzheimer's research at OMRF.

You can read more about Helen and Phyllis (and even get their chicken and noodle recipe) on page 18. And if you go online to **interactive.omrf.org**, you can hear Helen and Phyllis tell their stories in their own words and see a slideshow of the lives they shared with their late husbands.

People like Helen and Phyllis remind me of why I love working here. Sure, the science is wonderful. And so are the scientists. But at the end of the day, it's about the people we serve. And who serve us.

Of course, if you're looking for "why," look no further than page 10, where you'll meet Sandy Roark and Greg Watkins, two Oklahomans whose lives were transformed by an OMRF discovery. And you can also read about James Chapman (page 16), an unassuming rancher who made a fortune in the oil patches south of Tulsa, then used his riches to seed OMRF. Like Phyllis and Helen, he was a true believer in the power of medical research. In the power of turning dreams into reality.

Stephen M. Prescott

DNA A-Peel

I JUST RECEIVED YOUR LATEST issue of *Findings* over the weekend and thoroughly enjoyed a cover-to-cover reading of it and another trip down memory lane. I like the way author Greg Elwell ("Next of Kin," Summer 2008) set a first-person perspective on the current application of DNA analysis to the individual, his health and his prospects for a healthy future. He presented a very readable overview of how adenine, cytosine, guanine and thymine provide the alphabet of DNA and allow myriads of possibilities for genetic coding.

I got to study under Dr. (Petar) Alaupovic and others as a graduate student assistant at OMRF in the cardiovascular group and have enjoyed the updates published in recent OMRF *Findings*. Pleasant memories!

GAIL JERGENSEN
LONGMONT, CO

I WANTED TO LET YOU KNOW how much I like the new look of the *Findings* magazine I got in the mail yesterday. I really like the enhancements you have made. It looks great, really sleek and polished. It has a scientific and tech-y look that has a lot of appeal. It's awesome.

GINA LEEDS
OKLAHOMA CITY

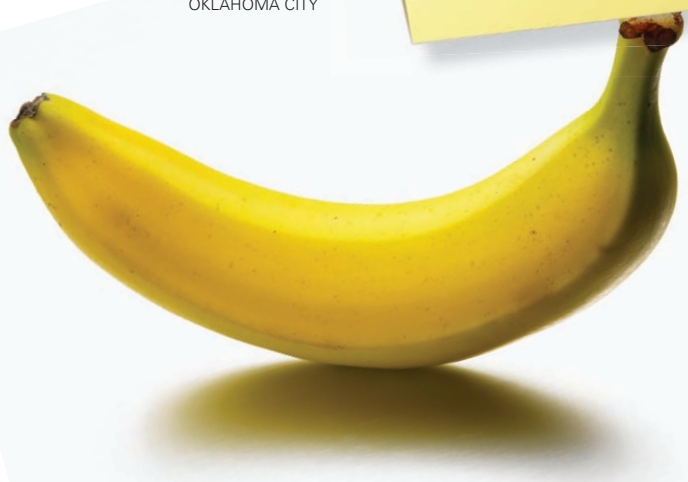
I REALLY ENJOY *FINDINGS* AND more importantly, the research that you do. We have had memorials for our dad right there through OMRF. So keep up the good work!

MICHELE WEBSTER
DEER CREEK, OK

WE'RE A LITTLE BIASED toward the subject (and author) of your last cover story, "Next of Kin," as he's our son, but we very much appreciated the chance to learn a little about our genetic heritage and how it affects both our sons and (we hope) the next generation of Elwells. As for the cover art, let's just say we always knew Greg was a little bananas—we just didn't realize the extent of their relation.

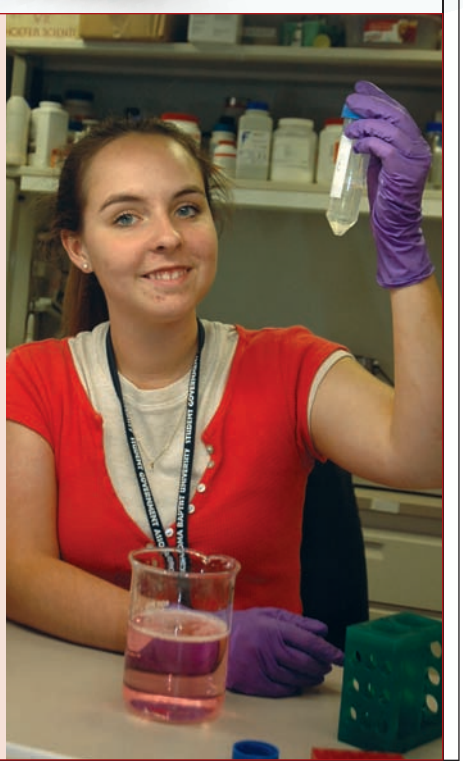
M.G. AND LAURA ELWELL
OKLAHOMA CITY

At the 31st annual Upper Case Awards in October, *Findings* won a pair of top prizes from the Oklahoma City chapter of the Public Relations Society of America. For the third time in the last four years, *Findings* took home the blue ribbon in the magazine category. "The Comeback Kid," our story about sepsis survivor Rayna DuBose, won for best feature writing, and it also took home the Best of Show award for all writing entries.



WHEN I WAS SELECTED AS a 2008 Fleming Scholar at OMRF, I didn't really know what to expect, but I was more than thrilled with the whole experience. The best part was getting to do experiments and ask questions that no one really knows the answers to. This experience has shown me that I want to do research as a career, because I enjoy this more than anything I've done before. Results from basic research lead to developments that help people who are fighting disease. One day I hope to become a physician-scientist, and now I have a better background for pursuing that career path. I also had the opportunity to make new friendships with other students from around the state. I wouldn't have wanted to do anything else with my summer.

STEPHANIE WILBURN
FITZHUGH, OK



WRITE TO US!

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

Tackling a New Challenge

When he crossed the Red River to play football at Langston University, **James Harding Jr.** expected to meet his most formidable foes on the playing field. Unfortunately, his toughest opponents were lurking inside his own body—diseases that would rob him of a promising athletic career and change his life forever. Luckily, Harding's move to Oklahoma put him in just the right place to deal with the challenges that lay ahead.

Last August, a routine run around the practice field left Harding, 19, unusually sore, his muscles aching from head to toe. He soon collapsed and was rushed to the hospital. There, the Lancaster, Texas, native learned that he suffered from an assortment of autoimmune diseases—lupus, polymyositis, Sjögren's syndrome—conditions in which the body's immune system attacks itself instead of fighting infections and diseases.

Of the three illnesses, lupus posed the most serious threat. The disease can be life-threatening and can strike multiple organs: the nervous system, lungs, heart and kidneys, as well as the joints and the skin. There is no cure, and often the treatments carry serious side effects. Harding learned that the key to long-term disease management lay in regular care, so he began treatment at OMRF's lupus clinic.

While there, the honors student (he carried a 3.8 GPA in high school and is a member of Langston's E.P. McCabe Honors Program) heard about an OMRF summer scholarship program where college students could participate in hands-on research for 8 weeks. For the one-time gridiron star, it quickly became clear that his future would depend more on brains than brawn.

"My goal now is to do whatever I can for people with lupus and other autoimmune diseases," says Harding. "OMRF's program presented the perfect opportunity for me to use my mental gifts to help improve the lives of others." He applied and was accepted as a 2008 OMRF Presidential Scholar. In the program, he spent his summer working in OMRF's Arthritis and Immunology Research Program, where he studied a little-understood research topic: the genetics of men who are suspected of having more than one X chromosome and how many of them develop lupus.

"The work was everything I hoped for and then some," says Harding, now in his sophomore year at Langston. Although his medical condition has put an end to his football career, it has given birth to new ambitions. "I did graduate-level work this summer, so I'm well ahead in school. My experience at OMRF also gave me an idea of what it takes to make it in the research field. My dream now is to go to medical school and then start my own search for a solution to lupus and diseases like it."

"My goal now is to do whatever I can for people with lupus and other autoimmune diseases." **JAMES HARDING, JR.**

OMRF finds new grounds for hope in treating MS

A good cup of coffee might be just the wake-up call scientists need to stop multiple sclerosis.

A new study co-authored by OMRF's **Dr. Linda Thompson** found that mice immunized to develop an MS-like condition were protected from the disease by drinking caffeine. The research, which appears in the *Proceedings of the National Academy of Sciences*, could lead to new ways to prevent and treat MS.

"This is an exciting and unexpected finding, and I think it could be important for the study of MS and other diseases," says Thompson, who holds the Putnam City Schools Distinguished Chair in Cancer Research at OMRF. In particular, she says, the research holds potential for lupus, rheumatoid arthritis and other autoimmune diseases—conditions in which the body uses the weapons of its immune system against itself.

In the study, done in collaboration with Cornell University and Finland's University of Turku, researchers followed the progress of mice that normally developed an MS-like condition. But the scientists found that when the rodents consumed the equivalent of six to eight cups of coffee a day, they did not develop of the condition.

According to Thompson, the caffeine stopped adenosine (one of the four building blocks in DNA) from binding to an adenosine receptor in mice. Adenosine is a common molecule in the human body and plays a vital part in the biochemical processes of sleep, suppression of arousal and energy transfer. When adenosine could not bind to the receptor, this prevented certain T cells—white blood cells that play a central role in immune responses—from reaching the central nervous system and triggering the cascade of events that lead to experimental autoimmune encephalomyelitis, or EAE, the animal model for the human disease MS.

While the results are heartening, Thompson says, there is much more work to be done for the prevention of multiple sclerosis in humans. "A mouse is not a human being, so we can't be sure caffeine will have the same effect on people prone to develop MS without much more testing." A retrospective study of people with MS to track their caffeine intake and the effects on the disease could be an important next step in the research process, says Thompson. "If you found a correlation between caffeine intake and reduced MS symptoms, that would point to further studies in humans."

MS is a disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech and bladder control. Believed to be an autoimmune disease in which the body's immune system attacks nerves in the brain and spinal cord, MS affects approximately 400,000 Americans and 2.5 million people worldwide.

Generation Next

OMRF Adds Scientists to Spur Growth, Discovery

A new wave of researchers has joined OMRF's scientific staff as part of the foundation's expansion. In total, OMRF has added seven principal scientists and promoted two staff scientists to faculty-level positions. The recruitments and promotions are part of an expansion that will increase the number of principal scientists from 50 to 80 and grow the total OMRF staff from 500 to 800.

"With the right resources, OMRF can make even more headway in the fight against disease," says OMRF President Stephen Prescott. "Those resources include facilities and equipment, but the real keys are the human engines that drive discovery. With these recruitments, we believe we've brought some of the brightest emerging minds to Oklahoma and OMRF.

The new researchers have come to OMRF from a variety of institutions across the U.S. and beyond, including Yale University, Duke University, the National Institutes of Health and London's Imperial College of Medicine. And their research interests range from studying the genetic roots of cancer to using wavelengths of light to understand cardiovascular processes that lead to heart disease.

Bringing in so much talent in a single year required significant recruiting efforts by OMRF's current faculty and human resources department. And while the weather did not always cooperate, OMRF's and Oklahoma's strengths shined through. Dr. Courtney Griffin, who joined OMRF with her husband, Tim, in September, made her first trip to OMRF during last year's ice storm. "I'd never been out here before, but even coming during the ice storm, I was impressed," she says. "When we came back together and checked out the neighborhoods and schools, it was a pleasant surprise. But the real selling point was OMRF and the promise that we'll be able to work in a place that prizes innovation, discovery and collaboration."

In the coming years, the foundation will continue to grow, Prescott says. "Our mission is to find new diagnostics and treatments for human disease. By growing our already formidable group of researchers, we can help bring healthier tomorrows to Oklahomans and people everywhere."

Dr. Tim Griffin joined OMRF from Duke University in September.

Hear about an unusual research project he did involving penguins and how they walk >>interactive.omrf.org

Dr. José Alberola-Ila, *Understanding the Genetic Networks that Control CD4 T Cell Lineage Commitment*, American Heart Association; *Role of PTPRK in CD4/CD8 Lineage Commitment*, Oklahoma Center for the Advancement of Science and Technology

Dr. Robert Barstead, *A Gene Knockout Resource for* C. elegans, National Human Genome Research Institute

Dr. Dean Dawson, *The Role of SLK19 in Mitotic Cell Cycle Progression,* Oklahoma Center for the Advancement of Science and Technology

Dr. Michael Dresser, *Mechanism of Force Generation at Telomeres*, Oklahoma Center for the Advancement of Science and Technology

Dr. A. Darise Farris, *Do Estrogen Receptors in B Cells and DC Mediate Sex Bias in Murine Lupus* National Institute of Allergy and Infectious Diseases; *Mechanism of Defective Suppresion in YAA+ Murine Lupus*, Oklahoma Center for the Advancement of Science and Technology

Dr. Patrick Gaffney, *Replication of SLE Candidate SNPs from Genome-wide Association Studies*, Arthritis Foundation

Dr. Joel Guthridge, *Gene Regulation of the C8orf13/BLK Locus in SLE*, Oklahoma Center for the Advancement of Science and Technology

Dr. John Harley, *Molecular Mechanisms and Genetics of Autoimmunity,* National Center for Research Resources

Dr. Kenneth Hensley, *Kynurenine Metabolites for Hypertension,* Oklahoma Center for the Advancement of Science and Technology

Dr. Judith James, *Kirkland Scholar Award,* Mary Kirkland Center for Lupus Research

Dr. Chandrashekhar Kamat, *Tocopherals in Cardioprotection,* Oklahoma Center for the Advancement of Science and Technology

Dr. Susan Kovats, *Dendritic Cell Function in Lupus-Prone Mice Lacking Estrogen Receptors,* Arthritis Foundation; *Estrogen Regulates Dendritic Cell Differentiation*, Oklahoma Center for the Advancement of Science and Technology

Dr. Rodger McEver, *Protein-Glycan Interactions in the Vascular System,* National Heart, Lung and Blood Institute

Dr. Kenneth Miller, *Identification of Synaptic Dag Effectors and Regulators,* Oklahoma Center for the Advancement of Science and Technology

Dr. Kevin Moore, *Identification of Tyrosine-Sulfated Proteins in the Male Genital Tract,* National Institute of Child Health and Human Development; *Mechanisms for Hypothyroidism in TPST-2 Deficient Mice*, Oklahoma Center for the Advancement of Science and Technology

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

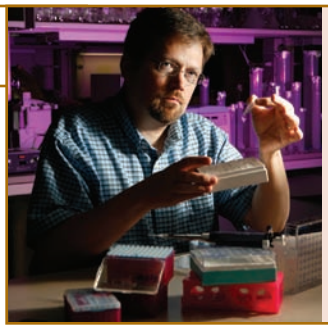
Dr. Dario Ramirez, *Free Radical and Redox Signaling Triggered by Lipopolysccharide in Macrophages,* National Institute of Environmental Health Sciences

Dr. James Rand, *Role of Neuroligin in Synapse Stability,* Autism Speaks

Dr. Susannah Rankin, *Sororin, Chromosome Cohesion and Cell Cycle*, Oklahoma Center for the Advancement of Science and Technology; *Sororin, Sister Chromatid Cohesion and Cell Cycle Control*, Pew Scholars Program in the Biomedical Sciences

Dr. William Rodgers, *Raft Protein Clustering by the Actin Cytoskeleton,* Oklahoma Center for the Advancement of Science and Technology

Dr. Luke Szweda, *Modulation of Mitochondrial Function by Pro-oxidants,* National Institute on Aging



DR. PATRICK GAFFNEY and Dr. Kathy Moser have discovered a gene variation that appears to cause the immune system to lose control, resulting in damage to the body and autoimmune disease. This new research, published in the journal *Nature Genetics,* could open new doors for treating lupus and other autoimmune diseases.

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

Dr. Yasvir Tesiram, *Advanced NMR/MRI Methods for Liver Cancer,* National Cancer Institute; In Vivo *Localization of Anthrax Toxins by MRI*, Oklahoma Center for the Advancement of Science and Technology

Dr. Rheal Towner, *Chemoprevention of Gliomas using Nitrones with Anti-c-Met Activity*, National Cancer Institute; *Biomedical Imaging in Oklahoma: OMRF Small Animal fMRI*, Oklahoma Center for the Advancement of Science and Technology; *Inhibition of INOS in Malignant Gliomas*, Oklahoma Center for the Advancement of Science and Technology

Dr. Jeffrey Van Komen, *Antigen Independent Functions of CD28 in T Cell Stimulation,* American Cancer Society

Dr. Andrew Westmuckett, *The Role of Tyrosine Sulfation in Atherosclerosis,* Oklahoma Center for the Advancement of Science and Technology

Dr. Lijun Xia, *Exogenous Mucins as Treatment for IBD,* Altheus Therapeutics, Inc.

Grants Awarded *(May-August, 2008)*

Prayers,

A Shawnee
preacher's wif

A rare disease

Sometimes

A

ife

A pair of OMRF scientists

hope is much closer than you think.

by Greg Elwell

nswered

A ticking time bomb

As her car pulled to a stop at the grocery store, Sandy Roark felt a rush of shame, but no blush came to her cheeks. She didn't have enough blood to show color.

Parking in the handicapped spot, even with her tag, she still drew looks. At age 60, she looked as healthy as anybody else. She wasn't in a wheelchair or using a walker. Yet each step from her car to the sliding glass doors was a battle.

"I would look at people walking, and I would get mad," she says. "They take for granted how easy it is to just get up and go without a second thought. I had nothing but second thoughts."

As she struggled through the supermarket aisles, other shoppers couldn't see the bruises her clothes disguised, the plum-colored blotches that mysteriously appeared on her body in places she didn't remember being hurt. And in the churches where her husband has preached, sitting in the pews, the other members of the congregation didn't understand the effort it took to get up in the morning just to be there. She looked just like the Sandy of old, the one with the energy to garden and travel and cook and visit after the final hymn. But she wasn't the old Sandy. No, right around her 60th birthday in 2000, that person had disappeared.

When she went to the doctor, blood tests at first revealed that her platelet levels had dropped to less than 10 percent of normal levels. After months of additional testing and countless consultations, physicians finally gave her a name for the pain: paroxysmal nocturnal hemoglobinuria, or PNH, a rare, incurable blood disorder.

"After I found out I had PNH and read about the disease, I was in a panic," she says. The threat of a developing a blood clot, she learned, was constant. The clots could form anywhere: deep veins, the abdomen, the kidneys, the liver. And the strong chance that one of those clots would break off and cause a fatal event—like an embolism or stroke— explained the most sobering statistic she encountered: Once diagnosed with PNH, a person could expect to live only another eight years.

Not even a decade. Not long enough to see her first grandchild graduate from college. Or to celebrate her 70th birthday. "Generally, I try to look at the glass half full," says Roark. But now when she peered into the future, she saw only darkness. "I thought my life was over."

She felt what anyone in her situation would feel: anger, frustration, despair. "I was searching for answers. Not just, Why did this happen to me? But why does this happen to anybody?" And the permanence of her situation only underscored its bleakness. "This wasn't a passing thing. It's not like I could get an operation and it would be gone. This was for the rest of my life"—however long that might be.

So she did the only thing she could: She asked the congregation, her family and everyone she knew to pray for her.

The prayers she requested did not seek a cure. Or even to bring an end to her pain. "I just asked them to pray for me to have the strength to face each day. To have the strength to fight the disease."

WHAT IS PNH? PNH is a rare disease in which the body makes red blood cells that are susceptible to damage from the first wave of the immune system. It causes fatigue, flu-like symptoms and can lead to death by blood clots or hemorrhaging. It affects about one or two people in a million.

You've probably never heard of PNH; only one or two people in a million are diagnosed with it each year. Still, the illness is as devastating as it is rare.

The disease has its roots in the body's complement system, a group of proteins that helps the immune system eliminate infectious microorganisms. When bacteria enter the human body, the complement system serves as the first line of defense. It creates proteins on the outer walls of invading cells that cause the invading cells to pop like balloons.

Normally, our red blood cells are immune to the proteins created by the complement system. But in PNH, which results from a genetic mutation, abnormal bone marrow cells make red blood cells that are susceptible to harm by the complement system. So when the complement system launches an attack, that same barrage bursts the red blood cells in PNH patients, spilling hemoglobin into the blood stream. This hemoglobin can also leak into the urinary tract, and the disease get its name because in these recurring (paroxysmal) episodes, the abnormal presence of blood (hemoglobinuria) is most notable in the dark-colored urine that has accumulated in the bladder during the night (nocturnal).

This loss of hemoglobin is the culprit behind many of the hallmark symptoms of PNH.

"Hemoglobin is the protein in red blood cells that carries oxygen to the tissues," says Dr. Stephen Prescott, OMRF's president and a vascular biologist. "When it's lost, that causes anemia, which manifests itself in symptoms like fatigue, weakness and shortness of breath." People with PNH are more prone to infections due to a deficiency of white blood cells, and they are also at greater risk of developing leukemias—cancers in blood-forming cells. "With PNH, you'll also see abnormal platelet function, and that causes problems in the blood clotting process."

The result can be deadly: Thromboses—blood clots—are the leading cause of death among PNH patients. The disease also can cause potentially fatal hemorrhaging. And unlike many illnesses, there is no predictable course to PNH.

"With this disease, there's no peace of mind. The worst could happen at any time," says Prescott. "PNH is like a ticking time bomb."

The low point

Following a round of blood work, doctors at first told Sandy Roark she was suffering from idiopathic thrombocytopenic purpura, or ITP. The condition is characterized by a low platelet count and often—as in Roark's case—by spontaneous bruising. But when she failed to respond to steroids, the standard initial course of

treatment for ITP, Roark's physicians sent her to a specialist for a bone marrow biopsy. That biopsy led to her diagnosis with PNH.

"That was a low point," says Roark. "I had always been healthy. Very healthy." And now, even if she survived, she was looking at a life where she was "too tired even to sit in a chair."

One of the worst symptoms she faced was "PNH flu"—fever, nausea and diarrhea. "It's just like the flu, except the flu goes away," she says.

The holidays, in particular, brought a stark reminder of how sick she had become. "There are 18 of us, and they would all come to our home. And before I got sick, I did everything." She would decorate indoors and out, hanging garlands and lights. Then she'd whip up a big meal—turkey, potatoes, dressing, desserts, the works—and wait. "I wanted everything to be prepared so that when my family arrived, we could talk and play games. I loved playing with the grandkids." She'd cuddle the babies and roll around on the floor with the younger ones. "I relished those times."

But once PNH struck, she could no longer cook for her brood. Or hang the holiday decorations. "I was stuck in the bedroom, going from the bed to the bathroom. All I wanted was to be out there with them, around the tree, at the dinner table," she recalls. "But my body wouldn't allow it."

At first, her grandchildren would inquire, Where's Nana? Isn't she coming to eat? Doesn't she want to be here when we open the presents? But soon enough, they stopped asking. "They knew I was in bed." Sometimes, they would come and stand at the bedroom door. "I was so sick, I was throwing up and feverish. I couldn't even tell them to come give me a hug, couldn't read them a book."

They would come for only a day or two, so Roark did her best to put on a happy face for the children. "I would try to get up and clean up, to sit with them for a bit. It was so hard, but it was important to me. Because I didn't want their memories of me to be an old woman sick in bed."

To stabilize her hemoglobin levels as the disease progressed, Roark received blood transfusions every few weeks. Doctors put her on cyclosporine and steroids to curb her immune system and,

A New Birthday

Technically, Greg Watkins was born on August 10, 1949. But if you ask the McAlester dentist his birthday, he might give you another answer. "I tell people that April 20 is my new birthday of a new life," he says. That's the day in 2007 that doctors began treating his PNH with Soliris—a drug born in the labs of OMRF.

The rare blood disease first struck Watkins 12 years earlier, as he was recovering from a mild intestinal virus. One night, he woke at 3 a.m. with a driving need to use the bathroom. "I looked down and my urine was blood. It was just pure, red blood," he says. "I was very alarmed, because I didn't know what was going on." Unbeknownst to Watkins, PNH had caused his body's complement system to attack his red blood cells, spilling hemoglobin into his urine.

The next morning, as Watkins waited to see his urologist, he felt an acute squeezing pain in his chest. "At the time, I thought I might have had a small heart attack," he says. He would later realize it was his first esophageal spasm—another symptom of PNH. The painful spasms are caused by the depletion of nitric oxide in smooth muscle and make swallowing extremely difficult.

Watkins's symptoms would confound physicians for months before a hematologist finally diagnosed him with PNH. By this time, though, the disease had already begun to take a toll on the self-described "running addict."

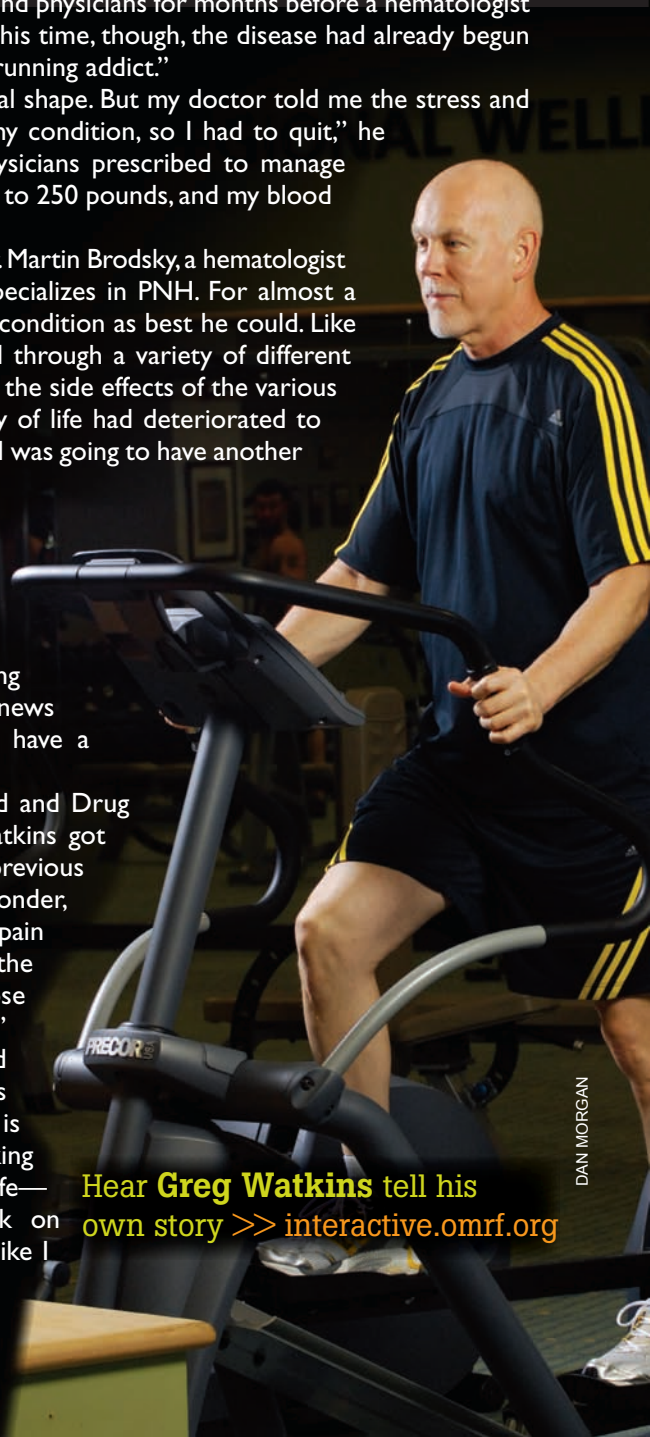
"Before PNH, I was in peak physical shape. But my doctor told me the stress and strain of running would only hurt my condition, so I had to quit," he says. With the anabolic steroids physicians prescribed to manage Watkins's symptoms, "I ballooned up to 250 pounds, and my blood pressure shot up, too."

Watkins eventually began seeing Dr. Martin Brodsky, a hematologist at Johns Hopkins University who specializes in PNH. For almost a decade, Brodsky managed Watkins's condition as best he could. Like most PNH sufferers, Watkins cycled through a variety of different drugs. Between the disease itself and the side effects of the various treatments, says Watkins, "my quality of life had deteriorated to one of worrying if today was the day I was going to have another PNH attack."

In early 2007, Watkins traveled to Baltimore for a routine visit with Brodsky. The hematologist asked the usual questions: What attacks have you had in the last two years? How are you feeling? Has anything unusual come up? Then he delivered news that floored his patient: "We now have a cure."

Less than a month after the Food and Drug Administration approved Soliris, Watkins got his first dose of the new drug. "In the previous 12 years, every day I'd wake up and wonder, How will I deal with the fatigue and pain of PNH? How will I make it through the day?" But with Soliris, he says, "those are no longer questions I ask myself."

Watkins's energy has returned and he no longer needs steroids. His blood pressure is back to normal, as is his weight. He has returned to working out regularly, and his professional life—once decimated by PNH—is back on track. In short, says Watkins, "I feel like I have a whole new life."



DAN MORGAN

Hear **Greg Watkins** tell his own story >> interactive.omrf.org

thus, reduce the rate of blood-cell destruction. As if the disease itself weren't enough, these treatments came with side effects—insomnia, mood swings, weight gain, fluid retention. Before long, says Roark, "I'd forgotten what it was like to feel good."

What she didn't know was that she would one day remember that feeling. And the discovery that would make it possible would come from just up I-40, from the labs of OMRF.

New hope

Drs. Therese Wiedmer and Peter Sims

For most couples, there's marriage, and then there's what you do with the rest of your life. For Drs. Peter Sims and Therese Wiedmer, though, the two worlds are one and the same.

Sims and Wiedmer came to Oklahoma and OMRF together from Duke University in the 1980s. The two scientists shared more than a partnership in life; they also both studied how healthy red blood cells resisted damage from the complement system, the precise part of the immune system that does the damage in PNH.

As is often the case in science, one way to figure out how something works is to study a model that's broken—and try to understand what went wrong. "That was where my interest in PNH began," says Sims. "It had been known for a number of years that there was something very unusual about the blood cells produced by PNH patients."

In particular, researchers knew that PNH patients had a higher degree of platelet activation, a process that plays a key role in initiating blood clotting. Clotting is an important function in the human body, repairing tears and breaks and preventing hemorrhaging. But when it occurs in the wrong place, as it does with PNH patients, it can form deadly blockages that can lead to organ failure or stroke.

So Sims and Wiedmer put their heads together with Drs. Chuck Esmon and Fletcher Taylor, two world leaders in the study of blood clotting, who also happened to be at OMRF. Working with Esmon and Taylor, Sims and Wiedmer developed a hypothesis. "Our suspicion was that a crossover from the complement system triggered the activation of a clotting mechanism in PNH patients," Sims says. "We thought the PNH cells held a secret. Whatever that unknown thing was"—a sort of shield that protected red blood cells from the complement system—"the PNH blood cell was missing."

For many years, physicians treated PNH patients like Sandy Roark by treating their symptoms. Doctors would tamp down patients' immune system with steroids and other drugs, and they'd replace red blood cells with transfusions. The one potential fix for the disease—bone marrow transplant—came with a two-year survival rate of only slightly better than 50 percent. And even when patients lived, the surgery was not always successful.

So Sims and Wiedmer decided to attack the problem from a different angle.

"We figured that if we could interrupt the complement system, it would protect the red blood cells from the proteins that were destroying them," Sims says. Working with red blood cells, they isolated the inhibitory molecule—the armor that, in everyone but PNH patients, protects red blood cells from the piercing attacks of the complement system. With that key piece of knowledge in hand, the pair developed a method to shut down the complement system by using a highly specialized antibody (a sort of defense protein) to disable a key protein in the complement system.

OMRF filed for a patent on the discovery in 1989. When the patent was issued in 1992, OMRF licensed the discovery to a biotechnology company that Sims had helped found. Over the next 15 years, that company, now known as Alexion Pharmaceuticals, built the discovery into a drug that could be administered to humans. The drug then underwent human clinical testing, a rigorous process that typically consumes a dozen years and hundreds of millions of dollars.

For most experimental drugs, this is where the story ends, as only 1 in 5,000 reaches the market. But this drug—which came to be known as Soliris—bucked the odds, building a remarkable track record of safety and efficacy throughout the three stages of testing in hospitals and clinics. As a result, in 2007 the U.S. Food and Drug Administration approved Soliris for the treatment of PNH. It was one of only 19 new drugs approved in all of 2007 and the first specifically approved for the treatment of PNH.

The moment when a discovery is transformed into a treatment for human disease, says Wiedmer, is one that every medical researcher dreams of. "We were so joyful."

Life, part two

In May 2007, after seven grueling years at the mercy of PNH, Roark began treatment with Soliris.

Before the drug, she was receiving blood transfusions every few weeks. Immediately after her first treatment, though, she saw a change. "I went three full months without a transfusion. It was wonderful."

Just as importantly, the drug helped restore Roark's quality of life. "What Soliris has done is it stopped all those symptoms," she says. Before, when her hemoglobin count would drop, her heart would throb just from the effort of beating, and esophageal spasms would make every breath a labor. Worst of all, abdominal cramps would trigger her greatest fear: a clot. "Now," she says, "I can keep going. I can work in the yard. I can do what I need to do. It's wonderful."

Roark is not alone. In PNH patients treated with Soliris, half had stable hemoglobin levels over six months without needing a transfusion. In a control group of PNH patients who did not receive the drug, not a single one showed similar results. The dramatic changes Soliris has made in the lives of PNH sufferers earned the drug the Prix Galien U.S.A. 2008 Award for Best Biotechnology Product. The award is considered the industry's highest accolade for pharmaceutical research and development.

"It's certainly gratifying that a drug born in Oklahoma and

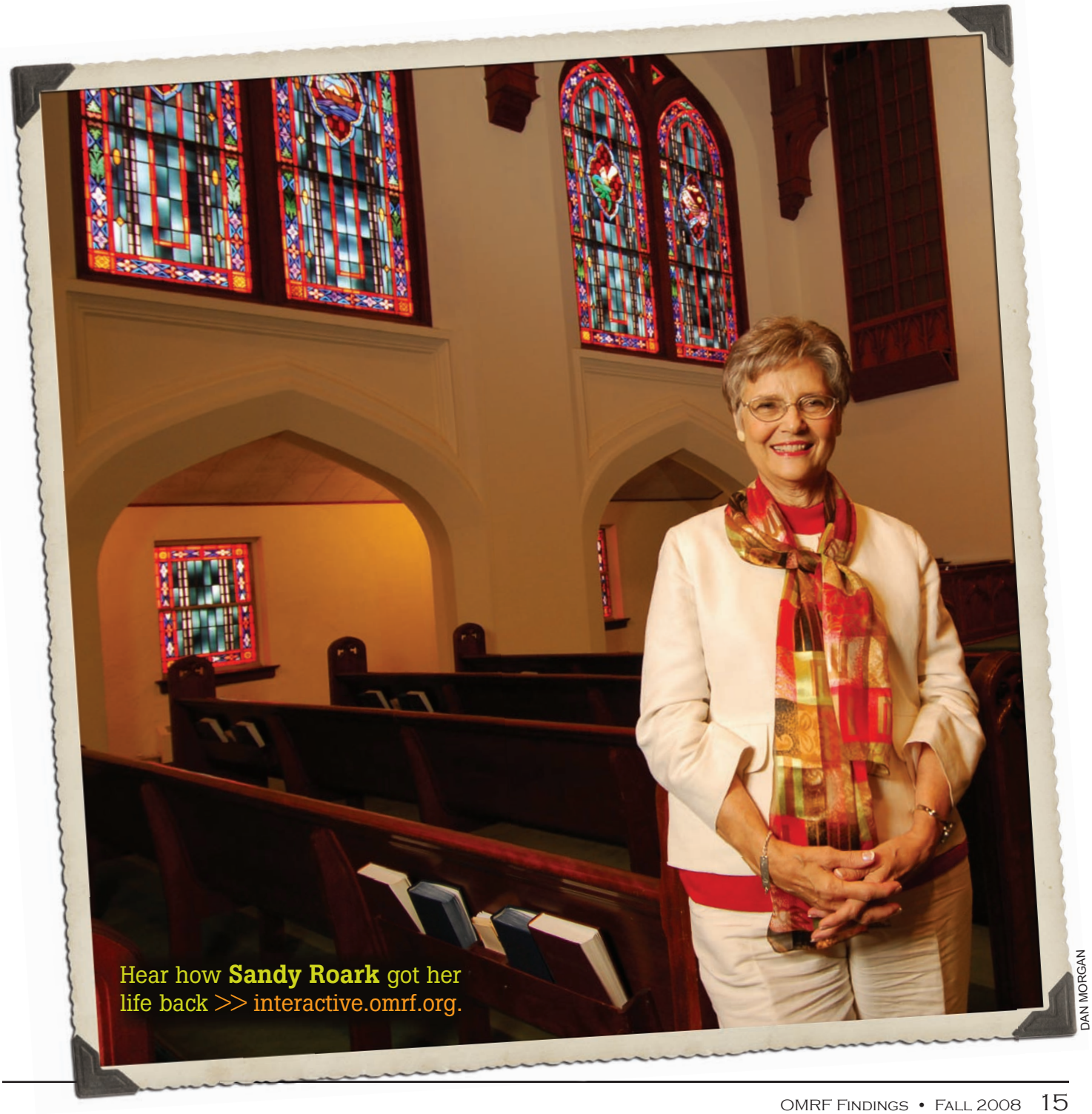
at OMRF received this honor," says OMRF President Prescott. "But what's most gratifying is that our scientists' work has changed the lives of patients suffering from a terrible disease."

Roark's life looks nothing like it did 18 months ago. "I'm a new person." Still, she sees some silver linings to her struggle with illness. "The bad things that happen to us make us pause and take stock of what's important in life. PNH did that for me." And, she says, "it caused my faith to take a big leap forward."

Before PNH, she hadn't given much thought to medical research. "I was thankful for it, but I didn't realize its importance." But when a drug born at OMRF changed her life, she took notice. "I became very interested in the depth and breadth of research. Things like stem cells and bone marrow. I'd read every article I'd see in the paper." And, she felt particularly blessed and proud that the research that saved her came not from afar, but from Oklahoma. "It was amazing. All of a sudden, I had a very close tie to OMRF."

That unexpected tie, she says, has been transformative. No longer is every day uncertain. She's looking forward to the holidays again, when she'll cook and decorate and visit with her family. And when she goes to church every Sunday, she no longer asks for her fellow congregants' prayers. No, these days, she's sending out all that positive energy to others. You know, the ones in need of help.

"To sum it up in a sentence, Soliris has given me my life back." It's a gift she never expected. But one for which she will never stop giving thanks. OMRF



DAN MORGAN

the Giver

BY SHARI HAWKINS

In photos, he looks for all the world like an ordinary farmer, sporting dusty boots and an open-collared shirt. Peering out from under his hat brim, he tolerates the camera's intrusion for but an instant, anxious to return to his work. But behind the solemn gaze and simple clothing stood one of Oklahoma's greatest oilmen. His head for business helped him build one of the country's largest petroleum empires. And his generous heart led him to transform his vast fortune into prosperity for others, people he would never know and who were far removed from the oil patch.

Jim Chapman's generosity helped make OMRF what it is today.

James Allen Chapman was born on April 3, 1881, near Waxahachie, Texas, where his family made their living as farmers and ranchers. After completing the eighth grade, he left school to devote his time to the family business. But at the age of 20, Chapman decided it was time to seek his fortune, so he headed north to Holdenville, Okla., where his uncle Robert McFarlin ran a cattle operation. Little did either man know that they were about to forge a partnership that would last the remainder of their lives and write a new chapter in the history of Oklahoma—and OMRF.

As part of their cattle operation, Chapman and McFarlin had been buying and selling land in the Tulsa area, mostly for agricultural purposes. But when oil was struck in 1905 at the "Glenn Pool" south of Tulsa, the pair realized that the greatest economic opportunity might not be found on the land but, rather, under it. So they formed the Holdenville Oil and Gas Company and drilled a single well on a modest 40-acre parcel of land near Kiefer, not far from the original Glenn Pool strike. The well was a gusher. Oil flowed in abundance, and within two short years, McFarlin and Chapman were millionaires.

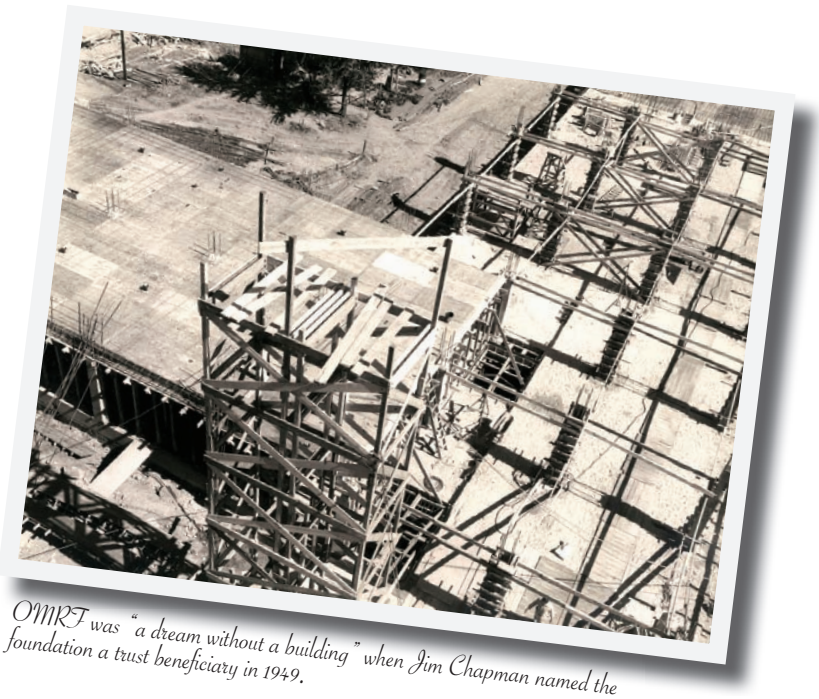
"They were essentially farm boys with ambition and good business sense," says Dr. Paul Lambert of the Oklahoma Historical Society. "They watched as others took tremendous risks, but they proceeded with caution. And it paid off handsomely."

Chapman married McFarlin's daughter Leta Mae in 1908. Now bound even more closely by family ties, the two built a petroleum empire that would stand among the best in the country. In 1912, the partners dissolved the Holdenville Oil and Gas Company and founded the McMan Oil Company, whose name was a blended version of their own. Their drilling ventures in the newly tapped Cushing field produced oil in such quantities that McMan found itself building a storage tank a day just to keep up with the flow.

In 1916, the pair sold McMan to Magnolia Oil Company, which would later become Mobil, for $39 million plus 20,000 shares of Magnolia stock. The cash portion of the sale alone would total nearly $800 million in 2008 dollars. Indeed, the transaction stood as the largest oilfield sale on record well into the 1950s.

Chapman and McFarlin were wealthy beyond all comprehension. Yet, like so many wildcatters, they yearned to return to the oil patch. "The two found that the oil business suited their temperaments and desires, for it allowed them to be outside breathing fresh air, it kept them close to the soil, and they were their own bosses," wrote Carl Tyson in his book *The McMan*. So later that same year, nephew and uncle started a second McMan Oil and Gas Company. They operated that company—again with much success—until 1930, when they sold it to Standard Oil of Indiana (now Amoco) for $20 million.

Despite his riches, Chapman still loved the simple life of farming and ranching he'd had as a young boy in central Texas. So he returned to his ranch in Osage County, where he and McFarlin's



OMRF was "a dream without a building" when Jim Chapman named the foundation a trust beneficiary in 1949.

nephew Horace Barnard maintained a cattle operation. Until well into his 70s, Chapman derived his greatest pleasure from riding around the ranch and doing the "dirty work"—herding, vaccinating and branding cattle.

On the heels of World War II, Chapman met with longtime McMan attorney John Rogers to discuss estate planning. He instructed Rogers to outline a plan that would give the majority of his estate to education, medicine and research. "Jim Chapman was a self-made man and believed in giving back to his community," says says Sharon Bell, who now serves as the individual trustee of a group of charitable trusts created by the Chapmans. "Education was something he could not afford, so he wanted to give people the opportunity to make something of themselves in the same way he had made himself." He focused on indigent care in hospitals to help those most in need of health care. And medical research? "Because doing basic research for the good of mankind here in Oklahoma appealed to him."

To that end, he asked Rogers to talk to his friends in Oklahoma City and organize a medical research foundation there. As luck would have it, at that same time, a group of doctors was already spearheading the creation of OMRF. After connecting with those physicians, Rogers became a key player in the formation of OMRF. In 1949—the same year that OMRF broke ground on its first building—it was one of seven charities named as beneficiaries of the newly formed James A. and Leta M. Chapman Trust. "OMRF was really a dream without a building when Mr. Chapman formed that first trust," says Bell.

In the six decades since, Chapman funds have provided a financial cornerstone that helped build OMRF and sustain its success. Donations from that first trust, as well as others the Chapmans later created, have not only paid OMRF's day-to-day operating expenses, they have provided start-up funds for new investigators, established an endowed chair and allowed for renovation and remodeling of OMRF's buildings. They have also made possible untold lectureships, scientific awards, matching funds and construction projects—including a major new research tower at OMRF.

Perhaps most importantly, those funds have given OMRF a unique position among charities. "The Chapman trusts provide funds to support OMRF's administrative and overhead costs," says OMRF President Stephen Prescott. "So when we receive a gift, we can tell donors that 100 percent of that donation will be used to support research. How many other charities can say that?"

Although the Chapmans gave to many, they chose to maintain their privacy and went to great lengths to remain anonymous. Just as he had been prone to do in the oil business, Chapman shunned the spotlight when it came to philanthropy. All beneficiaries were given two strict instructions: Remain a nonprofit organization and keep the source of their gift confidential—or risk losing the money. So insistent on secrecy was Chapman that it led some to dub him "Mr. Anonymous." However, he grudgingly agreed that, upon his and Leta's death, their names could be revealed.

Chapman died in 1966, and Leta passed away eight years later. "I know the Chapmans would be proud of OMRF and all it has become," says Bell. And just maybe, Jim Chapman would have tipped his dusty cowboy hat to those who carry out his wishes today—those who still share his vision for excellence and work hard to see it met.

"OMRF grew because Oklahomans believed in it and planted the seeds of success here through their gifts," say Prescott. "But Mr. Chapman planted the most prolific seeds of all when he created his trusts and chose us as a recipient of his hard-earned fortune. Just as he laid the foundation for his business success by working in the shadows, he did the same for OMRF. We all owe him a debt of gratitude for what we enjoy today."

At his Osage County ranch, Jim Chapman (left) was just another cowboy.

Leta (far left) at the Chapmans' ranch

Bon Appet

Helen Bloxsom and Phyllis Moriarty, Ponca City

DAN MORGAN

IT!

We've known each other for years, but Alzheimer's disease brought us closer together. Each of us lost our husband to Alzheimer's—one in 2002 and one in 2003.

Both of them were wonderful, thoughtful family men. Good daddies and grandpas. Thank God they didn't know everything that was happening to them. That's the only forgiving grace of this disease. You just have to realize that it's not them you're dealing with. It's the disease.

Our guys suffered so many years with it, and we see more and more people coming to our support group whose loved ones are suffering. It's so sad, but people come to help others cope.

We started our dinners, because we want to help find a cure for Alzheimer's disease. That's all there is to it!

Homemade chicken and noodles, salad, a roll, a brownie and half a peach. That's the menu for 2008. We thought preparing for 400 was a lot, but this year we raised it to 500. That's a lot of chicken to cook!

We just had the idea. After that, Ponca City got behind it. Some helped sell tickets and put up flyers. Others donated food. Local merchants gave money or donated items for door prizes. You can't do any better than that.

A couple of years ago, Phyllis found information about the Oklahoma Medical Research Foundation and Dr. Jordan Tang online. That very day there was an article about him in *The Oklahoman*.

We were so impressed with what he was doing that we decided to send all the proceeds from our dinners to OMRF. We just wish it could be more.

Phyllis Moriarty's Chicken and Noodles

1 large chicken, cut in pieces
1 inside tender stalk of celery with leaves, cut in small pieces
1 medium onion, chopped
2 medium cloves of garlic
2–3 bay leaves
Fresh or frozen noodles (homemade or store-bought)

Add water to cover chicken and boil until done. Taste broth. If it needs more chicken taste, add bouillon granules or chicken broth to taste. Add salt and pepper as desired. Remove chicken with slotted spoon and let cool. Take chicken off the bones and chop; discard skin and bones. Cook noodles in broth. Add chicken to the noodles and mix. Thicken with a little flour mixed with water, if desired.

a look back

A LOOK BACK

Once deemed the "largest one-man network in the world," this Oklahoma native got his start on a Tulsa radio station before becoming a household name. For a time, he attended the University of Tulsa, which, like OMRF, is a beneficiary of the J.A. and Leta Chapman trusts. The rest of the story? For a chance at a free OMRF tee, name this famous announcer (now 90 and still on the air). Send guesses to findings@omrf.org or call 405-271-7213.

P.S. No, it's not Dr. Frasier Crane!

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