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FEATURES

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There are people who suffer from rare diseases. And then there's **Sydney Rutz**, who has a genetic condition never before identified—until a group of OMRF scientists took on her case.

COMING TO AMERICA

As **Jordan Tang** toiled in a dead-end job in Taiwan's Fertilizer Bureau, he dreamt of traveling to the U.S. to study. But would the government let him leave? And even if it did, how would he pay for the education he so dearly desired?

ALSO IN THIS ISSUE

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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 cancer, diseases of aging, lupus and cardiovascular disease.

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COVER PHOTO: Brett Deering

Fountain of Youth?

One researcher tests if a diabetes drug can also be an anti-aging pill

For Dr. Ben Miller, staying active has always been "a no-brainer."

"I was raised to exercise," says the OMRF researcher. "I have always taken that as part of who I am." Miller took up cycling in the sixth grade. Late in college, he began competing, which he continues today, almost three decades later. He still gets up before dawn most mornings to ride, and he estimates he spends 10 to 15 hours each week on a bike.

When he's finished working out, Miller takes another ride—from his home in the Mesta Park neighborhood of Oklahoma City to OMRF. At the foundation, he devotes the balance of his days to researching how the human body ages. Specifically, he's focused on increasing people's healthspans, that period we're able to live without disease and disability.

"It's long been known that exercise slows the aging process," says Miller, "but there's a large portion of the population who are not going to exercise." For that group, "we're going to have to come up with alternatives."

In the lab, Miller studies the gamut of subjects, from gym rats to those who are completely sedentary. His goal is to find the most effective ways to blunt the toll of growing older in these divergent groups.

Recently, that work has centered on metformin, the world's most-prescribed diabetes drug. Scientists have thought the medication might also change how healthy people age. Experiments suggested that in addition to reducing blood sugar, it can cut inflammation and produce other beneficial cellular changes.

To test metformin's potential as an anti-aging pill, Miller and his research team recruited 53 sedentary men and women in their 60s, each with at least one risk factor for diabetes. The scientists assigned half of them to take metformin, while giving the others placebo. All of the volunteers then underwent a 12-week exercise program, regularly jogging on treadmills or riding stationary bikes.

The placebo group showed better aerobic fitness and blood-sugar control at the end of the study. Those who took metformin had fewer gains in both fitness and insulin sensitivity. In effect, the drug blocked normal exercise-related gains.

"Metformin does not appear to be the silver bullet for aging some thought it might be," says Miller. The findings turned heads in the world of aging research and garnered a story in *The New York Times*. But while the work showed metformin "didn't seem to play well with exercise," Miller believes the drug might still hold potential for less active people.

Going forward, he has received a grant to examine how metformin use impacts non-exercisers. Curiously, preliminary data suggests it might work best in those who are least metabolically healthy. "Now," he says, "we have to directly test this."

In the meantime, as he nears his own 50th birthday, Miller doesn't have to look far to find a role model for healthy aging. "Whenever I get together with my parents, my mom and I still try to go for a mountain bike ride together, and she's 72."

Dr. Ben Miller's Tips for Healthy Aging

1. **Remain active and physically fit**
2. **Stay socially and mentally engaged**
3. **Practice a diet of moderation (like the Mediterranean diet) and avoid extremes**
4. **Pick your parents well**

"None of these are rocket science," says Miller. "Everyone has heard them before; it's just that most people don't do them. So, we search for a pill."

Dr. Michael Beckstead is investigating whether one of the brain's naturally occurring chemicals plays a role in Alzheimer's disease.

Charting a New Course Against Alzheimer's

Just about every one of us knows someone who's been struck by Alzheimer's disease. In the U.S., nearly 6 million people suffer from the deadly, memory-robbing illness. Worldwide, the number is estimated at 44 million.

"It's the most commonly diagnosed neurodegenerative disorder," says OMRF's Dr. Michael Beckstead. And with a rapidly aging population, experts predict disease rates could triple by 2050.

Beckstead has spent two decades studying dopamine, a chemical responsible for voluntary movement and the perception of reward in the brain. "Dopamine is what makes you want to get off the couch and enjoy activities," he says.

He utilizes experimental models to examine what can happen when things go wrong in the brain with neurons that interact with dopamine. In the past, his work has largely focused on Parkinson's disease—when too little dopamine is present—and drug addiction, where there is too much of the chemical.

But since joining OMRF from the University of Texas Health Science Center at San Antonio in 2017, he's also begun investigating whether the chemical plays a role in Alzheimer's. "Although dopamine has never been studied in this context, we have a lot of evidence to suggest it's involved, especially in the initial stages of disease," he says.

Using mice that have been genetically engineered to develop a condition resembling Alzheimer's, Beckstead and his research team are looking for functional changes in the rodents' dopamine cells early in the disease process. In people, alterations in these cells can spark a variety of behavioral changes similar to those seen in the initial phases of Alzheimer's. "Before memory loss and cognitive impairment, patients show symptoms that include depression, trouble sleeping and apathy," Beckstead says.

In the mice, Beckstead's initial goal will be to determine whether dopamine changes accompany disease onset. "It's a simple question that nobody has ever asked." The reason, he says, is that "we've only had the technology to do this work for a few years."

The project has spurred the interest of the National Institute on Aging, which recently awarded Beckstead funding for the project. If successful, the work could plot a new path to develop a drug or other interventions to halt the progression of Alzheimer's in humans.

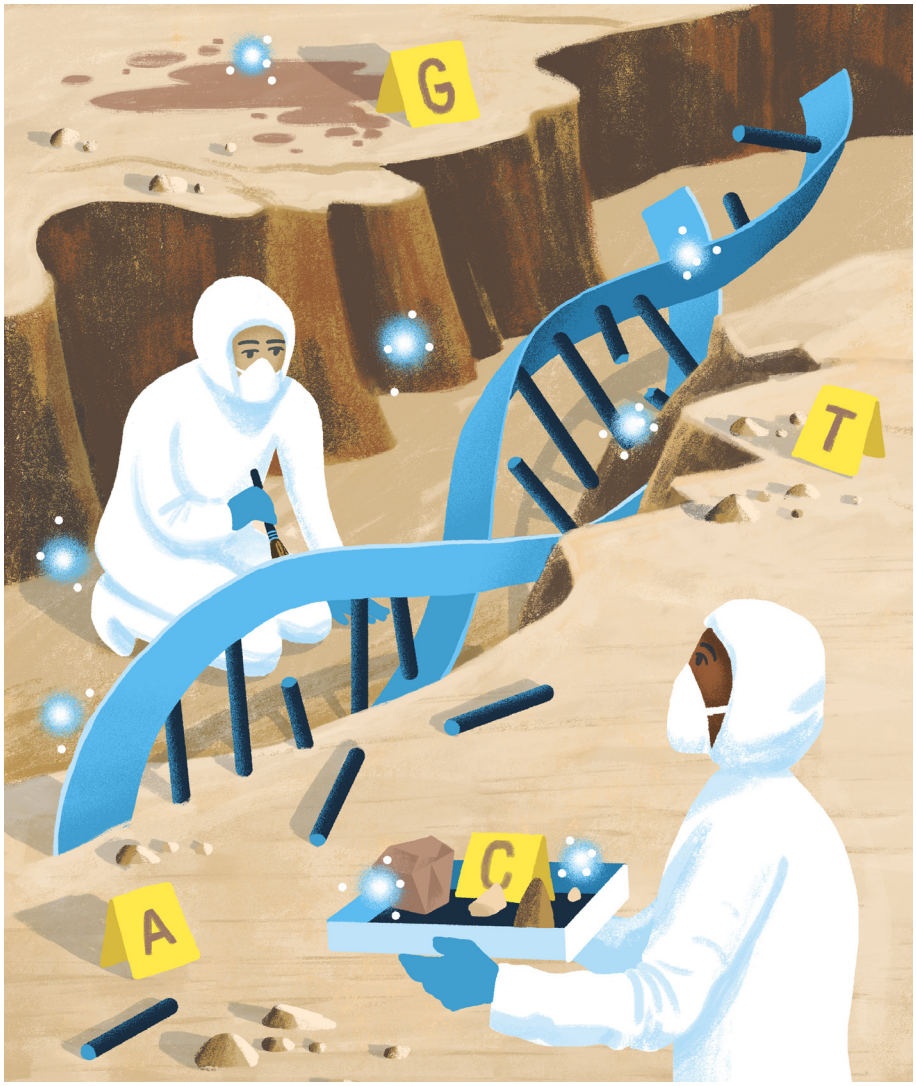
Despite the failure or abandonment of more than 100 experimental Alzheimer's drugs, Beckstead remains optimistic about the ultimate prospects for new therapies. "I'm a firm believer that treatments for a lot of brain diseases will come from targeting specific cellular pathways like this one."

CSI: Oklahoma

Dear Dr. Prescott,

It seems police are now routinely solving "cold cases" by using DNA evidence from crimes committed long ago. How is it they're still able to use DNA that's been around for a decade or more? Doesn't it go bad?

Regina Buckley
Bala Cynwyd, PA



Dr. Prescott Prescribes

Like all biological materials, human DNA has a shelf life. But that expiration date varies wildly, depending on storage conditions. The keys are protecting it from heat, water, sunlight and oxygen.

For example, if a body remains exposed to the elements, its DNA will be useful for testing only for a few weeks. On the other hand, if it's buried a few feet below ground, it will last 1,000 years or more. And if it's kept cold and protected, it can last much, much longer: A sample of Neanderthal DNA found in a Belgian cave dates back 100,000 years.

Since long before the advent of DNA sequencing technology, law enforcement investigators have been collecting biological evidence from crime scenes in ways that would preserve it. For example, that means gathering dry samples (hair, dried blood or other bodily fluids, cigarette butts with traces of saliva) and placing them in separate containers. This avoids cross-contamination with other samples and, when stored in cool, dry spaces, prevents spoliation caused by the growth of organisms like mold or mildew.

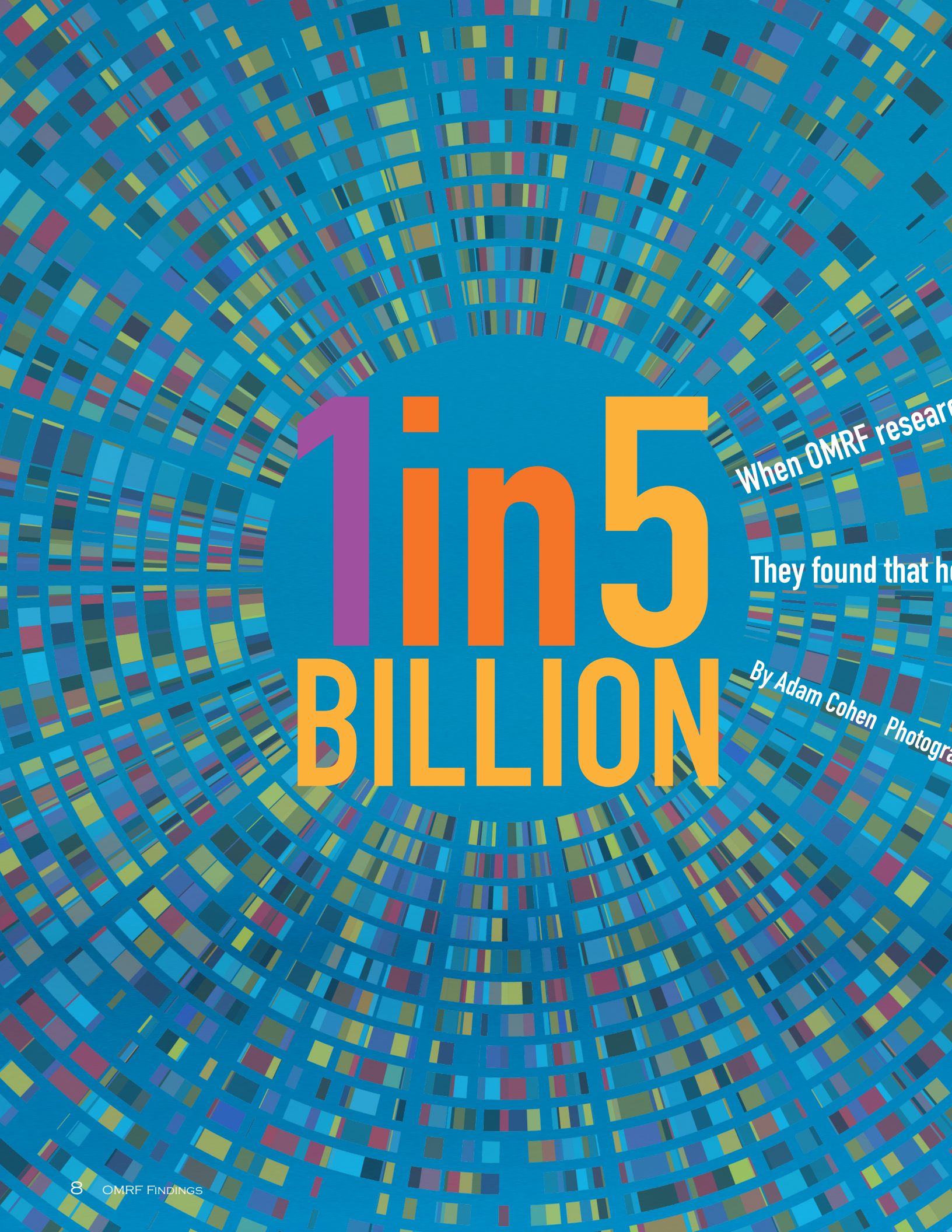
With certain pieces of wet evidence, forensics experts dry the samples, then store them in a similar way. For tissue or fluids, they're typically collected in vials and stored in refrigerators or freezers.

Obviously, sample storage procedures vary among police departments and have changed over time. Still, so long as those methods keep samples dry, relatively cool, out of the sunlight and uncontaminated by other substances, that evidence should remain "good" for DNA testing longer than anyone reading this will be around.

Science is like a sport, and as a lab head, you're the coach. You have to see the big picture. Then you let your team set goals, encourage them, and help them find ways to succeed.

Dr. Linda Thompson

An immunology researcher, Dr. Thompson holds the Putnam City Schools Distinguished Chair in Cancer Research at OMRF. She is also a die-hard University of Michigan and Oklahoma City Thunder fan.



When OMRF researc

They found that h

By Adam Cohen Photogra

chers sequenced Sydney Rutz's DNA...

er genes were unlike anyone's anywhere

aphs by Brett Deering

The nurse placed Mary Rutz's newborn daughter in her arms. Mary gazed lovingly at this being she'd just brought into the world and thought, "She looks like a tiny doll."

Sydney Rutz had arrived after a full nine months growing inside her mother. It had been an uneventful pregnancy. But as the birth date neared, Mary could feel that the child in her belly was not going to be as big as her two older daughters, each of whom had tipped the scales at roughly 8 pounds when they came into the world.

Still, Mary was surprised when she cradled Sydney against her chest for the first time. Four pounds, 9 ounces, the nurse said. Her head was more or less the size of Mary's fist.

Mary stands almost 6 feet tall. She wasn't used to a child so small, so seemingly fragile. At night, when she'd take Sydney into bed with her, she worried she might crush her young daughter. "She made me nervous," remembers Mary. "She was just so little."

Infant clothes didn't fit Sydney. Even preemie outfits proved too big. So, for several months, Mary dressed her doll-sized baby in doll clothes.

At regular check-ups, Sydney's doctor plotted her growth. At first, she charted out at the 5th percentile. But even that would prove a high-water mark; within her first year, she dropped off the chart altogether.

"She'll catch up," people said. When she didn't, Sydney's endocrinologist prescribed growth hormones for her. Mary, a physical therapy assistant, administered shots each night while her daughter slept. They seemed to have no effect.

Despite her diminutive stature, Sydney otherwise appeared to be progressing normally. She started walking and talking. She showed no cognitive delays.

But right before her third birthday, Mary noticed a "little bitty glint" in her daughter's eye. "The next day, her pupil was completely white." Within another day, Sydney's left eye had clouded over as well. Mary drove Sydney from their home in Yukon to the Dean McGee Eye Institute in Oklahoma City, where doctors performed surgeries to remove the cataracts from each of her eyes.

Soon after, doctors found a weak spot in her lower abdomen with tissue bulging through. They diagnosed her with an inguinal hernia, and another surgery followed.

As Sydney's bones and skeleton developed, they did so in a way that differed from other children. Her arms grew disproportionately long, as did her forehead and ears, while her jaw remained foreshortened. The bones in her spine twisted at an extreme angle, causing severe scoliosis. Her sternum began to protrude, causing a protrusion that Mary, affectionately, began referring to as "chicken chest."

For several years, doctors treated Sydney's symptoms individually. But when she was 6, Sydney's primary physician referred her to Dr. Klaas Wierenga, who at the time held the McLaughlin Family Chair in Genetics at the University of Oklahoma College of Medicine. As a pediatric geneticist, Wierenga specializes in diagnosing and treating young patients affected by rare conditions caused by mutations—changes or abnormalities—in the DNA.

Wierenga suspected that Sydney was just such a patient. But her symptoms didn't align with any known genetic disease.

During the course of Sydney's treatment, a blood test revealed she not only had issues with her bones, but she also had an enzyme problem. Specifically, it showed that a class of enzymes known as lysosomes weren't doing their jobs in her body.

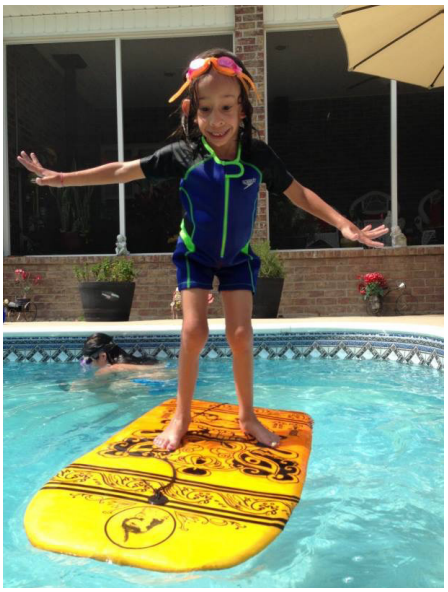
Lysosomes function as cellular garbage disposals, breaking down proteins the body no longer needs. When these lysosomes fail to do their job, it causes an accumulation of cellular junk. Over time, this build-up can interfere with proper cellular function and, ultimately, prove toxic.

Fortunately, Sydney's lysosomes seemed to be functioning just well enough to keep her healthy. Nonetheless, the test results led physicians to diagnose her with one of the almost 50 conditions known as lysosomal storage diseases, which are all characterized by an abnormal accrual of proteins in the body. Specifically, Sydney's doctors determined she suffered from an illness known as mucolipidosis, a severe congenital disease that often proves fatal.

Wierenga, though, wasn't so sure. In mucolipidosis, patients all show mutations in one of two specific

Sydney Rutz was born at a little more than half the weight of her older sisters—and her growth trailed off from there.

"I love watching Sydney come into my class every morning," said one teacher. "She's always smiling."



genes. But when he tested Sydney, those genes appeared normal. So, he reached out to OMRF's Dr. Patrick Gaffney for help.

A geneticist who holds the J.G. Puterbaugh Chair in Medical Research at OMRF, Gaffney had established a "next-generation" DNA sequencing facility in his laboratory. With an array of sophisticated equipment, he and his research team could perform analyses of people's genes that were far more sophisticated than those available through standard laboratory or commercial testing facilities. Specifically, using a technique known as exome sequencing, Gaffney could isolate and analyze that small part of the genome—less than 2 percent of the three billion nucleotides or "letters" that make up DNA—that tells cells how to build all the proteins in the body. It's in this precious real estate that errors leading to genetic diseases typically occur.

"Up until exome sequencing, you'd have to do other, less specific tests," says Gaffney. Even when results pointed to a genetic culprit, physicians often could not be sure. "But with the advent of exome sequencing, you could conclusively identify mutations."

When Gaffney performed an exome sequence on DNA from Sydney's blood, he confirmed Wierenga's findings. She didn't have the mutation for mucolipidosis.

However, she did have a mutation in another gene. In fact, she had two mutations in that same gene.

Known as MBTPS1, the gene was known to be involved with lysosome function. But, here, Sydney's bones were clearly affected, too.

When Gaffney and Wierenga searched the medical literature, they could find no cases of a patient with a disruption in this gene. Sydney, it seemed, was unique.

Wherever the Rutz family went, people would gravitate toward Sydney. In stores, other shoppers—and even workers—would follow her up and down the aisles, stealing surreptitious glances at this toddler-sized elementary schooler.

Children were often less subtle. They'd unabashedly stare at her. Or they'd approach her and blurt out a question: "You know you're small?"

Sydney typically resorted to humor to deal with the situation. "I had no idea," she'd say with a grin. If they asked about her protruding chest, she'd respond, "Oh, that? That's my heart." When their eyes widened, she'd let them in on the joke. "I was just messing with you," she'd say.

Testing had shown that Sydney's bones lacked density, making them prone to breakage. Her hips are compressed, and she wears a back brace to counter the curvature of her spine. "She can't run or jump," says Mary. Instead of a full jaw bone, "she has just a sliver."

Still, Mary balanced Sydney's special needs with the desire for her daughter to have a normal childhood. Sydney attended Yukon Public Schools, which assigned her an individual classroom

aide. Sydney walked and carried a backpack when she could—"She doesn't like to use a rolling one," says Mary—but sometimes pain forced her to use a wheelchair.

One day, Sydney's teacher took Mary aside. "I love watching her come into my class every morning," the teacher said. "Lots of kids show up grouchy, complaining. But here's Sydney, a child who has a real reason to mope, and she's always smiling."

Even though Sydney's orthopedist urged her not to play sports, Mary eventually succumbed to her daughter's pleas and allowed her to try gymnastics. "But I had to quit because of my back," says Sydney. "It hurt too much."

In spite of her physical challenges, though, Sydney was a kid surrounded by other kids. And sometimes, she'd forget about her limitations, with unfortunate results.

During a parents' night out, Mary received a frantic call. She arrived to find Sydney unable to walk: Her knee had buckled when she tried to jump. Another time, an attempted back roll off of playground equipment resulted in a fractured wrist.

The ensuing visits to the orthopedist frightened Sydney. "She'd worry he was going to say she needed surgery," says Mary. But he didn't. And, so, they soldiered on.

For Mary, it was nothing new. Two siblings had suffered from Friedreich's ataxia, a rare genetic disorder unrelated to Sydney's condition. The disease slowly robbed her brother and sister of the ability to control their limbs, to walk and, finally, even to speak. Both died in their 40s.

Still, says Mary, "In our family, you didn't say you couldn't do something." There was always a way—you just needed to find it.

That's how the Rutzes came to view Sydney's condition, too. "We don't look at her as handicapped," Mary says. "We just see her as different."

At OMRF, Sydney and her family underwent further testing, as Gaffney worked to understand what was going on within her body. He found her genetic condition resulted from a mutation in the MBTPS1 gene encoded in the DNA of her father, Jon, and another, different variation in that same gene carried by Mary. In Sydney's parents, those single variations didn't seem to affect how their bodies functioned. But, when combined in Sydney, they had profound effects.

"We thought this would be a simple project," says Dr. Lijun Xia. Instead, it took three years.

Or so it appeared. But without a deeper analysis, all Gaffney had found was an association between the genetic variation and Sydney's symptoms. While it was intriguing, this correlation fell far short of explaining what was happening on a molecular level. And without such an explanation, there could be little real hope of helping Sydney.

To get to the root of this medical mystery, Gaffney sought the help of Dr. Lijun Xia. A hematologist by training, Xia treated patients suffering from blood disorders in his native China before coming to OMRF in 1995 to focus on medical research. At OMRF, he initially studied the blood. But over time, his interests expanded. In particular, he developed expertise in the workings of a group of sugars known as glycans. These sugars seemed to play a key role in the function of lysosomes, the enzymes at the heart of Sydney's condition.

Still, Xia was going to have difficulty taking on the project. He serves as chair of OMRF's Cardiovascular Biology Research Program, where he oversees the work of more than 50 scientists and their staffs. As the Merrick Foundation Chair in Biomedical Research, he also has several National Institutes of Health grants of his own, all of which he and his research team needed to work on, and none of which had anything to do with Sydney's condition.

However, as luck would have it, a new post-doctoral fellow had recently joined Xia's lab. With a freshly minted Ph.D. from Nagoya University in Japan, Dr. Yuji Kondo needed an assignment that would allow him to get his feet wet and familiarize himself with lab operations.

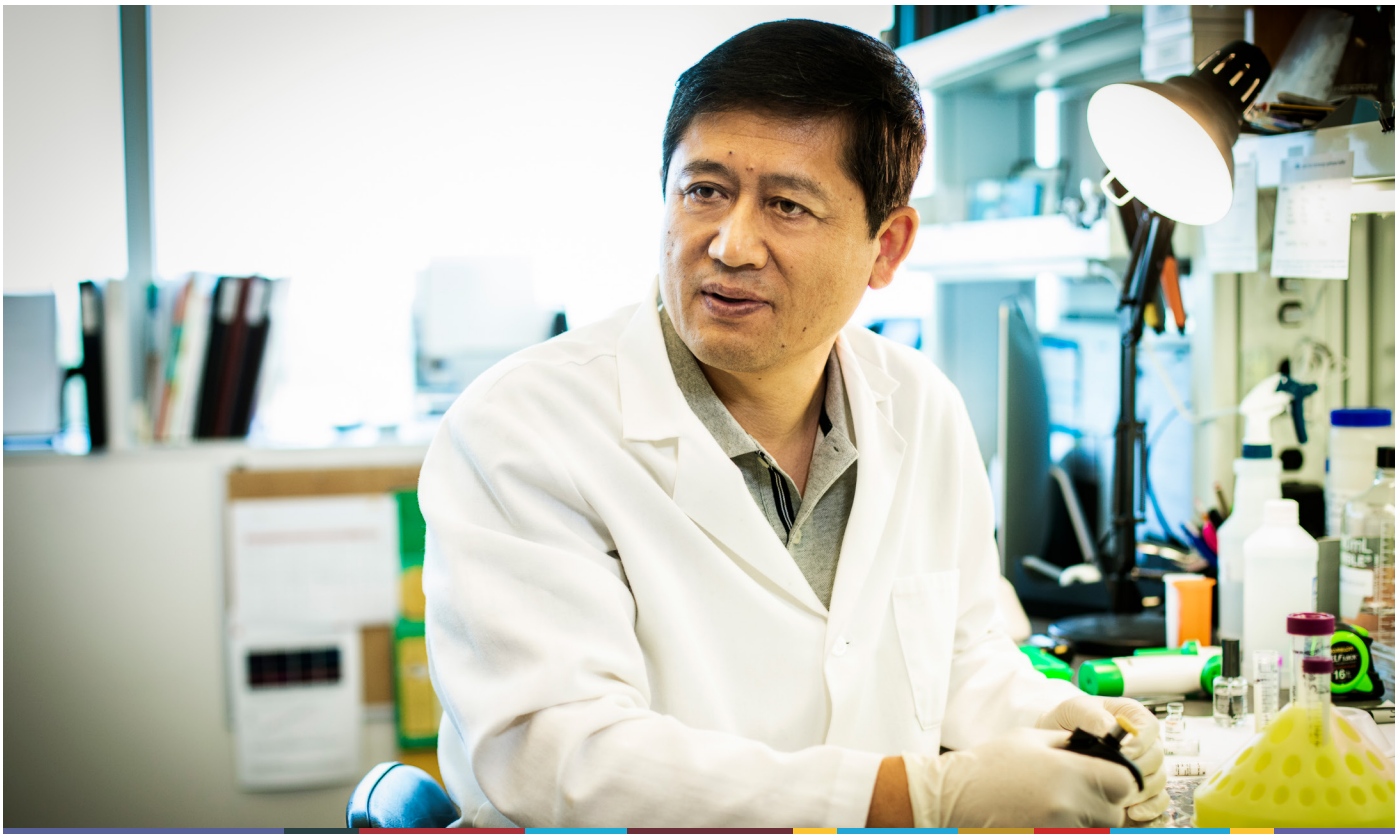
"We thought this would be a simple project," says Xia. "I estimated it would require a maximum of three months to finish." Instead, it took three years.

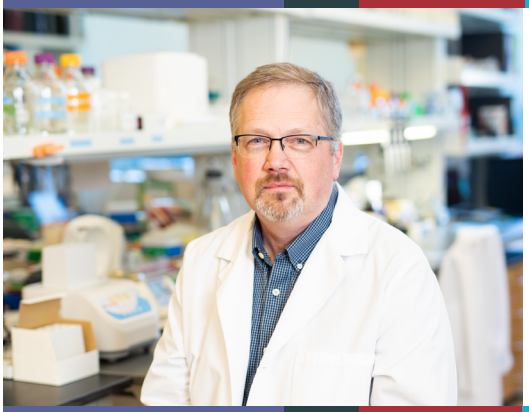
The project became more and more complex as it unfolded. Xia, Kondo and Dr. Jianxin Fu, another scientist in Xia's lab, discovered Sydney's genetic mutation had caused a failure in the cellular machinery responsible for bone growth. The malfunction centered on collagen, a protein the body creates to use as one of the building blocks for bones and connective tissues.

Sydney's cells were producing sufficient amounts of collagen, but without a properly functioning MBTPS1 gene, the protein was getting stuck where it shouldn't. As so often happens in the body, that breakdown gave birth to others.

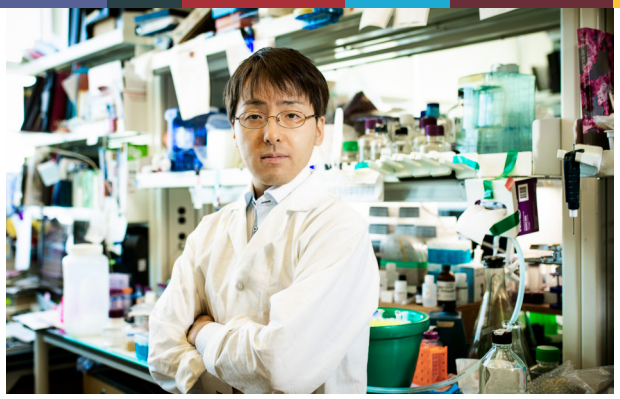
"Lack of collagen supply is an issue for bone growth, but the bigger problem is collagen accumulation," says Xia. Specifically, the build-up of proteins triggered the body's cellular garbage disposal system to kick into gear. And when it did, it not only swept away the collagen, says Xia, "but it also sends out a signal that causes the death of chondrocytes." These cells, says Xia, "are essential to bone growth."

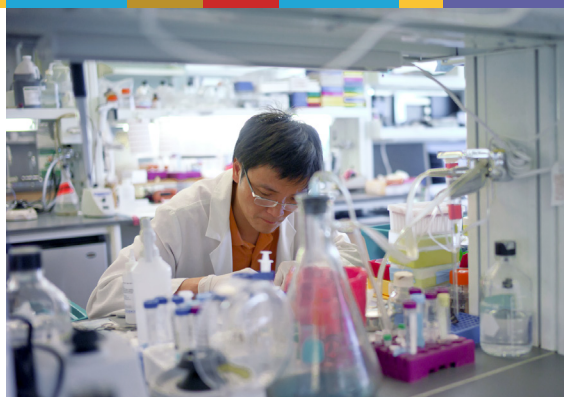
For Sydney, "at the age of 6 or so, the bones accelerated their growth," Xia says. "This made things worse." The body kicked into overdrive, producing more collagen. When excess collagen piled up, unable to reach its final destination, cellular trash collectors scooped it up—and, in the process, killed off most of her chondrocytes. "As a result, she essentially stopped growing."





The team of scientists who solved the genetic mystery at the heart of Sydney's condition (clockwise from top): Drs. Lijun Xia, Klaas Wierenga, Jianxin Fu, Yuji Kondo and Patrick Gaffney





Xia, Wierenga and Gaffney invited Mary and Sydney to OMRF to explain what they'd discovered about Sydney's condition. The science was, not surprisingly, difficult for mother and daughter to digest.

Xia attempted to make the findings more understandable by showing a snippet from a movie about a girl with a—different—rare genetic disease. While well-intentioned, the approach did not achieve the desired result; Sydney began to sob.

"I thought I was going to die," remembers Sydney, then 10.

Mary and the researchers, though, were quickly able to calm her down. They explained that while her condition made her different, nothing the scientists had found should make her worry.

In fact, they said, as far as they knew, she occupied a unique position in the world. She was the only person whose genes were this way.

"I'm special," she says.

The scientists explained that Sydney was so special they were going to write a paper about her. When it was published in the scientific journal *JCI Insight* in 2018, the paper created a new disease classification: spondyloepiphyseal dysplasia, Kondo-Fu type. (According to naming conventions for diseases, they bear the name of the first listed author on the research paper that first identified the condition. Here, because Kondo and Fu decided to share that distinction as first authors, the condition they discovered does, too.)

Sydney can't quite pronounce the name of "her" disease. "It's a mouthful," says Mary. But she's nevertheless embraced it as part of her identity.

Nowhere is that more evident than when she's playing her favorite online video game. In that world, all the other players know her simply by her username: Oneinfivebillion.

"I chose that name because I thought there were five billion people in the world, and I'm the only one with this condition," she says. "You have to own who you are."

These days, that person is 13 years old, an eighth grader at Yukon Middle School. She loves drama class and singing in the choir. Last year, she even had the chance to be in a production of Hercules, where she played the gatekeeper to the underworld.

Standing at a height of 3 feet, 10 inches, she made one-half of a memorable stage pairing. "The guy who played Hades is, like, tall," she says, giggling. "The two of us were really funny together."

She's also a long-time Girl Scout. When she attended Scout camp, her physical limitations threatened to derail her from participating in the rigorous schedule of activities until Mary came up with a solution: "I'd just pull her in a wagon when her back was giving her problems."

This past winter, she joined a school color guard team. The group performed flag ceremonies and competed with other squads. With a specially modified flag that she spun and tossed alongside her fellow team members, Sydney found the experience exhilarating. "She loved being a part of that," says Mary, "because she's never been on a team before."

Sydney understands her growth is likely at an end. But that realization in no way stunts her dreams.

"I really want to be a lawyer. Oh, and I also want to be an actress," she says. "So, maybe actressing can be a part-time job."

Sydney keeps talking, explaining that being a lawyer would let her

"yell at people." Mary, sitting nearby, cracks up. That's just Sydney being Sydney. Sassy and rambunctious. A typical teen.

It is, Mary says, what she most wants for Sydney.

"I don't want anyone to treat her any differently. I don't want her to be always scared."

Sydney is sitting beneath a sign that reads, "It's never too late to live happily ever after."

Mary looks over at her daughter and smiles. "I want her to have a full life."

For OMRF's Xia, Sydney's story is not over. "Our goal was to help. That was our motivation."

And they have helped. When Sydney's case was referred to them, she'd been given a diagnosis of mucolipidosis. That condition carried with it a dire prognosis: vision problems, diminished mental capacity and, often, death. "I looked it up," says Mary. "It was very scary."

Through their work, the researchers were able to give Sydney a correct diagnosis, one that came with far brighter prospects. Could the scientists say for certain what the coming years hold for Sydney? No. But they could honestly tell Mary that her daughter's fate, like so many of our tomorrows, would reveal itself only with time.

That wasn't all, says Xia. "Unlike many diseases, we now know its exact molecular mechanism." With that information comes the possibility of a treatment.

At OMRF, Xia has identified a compound that can reduce collagen accumulation. That compound has already been approved by the U.S. Food and Drug Administration for the treatment of another condition and is commercially available.

In laboratory experiments, they've found it decelerates collagen production and accumulation. "It may not resume the rate of normal growth," says Xia, "but it slows it down so the cells can handle it and maintain a low rate of growth."

"We don't look at Sydney as handicapped," says her mother, Mary. "We just see her as different."

Xia is now working with OMRF's Technology Ventures Department to devise a path to bring this therapeutic to patients. In addition to treating Sydney's mutation, he hopes this treatment approach will be effective on a wide range of rare skeletal disorders that stem from similar genetic variations.

Because Sydney is now a teenager, she's likely passed the point where such a therapy could stimulate bone growth. But, Xia says, it might still help her to avoid other, as-of-yet unforeseen problems down the road. "It's hard to know," Xia says, "what her future looks like."

Without a crystal ball, he says, the best hope is to continue to investigate every lead he can find. "Right now, all we know about the disease is from this one girl. This is not enough."

Using a database for rare diseases, he's identified another eight patients from around the country who might share this mutation. He is planning to contact their physicians in hopes he can gather more information from each of their cases. "Our goal is to track patients and analyze them in a systematic way. We want to learn how to diagnose them and how to manage their care."

Recently, a nurse practitioner from Broken Arrow contacted him. Her 6-year-old daughter had just been diagnosed with an MBTPS1 mutation and showed some—but not all—of the same symptoms as Sydney.

That got Xia thinking. "Even within Oklahoma, we have two patients already. And those are just the ones who've had genetic testing." How many more, he wonders, might still be out there?

For Sydney, the news that she was not the only one was, at first, a bit deflating. "But I told her to chill out," says Mary. "You'll always be the first."

Sydney's now excited to meet her genetic "twin." And, knowing there's someone out there just like her who could benefit, she now has a reason to keep donating her blood for studies. Even though she hates, hates, hates the needles.

"I'll help," she says. Then she rubs her forearm and widens her eyes for comic effect. "I just might be fashionably late for my appointment."

Additional reporting by Shari Hawkins

Jordan Tang (far right) with his parents and siblings, Shelly and Donald, at his family's home in Taipei in 1948

Coming to America

By Jordan Tang
(as told to Adam Cohen)

Dr. Jordan Tang spent more than a half-century at OMRF, where his research played a key role in understanding and developing experimental treatments for HIV/AIDS and Alzheimer's disease. Now an OMRF Distinguished Career Scientist and retired from the lab, Dr. Tang has been working on his memoirs.

In this excerpt, he shares the story of his journey from Taiwan to America—and Oklahoma.

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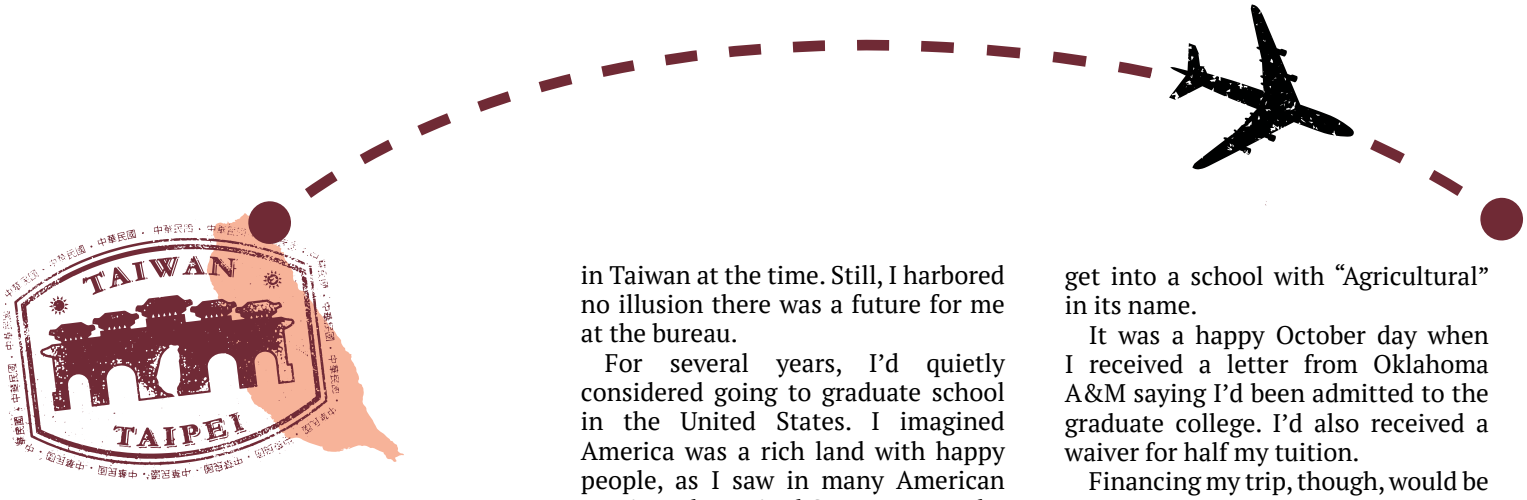


Once I'd completed college and my year of mandatory military service, I was assigned to work at the Fertilizer Bureau, a branch of the provincial government of Taiwan. In the summer of 1954, I reported to the bureau, a small agency whose mission was to oversee the production and utilization of chemical fertilizers.

The bureau was housed in a one-story building. It had a large space to accommodate about 20 workers, and I received a desk at the back of the room. For the first couple of weeks I sat idle, with no assignment or idea what to do.

But, eventually, my section chief came to me and said I was to work on farmer education. Apparently, even though chemical fertilizers were available, most farmers were still using traditional fertilizers, which included human and animal wastes.

Because most farmers were illiterate at the time, I thought I'd design posters to communicate with them. I'd done a considerable amount of artwork while in college, but the bureau's office was ill-equipped as an art studio. So, at home, I designed and painted a large poster. It showed a smiling farmer surrounded by tall, flourishing crops—all treated with chemical fertilizers.

My section chief was surprised and excited by my poster. He arranged to have 1 million copies printed and hung in villages all over Taiwan. After I created a second poster on a similar theme, he assigned me to design the cover of a fertilizer handbook.

In college, I'd studied agricultural chemistry for four years. But in three short months, I'd become the artist-in-residence for a government bureau. Indeed, my posters were perhaps the most viewed "artworks" in Taiwan at the time. Still, I harbored no illusion there was a future for me at the bureau.

For several years, I'd quietly considered going to graduate school in the United States. I imagined America was a rich land with happy people, as I saw in many American movies. The United States was at the forefront of science and technology, and many generations of Chinese students, including my father, had gone to study there. From my family's relationships with American missionaries, I also knew American people were friendly and kind.

Indeed, while visiting our home in Taipei, an American missionary had given my siblings and me our English names. To Jiennan, my given Chinese name, she'd added Jordan. When I later started to publish scientific papers, I decided to use my English name, as I thought it would be easier to pronounce. Today, almost everyone calls me Jordan.

Wishing to study in America was a long way from actually going. For one thing, Chiang Kai-Shek's government didn't permit army reservists (a role I was required to fill) to leave. Fortunately, though, children of highly ranked government officials with a status similar to mine also wanted to study in America. So, the government relaxed the rule once in a while to let those people go. My brother, Donald, had left during such a lull.

Still, I wasn't sure my academic record would qualify me for any graduate schools in the U.S. And then there was the question of what school to attend. There was no information available about American universities to which I could apply, where they were located, or even to whom I should write to ask about applying.

A friend had provided Donald with information about Oklahoma Agricultural and Mechanical College in Stillwater, Okla. He'd applied and was admitted to graduate school to study electrical engineering. So, I decide to apply there, too. I figured my undergraduate degree might help me get into a school with "Agricultural" in its name.

It was a happy October day when I received a letter from Oklahoma A&M saying I'd been admitted to the graduate college. I'd also received a waiver for half my tuition.

Financing my trip, though, would be another matter. My short tenure and meager salary at the Fertilizer Bureau left me with virtually no savings. As a principal at a teacher's college, my father made enough to support our family, but he had little left over. That left only the "money pool club."

The club, or Hui, consisted of about 12 families, all of whom knew each other well. Each month, they pooled a portion of their incomes, and one family would take the money to use it however it was needed. As my departure approached, my mother arranged it so the Hui would pay for part of my trip.

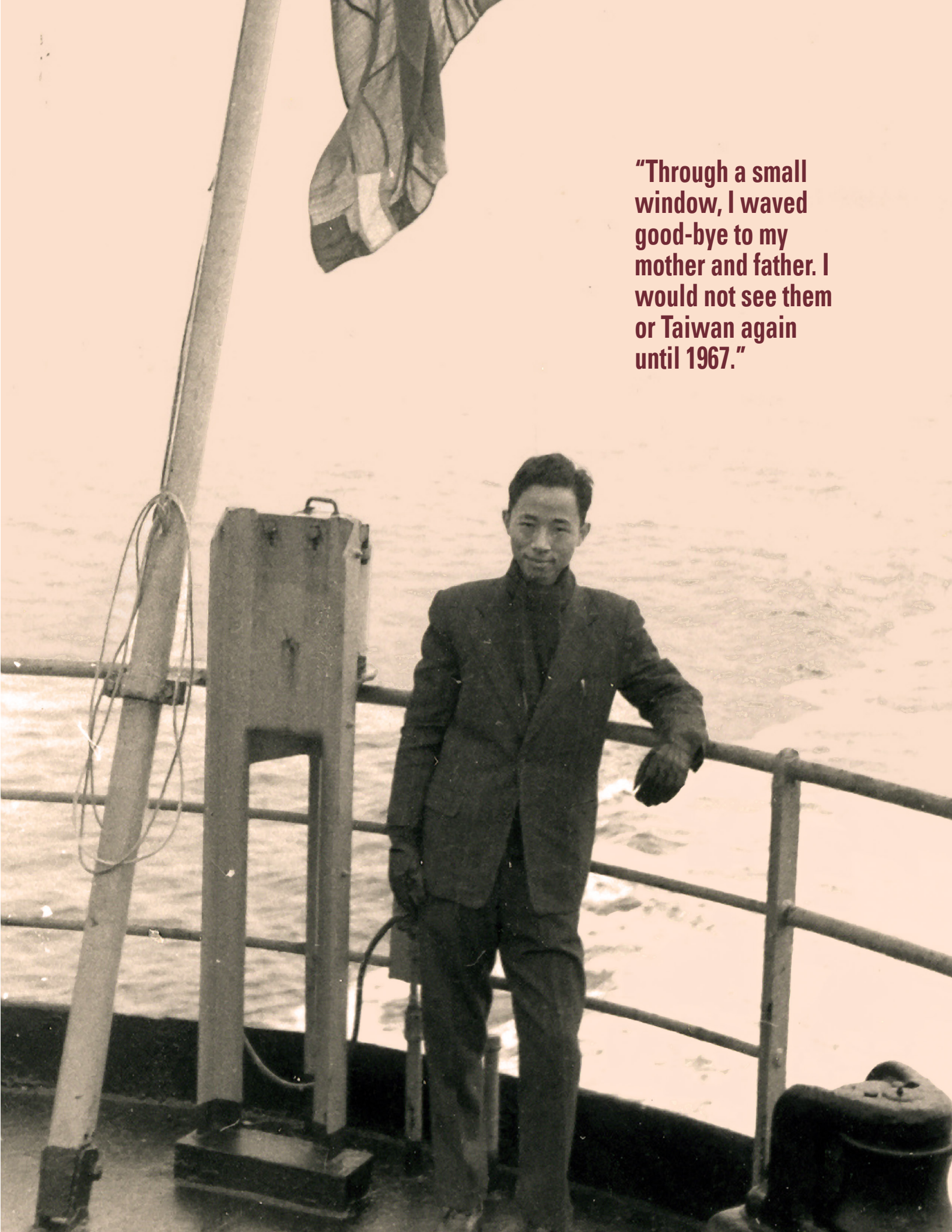
In December, the government relaxed exit permit requirements. I received a passport and a student visa. From second-hand stores, I purchased a suit, my first suitcase and, because my father was worried about Oklahoma's harsh winters, an oversized leather jacket.

On the eve of my departure, my parents gave me 300 U.S. dollars, the first foreign currency I'd ever seen. The next night, they drove me to the airport, where I boarded a two-engine, propeller-driven plane. Through a small window, I waved good-bye to my mother and father. I would not see them or Taiwan again until 1967.

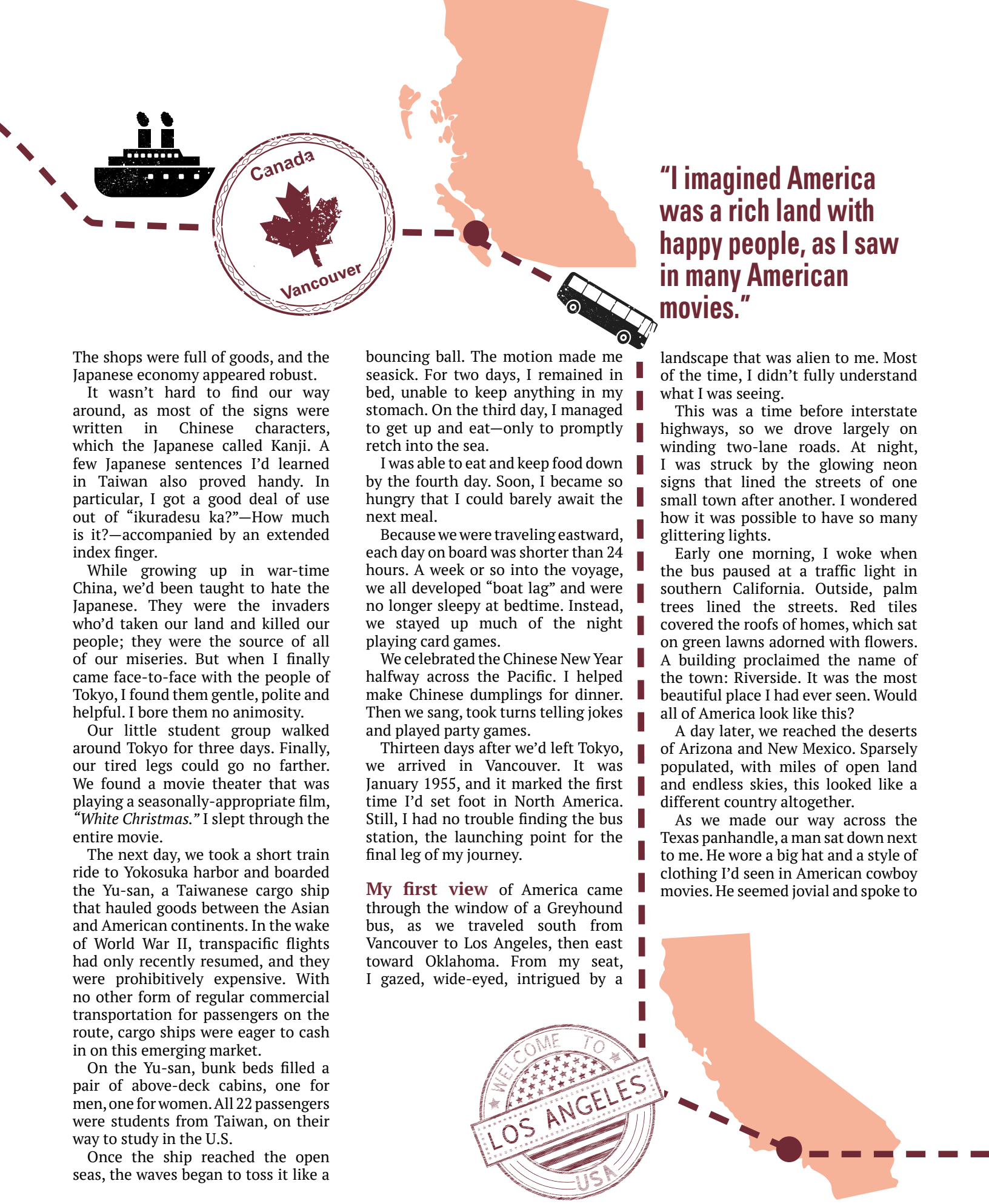
The small plane had a mighty, deafening roar. It bounced through angry skies over the darkened Pacific Ocean most of the way, but we safely reached our destination—Tokyo.

It turned out there were several students on the plane who would be joining me for the next leg of my journey, a ship ride to Vancouver. The boat's departure, though, was delayed by several days. That gave our group the chance to sightsee.

Only nine years before, American warplanes had devastated Tokyo. But no evidence of the bombing remained.



"Through a small window, I waved good-bye to my mother and father. I would not see them or Taiwan again until 1967."



"I imagined America was a rich land with happy people, as I saw in many American movies."

The shops were full of goods, and the Japanese economy appeared robust.

It wasn't hard to find our way around, as most of the signs were written in Chinese characters, which the Japanese called Kanji. A few Japanese sentences I'd learned in Taiwan also proved handy. In particular, I got a good deal of use out of "ikuradesu ka?"—How much is it?—accompanied by an extended index finger.

While growing up in war-time China, we'd been taught to hate the Japanese. They were the invaders who'd taken our land and killed our people; they were the source of all of our miseries. But when I finally came face-to-face with the people of Tokyo, I found them gentle, polite and helpful. I bore them no animosity.

Our little student group walked around Tokyo for three days. Finally, our tired legs could go no farther. We found a movie theater that was playing a seasonally-appropriate film, *"White Christmas."* I slept through the entire movie.

The next day, we took a short train ride to Yokosuka harbor and boarded the Yu-san, a Taiwanese cargo ship that hauled goods between the Asian and American continents. In the wake of World War II, transpacific flights had only recently resumed, and they were prohibitively expensive. With no other form of regular commercial transportation for passengers on the route, cargo ships were eager to cash in on this emerging market.

On the Yu-san, bunk beds filled a pair of above-deck cabins, one for men, one for women. All 22 passengers were students from Taiwan, on their way to study in the U.S.

Once the ship reached the open seas, the waves began to toss it like a bouncing ball. The motion made me seasick. For two days, I remained in bed, unable to keep anything in my stomach. On the third day, I managed to get up and eat—only to promptly retch into the sea.

I was able to eat and keep food down by the fourth day. Soon, I became so hungry that I could barely await the next meal.

Because we were traveling eastward, each day on board was shorter than 24 hours. A week or so into the voyage, we all developed "boat lag" and were no longer sleepy at bedtime. Instead, we stayed up much of the night playing card games.

We celebrated the Chinese New Year halfway across the Pacific. I helped make Chinese dumplings for dinner. Then we sang, took turns telling jokes and played party games.

Thirteen days after we'd left Tokyo, we arrived in Vancouver. It was January 1955, and it marked the first time I'd set foot in North America. Still, I had no trouble finding the bus station, the launching point for the final leg of my journey.

My first view of America came through the window of a Greyhound bus, as we traveled south from Vancouver to Los Angeles, then east toward Oklahoma. From my seat, I gazed, wide-eyed, intrigued by a landscape that was alien to me. Most of the time, I didn't fully understand what I was seeing.

This was a time before interstate highways, so we drove largely on winding two-lane roads. At night, I was struck by the glowing neon signs that lined the streets of one small town after another. I wondered how it was possible to have so many glittering lights.

Early one morning, I woke when the bus paused at a traffic light in southern California. Outside, palm trees lined the streets. Red tiles covered the roofs of homes, which sat on green lawns adorned with flowers. A building proclaimed the name of the town: Riverside. It was the most beautiful place I had ever seen. Would all of America look like this?

A day later, we reached the deserts of Arizona and New Mexico. Sparsely populated, with miles of open land and endless skies, this looked like a different country altogether.

As we made our way across the Texas panhandle, a man sat down next to me. He wore a big hat and a style of clothing I'd seen in American cowboy movies. He seemed jovial and spoke to

me about many things, most of which I didn't understand. He laughed a lot, and, despite the language barrier (I knew some English, but my vocabulary and conversational skills had yet to develop), I gathered that he was telling me jokes.

After a while, he reached into his pocket and pulled out what looked like a fountain pen. I was confused by why he was showing it to me. But then he opened it. And from the inside of this pen, he pulled out something I recognized from my military training: a bullet.

Surprised, I pointed at the pen and gasped, "A gun?"

"Shh!" He looked around to make sure no other passenger had heard me. In a hushed voice, he said, "You never know when you might run into a boogeyman."

I wondered what a boogeyman was. Eventually, I decided he meant a bad guy, perhaps like the ones who wore black hats in the Westerns I'd seen.

In Oklahoma, the land grew flat, which was odd to me. Where I'd lived previously, I could always see mountains. It was, I thought, curious that the trees here had no leaves and the grass was yellow. For the first time in my life I saw snow, plowed and piled along the highway.

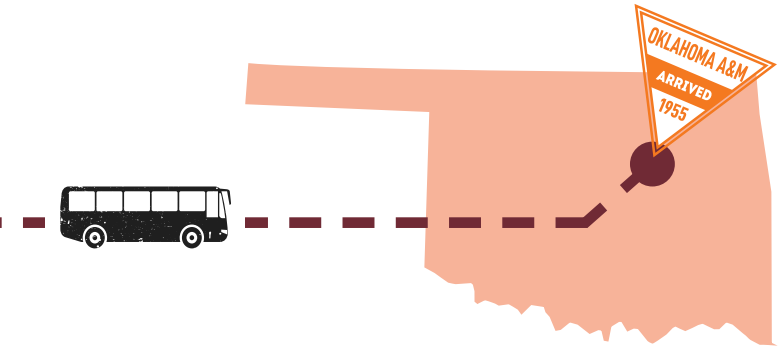
The bus stopped at Oklahoma City's Union Station. Several tall buildings dwarfed the single-story structure, which was nestled in downtown. I went inside and bought a new ticket, this one to Stillwater.

While waiting, I looked for a men's room. I found two: one marked "White," the other labelled "Colored."

I hadn't the faintest idea what this meant. But I decided that yellow was a color and chose accordingly. I still remember the curious looks I received while in there. It wasn't until years later, after studying Oklahoma history, that I understood those confused gazes.

Following a short ride, I arrived in Stillwater, my final destination. My journey from Taipei had taken nearly three weeks. It had carried me halfway around the world.

I stepped off the bus. At long last, I would get to see my brother again. My graduate studies would begin. I was excited and full of anticipation for my new life in America.



In Stillwater, Jordan not only completed his master's degree, but he met another graduate student from Taiwan, Kuen-I-Sun, whom he married in 1958. After earning his doctorate at the University of Oklahoma Health Sciences Center, he joined OMRF's scientific faculty and went on to an illustrious career in biomedical research. Jordan and Kuen have two children, Albert and Joseph. This year, they celebrated their 61st wedding anniversary, and on July 4 they became grandparents.

Triple Double

Three Pairs of OMRF Scientists, Three Sets of Twins

Dr. Susannah Rankin remembers when her twin sons, Grady and Zeke, first realized they were separate beings. She and her husband, Dr. Dean Dawson, each took one boy, then only a few months old, from the crib they shared and stood a few feet apart. The infants looked around until they locked eyes on one another. Baby grins and giggles followed. "It was kind of like a game of peek-a-boo," she says. "It was super cute."

By 2006, the boys, then 3, had swapped their shared crib for separate beds, and their parents—both cellular biologists—had moved from labs in Boston to OMRF. Once in Oklahoma, the researchers found a ready-made playdate for Zeke and Grady: Drs. Susan Kovats and Pepe Alberola-Ila, who'd come to OMRF the previous year, also had young twins of their own. When Drs. Courtney and Tim Griffin joined OMRF in 2008, it marked the foundation's third straight joint faculty recruitment where the couple brought not only sterling scientific credentials, but also a set of twins.

The kids were all within two years of one another, and the three families became fast friends. In the ensuing decade, they've shared Christmases and New Year's Eves, sent the kids to many of the same summer camps, and spent countless hours together. "It's been really special, because none of us have families nearby," says Tim Griffin. "So, this is like our extended family."

Being scientists, the parents couldn't help but make the stray "nature versus nurture" observation when their children shared (or didn't) certain behaviors or traits. But, mostly, says Susan Kovats, raising twins "helps take you away from the stress of research."

Having two children at once, says Kovats, "certainly was more efficient." Still, none of the parents miss the "chronic" sleep deprivation that came with caring for two babies. "I remember driving to work and literally falling asleep at traffic lights," says Courtney Griffin." Each of the couples divvied up the child-rearing tasks, which helped ensure they'd have ample—or at least enough—time to pursue their research.

As they grew, the kids learned to keep the drama to a minimum at certain times. "We see how much stress our parents are under when they're writing grants," says Olivia Griffin. That's when they stay up until the wee hours, says Isabel Alberola, "clacking on the computer."

As the offspring of scientists, the twins have enjoyed a slightly different perspective on life than their peers. Bringing tanks of frogs to class to explain genetics seemed pretty normal. Ditto when your mom lights junk food on fire in order to demonstrate its fat content. And no one seemed surprised when the parents swapped out candy for math problems, word games and trivia at the annual Easter egg hunt.

This fall, Zeke and Grady Dawson and Delancey and Olivia Griffin will all be juniors at the Classen School of Advanced Studies. Meanwhile, the Alberolas will head to college, with José attending UCLA and Isabel off to Barnard College in New York.

The transition may prove tough for their parents, not to mention the quartet of twin friends they're leaving behind. But it looks like OMRF scientists will continue seeing double: This past year, Drs. Bob Axtell and Rose Ko welcomed twin baby boys, Oliver and John. If the past is any indicator, they should have no trouble finding playmates.

The Kovats/Alberola-Ila family: Susan, José, Isabel, Pepe; the Rankin/Dawsons: Susannah, Zeke, Dean, Grady; the Griffins: Tim, Courtney, Delancey, Olivia

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Wheat Feat

"This grain of wheat reminds me of the endeavor of all of us who grow wheat to provide for this year's harvest, to give as many bushels as we possibly can for the Oklahoma Medical Research Foundation." With this signed pledge, 450 farmers from 34 Oklahoma counties donated the proceeds from the sales of 9,000 bushels of wheat to OMRF during the 1961 Wheat Campaign.