FINDINGS
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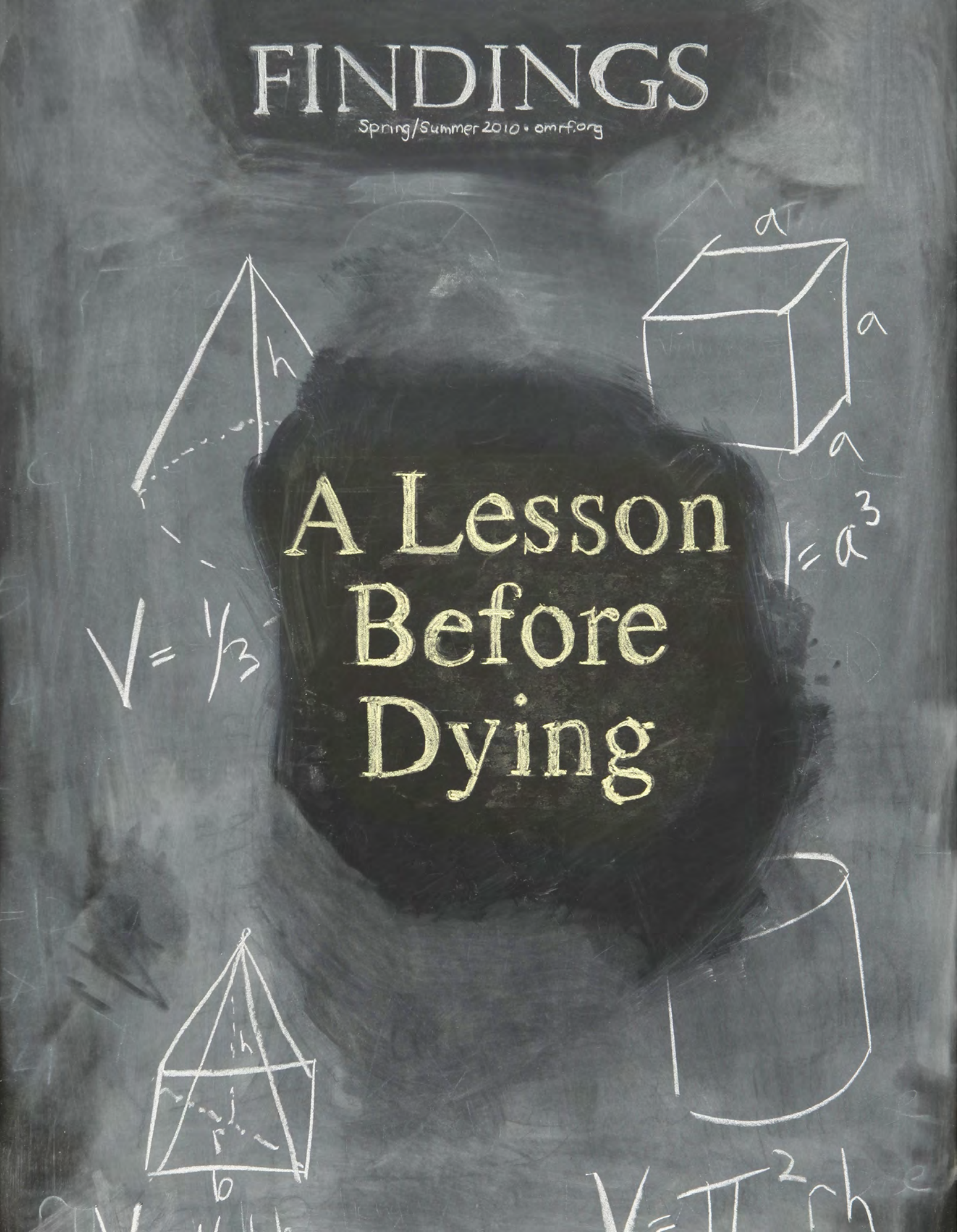

A Lesson Before Dying

How many more lives can you help us save?

These six people know firsthand that OMRF's work can make the difference between life and death. Without the work of OMRF scientists, they might not be alive today. Since 1946, OMRF has been dedicated to understanding and developing more effective treatments for human disease. Please help us continue to make discoveries that make a difference.

OMRF

The more you give...

With OMRF's one-of-a-kind state tax credit, making the decision to give has never been easier. For every $2 you donate to OMRF, you'll get a $1 tax credit (for gifts up to $4,000 for joint filers and $2,000 for individuals). It's simple—the more you give, the more you save.

FINDINGS

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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

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AN EDUCATION When she was diagnosed with breast cancer, Debbie Ocker knew she had much more to teach her students than geometry. For six years, she opened their eyes to what it meant to live with the disease, sparing no detail. Then doctors told her that the cancer had spread—she had only months to live.

WEB BONUS

Hear Debbie Ocker tell her story and meet her students at Putnam City High School

>>interactive.omrf.org

WHY HAVEN'T WE CURED CANCER?

It's a question I hear all the time. And it's one that has no easy answer.

Each year, federal agencies like the National Institutes of Health, private nonprofits like the American Cancer Society and for-profit pharmaceutical and biotech companies spend a total of more than $10 billion seeking to put an end to the more than 100 forms of cancer. Yet this year, cancer is set to surpass heart disease as the nation's leading killer.

In the last four decades, we've made major inroads against heart disease. We've seen a significant decline in smoking. Researchers have developed better methods of controlling high blood pressure and cholesterol. Acute care for victims of heart attacks and stroke have improved markedly. As a result, the age-adjusted mortality rate for heart disease has fallen 70 percent.

During that same time, we've seen only a 7.5 percent improvement in cancer survival rates. That's hardly the sort of victory President Nixon or anyone else envisioned when he made the "conquest of cancer a national crusade" 39 years ago.

There are many reasons progress against cancer has proven so slow. First, cancer is not a single disease. Or if it is, we've yet to discover a shared weakness that could lead to its extinction. Other than smoking cessation, we've made few inroads in preventing cancer. Despite much marketing to the contrary, there's little evidence that diets, vitamins or exercise are effective methods of prevention.

Although new drugs have continued to reach the market, most lengthen lives only by a few weeks or months. This incremental approach has plagued medical research as well; granting agencies all too often fund projects that tweak existing treatments rather than supporting innovative but riskier projects.

Lost in this picture, though, are many smaller victories. The drug Gleevec has transformed chronic myelogenous leukemia from a death sentence into a disease with a five-year survival rate of 89 percent. Breast cancer deaths have dropped by almost one-fourth since 1975. And testicular cancer survival rates have skyrocketed.

But for every Lance Armstrong, there's a Debbie Ocker. In this issue, you can read about Debbie and her journey since she was diagnosed with breast cancer in 2003. It's a story that's both unique and all too familiar, uplifting and painfully sad at the same time.

Debbie—and the millions upon millions who have shared her plight—are the reasons that OMRF does what it does. She's why our scientists are working to solve cancer's mysteries, to help speed new treatments to hospitals and clinics. Right now, researchers in OMRF's labs are testing new approaches to treating brain and breast cancers. They're also studying the cellular processes that lead to prostate and ovarian cancers, leukemias and lymphomas.

We hope this research will contribute to a deeper understanding of cancer. And that one of these projects will one day yield a new treatment to extend the lives of cancer patients.

In the meantime, we will keep chipping away at the disease, one experiment at a time. That work, we hope, will help spare future cancer patients from the long and difficult odyssey that all the Debbie Ockers of the world have made.

FINDINGS FAN

After reading the fall 2009 issue of *Findings*, I had to let you know how much I enjoyed it. I read with interest about Fleming Scholar Sean Olsen; I work at the Oklahoma City Community Foundation, which administers the endowment for the Fleming program. I also truly enjoyed reading "Higher Powers." Not only is the Alzheimer's research incredibly interesting, but the writing was really well done ,and the photography was very nice. Kudos to author Greg Elwell, photographer John Clanton and all of your staff.

Cathy Nestlen
Oklahoma City

FAMILY PRIDE

I was so proud of your article on Sean Olsen in the fall issue of *Findings*. He happens to be my great-nephew. I'm very excited for him and hope he continues in the medical field.

Francis Atkins
Sulphur

WHITE COATS

With a title like "Cooties in the Lab," how could I resist reading your article about the potential ban on lab coats in hospitals? It's great to see a bit of humor in the pages of your magazine. Well done.

Susan Cahoon
Atlanta, Ga.

TOUR DE FORCE

On a recent tour of OMRF, we were delighted to discover works by internationally respected photographers, sculptors and other artists in a world-class research institute so close to home. In particular, the granite installation in the lobby by Jesus Moroles is breathtaking! This collection is truly one of the many treasures of Oklahoma City, and we are grateful to have had the opportunity to enjoy seeing it.

Peggy Megginson
Norman

God bless each and every one of you working to find a cure. I have had cancer and lost my husband in 2004 to colon cancer and leukemia. They can put a man on the moon but can't find a cancer cure, but you will someday. Thanks for caring and for the work you do.

Betty Andrews
Perry

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!

WE ARE THE WORLD

Although OMRF's labs are physically located in Oklahoma City, foundation scientists work in collaborative efforts that span the globe. Last year, OMRF researchers published papers or joined on grants with scientists from nearly two dozen countries. And earlier this year, OMRF further expanded its international reach when it formed a new strategic partnership with the Institute of Biophysics, Academy of Chinese Sciences in Beijing.

The institutions will share researchers and equipment in the field of structural biology. The collaboration will include exchange visits by researchers at each institution and is aimed at combining efforts to understand the molecular structure of disease.

Founded in 1958, the Institute of Biophysics is one of China's premiere research facilities. With 64 principal scientists and an estimated 600 research and support staff, the IBP focuses on the fields of protein science and brain and cognitive sciences.

This represents the fourth strategic partnership OMRF has developed in the past 18 months with a foreign research institute. OMRF has also partnered with the Rajiv Ghandi Institute of Medical Sciences in Kadapa, India, for cardiovascular research, the Oswaldo Cruz Institute in Rio de Janeiro, Brazil, to study infectious disease and vaccinations, and the Christian Medical College in Vellore, India, to investigate the genetics of lupus.

"OMRF is a relatively small research institute focusing on a few key areas: autoimmune diseases, cancer and cardiovascular diseases," says OMRF President Stephen Prescott. "Diseases are so complex that it takes teams of researchers across a variety of specialties to make scientific advancements. These partnerships help us 'fill in the blanks' and speed the process of medical innovation."

The move puts the foundation in a better place to expand several areas of research, says Dr. Tim Mather, OMRF's director of research administration. "The IBP has the facilities and equipment to do large-scale crystallography studies, which can be used to reveal the atomic structures of molecules." Crystallography allows scientists to see how microscopic chemicals fit together and interact and has become vital in the development of new drugs.

In partnership with crystallographers at the IBP, Dr. Rod McEver of OMRF will explore the role of circulating blood cells that attach to blood vessel surfaces during injury or infections. OMRF's Dr. Roberto Pezza will expand his research on how cell division is related to birth defects, and OMRF immunologists will look for the structural makeup of a protein mutation that may affect lupus.

"Our main goal is simple—improve human health," Mather says. "To do that, we work with organizations with similar interests but different approaches. We think of it as complementary science, and it allows us to work more efficiently and make more discoveries."

THE LONG AND WINDING ROAD

When Willis Johnson did his tour of duty during the Vietnam War, the U.S. military sprayed millions of gallons of chemical defoliants in the jungles of South Vietnam. Johnson was one of many American soldiers exposed to the herbicides in the process.

The chemicals in so-called Agent Orange and other defoliants were found to cause a wide variety of illnesses and medical problems, and the U.S. military stopped using them in 1971. But their impact would be felt for decades to come.

In 1992, doctors diagnosed Johnson with type 2 diabetes. The condition is one of many that have been linked to Agent Orange exposure.

Over the next five years, the Fairview resident gained 100 pounds, and health problems forced him to retire at the age of 53. Johnson realized that he had arrived at a crucial juncture. "I started thinking about how I was going to write the next chapter in my life," he says. "As I looked in the mirror one morning, I decided the one thing I could control was my weight."

Johnson began walking, then running, to control his weight and manage his disease. In six months, he had shed 60 pounds. After a year, he was below his weight when he was diagnosed.

"To date, I have lost 116 pounds and kept it off for more than 10 years," he says. "By running and watching my diet carefully, I have been very blessed that I have not had to go on any diabetes medications so far."

Johnson even completed a marathon. This spring, at the age of 65, he decided he wanted to run a second 26.2-mile race, the 2010 Oklahoma City Memorial Marathon. And his efforts, he decided, should have a larger meaning. So using the tools on OMRF's website, he set up a page to raise money to support diabetes research at OMRF.

"OMRF scientists are the experts in their field," he says. "They know what needs to be accomplished to help find a cure for diabetes or even how to help those of us with the disease to live an enhanced life."

The page—adorned with a photo of Johnson in his Vietnam days, decked out in combat gear in front of a tank—occasioned quite a response. Thirty-nine friends joined "Team Orange" (nicknamed for Johnson's love of Oklahoma State University) and pledged funds to OMRF to support his efforts.

The morning of the marathon, Johnson woke up sick. As he and his wife drove east toward Oklahoma City hours before dawn, Johnson told her, "I don't know if I can do this today."

Yet there he was at the starting line at 4:30 a.m., lined up for the early start. He would, he decided, just start walking and see how far that would take him.

He made it past the Capitol. Up Western and Classen Boulevards. Through Nichols Hills and out Britton Road. Along Lake Hefner, back through Nichols Hills and down Classen. Then it was Heritage Hills and down Broadway for six, final blocks.

The crowds had thinned by the time Johnson crossed the finish line. A volunteer hung a medal around his neck and wrapped a Mylar blanket around his shoulders. It had taken him seven hours and five seconds to complete the course, an average of about 16 minutes per mile.

Still, on a day he'd doubted he had the strength even to start, Johnson had finished. He'd taken control of a disease that once had controlled him and, in the process, raised nearly $2,500 for diabetes research at OMRF. Willis Johnson may have come in 2,576th out of 2,634 marathoners, but there was no question that he was a winner.

> "OMRF scientists are experts in their field. They know what needs to be accomplished to help find a cure for diabetes or even how to help those of us with the disease."
>
> WILLIS JOHNSON

NEW HOPE FOR TRAUMATIC INJURIES

More than 119 million people visit U.S. emergency rooms each year. As many as 42 million of those cases stem from traumas, many of which can result in loss of limbs, organ function and, often, lives. But a new discovery by OMRF scientists could help change those statistics.

While studying the blood of patients suffering from severe blood infections, OMRF's Dr. Jun Xu noticed fragments of proteins called histones. The proteins normally keep DNA wound inside a cell's nucleus, so Xu and his mentor, Dr. Charles Esmon, wondered what they were doing floating in the bloodstream. "People had seen histones in the blood before," says Xu, "but no one realized they might be causing some of the trauma."

In a paper published in the scientific journal *Nature Medicine*, Esmon and Xu explained how histones can enter the bloodstream and begin to kill the lining of blood vessels, resulting in uncontrolled internal bleeding. Building on this work, they have found an antibody that could counter this deadly process.

"This discovery could open the door to new ways to treat soldiers injured by roadside bombs, gunshot wound victims and people who suffer a traumatic injury," says Esmon, who holds the Lloyd Noble Chair in Cardiovascular Biology at OMRF. "When we realized that histones were so toxic, we immediately went to work looking for a way to stop their destructive tendencies."

Inside the cells, histones perform an important function, keeping DNA coiled and compressed inside the nucleus. But the OMRF researchers found that when cells become damaged and burst, histones can enter the bloodstream and begin to kill the lining of blood vessels. This results in uncontrolled internal bleeding and fluid build-up in the tissues, conditions that are life-threatening.

Working with collaborators at Temple University, the researchers developed an antibody that blocks the histones' ability to kill. In preclinical testing, it showed promising results and no adverse effects. A potential future step, says Esmon, would be human trials. "When a patient is suffering from severe bleeds, these antibodies could prevent multi-organ failure."

According to OMRF President Stephen Prescott, the implications of the discovery reach well beyond injuries suffered on the battlefield or in other traumas like car accidents. "These findings have the potential to create new treatments not only for traumatic injuries but also for diabetes, pneumonia and any other condition that results in tissue death."

GRANTS AWARDED (July-December, 2009)

DR. MARTA ALARĆON-RIQUELME, *Fine Mapping and Replication of a Genome-Wide Scan for SLE in Hispanics*, National Cancer Institute; two additional grants

DR. JOSÉ ALBEROLA-ILA, *Understanding the Genetic Networks that Control CD4 T Cell Lineage Commitment*, American Heart Association; one additional grant

DR. HONG CHEN, *Epsin in Angiogenesis and Vascular Remodeling*, National Heart, Lung and Blood Institute; two additional grants

DR. MARK COGGESHALL, *Molecular and Immunologic Analysis of the Pathobiology of Human Anthrax*, National Institute of Allergy and Infectious Diseases

DR. DEAN DAWSON, *The Role of SIK19 in Mitotic Cell Cycle Progression*, Oklahoma Center for the Advancement of Science and Technology

DR. CHARLES ESMON, *Validation of Extracellular Histones as Biomarker and Therapeutic Target in Sepsis*, National Institute of General Medical Sciences

DR. DARISE FARRIS, *Do Estrogen Receptors in B Cells and DC Mediate Sex Bias in Murine Lupus?* National Institute of Allergy and Infectious Diseases

DR. ROBERT FLOYD, *Evaluation of Extracellular Endosulfatase Hsulf-2 in Breast Cancer Cell WNT Signaling,* US Army Medical Research Acquisition Act; two additional grants

DR. PATRICK GAFFNEY, *Candidate Casual Variants in Systemic Lupus Erythematosus*, National Institute of Arthritis and Musculoskeletal and Skin Diseases; two additional grants

DR. GARY GORBSKY, *Chromosome Movement in Prometaphase*, National Institute of General Medical Sciences

DR. COURTNEY GRAY-MCGUIRE, *African American Sarcoidosis Genetics Resource*, Natonal Heart, Lung and Blood Institute

DR. COURTNEY GRIFFIN, *ATP-Dependent Chromatin-Remodeling Complexes and Vascular Development*, National Heart, Lung and Blood Institute

DR. TIM GRIFFIN, *Biomechanical Regulation of Mitochondrial Function in Osteoarthritis*, 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, *Lupus Family Registry and Repository*, National Heart, Lung and Blood Institute; four additional grants

DR. KENNETH HUMPHRIES, *Mitochondria in Cardiac Ischemic Preconditioning*, Oklahoma Center for the Advancement of Science and Technology

DR. JUDITH JAMES, *Science in a Culture of Mentoring,* National Center for Research Resources; two additional grants

DR. SUSAN KOVATS, *Do Estrogen Receptors in B Cells and DC Mediate Sex Bias in Murine Lupus?* National Institute of Allergy and Infectious Diseases; three additional grants

DR. FLOREA LUPU, *EPCR, TAFI as Regulators of PMN/Endothelial Interaction*, National Institute of General Medical Sciences; one additional grant

DR. SATOSHI MATSUZAKI, *Tocopherols in Cardio Protection*, Oklahoma Center for the Advancement of Science and Technology

DR. RODGER MCEVER, *Mechanical Regulation of Selectin-Ligand Binding Kinetics*, National Institue of Allergy and Infectious Diseases

DR. KENNETH MILLER, *Forward Genetic Analysis of the Synaptic Gs Pathway*, Oklahoma Center for the Advancement of Science and Technology

DR. KEVIN MOORE, *Mechanisms for Hypothyroidism in TPST-2 Deficient Mice*, Oklahoma Center for the Advancement of Science and Technology

MICHAEL MORGAN, *Health Care and Other Facilities*, Department of Health and Human Services

DR. KATHY MOSER, *Suseptibility Genes in Primary Sjögren's Syndrome*, National Institute of Dental and Craniofacial Research; one additional grant

DR. STEPHEN PRESCOTT, *Presbyterian Health Foundation M.D/Ph.D Project*, Presbyterian Health Foundaton

DR. JAMES RAND, *Role of Neuroligin in Synapse Stability*, Autism Speaks

DR. SUSANNAH RANKIN, *Sororin Sister Chromatid Cohesion and Cell Cycle Control*, The Pew Charitable Trusts

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; one additional grant

DR. YASVIR TESIRAM, *Advanced NMR/MRI Methods for Liver Cancer*, National Cancer Institute

DR. LINDA THOMPSON, *Immune Function and Biodefense in Children, Elderly and Immunocompromised Populations*, National Institutes of Health; one additional grant

DR. RHEAL TOWNER, *Chemoprevention of Gliomas Using Nitrones with Anti-c-Met Activity*, National Cancer Institute; one additional grant

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*, Oklahoma Center for the Advancement of Science and Technology; one additional grant

DR. JANE YACIUK, *Role of PTPRkappa in Lck Regulaton During T Cell Development*, National Institute of Allergy and Infectious Diseases

The Last Lesson

by Adam Cohen and Shari Hawkins

Dear Friends,

I don't know the last time we spoke or heard from each other, but recently I have received news from my oncologist that things aren't going so well.

On November 10, because my chin and left part of my jaw were tingly (like Novocain wearing off) I had an MRI: It was discovered that my breast cancer had spread to the cranial fluid surrounding my brain. The prognosis was 2-3 months without treatment, 4-5 months with treatment. The treatment would have involved brain surgery and many treatments, with poor quality of life during that time.

Needless to say, I have chosen the former.

Debbie Ocker wrote this letter in November of last year. That was 38 years after President Richard Nixon declared war on cancer in his 1971 State of the Union speech, then signed the National Cancer Act to make the "conquest of cancer a national crusade." Her letter came after the federal government, drug companies and private nonprofits had spent roughly $200 billion in search of cures. It followed an estimated 1.5 million papers that scientists, including many at OMRF, had written analyzing the basic biology of cancer.

Yet there Ocker still was, counting the months.

The 58-year-old math teacher at Oklahoma City's Putnam City High School was far from alone. In 2009, cancer took the lives of more than a half-million Americans. That's 1,500 people every 24 hours, the equivalent of the *Titanic* sinking 365 days a year. It's also 230,000 more U.S. lives than cancer claimed in 1971. To be fair, our country's population is significantly larger and older than it was four decades ago. But in a given year, the disease still kills 184 out of 100,000 Americans, an improvement of only 7.5 percent since 1975.

The picture is not without bright spots. From 1975 to 2005, death rates from childhood leukemia plummeted from 75 percent to 27 percent. Prognostic testing and early intervention against colorectal cancer have saved roughly 80,000 lives in the last 20 years. And survival rates in testicular cancer have more than tripled since 1973.

Still, those isolated victories do not a cure make. "Forty years ago, we thought curing cancer would be easier," says Dr. Stephen Prescott, OMRF's president. "But in many ways, we were dealing with a complete scientific mystery."

Prescott should know. He spent decades probing how cells communicate and how mistakes in these processes allow cells to develop into cancerous tumors. Consequently, this area has been the focus of much research, with scientists searching for ways to interfere with this process in order to stop the growth of malignant tumors. Prescott's work in the lab ultimately led him to the helm of the University of Utah's Huntsman Cancer Institute, where he served as director for six years before coming to OMRF.

"We started the so-called war on cancer with the mistaken assumption that cancer was one thing," he says. "But really, it's many different problems that share certain common features."

According to the National Cancer Institute, more than 100 different diseases sit beneath cancer's umbrella. Each of these conditions is marked by abnormal cells dividing out of control and invading other cells. These illnesses also share the ability to metastasize—to spread to other parts of the body through the blood and lymphatic systems.

Yet after that, things get trickier. In most cancers, the uncontrolled growth leads to clumps of abnormal cells. But in others, tumors rarely form. Lung cancers grow quickly. Prostate cancer typically progresses at a slow pace. The human papilloma virus causes cervical cancer. Other cancers seem to have no connection to viruses. If there's a weak link that unites these many illnesses, scientists have yet to find it.

When you examine something at length and in depth, conventional wisdom suggests the picture should become clearer. But, Prescott says, the opposite has proven true in the realm of cancer research. "The more we've studied cancer, the more complex it seems."

Physicians diagnosed Debbie Ocker with breast cancer in June of 2003. That summer she underwent a pair of surgeries. Her first round of chemotherapy followed, just weeks before the beginning of the fall semester.

The treatment left her fatigued, but she resolved not to let it disrupt her teaching. Still, as summer came to an end, she faced a problem she could not have imagined only months before. "I was panicking, because I could not find a wig to fit my head," she remembers. "I thought I was going to have to show up the first day of school bald-headed."

A last-minute acquisition of a right-sized wig eased her fears. She donned the new locks and topped them with a cap. But artificial hairpieces, she soon discovered, can itch.

Ocker had not kept her lack of hair from her students. So one afternoon, with her wig driving her to distraction, she decided she'd had enough of keeping up appearances. "I asked the students if they would mind if I went to the ladies' room to take off my wig and put on my cap." A student raised her hand and asked to witness the wig removal. The girl said she'd never seen anyone who'd lost her hair. Another hand shot up. Then another. Nearly every student in the class wanted to watch.

So Ocker stood in front of the class and took off her wig. Then she did a slow pirouette, letting the students soak in her gleaming pate from every angle. As she turned, she wondered how the teens would react. Would they be frightened? Disgusted? Shocked? Or would they laugh and point their fingers?

"There wasn't a snicker to be heard," says Ocker. Instead, the students began sharing stories of loved ones who'd suffered from cancer. They told of family members who'd survived the disease and of others who had not. It didn't take long for Ocker to realize that her own personal struggle with cancer could have a silver lining.

Some form of cancer strikes 1 in 3 women in America and 1 in 2 men. Odds are, the disease would, one way or another, eventually touch every student Ocker taught. "They would have many important people in their lives succumb to this disease. I wanted them to know that these people could still have a life filled with hope, with love, with friendship, with faith."

Right about then, Ocker made a promise to herself. Like her hairless head, her battle with cancer would not remain hidden. She would share her experiences with her students. No matter what the future might hold.

"I wanted my students to know that people with cancer could still have a life filled with hope."

Despite the work of advocacy and fund-raising groups like the Susan G. Komen Foundation and the Lance Armstrong Foundation, cancer claimed the lives of more than 500,000 Americans last year, including Sen. Edward Kennedy and actors Farrah Fawcett and Patrick Swayze.

If you read newspapers or magazines, pass billboards on your daily commute, or watch television, you've seen the advertisements for cancer care. They use phrases like "Life without cancer" and "Making cancer history" and talk about cure rates and cutting-edge treatments. And all too often, they (and even, on occasion, this magazine) refer to "fighting" or "battling" the disease.

"It's great to be upbeat and talk about battles and cures, but it can create false hope," says Prescott. After all, calling something a battle suggests the possibility of winning. "We've made great progress against some cancers, but others have us stumped, at least for now."

One type of cancer that has proved particularly difficult to treat is malignant glioma. This aggressive form of brain cancer strikes almost 9,000 Americans each year. Survival statistics are grim, and for the most deadly form, glioblastoma, life expectancy is only 15 months. Glioblastomas have claimed a number of high-profile victims: Oklahoma native and New York Yankee stalwart Bobby Murcer, entertainer Ethel Merman, Republican political strategist Lee Atwater and, most recently, Massachusetts Senator Edward Kennedy.

Although malignant brain tumors rarely spread elsewhere in the body, they continue to grow within the brain. As the tumors increase in size, they cause increased pressure within the skull, resulting in a cascade of symptoms ranging from headaches to seizures and loss of vision.

The preferred course of therapy involves surgery followed by radiation and chemotherapy. In many cases, though, surgery is not an option because the tumor is too deep or located too close to critical brain regions. But, says Prescott, even with surgery, the outlook is bleak. "Glioblastomas spread by extending tendril-like growths deep into surrounding tissue. It's almost impossible to remove the entire tumor." As a result, of every 50 patients diagnosed with glioblastomas, only one will live five years.

At OMRF, Drs. Rheal Towner and Robert Floyd are exploring a new therapy they hope will change those statistics. Working with an experimental compound, they've performed a series of tests using glioblastomas that have been implanted in rodents. "In mice and rats, we've seen a dramatic shrinkage in tumors," says Floyd, who holds the Merrick Foundation Chair in Aging Research at OMRF.

The next step, says Towner, "will be to initiate clinical trials to study the drug's efficacy in humans." The researchers are currently working with the Food and Drug Administration to initiate a trial for glioblastoma patients who have failed standard therapies. "We'd hope to see the experimental drug slow or even prevent the tumors from growing," says Towner.

"If the drug worked in humans as it has in rodents, it would extend lives," says Floyd. "And if it worked really well, it might keep the tumors in check indefinitely."

The good news is that the experimental drug has already gone through multiple phases of human trials and been shown to be safe when it was tested for another clinical indication. But the FDA has yet to okay trials to test the drug's effectiveness in treating glioblastomas. And even if the trials eventually receive a green light, the drug would have to undergo multiple phases of testing—a process that takes years and can cost hundreds of millions of dollars—before possible FDA approval.

"At this stage, it's impossible to know how this will play out," says Prescott. "But right now, a diagnosis of glioblastoma is pretty

close to a death sentence. So we owe it to brain cancer patients to keep moving down this road, no matter how many obstacles may lie ahead."

Unlike glioblastoma, breast cancer enjoys a reputation as a "treatable" cancer. Indeed, if you are diagnosed with the disease, your five-year odds of survival are almost 90 percent. Since President Nixon's declaration four decades ago, death rates have fallen by almost a quarter. Today, breast cancer claims only 24 victims per 100,000 people.

The improved survival rates are due largely to two factors: earlier detection and more effective treatments. Increased clinical vigilance and better diagnostic tools have enabled earlier and more effective clinical intervention. In combination with traditional therapeutic options of surgery, radiation and chemotherapy, oncologists have in recent years turned to a new generation of cancer drugs—so-called targeted therapies—to improve patients' odds of survival.

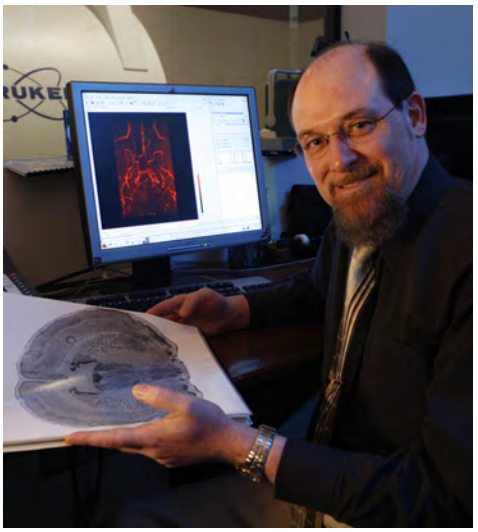
The seed for these therapies was planted in 1982, when biomedical researchers found a gene involved in cancer. They eventually demonstrated that this gene, called HER2, played an active role in causing breast cancer. Scientists went on to discover an antibody that attaches to and disrupts HER2. In 1998, the FDA approved that antibody, Herceptin, for use in breast cancers caused by HER2. In the dozen years since, the drug has proved a tremendous success, curing thousands of women. Scientists have similarly discovered that breast cancers with estrogen receptors can be treated with drugs like Tamoxifen and Evista, which interferes with estrogen receptors.

Yet even with breast cancer, not every case has a happy ending. "If your breast cancer has HER2 or estrogen receptors, it likely will respond to treatment," says Prescott. "But many breast cancers don't fit this pattern." As medical researchers continue to work to unmask the molecular codes underlying the many different forms of breast cancer, oncologists are doing their best with the tools at their disposal.

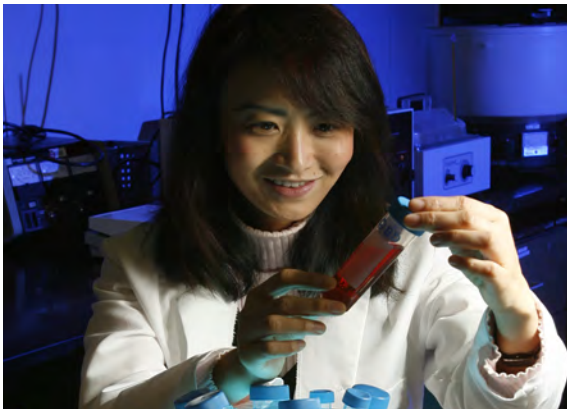
"Surgery can be effective, but a lot of its success depends on the molecular signature of the particular cancer," Prescott says. "In some cases, no matter how early a cancer is detected and how complete the excision appears to be, it's going to metastasize." Chemotherapy, he says, has proven "tried and true" at slowing this process, but in the end its results are not typically dramatic. So sometimes, despite physicians' best efforts, a patient with breast cancer is going to run out of treatment options.

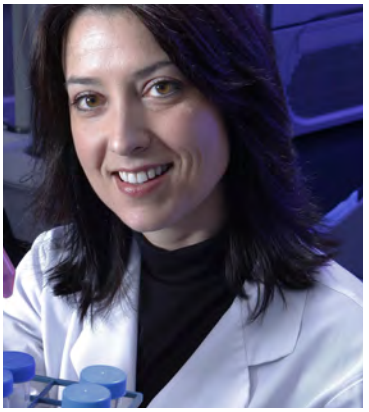
After Debbie Ocker's initial diagnosis and treatment—a lumpectomy followed by chemotherapy and radiation—her life pretty much returned to normal for four years. But in 2007, she learned that the cancer had spread to her bones. A year of drug therapy didn't seem to help. She went on an extremely low-carbohydrate diet and lost 65 pounds. Her tumor markers dropped, but her doctor worried that her weight was too low.

In the fall of 2009, just like in each of the previous six school years, she told her students about the cancer. As had become her way—it was almost a part of the lesson plan by now—she waited several weeks into the semester to tell them. And then she opened the floor for questions.



OMRF's cancer research efforts span many different areas. Drs. Rheal Towner (left) and Robert Floyd (right) have developed an experimental treatment for deadly brain cancers known as gliomas. Meanwhile, (below, left to right) Drs. Paul Kincade, Hong Chen and Courtney Gray-McGuire are studying leukemias and lymphomas, breast cancer and colon cancer.





One day last November, Ocker told her students that her cancer had spread to the fluid surrounding her brain. There were lots of tears that day.

The students were tentative at first. But as it became clear that their teacher meant it when she told them to ask her anything, they took her at her word. How does it feel, Ms. Ocker? What, exactly, are the treatments like?

The questions gave Ocker pause. At that time, she was undergoing assessments of her lymph nodes that involved numerous shots in sensitive areas of her breasts. The procedures were, she says, "excruciatingly painful."

What to tell her students? Was this too graphic, too hard for 16- and 17-year-olds to process?

No, she decided, she would not candy-coat things. Since doctors had first diagnosed her, Ocker had pledged to use her experiences as a way to make cancer real to her students. Yes, the disease was scary. But obscuring the details—"I'm sorry, I don't want to talk about it"—would only fuel her students' fears. If Ms. Ocker won't tell us, they'd think, it's got to be pretty awful.

She warned the students that what she was about to tell them would contain details that might make them uncomfortable. She gave them the chance to leave the room. None did.

The teens asked what it was like to have a portion of her breast removed. The toll that cancer drugs exacted on her body. If she was scared to die.

Ocker pulled no punches in her answers. "I expected there would be calls from outraged parents, but I didn't care. Their questions needed to be answered."

The calls never came.

Since 1975, the Putnam City Schools have conducted an annual fund drive to raise money to support cancer research at OMRF. What started out as a door-to-door change collecting effort at a single school has evolved into a district-wide campaign involving all manner of events—bake sales, carnivals, volleyball marathons, car washes, auctions. During the 2008-09 school year, the drive raised more than $100,000.

For the 2009-10 school year, Ocker agreed to serve as the "poster child" for the Putnam City High cancer drive. The activities director at Putnam City came up with a theme for that year's drive: "Ocker's Army." When Ocker arrived at work on what she thought would be a typical Friday that fall, she was greeted by hundreds of students and colleagues donning tee shirts bearing her name.

Like every other part of the drive, proceeds from the sales of those tee shirts will go to support cancer research at OMRF. Among OMRF's current efforts in that area are two projects focused on breast cancer.

In the first, Dr. Hong Chen has discovered a molecular pathway that appears to play a crucial role in the growth and metastasis of breast cancer. She has hypothesized that disrupting this pathway could have important therapeutic affects, both in reducing primary tumors and the spread of breast cancer. A second project led by Dr. Robert Floyd has received a grant from the U.S. Department of Defense to conduct pre-clinical testing of a compound that, in the laboratory, has been shown to stop tumor growth.

The most exciting aspect of these projects, says Prescott, is that they are not "tumor-specific." In other words, "If either or both of these strategies work, they could be used to treat any form of breast cancer," as opposed to the currently available treatments like Tamoxifen and Herceptin, which only work in breast cancers with a specific molecular signature.

Like all basic research, cautions Prescott, these projects face countless hurdles before they could reach hospitals and clinics. Even if everything plays out as the scientists hope, it will be years before a treatment reached patients. Unfortunately, that will be too late to help Debbie Ocker.

On Tuesday, November 10, after experiencing "tingly" sensations in her jaw and chin, Ocker had an MRI. "That's when they discovered the cancer had spread to the cranial fluid surrounding my brain," she says.

Doctors told her that without treatment, her life expectancy was three months at best. Treatment might add another few months. But treatment would entail brain surgery followed by intensive rounds of chemotherapy and radiation. Ocker did not want her life to end that way.

The next day, Ocker told her students and colleagues the news. Her last day of work would be Friday, November 13.

There were a lot of tears that day. And in the days that followed. But there was also a tremendous outpouring of love. Ocker was flooded with flowers, gifts, cards, emails and letters from students and former students, parents and faculty. On her last day, there was a party. Four hundred people showed up. They donated $1,200 in her honor to OMRF through the Putnam City Cancer Drive. And, for the most part, they obeyed two rules that Ocker had made a condition of the celebration: no sad speeches and no crybabies. "My message has always been about living with cancer, not dying from it," she says.

She woke up around 3:00 the next morning. When she switched on her light, she saw the stacks of cards that her Putnam City family had given her the previous day. With the swirl of events, she'd not yet had time to read them. So she picked up the stack, tore open that first envelope and began to read.

The cards told Ocker of the love she'd spread and the lives she'd impacted. They thanked her and told her they loved her. They volunteered to do whatever they could to help her. They sent prayers and blessings and love.

Before she knew it, in those wee hours, Ocker had read hundreds of cards. It was, she says, "the most amazing gift I have ever received."

"My message has always been about living with cancer, not dying from it."

She'd said good-bye to her students, her colleagues. She'd retired from her job of 22 years and given away most of her belongings. Then for two or three days at a time she wouldn't leave the house, wouldn't even take off her pajamas. Her life as she'd known it, she realized, was over.

Yet there Ocker still was.

She decided to pay a visit to her sister in Chicago. There was a nice guest room on the main floor of her home. She could stay as long as she wanted. And her sister had even set up a studio where Ocker could do one of her favorite things: quilt.

Maybe it was doing something she loved. Or the distraction from her condition. Or perhaps it was the feeling of once again being productive, of being, well, alive. But whatever it was, the quilting helped Ocker reconnect with the world. As she did, other little pieces of normalcy began to return. She started taking a shower every morning, getting dressed. She even began putting on makeup again.

A few weeks before Thanksgiving, her doctor had given her three months to live. But February 10 came and went without incident.

Not long ago, she decided to send another letter to her friends. To let them know about her current situation. And that she was, in her words, "still kicking."

She continues to stay with her sister. Although she isn't in any pain, her vision has begun to fail. And getting around has become a challenge; she's using a walker and has a wheelchair on order.

Yet each morning she rises before dawn, she makes a breakfast of frittatas and fruit, then drives to her "office," the quilting studio. There, she keeps her sewing machine, fabrics and a felt board where she hangs fabric cut-outs. A couple of weeks ago, her sister bought her a futon so she can take mid-afternoon naps. So far, she's made at least a dozen quilts, and she has plans for more.

Still, Ocker is clear-eyed about her future. "I don't know how much time I will have on this earth." But she's grateful for the life she's enjoyed and for these last, extra months. "I don't have a place big enough to hold my blessings."

Most of all, she hopes her students will remember all she tried to teach them. Challenge yourselves. Have faith that you can achieve your goals. And always tell it like it is, no sugar-coating.

On May 18, as this issue went to press, Debbie Ocker died.

START

4:30 am
Delancey has a nightmare. Lie down with her so she can sleep.

Lose a turn (and an hour's sleep)

6:00
Manage to sleep-talk myself out of bed.

Out of milk!

Spin Again

Looks like it's pancakes for breakfast! Aren't "only add water" mixes the best?

Play another day

The GRIFFIN Game of LIFE

Like many working parents, Drs. Tim and Courtney Griffin would give just about anything for a 26-hour day. But until researchers figure a way to alter the march of time, the OMRF scientists and parents of twins (Delancey and Olivia, 6) will continue to do the best they can with the standard 1,440 minutes. Here, mom/cardiovascular biologist Courtney and dad/bioengineer Tim share a typical day.

11:58
Finally stumble to bed, only to have Tim convince me to watch an episode of *The Office*. I'll regret this tomorrow!

Almost fall asleep at the computer.

10:45
Write an animal protocol. Review a manuscript.

10:30
Begin work on poster presentation for an upcoming meeting.

Advance careers 1 space

9:20
Empty the dishwasher. Discuss whether we're applying for enough grants. Talk to my parents.

8:32
Prep girls' lunches for tomorrow. Chat about scientific benchmarks and goals. It's good to be teammates in this endeavor.

Bonus round

8:15
Read the story of Frederick the mouse to the girls. Send them off to bed with lots of hugs.

7:42
Oversee homework on capitalizing proper nouns.

7:00
Back home (with balloons) for a tasty shrimp dinner. Try to convince twins that scallions won't kill them.


Add 2 New Players
7:04
Field Olivia and Delancey's questions about how paper money is made (thank you, tooth fairy) while boiling mac and cheese for lunches.
7:50
Walk the girls to school, dodging sprinklers.
Choose Player
8:30
Hello, OMRF. Time to study the ways in which obesity contributes to arthritis.
8:47
We're ending a 6-month-long experiment today. Hope no one sneezes into the test tubes!
9:52
So far so good. Exciting and scary to think that we'll be analyzing this data for years to come.
10:30
Discuss methods for collecting biological samples from mice with lab member. Who says research isn't exciting?
Spin to Win!
11:25
Learn that our obese mice run more than the lean ones when the lights are off. Hmmm . . .
1:20 pm
Nothing like measuring mouse body fat to make you skip the burger and fries.
4:37
Visit OMRF's Center for Genetic Research (a.k.a. the mouse house) to check on the critters.
Team Play
5:55
Kids remind us of PTA meeting tonight. Decide to skip, lest the family starve to death.
5:58
Tim starts a discussion on low diffusion rates of mylar balloons.
Go directly to party store
5:01
Late to pick up the kids. Argh!
3:02
My lab has been operating full throttle all afternoon. All hands on deck to handle a ton of samples.
12:00 pm
Attend fascinating talk on multiple sclerosis.
Pick another research topic
8:52
Rush down to the lab to start experiments on blood vessel formation.
8:30
Arrive at the office. Read an article about the disparity in success rates between male and female scientists.
CAREER

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A LOOK BACK

When President Richard Nixon declared war on cancer in 1971, it brought the disease into the national spotlight. Just three years earlier, Nixon and his wife, Pat, visited Oklahoma City on the campaign trail. Along for the ride were two well-known Oklahoma governors, pictured above with the Nixons. If you can name either (hint: one was also an OMRF board member) your name will be entered in a drawing for a free OMRF T-shirt. Take your best shot at findings@omrf.org or call 405-271-7213.