FINDINGS

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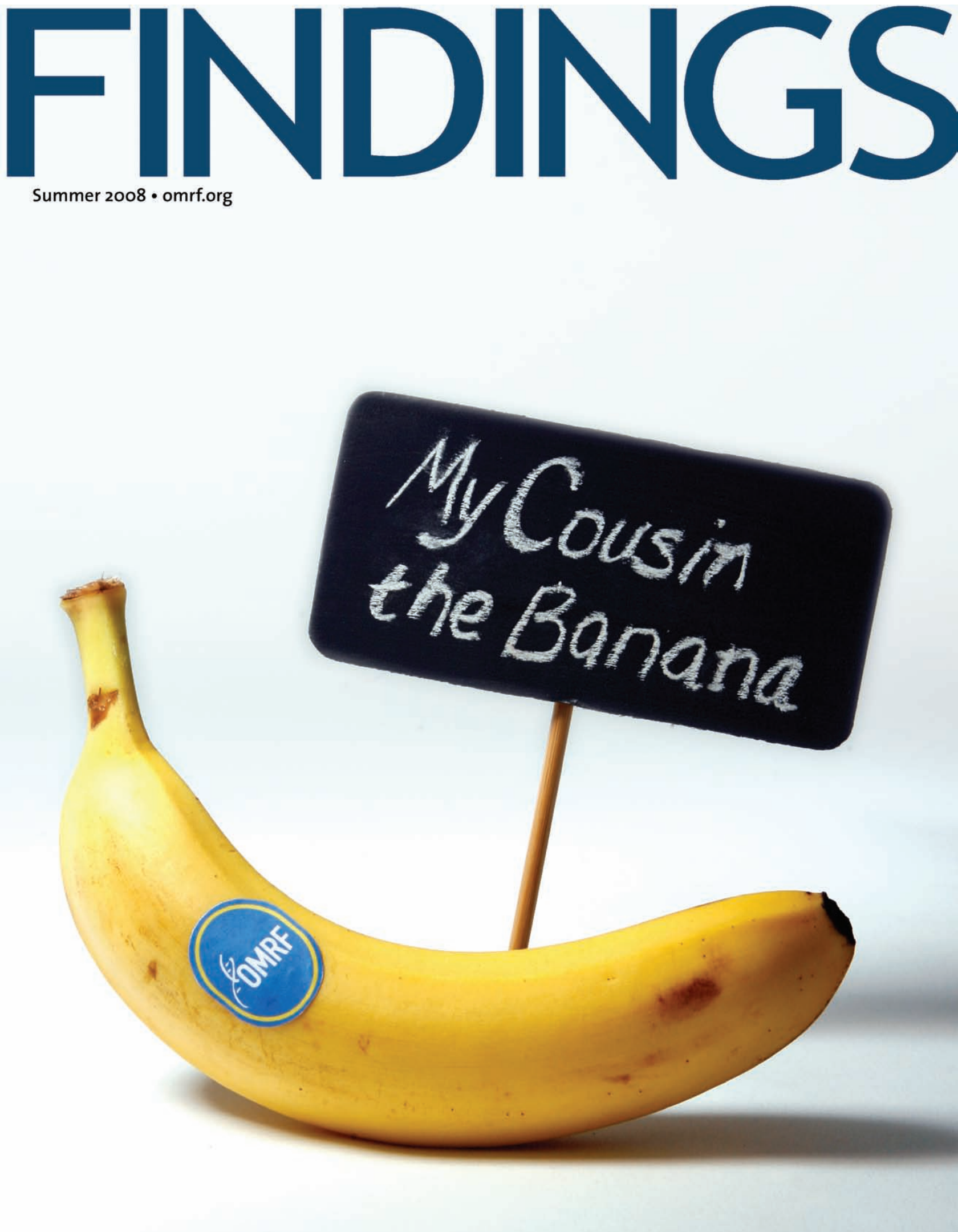

Little things can make a BIG difference

A red blood cell is only six micrometers across, but when an infection like sepsis enters your bloodstream, the damage can be monumental. At OMRF, scientists helped create the only FDA-approved treatment for this deadly blood infection. And they're dedicated to finding better treatments for all human diseases–from cancer to heart disease and Alzheimer's.

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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 **It doesn't matter if you're a banana, fruit fly or writer; DNA is inside all your cells. Join OMRF's Greg Elwell as he peels back his own genetic skin.**

WEB BONUS

Watch what happened when Greg Elwell looked inside his own genome at interactive.omrf.org

This Drug's for You

The personalized medicine revolution is here. Sort of.

Three years ago, the U.S. Food and Drug Administration issued guidelines to encourage drug companies to pursue personalized medicine—genetic testing that would determine what course of treatment, exactly, was right for a given individual.

Sounds great, right? Instead of having to try this blood pressure medication or that, you could simply take a one-time test that would tell you which blood pressure drug would be most effective at controlling your hypertension while, at the same time, carrying the lowest risk of side effects.

No longer would patients' (or doctors') decisions be driven by marketing. Instead, hard data would guide treatment.

You liked that ad featuring the couple in the bathtub? Your physician attended a conference sponsored by the manufacturer of that anti-depressant? Doesn't matter—the genetic test shows that a pill made by another drug company would work better for you. So that's the one you'll get. End of story.

Or not. Because three years later, we've hardly moved off of high center.

It's not for lack of technology. Companies, primarily smaller biotechs, have developed numerous innovative genetic tests that can predict whether patients are likely, or in some case certain, to develop various diseases. They also have created tests that will indicate whether given courses of treatment are likely to prove effective (or dangerous).

Yet three major obstacles have prevented the widespread use of such testing: drug companies, insurers and patients.

Drug companies are hardly wild about diagnostic tests that stand to cut the use of their most popular products. If it turns out that only 10 percent of all diabetics stand to benefit from an expensive drug that now has a 60 percent market share, who's the big loser?

You'd think that insurers would be eager to cut unnecessary treatments and the attendant merry-go-round of physician and hospital visits. After all, getting their clients on the right medications will presumably cut significant costs in the long run, especially when many of those medicines will be older, cheaper drugs than those patients currently take.

Yet insurance companies have repeatedly balked at the up-front costs for such tests, deeming them "elective" (read: unnecessary). This kind of short-sightedness is hardly surprising, but the pennies saved today will come at the expense of dollars spent on (avoidable) treatments tomorrow.

Finally, many patients themselves have been reluctant to use predictive tests. Of course, it doesn't help when insurers leave them holding the bag for the full cost of testing. Add in the fact that many are worried that negative results might prevent them from getting health insurance, and you can understand why the personalized medicine revolution has not yet been televised.

And that's a shame. Because these tests, like the OncoVue breast cancer risk assessment test from Oklahoma's own InterGenetics, really can make a tremendous impact on people's lives. They can spell the difference between needless pills and targeted therapy. Between preventative regimens and aggressive treatment. Between anxiety and peace of mind.

To get a glimpse into the world of personalized genetic testing, read Greg Elwell's article that begins on page 10. As you'll see, it's a brave, if not quite perfect, new world. But the possibilities these technologies hold for tomorrow are staggering.

Like all revolutions, this one will not come without some pain. But it will keep coming, because the payoffs are too big and too important to ignore.

Stephen M. Prescott

DR. STEWART WOLF'S RESEARCH LAID THE GROUNDWORK FOR FUTURE BREAKTHROUGHS IN GASTRIC STUDIES WORLDWIDE.

Little Feat

I WAS SO SURPRISED TO read your article, "The Man with a Hole in his Stomach (Winter/Spring 2008)," because it was almost a direct parallel to my mother's physical disability. She, too, drank lye as a young child and eventually, scar tissue began to close her esophagus. Mother was slowly starving from being unable to eat. Her parents took her to Quanah, Texas, to see a young, new doctor who helped stretch the scar tissue enough to let food pass through. She lived a long, successful life and had two daughters, two husbands and many good friends and relatives. Maybe if Tom Little had lived in southwest Oklahoma in the early 1900s, he might have had a similar outcome early in his life.

LOU ANN DOAK
MIDWEST CITY

I FOUND YOUR STORY ABOUT Tom Little absolutely fascinating, especially in light of the fact that my mother had a feeding tube placed in her stomach temporarily and all the trauma that was associated with it. I can't imagine what it must have been like in those days and to deal with it every day of your life. What a remarkable story!

KAREN SCHOTT
OKLAHOMA CITY

THE ARTICLE ON TOM LITTLE'S life and the groundbreaking research conducted by Dr. Stewart Wolf at OMRF was simply incredible. When I read this story, it seemed like an episode straight from Paul Harvey's "The rest of the story." Although considered unconventional at the time, Dr. Wolf's research laid the groundwork for future breakthroughs in gastric studies worldwide. This is one more example of how OMRF has made a difference in medical research over the last six decades.

PAUL I. SCHULTE
KINGFISHER

YOU AND YOUR STAFF OUTDID yourselves on the latest issue of *Findings*. "The Man with a Hole in his Stomach" deserves to win an award. It was one of the most interesting articles I have ever read in any magazine.

SUE CAMPBELL
OKLAHOMA CITY

HOMETOWN GIRL

I READ YOUR MAGAZINE every time we get it and enjoy all the interesting stories. Lamont is just 15 miles east of Pond Creek where Dr. Judith James grew up. We watched her grow up and run into her family many times a year. It makes us feel really proud to know someone who is doing so much in research.

KAY CARDWELL
LAMONT

PAGING DR. SCREWDRIVER

At first, I thought the answer to your history mystery question was "screwdriver." However, on further observation, there were no ice cubes, and I began to doubt that you once had a preeminent scientist named "Dr. Screwdriver" at OMRF. So I decided to go with "Tang."

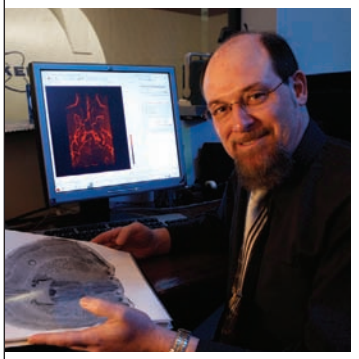
RON TOTH
SALT LAKE CITY, UTAH

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.

Taking Aim at Brain Cancer

Dr. Robert Floyd



Dr. Rheal Towner

When doctors diagnosed Sen. Edward Kennedy with a malignant brain tumor this spring, the prognosis was bleak. Experts said the average prognosis for the most aggressive form of this tumor, known as a glioma, was approximately 15 months, while those suffering from slower growing tumors might expect to live two to four years.

At OMRF, two scientists are exploring a promising new therapy that could one day change those grim statistics. Working with an experimental compound, Drs. Robert Floyd and Rheal Towner have found that, in rodents, the drug significantly shrinks the tumors.

"In rats, we've seen dramatic effects on the same kind of tumor that Senator Kennedy has," says Floyd, who holds the Merrick Foundation Chair in Aging Research at OMRF. "If the drug worked the same way in humans, it would, at a minimum, extend lives. And if it worked really well, it might suppress the tumors indefinitely."

The compound has already been tested for safety in humans in large-scale clinical trials, and it was found to be safe. "The next step will be to initiate human trials to study the drug's efficacy in treating gliomas," says Towner. "We expect to begin those trials in the near future."

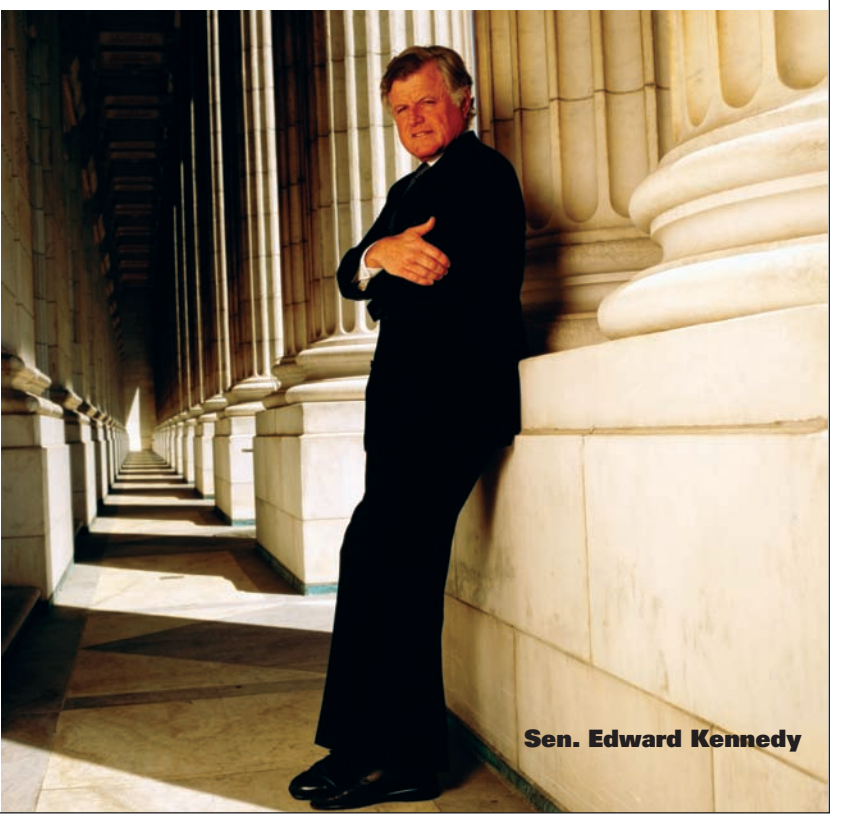
To that end, Floyd and Towner have formed a new biotechnology company: Onconos. The company's near-term focus will be on conducting clinical trials for the experimental drug, with a long-term goal of obtaining FDA approval for the drug's use in treating gliomas.

According to the American Cancer Society, more than 21,000 Americans will develop brain and nervous system cancers in 2008, and about 13,000 people will die from these conditions this year. Gliomas and other tumors are often accompanied by headaches and seizures.

As with Sen. Kennedy, patients sometimes undergo surgery to remove all or portions of the tumor, with radiation and chemotherapy following. However, in some cases surgery proves impossible due to the tumor's location in the brain. And even if possible, surgical treatment often proves ineffective.

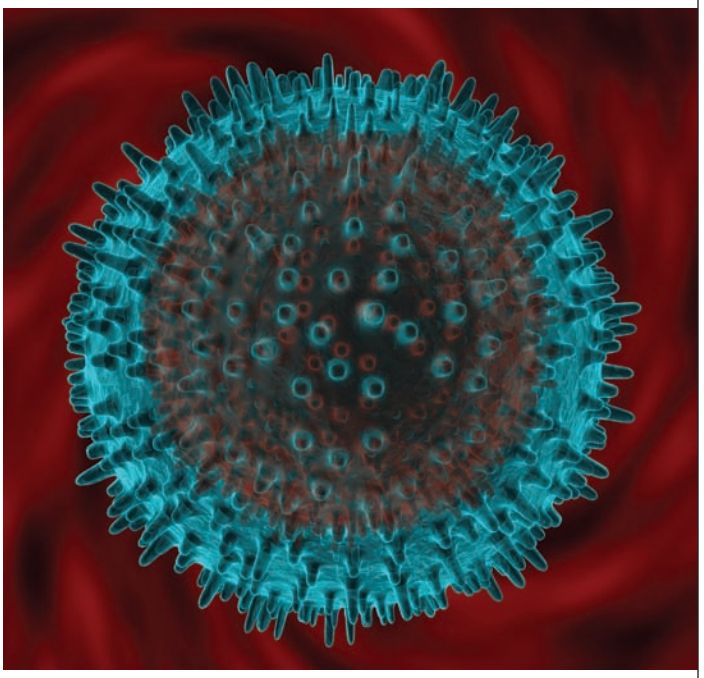
"Brain cancers are a devastating medical problem," says OMRF President Stephen Prescott. "The work Drs. Floyd and Towner have done is extremely exciting. Although there's still a long road ahead, this research holds the potential to change lives."

MORE THAN 21,000 AMERICANS WILL DEVELOP BRAIN AND NERVOUS SYSTEM CANCERS IN 2008, AND **ABOUT 13,000 PEOPLE WILL DIE** FROM THESE CONDITIONS THIS YEAR.



Sen. Edward Kennedy

The Most Natural Drug



In the fight against infection, the human immune system isn't ready for a war.

While vaccines help create defenses against illness, they take time to work. But a new process developed by OMRF scientists stands to revolutionize the process.

In the journal *Nature*, OMRF researchers detailed a method that can identify and clone human antibodies specifically tailored to fight infections. The new technology holds the potential to quickly and effectively create new treatments for influenza and a variety of other communicable diseases.

When an infection invades, the immune system goes to work manufacturing antibodies to fight it. Most of the antibodies created will have no effect, but a very few will bond to the invader and replicate to neutralize the enemy.

The new process develops a "smart bomb" for the immune system, using fully human monoclonal antibodies specifically designed to fight the infection without doing any harm to the body. The research, says Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases in Washington, DC., "opens the way to producing monoclonal antibodies that potentially could be used diagnostically or therapeutically not only for influenza but for other infectious diseases as well." The work has drawn worldwide attention, including write-ups by *Scientific American* and *The Journal of the American Medical Association*.

In the past, it took years of work and great expense to create what are known as monoclonal antibodies—lab-produced antibodies derived from a single line of cells. "It was kind of the 'needle in a haystack' approach," says OMRF's **Dr. Patrick Wilson**, senior author on the paper. "The problem is they couldn't pick the cells that made the antibodies against the pathogens that you wanted to fight."

A second method, making hybrid antibodies from mouse B cells (white blood cells that produce infection-fighting antibodies), is faster but more dangerous. If the proteins in the hybrid antibodies weren't compatible, the body could reject the antibodies or react with them in unforeseen ways.

The new process doesn't use traditional antibody derivation methods or human-mouse hybrids. Instead, the OMRF researchers, working with colleagues at Emory University, isolated antibody-secreting cells (plasma cells) from people who had received the influenza vaccine, then cloned the antibody genes from these cells. "We can recognize which cells are made and then make antibodies from them directly," Wilson says. "It's a rapid and efficient way to make fully human antibodies."

While the research is aimed at combating influenza, it can be used to create treatments for any condition—such as anthrax or smallpox—for which there is already a vaccine. Antibodies might also be produced from the immune responses of people with active or chronic infections. This technology has the potential to serve as therapy for someone who is already infected or provide passive immunity to protect against future infection. With more research, this new technology could also be key to fighting diseases such as multiple sclerosis and cancer.

Wilson and his clinical collaborator, **Dr. Judith James**, are currently working to make more antibodies from other infections—including hepatitis C, pneumococcal pneumonia and anthrax. They're also seeking a partner to help produce large quantities of the influenza antibodies. "We now have an outstanding opportunity to create antibodies against a host of diseases," says James, who holds the Lou C. Kerr Chair in Biomedical Research at OMRF. "This discovery has great clinical potential."

A Male Birth Control Pill?

Having a child is a big responsibility for both fathers and mothers. In the same way, when a couple doesn't want to conceive a child, the responsibility of preventing a pregnancy belongs to both partners.

For men, contraceptive choices are limited. While condoms are effective, they have a 15 percent failure rate in real-world application. Vasectomies have become easier and more available, but they're both expensive and might not be reversible in some men. But another option—a safe, reversible and non-hormonal pill—could be around the corner, thanks to a discovery by OMRF's **Dr. Kevin Moore.**

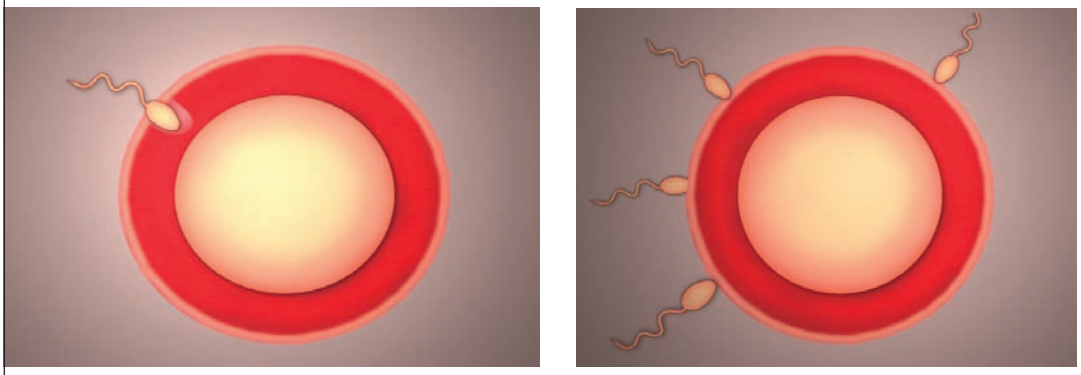
Moore's lab was the first to identify and clone two closely related enzymes, called tyrosylprotein sulfotransferases (TPST) 1 and 2. In experiments, they found that mice lacking the second enzyme, TPST-2, were infertile. "They couldn't fertilize eggs," says Moore. "Other than that, they seemed normal in every way."

The mice created sperm, and the sperm was motile, but it couldn't bind with the egg to cause conception. Moore realized that a compound to block the action of the TPST-2 enzyme might act as a male contraceptive in men. And an enzyme blocker would likely have fewer negative side effects than hormonal birth control, the kind most often used by women.

"In the last 60 years, science has developed a clearer understanding about the effects of hormonal contraceptives on women, including increased risk of breast cancer and cervical cancer," says Moore, who is the Fred Jones Distinguished Scientist at OMRF. "Knowing what we know now, why would we want to mess with the hormones of the other half of the population?"

Blocking enzymes, the approach employed by the popular cholesterol-reducing drugs known as statins, can better target biological processes than the manipulation of hormones. It should also avoid a host of side effects, including the weight gain and increase in bad cholesterol that can accompany treatment with hormone-based compounds. And, says Moore, "An enzyme-blocker would be reversible," an important fact for men who might later want a family.

Next up will be work to identify compounds that block the TPST-2 enzyme. If these efforts prove successful, years of drug development and testing would follow.



DO NOT PASS GO In normal mice (left), sperm can fertilize an egg. But OMRF's Dr. Kevin Moore discovered that in mice lacking an enzyme known as TPST-2 (right), sperm are unable to bind with eggs, preventing conception.

Dr. Dean Dawson, *The Segregation of Error-Prone Chromosomes in Meiosis*, National Institute of General Medical Sciences

Dr. Robert Floyd, *Pre-Clinical Study of Combination Oral Treatment for Acute Acoustic Trauma*, Office of Naval Research

Dr. John Harley, *Genes from SLEGEN, The Lupus Genetics Consortium,* Alliance for Lupus Research*; Genetic Linkage in Lupus*, National Institute of Allergy and Infectious Diseases; *Genetic Association in American Blacks with Lupus*, National Institute of Musculoskeletal and Skin Diseases

Dr. Kenneth Hensley, *Metabolic Thioether Derivatives for Huntington's Disease*, Hereditary Disease Foundation; *Acetaminophen for Amyotrophic Lateral Sclerosis*, Muscular Dystrophy Association

Dr. Judith James, *Science in a Culture of Mentoring*, National Center for Research Resources

Dr. Paul Kincade, *Developmental Stage-Related Changes in Lymphopoiesis*, National Institute of Allergy and Infectious Diseases; *Early Events in Mammalian B-Cell Differentiation*, National Institute of Allergy and Infectious Diseases

Dr. Susan Kovats, *Regulation of Dendritic Cells by Estrogen Receptor During Lupus Nephritis*, Alliance for Lupus Research

Dr. Joan Merrill, *Lupus Clinical Trials,* Lupus Clinical Trials Consortium, Inc.

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

Dr. Swapan Nath, *Identifying the Novel SLE Susceptibility of Gene on 5p15.3,* National Institute of Allergy and Infectious Diseases

Dr. Stephen Prescott, *Support Fund for New Faculty Scientist,* Presbyterian Health Foundation

Dr. Xiao-Hong Sun, *Mechanism of T Cell Lymphoma in E Protein Deficiency,* National Cancer Institute

Dr. Kenaz Thomas, *Database Development/Collection Committee of the Biomarkers Working Group,* Lupus Foundation of America

Dr. Rheal Towner, *Inhibition of iNOS in Malignant Gliomas,* Oklahoma Center for the Advancement of Science and Techonology

Dr. Carol Webb, *Bright Function in the Immune System,* National Institute of Allergy and Infectious Diseases

Grants Awarded *(January-April, 2008)*

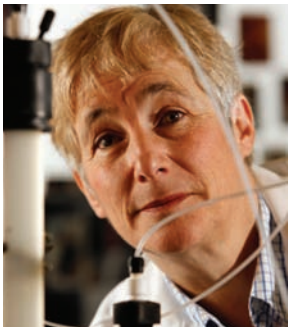
OF NOTE

After a nationwide competition, **Dr. Susannah Rankin** was named in June as Oklahoma's first ever Pew Scholar in Biomedical Research. The honor includes a $240,000 award over four years.

At OMRF's annual honors and awards banquet in May, the foundation welcomed three new directors: **Christy Gaylord Everest** of Oklahoma City, Rebecca Switzer of Norman and Susan Loosen of Okarche.

OMRF has received the highest possible rating from **Charity Navigator,** the nation's largest charity evaluator. OMRF's score ranked it as the state's top charity and 3rd out of 77 medical research institutes nationwide.

When the Oklahoma Hall of Fame welcomes its 2008 class, OMRF will be doubly represented—by the **Honorable Robert H. Henry**, an OMRF director, and Dr. Jordan Tang, the first OMRF scientist so honored.



On May 29, top heart disease researchers from around the world gathered at OMRF for the Thrombosis Symposium. Organized by **Dr. Naomi Esmon**, the event focused on a condition responsible for millions of deaths every year.

NEXT OF KIN

By Greg Elwell

It turns out I have a lot more in common with a banana than I first thought. No, I don't have yellow skin. I don't bruise easily. And nobody waits until I am over-ripe to bake me into delicious bread. But under my skin, inside it even, I share one very important thing with bananas: deoxyribonucleic acid. ■ DNA serves as the basic building block of all life, and about half of mine (and yours) is identical to that of a banana. Granted, ours is a bit longer (23 pairs of chromosomes to just 11 pairs in the fruit that made Chiquita famous) and more complex, but there's a genetic kinship there that will make me think twice before ordering my next smoothie. If that half-banana stat has got you thinking about checking the "fruit" box next time you're asked your ethnicity, here's another fun fact for you: All human DNA is 99 percent identical. It's that one percent that accounts for all of our differences. The spots where there are changes are called single nucleotide polymorphisms, or SNPs, and they can change the color of your hair, the moisture in your earwax and your probability of developing diseases during your lifetime. It's those portions of the DNA that scientists at the Oklahoma Medical Research Foundation—and throughout the world—are focusing on as they seek to unlock the secrets of human disease. ■ DNA is inside the cells of every living thing. It doesn't matter if you're a banana, a fruit fly, a tree or an almost-middle-aged writer. Here's what I found when I peeled back the skin of my own DNA.

HERE'S WHAT I FOUND WHEN I PEELED BACK THE SKIN OF MY GENOME.

FOR AS LONG AS PEOPLE HAVE BEEN STUDYING the human genome—the complete sequence of DNA in each of us—that exploration has been the province of elite scientists in research laboratories. But in the past few years, that has changed. ■ When the Human Genome Project finished assembling the first complete human genome in 2003, the price tag of the entire project came to about $300 million. Five years later, a growing number of companies, with names like deCODE Genetics and 23andMe, now offer a glimpse of your own genetic code for about $1,000. Rather than sequence the whole genome, these companies take a DNA sample and analyze more than a half-million SNPS (pronounced "snips"), targeted areas that have already been linked with a disease or condition. ■ It's pretty simple, really. Just go onto a website—I chose 23andMe's—punch in your credit card number and wait for the testing kit to arrive. Being new to this whole genotyping thing, I wasn't quite sure what to expect when the mail arrived. ■ What I got was a box conceived like a Russian nesting doll; everything I opened had something else inside. The only thing that really mattered, though, was a test tube, which I had to fill with saliva. When I filled it to the line, I snapped on the cap and mailed my test tube back to the company.

And then I waited.

ALTHOUGH DNA has been around as long as life itself, the study of genetics didn't begin until 1865, when an Austrian monk named Gregor Mendel experimented with pea plants in his garden and found that traits could be passed down through the generations. Scientists spent much of the next century trying to determine how the transfer of information was made. Oddly enough, says OMRF's Dr. John Harley, "DNA was largely dismissed as just a bunch of mucus inside the nucleus of the cell until 1943." That's when microbiologist Oswald Avery figured out that DNA was the mechanism of genetic transfer, the way that one generation passes along to the next the blueprint for making all the structures and materials the body needs to function.

Although Harley wasn't yet born, Avery's discovery would prove to be a seminal moment in his career. As head of OMRF's Arthritis and Immunology Research Program, his work focuses on pinpointing the genetic roots of lupus, the devastating autoimmune disease that affects as many as 2 million Americans and 15 million people worldwide.

The roots of lupus, like most diseases, are not fully known. But thanks to the work of Harley and others in the field, it is now all but settled that the disease is "multigenic," meaning that it is caused by defects at multiple sites on the DNA.

Harley spearheaded a massive research effort that involved 150 scientists and staff at more than a dozen institutions in the U.S. and Europe. Using SNP genotyping—the same process that would soon tell me whether I can taste certain bitter flavors or am more likely than average to develop colorectal cancer before the age of 89—the researchers studied the DNA of 720 women with lupus and 2,337 women without lupus (the disease strikes women nine times as frequently as men).

Scanning each subject's complete sequence of DNA—3 billion chemical pairs that together make up a person's "genome"—they homed in on 317,000 specific locations where a single unit of DNA might vary from one person to the next. The scientists confirmed these results in another independent set of 1,846 women with lupus and 1,896 women without lupus.

To most, those results would read like alphabet soup, a seemingly senseless concoction of A's, C's, G's and T's. But to Harley and his research army, the four letters (which stand for adenine, cytosine, guanine and thymine) read like a recipe. And the order in which those ingredients are arranged will determine everything about us, from hair color to susceptibility to disease.

When Harley's team culled through the seemingly endless data they'd generated, they discovered 13 different regions on the DNA—genes—associated with lupus. These included three genes previously thought unconnected to the disease and a region once believed to be "junk DNA," a piece of genetic material without a known function. In addition, the scientists uncovered further evidence strengthening the genetic case against nine genes linked to lupus and other autoimmune diseases.

Harley's work, which appeared in the journal *Nature Genetics* earlier this year, is one of several recent projects that have made major advances toward unmasking the genetic culprits behind lupus. And later this summer, OMRF's Dr. Patrick Gaffney will unveil—again in *Nature Genetics*—a new, genome-wide study that will reveal yet another potential genetic culprit behind lupus.

"We're making extraordinary progress," says Harley. "Less than a year ago, we were only aware of nine genes that contributed to lupus. Since that, we've identified another 16 genes associated with the disease." These new genetic findings, he says, "have opened many new doors. And we're excited to investigate what's behind each of them."

Live the genotyping experience

Go to interactive.omrf.org to watch Greg try to decode his own genetic blueprint. And while you're there, check out Gregipedia, his new blog.

THE FOUR CHEMICAL BUILDING BLOCKS OF DNA—A(DENINE), C(YTOSINE), G(UANINE), T(HYMINE)—ARE CALLED BASES.

DNA, SHORT FOR DEOXYRIBONUCLEIC ACID, IS A CHEMICAL FOUND PRIMARILY IN THE NUCLEUS OF CELLS. DNA CARRIES THE INSTRUCTIONS FOR MAKING ALL THE STRUCTURES AND MATERIALS THE BODY NEEDS TO FUNCTION.

WHEN MY TEST RESULTS ARRIVED in the form of a link from 23andMe, I took a deep breath and clicked. What I expected was a moment of revelation. What I got was decidedly unenlightening: raw data and research studies (like Harley's) linking this or that genetic sequence to an increased or decreased risk of various medical conditions. I spent the remainder of the day with my head buried in their—my—data, trying to make heads or tails of my genes.

"I'm going to get Lou Gehrig's disease," I announced to my wife when I got home from work that evening.

"What?! Is that what your report said?" She sat frozen on the edge of our bed. Somehow, taking off her socks had become less important now that I had introduced the specter of the incurable neurodegenerative disease.

"Well, it's not a lock," I admitted. "But I am 1.3 times more likely to get it than other people of European descent."

We spent the rest of the night and much of the next few days talking about the test. Some of the information was useless but nonetheless amusing: Apparently, I have wet ear wax and the same fast-twitch muscle SNPs as some Olympic athletes. But most of what I learned was vaguely scary. I say vaguely because I was having trouble understanding what, exactly, it all meant. I say scary because the report contained much discussion of and statistics relating to the risk of contracting just about any disease under the sun.

Thankfully, I work with some very smart people. In fact, I work for one of them, Dr. Stephen Prescott. And when I sat down with him, OMRF's president told me what I was longing to hear: Don't worry.

"The problem is, people don't really understand risk at all," he said.

"It's like when somebody talks about how risky it is to fly. Is it riskier than staying home? Probably. But it's much safer than driving a car, and people aren't too hesitant to get behind the wheel."

With disease, he explained, we're too often told about relative risks. "That's risk by comparison to others, which is what your genome results talked about." Compared to this group of people, having a certain SNP makes me that much more or less likely than the average Joe to have Disease X. But absolute risk is a different matter.

So, take the bomb I dropped about Lou Gehrig's disease. What I read in my genome was that my SNPs give me a 30 percent higher relative risk of developing the neurological disorder at some point in my life. On average, about 1 in 100,000 people develop Lou Gehrig's disease; if my risk goes up 30 percent, my absolute odds are still only 1.3 in 100,000.

I felt a lot better after that discussion. And, once I conveyed it to her, so did my wife.

HELLO, GINA

One major hurdle to genetic testing has been fear. Naturally, many have shied away from testing because they are afraid to learn the health risks that may await them. But many Americans considering genetic testing have also faced another concern—that health insurers or employers may use that genetic information against them.

In May, President Bush moved to put an end to the threat of genetic bias when he signed into law GINA-the Genetic Information Nondiscrimination Act. The law prohibits health insurance companies from using genetic information to deny benefits or raise premiums for individual policies. (It is already illegal to exclude individuals from a group plan because of their genetic profile.) Employers who use genetic information to make decisions about hiring, firing or compensation could face fines as high as $300,000 for each violation.

"This clears away what in many people's mind had been a real cloud on the horizon," said Dr. Francis S. Collins, director of the National Human Genome Research Institute at the National Institutes of Health, after Congress passed the bill by an overwhelming margin. "Families with a strong history of genetic disease will have one less worry about the circumstances they find themselves in, and hooray for that."

STEVE SISNEY

The DNA Age Dr. Linda Thompson's work has already helped create the first genetics-based risk assessment test for breast cancer.

SADLY, MY ABSOLUTE RISK for cancer is much higher. As a man of European descent (my genome tells me I'm 99 percent European), my odds of getting prostate cancer by the time I'm 89 should be 1 in 4. But mine are 1 in 3. And I've got higher risk for other types of cancer as well, like a 10 percent chance of getting colorectal cancer before I'm 90.

I won't lie; those numbers made me nervous. So I went to talk to Dr. Linda Thompson, who holds the Putnam City Schools Distinguished Chair in Cancer Research at OMRF.

Thompson's research played a key role in creating OncoVue, a genetic-based test to assess breast cancer risk. The test involves a spit-in-the-vial process similar to 23andMe's. But instead of looking at a half-million SNPs, OncoVue focuses on a panel of 20 to 30 regions of the DNA that have been associated with breast cancer, the ability for DNA to repair itself, and other risk factors for the disease. In conjunction with a lifestyle questionnaire, OncoVue can tell a woman her lifetime risk for developing breast cancer.

The first question Thompson asked me was, "Did they provide you with a genetic counselor?"

No, I said. She didn't much like that answer.

To use OncoVue, she explained, you must agree to talk with a genetic counselor. "They explain the risks, manage expectations and talk about what to do with the information." For someone who finds she's at an increased risk for breast cancer, the genetic counselor can help her decide whether the results warrant more frequent mammograms as opposed to, in rare instances, a preventative mastectomy.

"The data genetic tests generate are complicated, and their implications can seem frightening," Thompson told me. "Whatever the test, it's important to have some guidance."

My guide turned out to be Dr. Swapan Nath, who spends his days decoding the genome as a scientist in OMRF's Arthritis and Immunology Research Program. "Even if part of your DNA says you're likely to get cancer, there could well be another part that says you're immune," he explained.

Huh?

"You might have genes that will give you protection against cancer—or Lou Gehrig's disease or all sorts of other conditions. They just may not have been discovered yet."

In other words, "We still have a lot of work to do."

DOES THAT MAKE TODAY'S genetic tests a waste of time? No, says Prescott.

"It's going to take early adopters"—like me!—"to push the human genome out of the lab and into the mainstream." In other

THE PACKAGES FOR DNA ARE CALLED CHROMOSOMES. A LIVING ORGANISM HAS ROUGHLY 5 FEET OF COMPACTED DNA WITHIN THE NUCLEUS OF EACH CELL, AND THIS GENETIC MATERIAL IS WOUND UP INTO 23 PAIRS OF STRANDS LIKE COILED ROPE—CHROMOSOMES—THAT TAKE THE SHAPE OF AN X.

words, I am playing a small role in the genetics revolution that is fast upon us.

"I predict that personalized medicine, based on genomic testing, will be commonplace within a generation," Prescott says. "As better genetic information becomes available, the test results you receive will become more informative. And useful."

Some day in the not-too-distant future, he says, doctors will be able to look at your genome and know that for your high blood pressure, a certain class of statin drugs won't work. So instead of, say, prescribing Lipitor, a so-called natural statin, your physician will give you a prescription for Zocor, a synthetic statin.

"There will be no more one-size-fits-all medicine," Prescott says. "Marketing and advertising campaigns will drop out of the picture. Instead, it will be about what particular course of treatment works for you as an individual. Period."

In fact, we're already to that point with OncoVue and the growing number of genetics-based risk assessment tests. There's no longer a need for physicians to guess whether to prescribe the drug Tamoxifen in hopes of staving off a case of breast cancer that may never develop. With the multi-layered genetic data provided by OncoVue, they can make well-informed decisions based on a person's unique genetic make-up.

"New discoveries are being made every day, and I, for one, am excited to see what comes next," says Prescott. "OMRF is on the cutting edge of genomic research because we're confident the future health of Oklahomans and people around the world will be better for the work our scientists are doing."

Brain
Much less efficient at learning to avoid errors

Ears
Wet earwax

Heart
17.5 percent chance of heart attack by age 84, slightly less than average

Stomach
1.5 percent risk of developing stomach cancer, higher than average

Joints
8.3 percent chance of developing rheumatoid arthritis by age 94, almost double the average

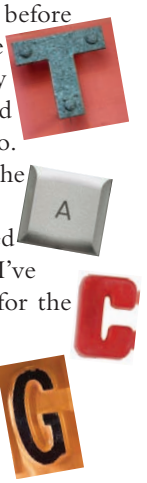
GENES ARE THE FUNCTIONAL PIECES OF DNA THAT DIRECT THE FORMATION OF PROTEINS. IN CONTRAST, SO-CALLED "JUNK" DNA ARE THOSE PORTIONS OF GENETIC MATERIAL BELIEVED TO HAVE NO FUNCTION. THE GENOME IS THE COMPLETE SEQUENCE OF DNA IN A CELL OR ORGANISM.

One of the first things I read when I started this project was an article in *The New England Journal of Medicine* about "letting the genome out of the bottle." It questioned the accuracy of tests like 23andMe's, whether they gave a clear picture of risk and just how useful a $1,000 genetic test really is.

After Googling my own genome, I found myself revisiting that article. There was nothing in my experience that led me to question the accuracy of the results (though, conversely, I have no real proof they're right either). Rather, I kept wondering about the utility of the whole experience. Despite my newfound knowledge of more than a half-million sites on my genome, I can't exactly walk into the doctor's office tomorrow, slap down a printout of my test and say, "Fix me." Still, that day might not be so far off.

Besides, the utility I've found in my genetic information is less about what's on the test and more about what the testing stirred up. Even before I received my results, even before I put my saliva in an envelope and mailed it off, I became more conscious of my health than ever before. I'm old enough not to believe myself immortal, but I'm still young enough (and who among us is not?) to shudder at a future that could deliver malignant tumors, heart disease and rapid memory loss.

The truth is, receiving results that showed an increased risk of cancer didn't exactly make my day, but I had the same risk before I'd ever heard of 23andMe. Testing or no, there's a chance I've inherited cancer genes from both sides of my family tree. Jack Martin, my maternal grandfather, is still alive and kicking after facing down prostate cancer a few years ago. Velda Lee Elwell Nevill, my dad's sister, wasn't so lucky; she beat thyroid cancer the first time, but not the second.



More than anything, the testing experience has served as a wake-up call. Whatever my risk for various diseases, I've resolved to do what I can now to keep myself healthy for the future.

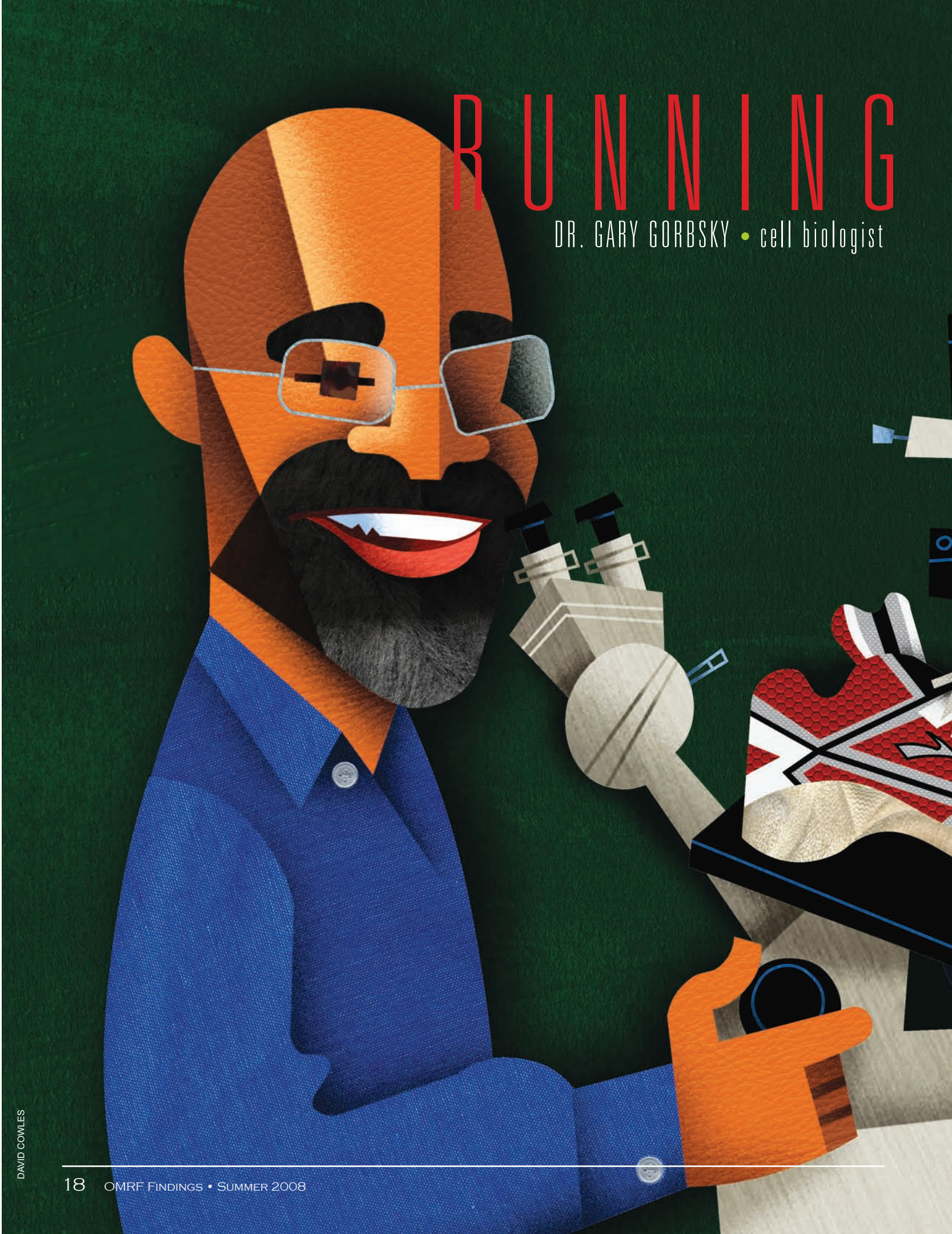
Since starting this project, I've begun watching my diet and joined a gym. That regimen has helped me lose a little more than 15 pounds. I've still got a ways to go before I'm a model of fitness, but I can assure you of one thing: There's not a banana out there that can keep up with me on the elliptical trainer. OMRF

JOHN CLANTON

Family Matters Jerry (left), Laura, Harry and Greg Elwell

RUNNING

DR. GARY GORBSKY • cell biologist



DAVID COWLES

MAN

I was a javelin thrower on the high school track team until our school moved to a league where they didn't have that event. My older brother was on the track team, too, so I had to stay on the team just to get my ride home. That's when I started running.

I've run for exercise off and on all through my life since then.

Maybe two years ago, a little after I turned 50, I joined a health club. I think it was a fear of getting old; I wanted to try to stave that off as long as possible.

Lately, I've been running six days a week, mostly on the treadmill. I run probably 30 miles a week.

On Saturdays, I meet up with another cell biologist, and we'll run about 10 miles. Then we sit around, drink coffee and shoot the breeze afterwards.

Sometimes we talk science when we're running. Sometimes, I just want to forget about everything.

I did my first half-marathon in February in Austin. There was so much going on—bands at every corner, tons of enthusiastic people. It was the first time I'd ever participated in a huge race like that. It was great.

I've run two more since then. The most recent one was the Oklahoma City Memorial Half-Marathon. I ran a personal best—1:41:20—and came in fourth in my age division. I was pleasantly surprised.

There's probably a marathon in my future. But as a scientist I work pretty long hours, so the idea of running practice 20-milers is a little daunting.

Exercise increases efficiency in the other parts of my life. It clears my mind and helps me think better.

I sleep better, too.

This spring, my lab manager ran a half-marathon along with his dad. We've sort of egged each other on.

I don't use an iPod. Once in a while, I'll take a radio and listen to NPR.

When you meet another person who's a runner, you immediately have a connection. You can talk about training experiences, racing experiences, what motivates you, what funny experiences you've had. I really like being able to say, Yes, I'm a runner.

Even if my sons don't run with me, I want them to see that I value exercising and keeping active. I don't care what they do in terms of physical activity, so long as they stay physically fit.

Retired running shoes are usually what I wear to work. I like the colorful ones. Just not fluorescent orange and yellow together.

A LOOK BACK

Deoxyribonucleic acid, or DNA, has been around for as long as life itself. Yet it wasn't until 1953 that a pair of scientists—an ex-physicist and a former ornithology student—walked into the Eagle pub in Cambridge, England, and announced that they "had found the secret of life." In fact, what they'd done was discover the structure of DNA. For a chance at an OMRF tee, can you name at least one of the scientists? Send your guesses to findings@omrf.org or call 405-271-7213.

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