

WINTER/SPRING 2008

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SEE INSIDE
HIS STOMACH!



YOU WON'T BELIEVE
YOUR EYES

AMAZING TRUE STORY

THE STRANGE
CASE OF

TOM

LITTLE



HE HASN'T SWALLOWED
IN MORE THAN 60 YEARS!





what will your legacy be?

Byron and Kathy Strawn turned a lifetime together into a legacy of hope and discovery for others. Their generous bequest supports the development of ground-breaking new treatments for Alzheimer's disease. Consider leaving a gift to OMRF in your will. Your gift can help fund the discoveries of tomorrow.



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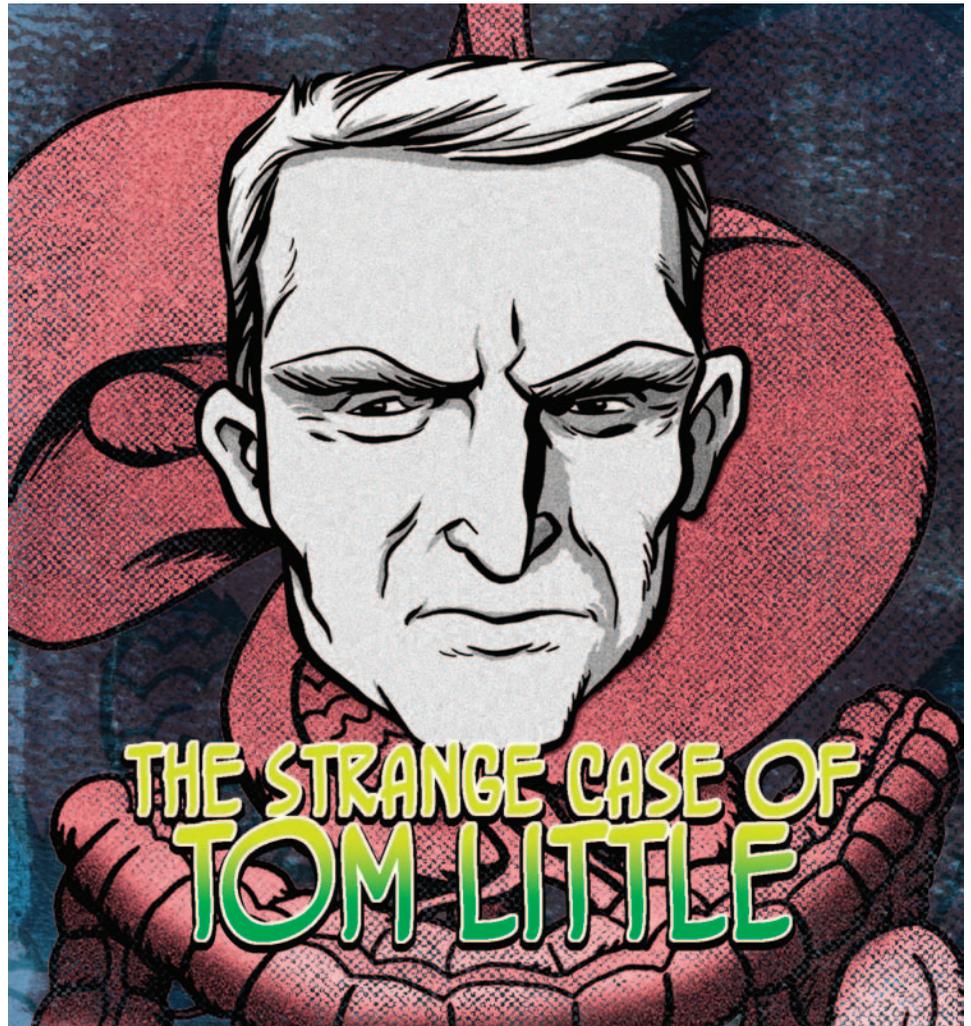
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Chartered in 1946, OMRF is an independent, nonprofit biomedical research institute dedicated to understanding and developing more effective treatments for human disease. Its scientists focus on such critical research areas as Alzheimer's disease, cancer,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



A United Way Partner Agency



10 A freak accident sealed Tom Little's esophagus. But his service as a research volunteer taught OMRF scientists volumes about human digestion

PRESIDENT'S LETTER

04 Happy Endings

DIALOGUE

05 Slam Dunk

DISPATCHES

06 An Alzheimer's Vaccine?

07 In the Genes

08 Stealing Science

09 Of Note; Grants

FEATURES

COVER STORY 10 The Man With a Hole in his Stomach

FIRST PERSON

19 Family Matters

Happy Endings

Rayna DuBose came to say thank you. And thank you and thank you and thank you.

In February, the subject of our last *Findings* cover story paid OMRF a visit. The 24-year-old Virginian had never set foot in our labs before. But make no mistake; this was a homecoming.

“OMRF, the scientists and doctors—it’s good to meet the people who helped save me,” Rayna told an auditorium packed with OMRF employees. “I just wanted to say thank you. I can’t say it enough.”

In the spring of 2002, Rayna, then a burgeoning star on the Virginia Tech University women’s basketball team, contracted bacterial meningitis. Then sepsis, a deadly blood infection, took hold. Rayna slipped into a coma, and her physicians didn’t know whether she’d ever emerge. She had a heart attack, her vital organs began to shut down, and gangrene set in, turning her extremities completely black.

“The doctors tried everything,” she said. Yet the standard courses of treatment—respirators, fluids, antibiotics—all failed. The prognosis was grim; sepsis kills about 250,000 Americans each year, and it is the leading killer in the country’s intensive care units. “Pretty much, I was dead. Then they gave me Xigris, and I came back to life.”

Approved by the Food and Drug Administration just months before, Xigris is a synthetic version of a human protein. The drug has its roots in discoveries made at OMRF by Drs. Chuck Esmon and Fletcher Taylor.

The drug saved Rayna’s life, but prolonged loss of circulation forced the amputation of her hands and feet. “My lowest point



was when my doctors, parents and friends told me they’d have to amputate,” she said. “I cried for five minutes, then I sucked it up and said, ‘Let’s do this.’”

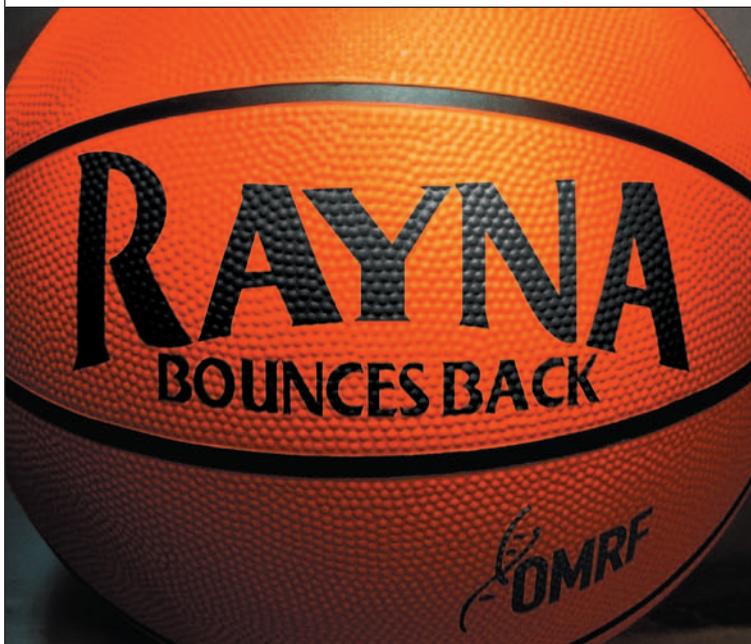
She attacked her rehabilitation with the fiery determination of an athlete, and today most who meet her can’t tell she’s walking on prosthetic legs. Little more than a year after the surgery, she returned to Virginia Tech. And this past summer, she earned her degree.

After the presentation, dozens of OMRF employees lined up to thank Rayna for coming to OMRF, for sharing her story, and for inspiring anyone who’s faced an obstacle that seemed too big to overcome. Among those employees was Chuck Esmon. “When Fletch and I started working on this project, our fondest hope was that it might actually help people. It’s great to see that hope come to fruition in someone special like Rayna. Her spirit is contagious.”

Rayna’s story is remarkable and touching, and her visit to OMRF served as a poignant reminder of our mission: helping people live, longer healthier lives. Rayna is the living embodiment of that mission. Her very presence explained—in a way words cannot—why we do what we do.

When it comes right down to it, Rayna shouldn’t be thanking us. We should be thanking her.

Stephen M. Fuscott



Nothing but Net

YOU TRULY OUTDID YOURSELVES on the fall 2007 issue of *Findings*. Your brilliant story, “The Comeback Kid,” brought me to tears. As the mother of college sons, my heart broke for Rayna DuBose, her family and the challenges she faced—and will face in the future. But the fact that she survived at all is due in large part to the contributions made to medical science by Chuck Esmon and Fletcher Taylor. Thanks to them and organizations like OMRF, Rayna’s story is triumphant instead of tragic.

ELISSA CROCKER
OKLAHOMA CITY

I WAS PROFOUNDLY MOVED by Rayna Dubose’s powerful, inspiring and life-affirming story. She is quite remarkable and a testament to the unbeatable combination of a good drug and a good attitude! Thank you for the extraordinary service that OMRF continues to provide day-in, day-out.

LINDA P. LAMBERT
OKLAHOMA CITY

WHEN FINDINGS HITS MY DESK, I know what awaits me within its pages—insightful, intriguing and, often times, moving stories that reach beyond the technical to find the humanity that propels all scientific research. The most recent issue of *Findings* is no exception. Beyond the eye-catching design and the quality writing throughout, Adam Cohen’s story, “The Comeback Kid,” stands out as remarkable, not just for its prose but for its message. Cohen shows

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.

the reality and emotion of how scientific exploration is bettering the world and the people around us. It’s another excellent story from a publication and an organization known for excellence.

ADAM CALAWAY
ARDMORE

MAKING GRANDMA PROUD

I ENJOY READING FINDINGS and about the new discoveries at OMRF. My granddaughter, Heather Rice, graduated with honors from OU in May and is now attending Harvard University where she is furthering her education in medical research. I believe it was her involvement with OMRF as a Fleming Scholar that spurred her interest in finding cures for diseases. I’m just a proud grandmother!

EMILY SPAHN
WATONGA

Crusader

I thought you might appreciate a poem I’ve written honoring Dr. Jordan Tang for his nationally known research on Alzheimer’s disease. Dr. Tang deserves all the credit that he can receive. I expect that in the future his research will save many lives.

*He fights the fog in brains
chasing magic scissors to cut
the plaque in minds.*

*He put off his treatment for cancer
risking self that others might live
as he campaigned and pleaded for cash
life blood to develop an Alzheimer’s drug.*

*Even as his tumor grew
he found 50 million in seed money.*

*Only then did he yield to his doctors
to battle non-Hodgkins lymphoma
six treatments of R-CHOP chemo
that took his hair yet killed the beast.*

*Somehow he finds time to make art
oil on canvas stereo paintings
like “Sculpture Park at Night”
an explosion of blues and reds*

*crafted like his medical models
presented
in three
dimensions.*

ROBERT FERRIER
NORMAN

*The author was nominated to serve as Oklahoma’s
Poet Laureate in 2006.*



An Alzheimer's Vaccine?

Could a vaccine be the key to stopping Alzheimer's disease? A new research study from OMRF shows that immunization could offer a way to blunt or even prevent the deadly, memory-robbing disease.

OMRF scientists immunized Alzheimer's mice with a protein believed to play a key role in the disease-causing process. The animals that received the vaccination showed a significant reduction in the build-up of protein plaques that, when present in the brain for long periods of time, are believed to cause the cell death, memory loss and neurological dysfunction characteristic of Alzheimer's. The immunized mice also showed better cognitive performance than controls that had not received the vaccine.

"These results are extremely exciting," says **Dr. Jordan Tang**, who led the study. "They certainly show that this vaccination approach warrants additional investigation as a therapy for Alzheimer's disease." The research appears in *The Journal of the Federation of American Societies for Experimental Biology*.

Tang and his team at OMRF previously had identified the cutting enzyme (known as memapsin 2) that creates the protein fragments believed to be the culprit behind Alzheimer's. In the current study, they used mice that had been genetically engineered to develop symptoms of Alzheimer's, then immunized the animals with memapsin 2.

"What we saw is that the mice immunized with memapsin 2 developed 35 percent fewer plaques than their non-vaccinated counterparts," says Tang, who holds the J.G. Puterbaugh Chair in Medical Research. "Those immunized mice also performed better than control mice in tests designed to assess their cognitive function."

Tang's work with memapsin 2 also has led to the creation of an experimental drug to treat Alzheimer's disease. That drug, which works by inhibiting the cutting enzyme, recently completed the first phase of human clinical trials.

Tang emphasized that the vaccine approach should be viewed as a supplement to—rather than substitute for—the experimental inhibitor and other treatments currently in development for the illness. "Alzheimer's is a complicated, multi-faceted disease. As with illnesses like cancer and heart disease, Alzheimer's demands that we develop many different approaches to combat it. We cannot rely on a 'one-size-fits-all' strategy, because what works in one patient will not necessarily work in another."

A vaccination approach—getting the immune system to clean up the plaques—has been considered a promising way to tackle the disease, but its success has been limited. In 2002, for example, the pharmaceutical company Elan halted trials of a different vaccine after 15 patients suffered swelling of the central nervous system.

OMRF President Stephen Prescott is hopeful that Tang's work will avoid the pitfalls that beset Elan's vaccine. "This vaccination stimulates the immune system more gently than previous Alzheimer's vaccines, so we are optimistic about its prospects going forward. Once again, Dr. Tang has found an innovative way to make inroads against a devastating and poorly understood disease."

The next step, says Tang, will be to progress the work to the point that it can be tested in humans. "There currently is no effective treatment for Alzheimer's disease, so we must explore every possible option to find a way to stop it."

ALZHEIMER'S DISEASE IS A NEUROLOGICAL DISORDER CHARACTERIZED BY SLOW, PROGRESSIVE MEMORY LOSS DUE TO THE GRADUAL DEATH OF BRAIN CELLS. ACCORDING TO THE ALZHEIMER'S ASSOCIATION, THE DISEASE AFFECTS MORE THAN **5 MILLION AMERICANS**, INCLUDING APPROXIMATELY 77,000 OKLAHOMANS AND NEARLY HALF THE NATION'S POPULATION OVER THE AGE OF 85.



In the Genes

An international consortium of scientists led by OMRF's **Dr. John Harley** has identified 13 genes linked to lupus, a devastating autoimmune disease that affects as many as 2 million Americans and 15 million people worldwide. The disease can strike any part of the body and has no known cure.

The researchers studied the DNA of 720 women with lupus and 2,337 women without lupus. They scanned the entire genome of each subject, in each case examining 317,000 separate locations on chromosomes where a single unit of DNA, or genetic material, may vary from one person to the next. The goal was to identify those regions on the chromosome linked to the disease.

The scientists confirmed these results in another independent set of 1,846 women with lupus and 1,896 women without lupus. OMRF scientific staff analyzed all 3,671 specimens in their laboratories in Oklahoma City. The findings appear in two related articles in the February edition of the journal *Nature Genetics*.

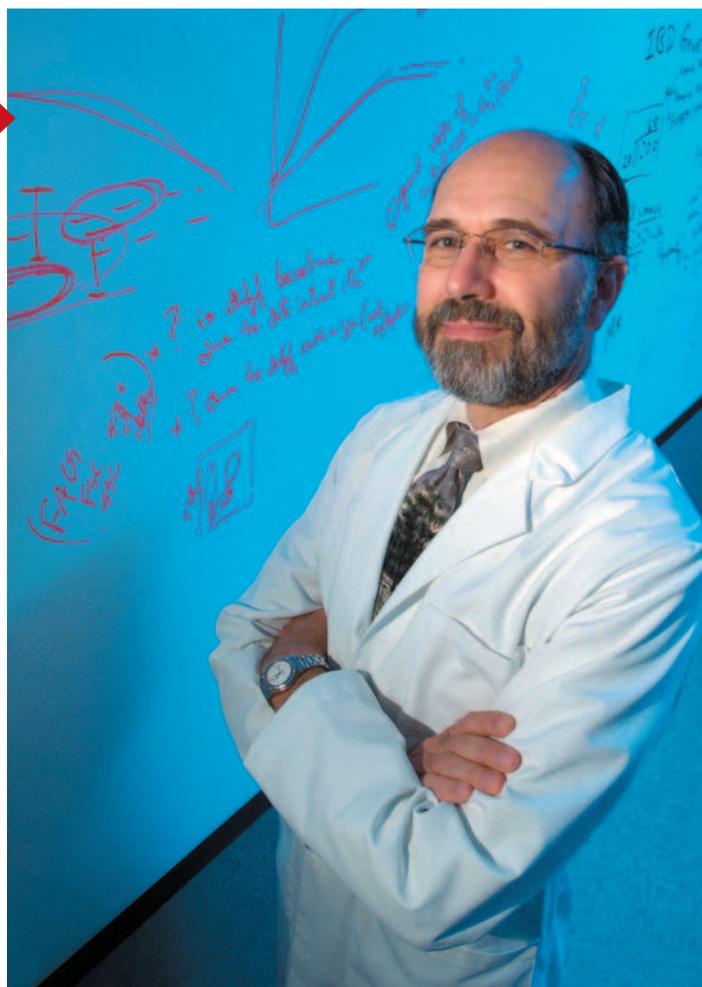
In the new study, the scientists discovered a link with three genes previously thought unconnected to lupus. They also identified a link between the disease and a DNA region once believed to be “junk DNA”—a piece of genetic material without a known function. In addition, they uncovered further evidence of association for genes previously linked to lupus and other autoimmune diseases.

“Lupus is a decimating illness,” Harley says. “As clinical investigators, our goal is to reduce the burden of suffering caused by this disease. These findings have opened many new doors, and we’re excited to investigate what’s behind each of them.”

A second *Nature Genetics* paper in the same issue by OMRF's **Dr. Swapan Nath** focused specifically on one gene on chromosome 16 and its relationship to lupus. Using data gathered from more than 4,000 patients, Nath and his colleagues determined that the gene likely plays a role in the disease and is present in 25 to 30 percent of lupus patients.

“This was an extraordinary effort, involving 150 scientists and staff and nearly 7,000 research volunteers,” says Harley. “The results promise to transform our understanding of lupus and to accelerate the day when safe and effective therapies are available.”

If you're interested in volunteering for future lupus studies at OMRF, call 888-OK-LUPUS (888-655-8787). Both healthy individuals and those with a lupus diagnosis are encouraged to participate.



Stealing Science

Much like the world of college essays, scientific journals are too often faced with authors trying to publish someone else's work as their own.

For OMRF's **Dr. Jonathan Wren** the issue hit home as part of his duties as an editor for the journal *Bioinformatics*, when a reviewer recognized a paper as having been published in another journal. Today, Wren has transformed that experience into a tool for sniffing out research retractions.

"I got to thinking about the nature of plagiarism and what could be done about it in the context of science," says Wren, whose research at OMRF specializes in bioinformatics and data analysis. Wren knew that his former mentor, University of Texas Southwestern professor Dr. Harold Garner, had created a program called eTBLAST. Garner developed the program to identify other researchers working on similar topics. But, says Wren, "After he developed eTBLAST, he used it to select student papers and make sure they weren't plagiarized."

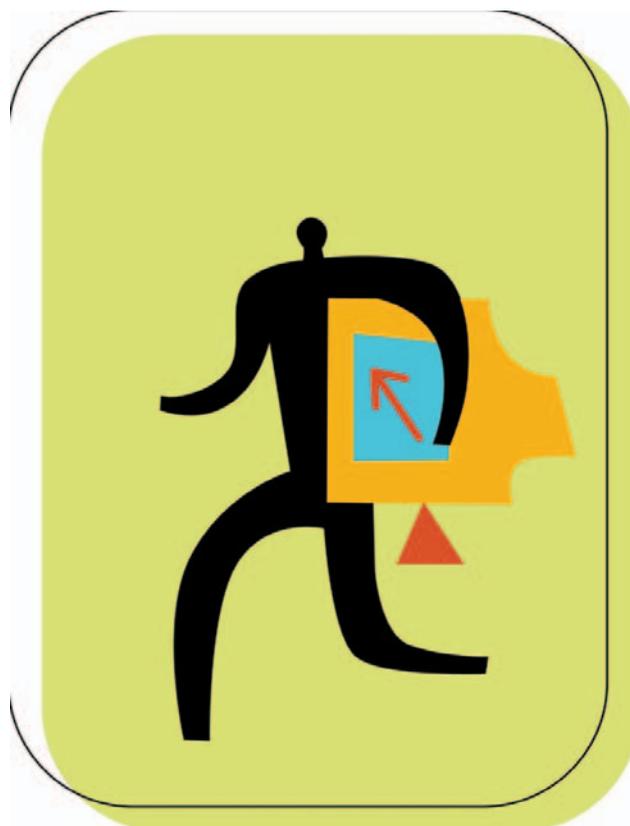
In light of his experience with the journal, Wren suggested a wider reach for the program: putting it to use at scientific journals to detect plagiarism among researchers. Wren saw a natural testing ground, a place where plagiarism could essentially hide in plain sight—Medline, the National Library of Medicine's database of more than 10 million scientific articles.

"Rather than just providing answers about whether one paper is plagiarized, eTBLAST could put us on the path of asking some more interesting questions about plagiarism," Wren says. "Who does it? Is it something many do occasionally or a few do frequently? Do people plagiarize more at some point in their careers, such as before tenure reviews or grant deadlines? Is plagiarism on the rise?"

DR. JONATHAN WREN FOUND THAT MORE THAN 70,000 SCIENTIFIC PUBLICATIONS BORE MULTIPLE SIMILARITIES TO OTHER PUBLISHED WORKS.

The answer was shocking: In a wide-ranging scan of scientific periodicals, Wren and Garner used eTBLAST and found that more than 70,000 research articles and abstracts bore multiple similarities to other published work. The results of their study appear in the journal *Nature*.

According to Wren, eTBLAST uses a more advanced algorithm than plagiarism detectors used by universities. "It not only looks for blocks of similar text, but it also examines sentence structure, looking at things like associations and proximity with other words." As powerful as eTBLAST is, Wren emphasized that it is not a judge and jury. "Any papers the program identifies still need to be examined by human eyes to determine if the plagiarism is real or just a coincidence."



Dr. José Alberola-Ila, *Role of GATA-3 during CD4/CD8 Lineage Commitment*, National Institute of Allergy and Infectious Diseases

Dr. Mark Coggeshall, *Molecular and Immunologic Analysis of the Pathobiology of Anthrax*, National Institute of Allergy and Infectious Diseases

Dr. Patrick Gaffney, *Replication of SLE Susceptibility Genes from Genome Wide Association Studies*, Lupus Foundation of Minnesota; *Comprehensive Candidate Pathway Analysis in SLE*, National Institute of Allergy and Infectious Diseases

Dr. Gary Gorbsky, *Chromosome Movement in Prometaphase*, National Institute of General Medical Sciences

Dr. John Harley, *Lupus Family Registry and Repository*, National Heart, Lung and Blood Institute; *Genetic Association in Sjögren's Syndrome*, National Institute of Dental and Craniofacial Research

Dr. Judith James, *Native American Research Centers for Health*, Chickasaw Nation; *Oklahoma Rheumatic Disease Research Core Centers*, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Dr. Paul Kincade, *Replenishment of the Innate Immune System*, National Institute of Allergy and Infectious Diseases

Dr. Shinichiro Kurosawa, *Shiga-Toxins: Pre-clinical Animal Model Development and Therapeutic Testing*, National Institute of Allergy and Infectious Diseases

Dr. Florea Lupu, *EPCR, TAFI as Regulators of PMN/Endothelial Interaction*, National Institute of General Medical Sciences

Dr. Kathy Moser, *SLE Genetics Initiative (SLEGEN III)*, Alliance for Lupus Research; *Isolating the Human SLE Susceptibility Gene on Chromosome 16Q13*, Arthritis Foundation; *Genetic Mapping of the Insulin-like Growth Factor Receptor Precursor (IGF-IR) Gene in Human SLE*, Lupus Foundation of Minnesota

Dr. Stephen Prescott, *M.D./Ph.D. Fellowship Program*, Presbyterian Health Foundation

Dr. Philip Silverman, *Organization of Plasmid TRA Proteins*, National Science Foundation

Dr. Linda Thompson, *Immune Function and Biodefense in Children, Elderly and Immunocompromised Populations*, National Institutes of Health

Grants Awarded September-December, 2007

OF NOTE



Dr. Judith James

The American College of Rheumatology awarded Dr. Judith James the Edmund L. Dubois Memorial Achievement Award. The annual prize, presented at the world's largest gathering of rheumatologists, is given to an outstanding investigator in the field of lupus research.



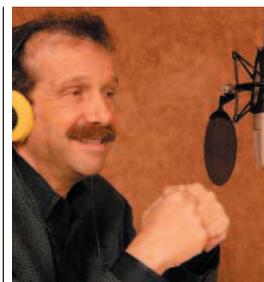
John Snodgrass

At the semiannual board meeting Nov. 14, OMRF honored John Snodgrass of Ardmore and Ann Alspaugh and Galen Robbins, both of Oklahoma City, for their service on the foundation's board. All three have served as OMRF directors for 25 years.



Dr. Robert Floyd

Dr. Robert Floyd received the 2007 Discovery Award at the annual meeting of the Society for Free Radical Biology and Medicine in Washington, DC. Floyd was saluted for his study of antioxidants and their role in disease formation, prevention and treatment.



Dr. Zorba Paster

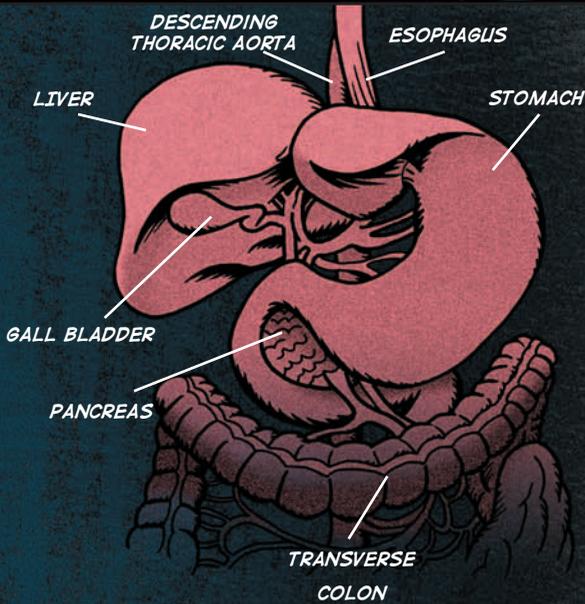
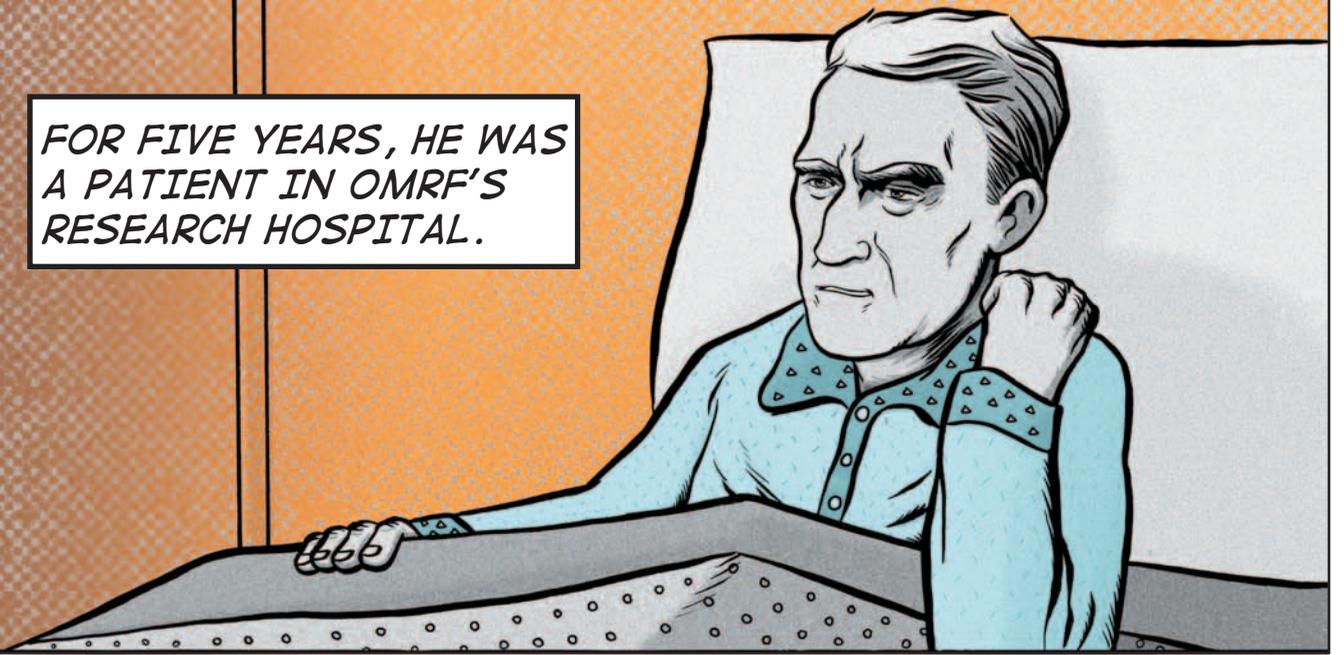
In November, OMRF and KGOU Public Radio sponsored a public talk by national radio personality and family physician Dr. Zorba Paster. The event took place at OMRF, where Paster fielded questions about health and medical news from the audience.



Dr. Michael Anderson

The Presbyterian Health Foundation awarded OMRF a \$500,000 grant to provide start-up funds for a new researcher. "This grant will develop new opportunities at OMRF and in Oklahoma," says Presbyterian Health Foundation President Michael Anderson.

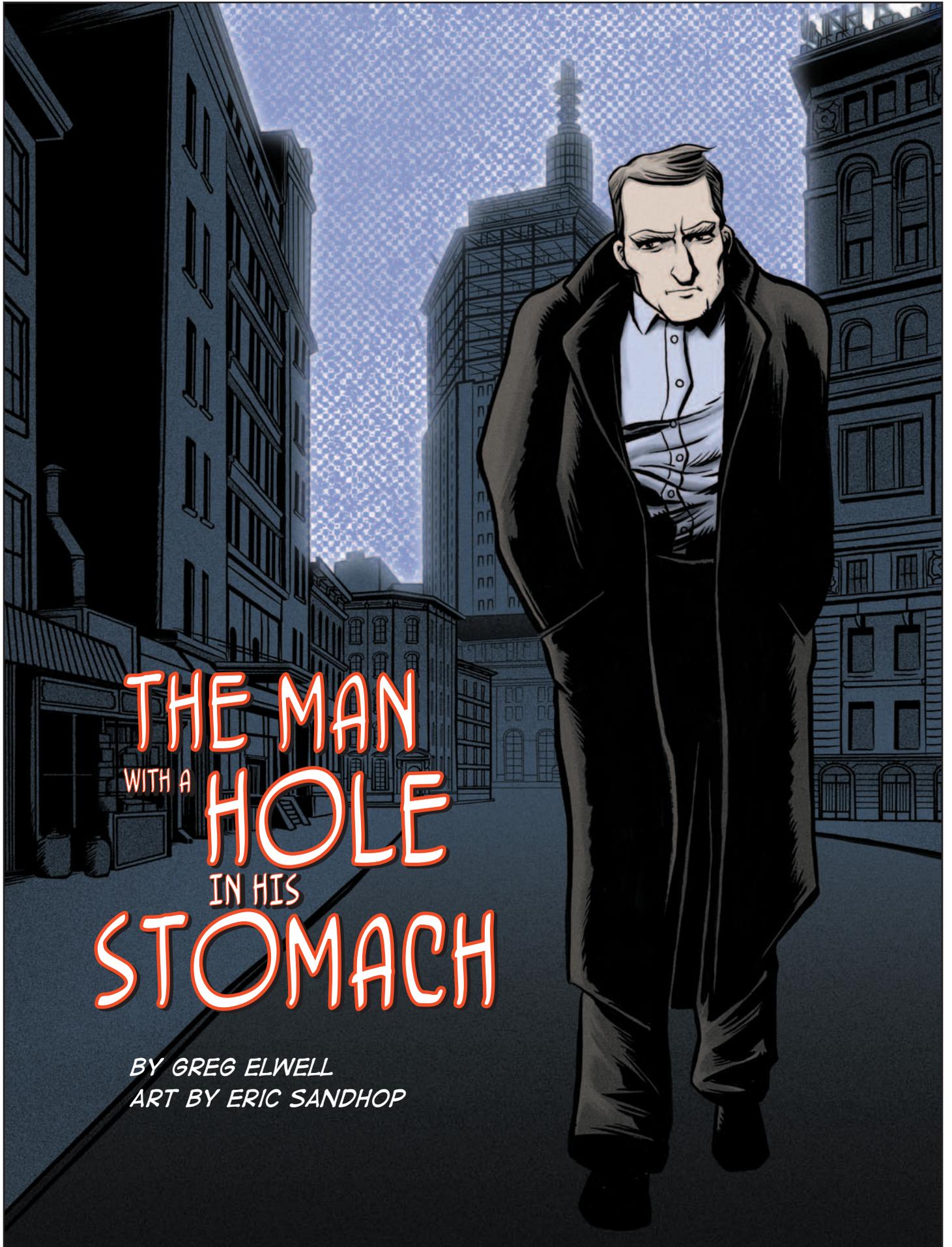
FOR FIVE YEARS, HE WAS A PATIENT IN OMRF'S RESEARCH HOSPITAL.



HE WAS A LIVING TEXTBOOK OF THE HUMAN DIGESTIVE SYSTEM.



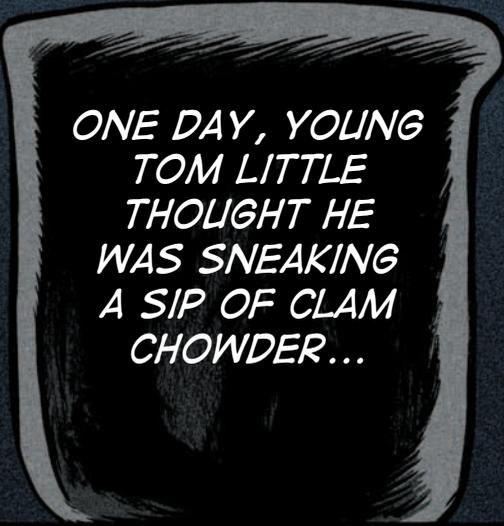
MEET TOM LITTLE...



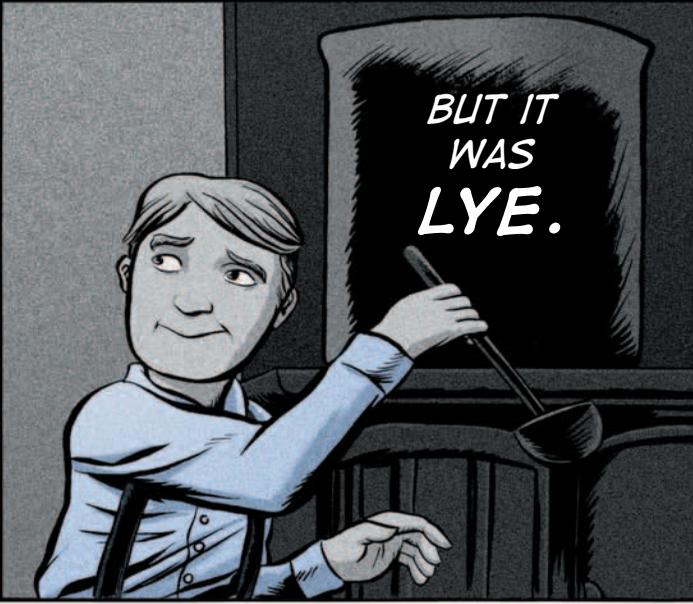
THE MAN
WITH A
HOLE
IN HIS
STOMACH

BY GREG ELWELL
ART BY ERIC SANDHOP

THE YEAR WAS 1894...



ONE DAY, YOUNG
TOM LITTLE
THOUGHT HE
WAS SNEAKING
A SIP OF CLAM
CHOWDER...



BUT IT
WAS
LYE.



PAIN!

IT WAS THE LAST
TIME HE WOULD
SWALLOW
**ANYTHING
EVER AGAIN!**

Born on the outskirts of New York City in 1885, Tom Little was the third of four children in an Irish family that was long on discipline and short on affection. The family wasn't rich, but as a mechanic, his father brought in a stable income and no one went hungry.

Tom was an athletic child and gregarious, to boot. He wasn't much of a student, but his parents didn't particularly care, so long as he did what he was told at home. And he usually did.

But one cold day, 9-year-old Tom slipped beneath his mother's radar, snatching a ladle of hot liquid simmering on the stove. So involved was the youngster in gulping what he thought was soup that he didn't catch the scent of lye as he held the ladle to his lips. The caustic chemical went down the hatch, searing his esophagus as it went.

Doctors were able to keep his esophagus open for a few days, yet scar tissue eventually closed the passageway, leaving Tom's physicians no choice but to cut a hole in the wall of his stomach. The opening was about an inch-and-a-half across, and with a sealed esophagus, it was the only way Tom could eat. Still, old habits die hard, and for the rest of his life Tom would chew his food thoroughly and savor the flavors before pushing it down a funnel, through a plastic tube and into the hole in his stomach.

Now you might think it would be impossible to keep a hole in your side secret, but Tom was terribly ashamed of being different, and he focused on keeping his malady to himself. He told few about his accident and allowed no one but his family to see him eat. Each day, before he left home, he wrapped his abdomen with gauze, which kept the leaking of blood and stomach acid to a minimum. Tom's condition, one of his doctors later wrote, "constituted a constant threat to his ideal of physical integrity and fitness, as well as his desire to 'belong,' and he took elaborate pains to keep it secret."

Sometimes, though, belonging came at a steep price.

At age 17, during a rough-and-tumble football game with friends,

Tom was pinned at the bottom of a pile. There, the tip of the ball drove into his gut, herniating the stomach lining. A physician later described the injury: "In the early hours of the following morning he was awakened by an excruciating pain throughout the lower portion of the abdomen, and, examining his stomach for the first time, he found a large portion of

his [stomach lining] protruding through his opening."

Tom went to the doctor—something he had done his best to avoid since his initial injury—and learned that surgeons would have to enlarge the opening in his stomach. While the procedure relieved his pain, the larger incision made it more difficult to contain the contents of his stomach—and to disguise his condition.

Although Tom held the doctors who saved his life at age 9 in high esteem, he was suspect of other physicians. Even the doctors he first encountered while receiving outpatient care were, in Tom's opinion, too curt and less interested in him than his "medical oddity." Less than a year after his football injury, Tom visited a hospital seeking some sort of belt to help contain his stomach contents. But, in Tom's eyes, the doctor was more interested in poking around his midsection than in helping him.

So Tom stomped out of the hospital mid-visit. It would be 36 years before he would allow another physician to examine his stomach.

Tom was only 10 years old when he dropped out of school to take a job as a plumber's assistant. It would pave the way for a life of menial positions, from stage manager to sewer maintenance worker.

Tom lived with his sister until age 28, when he married a woman a few years his senior. She was a widow who already had three children. "I could have gotten plenty of younger ones, but I was afraid a younger woman might eventually get disgusted with the way I feed," he said.

Caring for his family was hard, and work for an uneducated man like Tom was too often scarce—and temporary. The Great Depression only worsened matters. When even able-bodied men could scarcely find a job, who would consider hiring a man with a hole in his stomach to perform physical labor? That made concealing his condition a necessity.

It was in 1939, while digging ditches, that the strain of Tom's work became too much. Tightly fitted gauze around his stomach began to chafe, ripping at the edges of the incision and causing it to bleed continuously. The loss of blood left him unable to work, and only after his wife begged and pleaded did Tom, then 53 years old, finally consent to see a doctor.

Physicians fixed the problem but caused another. In the process of stopping the bleeding, they were forced to remove some of Tom's stomach lining; this resulted in further leakage of stomach acid and food from the hole.

With this added burden of concealment, "honest" work proved even harder to come by. An extremely proud man, Tom wasn't about to take charity. When his physicians approached him about the possibility of becoming a research subject, Tom was hardly enthused by the prospect. But times were tight. "If I couldn't support my family, I'd as soon jump off the end of the dock," he said.

Still, it took doctors two years to convince Tom to allow doctors to study him. It happened only after a young physician named Stewart Wolf was able to win Tom's trust. That trust would make the two fast friends—and ultimately bring Tom to OMRF.



TOM DISTRUSTED DOCTORS...



Dr. Stewart Wolf earned his medical degree from Johns Hopkins University in 1938, then headed north to train at Cornell-New York Hospital. While a resident at Cornell, Wolf met Tom Little. Immediately, the young doctor understood that Tom could provide a unique window into how the human digestive system functions. And he could do so while helping Tom.

That left but one obstacle: Tom.

"It took four months to create adequate rapport with the patient," Wolf later wrote in his book, "Human Gastric Function," which was largely devoted to Tom's case. Tom, it seemed, was too proud to accept payment "merely" for serving as a research subject. So Wolf proposed a compromise. In the mornings, Tom would come to the lab without eating breakfast and submit to a series of experiments and observations, all with the goal of improving his quality of life. In the afternoons, he would work as an assistant and handyman in the lab.

The arrangement would help Tom preserve his self-respect. It would also give him the job security that had eluded him in his working life. "Finally," wrote Wolf, who died in 2006 at the age of 91, "Tom was convinced of our interest in and solicitude for his welfare, both physical and economic." He accepted the deal.

For a decade, Tom reported to Cornell every weekday. Wolf was particularly interested in how the mind and body interacted, and he focused on the ways in which Tom's stomach changed with his emotions. During World War II, Wolf put Tom's case on hold to run a 1,000-bed hospital in the southwest Pacific. Wolf's colleagues

continued to work with Tom in his absence, and when the young physician returned, he and Tom picked up where they'd left off.

In 1953, Wolf joined OMRF as its first supervisor of clinical medicine. The foundation's newly opened research hospital represented a perfect site for Wolf to continue to care for Tom while also exploring his unique physiology. So for the remainder of Tom's life, he made pilgrimages to OMRF twice a year.

The relationship between the two men was complex, both intellectually and emotionally. Though younger by nearly 30 years, Wolf took on the role of elder in the relationship, acting in some ways as a father figure and confessor to his patient. "Stewart felt responsible for Tom," recalls Dr. Kent Braden, a retired Oklahoma City neurosurgeon who served as a resident under Wolf. "They were close friends in addition to their working relationship."

Wolf cared for his patient with a compassion and thoroughness that Tom had never experienced. Yet Wolf's work as a researcher required him to delve into the effects of trauma on Tom's digestive system. To this end, Wolf stepped out of his role of caregiver.

"Dr. Wolf was quite an actor," says Dr. Bill Hood, a physician who worked with Wolf at OMRF. "They kind of had a love-hate relationship. Tom was devoted to Dr. Wolf, but then he'd get furious with him because he'd purposely antagonize him or make

him depressed, just to see what would happen to the lining of the stomach.”

Wolf would play-act, with Tom’s stomach as the audience. When enraged, Tom’s stomach lining would become a deep red and tighten. When relaxed, it was pink and wrinkled. If frightened, Tom’s stomach would turn white. And if depressed, digestion slowed to a near stop.

The studies, says OMRF President Stephen Prescott, might seem unorthodox by today’s standards. “But that was a different era. Researchers did not have the sophisticated research tools they do now. For instance, scientists didn’t have the luxury of longitudinal, blinded tests involving hundreds or thousands of subjects. And their methodologies were often more direct, more oriented toward answering questions about basic human physiology than improving outcomes for an individual patient.”

Still, even a half-century ago, the research was not without controversy. Wolf subjected Tom’s stomach to a variety of different “insults”—in addition to behavior designed to evoke different emotional reactions, he also experimented with different foods and even mild physical trauma—to gauge his body’s reaction. When Wolf presented his findings on the effects of stress on gastric acid production to the Gastroenterological Society, some members balked because the research represented but a single case. Yet the groundbreaking basic observations Wolf made proved invaluable.

“He was so successful that people don’t even think about it

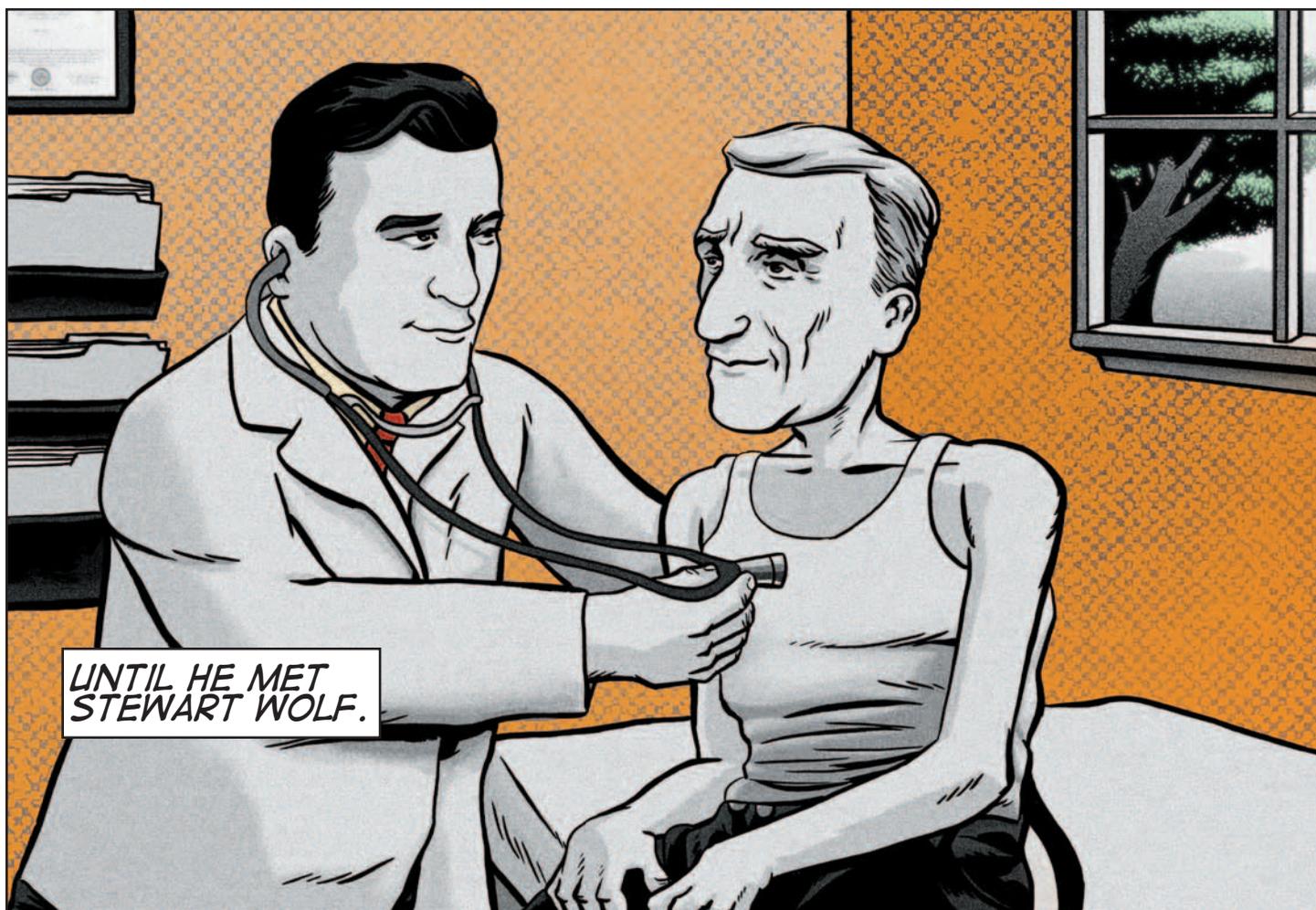
anymore,” says Prescott. “Psychosomatic medicine holds so many implications for common disorders, and we all accept that emotions have a bearing on physical conditions now. But it wasn’t that way back then.”

Dr. Kent Braden had heard Wolf’s stories about Tom, but the tales took on a human face during his gastroenterology rotation in OMRF’s research hospital. “When I was a resident, Dr. Wolf brought Tom into the research hospital, and I took care of him while he was there,” Braden says. Little was suffering from inflammation around the site of his incision, but the discomfort did not dampen his gregariousness.

“He was Irish (like me) and very talkative, so we visited a great deal,” Braden remembers. He told the young physician many tales, including how he came to have a hole in his stomach. “What I remember most was his story-telling. He was a lot of fun.”

Braden and the OMRF staff were able to reduce the inflammation, and Tom was discharged after a few days. While Tom seemed grateful for his care at OMRF, says Braden, it was something else that cemented the bond between doctor and patient. “I earned his confidence when I was able to find the black pipe tobacco he smoked, and I kept him supplied with it while he was here.”

While Tom created a human legacy with the OMRF staff, his larger contribution lives on in the research seeds he sowed.

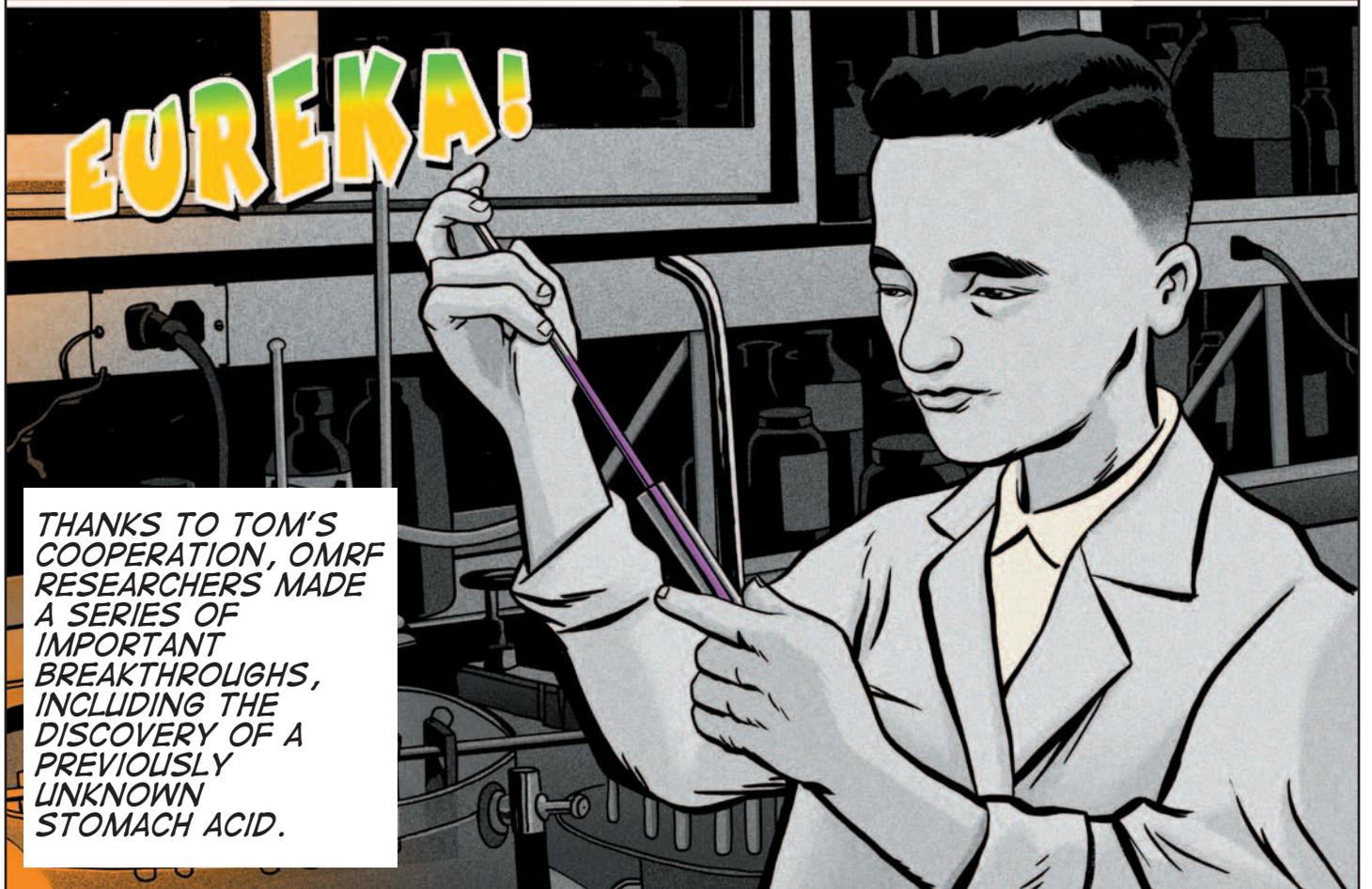




TOM, I'VE FOUND THAT IF YOU'RE ANGRY, IT INTERFERES WITH YOUR STOMACH'S ABILITY TO ABSORB FOOD.

RELAX, MY FRIEND.

THE WINDOW INTO HIS STOMACH PROVIDED A NEW WINDOW INTO HOW THE DIGESTIVE SYSTEM WORKS.



EUREKA!

THANKS TO TOM'S COOPERATION, OMRF RESEARCHERS MADE A SERIES OF IMPORTANT BREAKTHROUGHS, INCLUDING THE DISCOVERY OF A PREVIOUSLY UNKNOWN STOMACH ACID.



Dr. Ranwell Caputto used data from Wolf's experiments with Little to discover an enzyme that turns creatine into creatinine, a major step forward in the study of muscular dystrophy. With gastric juices from Little's stomach, Dr. Jordan Tang isolated the protein-digesting enzyme gastricsin—only the second gastric enzyme ever discovered. That breakthrough proved an important building block in the understanding of human digestive processes. The enzyme also became the basis of a diagnostic test for stomach cancer.

Using biological samples contributed by Little, Tang and OMRF's Dr. Raul Trucco were also the first to crystallize human gastric juices using a resin column technique developed by Dr. Wolf's group at OMRF. That crystallization allowed separation of the fluids and, thus, enables researchers for the first time to study the elements and their roles in digestion individually.

"You'd be hard-pressed in this day and age to find a single research subject whose contributions made as much of an impact as Tom Little's," says Prescott. "It's a remarkable legacy."

At the age of 73, his 5-ft. 4-in. frame wasted to 90 pounds, Tom died from cancer and kidney complications.

He'd spent most of his life trying to be unremarkable. Trying to blend in. Throughout his years working with Wolf, he'd insisted on anonymity. In Wolf's many publications, at his patient's behest, the physician referred to his subject only as "Tom."

Grudgingly, Tom finally agreed to pull back the veil. But it would have to be on his terms.

Tom agreed that upon his death, Wolf could share the details of Tom's 73 years with *Time* magazine. He would tell the story of the accident and the unique life that followed. Of the unlikely friendship that formed between patient and physician, researcher and subject. Of the bounty of knowledge this relationship yielded.

The story ran on Jan. 12, 1959. Only in the final sentence of the article did *Time* reveal Little's surname. And at last, millions of readers understood what Dr. Stewart Wolf had known for so long—that Tom Little's life was anything but unremarkable. 

ONLY AFTER TOM DIED DID HE ALLOW THE WORLD TO LEARN HIS NAME - IN A STORY ABOUT HIS LIFE THAT MILLIONS READ.



FAMILY MATTERS

DR. KATHY MOSER



When I pick a movie, it's always a mystery, because I love having something to solve. It's no wonder Sjögren's syndrome fascinates me. **I imagined I'd be a ballerina or a piano teacher. But in a college immunology class, I found a real-life mystery to tackle when I learned how much can go wrong in the immune system.** Most people study a disease because someone they love has it or died from it. It was purely by chance that Sjögren's turned out to run in my family. My grandmother was the first to be diagnosed. **A journal article I read described my mother's health issues completely, and her physicians agreed—she also had Sjögren's.** My mother is a classic example of Sjögren's. The dry eyes and mouth, severe nerve and gastrointestinal problems, asthma and ongoing infections. The things she deals with just to survive are almost unbearable. **Sjögren's typically strikes women around age 55. While that's still a few years away for me and my daughter, our family history will certainly keep me vigilant.** Only three or four clinics like our Sjögren's clinic at OMRF exist. No matter how much research money we have, we must have patients. Without them, the research can't happen. **For the sake of all the patients out there, I hope Sjögren's is not a mystery that takes 20 years to solve.**

In Sjögren's syndrome, the immune system gradually attacks and destroys the salivary glands and nervous system. Common symptoms include dry eyes, dry mouth, severe fatigue, arthritis, short-term memory loss and kidney problems. **To participate in the Sjögren's research study, call 405-271-2574 or 800-605-7447.**

a LOOK BACK back

What's in a name? Not much, we thought, until we recently discovered that one of OMRF's pre-eminent scientists started work here in the same year (1957) that General Foods launched a drink that shared his name. For a chance at an OMRF tee, can you name that orange-flavored beverage? Send your guesses to findings@omrf.org or call 405-271-7213.



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