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DANIELLE'S PAIN

The story of one woman's life with sickle cell disease — and the OMRF drug that transformed it


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FINDINGS

Winter/Spring 2021

FEATURES

THE LONG AND WINDING ROAD

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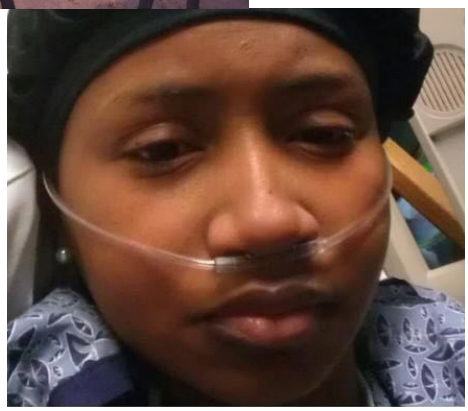
From West Bengal, India, to America's heartland, Dr. Jasim Ahamed's path to Oklahoma began by the light of a kerosene lamp.



Cover Story

DANIELLE'S PAIN

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Danielle Jamison lived her entire life with the crippling pain of sickle cell disease, until a groundbreaking drug born at OMRF brought her relief.

ALSO IN THIS ISSUE

OMRF

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: Kim Craven
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Back to the Bench

OMRF adapts to a changed research environment

When Dr. Dave Forsthoefel left his lab the evening of Friday, March 20, 2020, he sensed the enormity of the moment. With the first wave of Covid-19 breaking on Oklahoma, OMRF administration had instructed scientists to bring research operations to a halt. For Forsthoefel, who studies regeneration using tiny flatworms called planarians, that meant a week of scrambling. With the four other members of his laboratory, he organized and consolidated his worm colony, which would enable team members to come in periodically to feed the animals and keep them alive until it was safe to restart experiments.

"I looked around the lab and thought, 'I don't know when I'm going to come back,'" remembers Forsthoefel. "I knew we were doing the right thing by locking down, but when you're chugging away on your research for 15 years, not working in the lab is not something that comes naturally." Flatworms and microscopes don't typically inspire emotions, but at that moment, he says, "I got choked up."

During the next three months, OMRF existed in a state of suspended animation. To keep the heart of the foundation beating while others worked remotely, the foundation relied on a handful of employees who came to be known as the "skeleton crew": technicians who maintained experimental animals (mice, worms, fruit flies, fish and frogs) and cell lines; facilities staff who tended to equipment and mechanical systems; and health care providers who saw patients in OMRF's two clinics.

For Dr. Gabriel Pardo, director of OMRF's Multiple Sclerosis Center of Excellence, the first step entailed remaking the clinical environment to ensure it was safe for patients and staff. Procuring sufficient amounts of personal protective equipment was key, as was reducing human density. "We switched roughly 60% of our patients to telemedicine," he says. "That allowed us to prioritize those who actually needed to be seen in person" – patients experiencing new disease manifestations, those who required infusions with IV drugs, and patients also participating in research studies. That final group, Pardo says, proved critical, because

Photo by Brett Deering

"I knew we were doing the right thing by locking down," says Dr. Dave Forsthoefel, "but when you're chugging away on your research for 15 years, not working in the lab is not something that comes naturally."

"we were able to preserve the integrity of our clinical trials."

As a result, he and his staff could continue to administer experimental medications to those living with MS. "That benefits our patients," says Pardo. "And the more quickly we can complete clinical trials, the sooner new drugs can reach MS patients around the country."

In June, OMRF loosened restrictions, enabling scientists and lab members to return onsite. "People were anxious to jump back," says Dr. Xiao-Hong Sun, who's been studying the immune system at OMRF since 1999. Like many of her fellow scientists, Sun had used the three months when the foundation was locked down to compile and analyze data from previous experiments, write papers and submit grant proposals. But when she and her lab got the green light to resume operations, "We were waiting at the door," she says. In particular, she was eager to begin an experiment in OMRF's flow cytometry facility, where she could analyze the characteristics of individual cells taken from mice she'd specially developed. "This isn't something you could do at home."

As with the rest of the world, the OMRF that Sun and her colleagues returned to wasn't the same one they'd left pre-pandemic. Still, onsite restrictions – mask-wearing, physical distancing – haven't put a major crimp in her work. "Each person in my laboratory has their own lab bay, so we're able to socially distance," she says. Without in-person meetings, she relies on Zoom teleconferences to interact with colleagues. "It's not as good as seeing people face-to-face, but with a mask on, you can't see their facial expressions anyway."

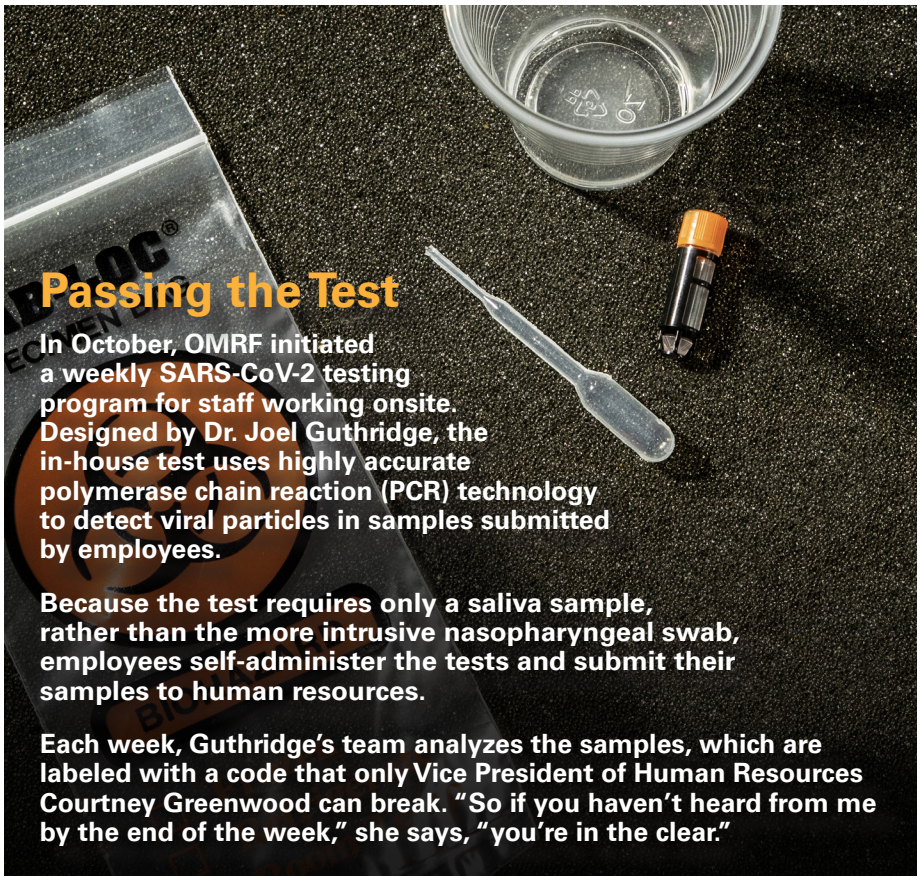
On a weekly basis, several hundred OMRF scientific staff members and affiliated personnel have returned onsite, down from a pre-pandemic headcount of about 500. Those who come to OMRF stagger shifts and keep their time at the foundation to a minimum, performing whatever portions of their jobs that they can from home.

Dr. Xiao-Hong Sun

Photo by Rob Ferguson

With only a handful of exceptions, OMRF's administrative staff continues to work entirely remotely, and there's not yet a timeline when they'll be back at the foundation. "That will depend on widespread vaccination and viral levels dropping significantly in the general population," says OMRF President Dr. Stephen Prescott. "Realistically, I don't expect that to happen until well into 2021."

In the meantime, OMRF has instituted a weekly Covid-19 testing program for all onsite personnel. "We're still insisting that everyone wear masks and socially distance to decrease risk," says Vice President of Clinical Affairs Dr. Judith James, who helped lead the testing initiative. "With community-based spread, testing adds another layer to help keep our workforce safe."



Passing the Test

In October, OMRF initiated a weekly SARS-CoV-2 testing program for staff working onsite. Designed by Dr. Joel Guthridge, the in-house test uses highly accurate polymerase chain reaction (PCR) technology to detect viral particles in samples submitted by employees.

Because the test requires only a saliva sample, rather than the more intrusive nasopharyngeal swab, employees self-administer the tests and submit their samples to human resources.

Each week, Guthridge's team analyzes the samples, which are labeled with a code that only Vice President of Human Resources Courtney Greenwood can break. "So if you haven't heard from me by the end of the week," she says, "you're in the clear."

A Mistake That Paid Off

A misstep on his med school application made all the difference for OMRF's newest rheumatologist

All he did was check the wrong box. But that error would end up changing Matlock Jeffries' life – for the better.

Raised on his family's ranch in Fairland, a northeastern Oklahoma town that boasted 28 students in his high school graduating class, the Oklahoma Regents Scholar was the first person in his family to go to college. He earned a degree in biochemistry from the University of Oklahoma, but a mistake on his medical school application delayed his acceptance by a year.

With time on his hands, Jeffries applied for a position as a research technician in OMRF's Arthritis and Clinical Immunology Research Program. It was the first time he'd set foot in a working research laboratory, and it opened a new world for him.

"Before that, I'd always planned to be a plastic surgeon," says Jeffries. "In small towns like the one where I grew up, the only people in science were family doctors or surgeons."

At OMRF, his laboratory projects focused on lupus and other rheumatological diseases, conditions that affect the joints, muscles and ligaments. So when he later enrolled in medical school, he opted to specialize in rheumatology. He charted a career path as a physician-scientist, both treating patients living with rheumatological disorders and researching those diseases in the lab.

Specifically, Jeffries focuses on the most common form of arthritis, osteoarthritis. OA stems from the loss of cartilage between bones and joints. It affects more than half of Americans over age 65. It's one of the leading causes of disability and the primary reason for joint replacements in the U.S.

One person who knows that all too well is Jeffries' mother, Reta.

Photo by Brett Deering

"I never imagined doing research that could help my own family," says Dr. Matlock Jeffries, whose mother, Reta, has osteoarthritis, the disease he studies.

Despite an active life working on the family ranch and as a nurse and case manager at OMRF (she retired in 2019), she's had a pair of knee replacements and will need a hip replacement soon.

"It's aggravating that I can't do things I used to do, and it keeps getting worse," she says. "But I trust Matlock," who helps manage her care, "and I know he'll do everything he can to help me."

Part of that help, he hopes, will include new methods of catching OA before it debilitates its victims. Using epigenetics, the chemical changes in the genome that affect how DNA is expressed, and the microbiome, tiny organisms living in our digestive tracts, Jeffries is searching for ways to catch osteoarthritis earlier and develop new ways to treat it.

"For years, we assumed OA resulted from overloading or wear and tear on the joint," he says. "Now we know OA has genetic and microbiome components, and we're finally developing some disease-modifying drugs for it."

After starting his career at the University of Oklahoma Health Sciences Center, Jeffries joined OMRF's scientific staff in August. It's been a seamless transition, as he's had a lab at the foundation for years, and he recently secured a pair of new grants from the National Institutes of Health. Although laboratory investigation occupies the lion's share of his time, he's also treating osteoarthritis patients in OMRF's Rheumatology Center of Excellence two days a week. That clinical experience gives him unique insights into a disease whose mysteries he hopes to crack in the lab.

"I'm not doing what I expected I'd be doing at all," he says. "I assumed I'd be a doctor seeing patients all day. I never imagined doing research that could help my own family."

For both mother and son, those breakthroughs can't come soon enough.

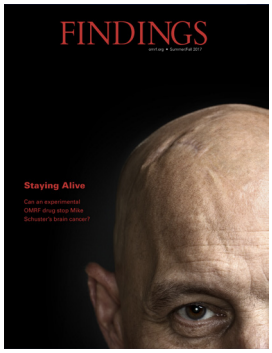
Beating the Odds

Mike Schuster celebrates an anniversary that once seemed unthinkable

"I'm sorry to bother you, but are you Mike Schuster?"

It was 2017, and the man who was, in fact, Mike Schuster sat in a waiting room at the OU Health Stephenson Cancer Center. He was there for a routine checkup when a woman approached him, clutching a copy of Findings magazine.

On the cover was a photo of Mike's head, crowned by a scar reminiscent of baseball stitching. Alongside the photo, there was a question: "Can an experimental drug stop Mike Schuster's brain cancer?"



The woman was there with her husband who, like Mike, had glioblastoma, one of the most aggressive forms of brain cancer. The couple read about Mike's experience with OKN-007, an investigational drug born in the OMRF labs of Drs. Robert Floyd and Rheal Towner. They had come to Oklahoma City in search of a cure.

"I told her, 'Nobody deserves to get cancer,'" remembers Mike. "'But if you get it, you're in the right place.'"

Mike's diagnosis had come the day before Thanksgiving in 2015. Despite two surgeries, chemotherapy and radiation therapy, the cancer had grown back. So he decided to enroll in a clinical trial of OKN-007.

"I remember telling my doctor, 'If you think it's a good idea, I think it's a good idea,'" says Mike. "Turns out, it was a good idea."

Two years later, Mike was declared cancer-free. And this past November, he celebrated an anniversary he'd only dreamed possible, becoming one of just 5% of glioblastoma patients to survive five years from diagnosis.

In that half-decade, Mike saw his son Connor graduate from high school and college. Parker, his older son, earned his bachelor's degree in mechanical engineering. Mike celebrated his 55th birthday on the heels of his grandmother's 105th. And in August, Mike and his wife, Teresa, sat hand-in-hand and watched Parker get married.

"It's impossible not to make mental notes. I'm always stepping back and thinking, 'I can't believe I'm here,'" says Mike, who now serves as a spokesman for a nonprofit that advances cancer research through clinical trials. "I'm incredibly fortunate."

But recovery has tested him, too. Surgery left a wound on his head that's resistant to healing and prone to infection, and therapy to help the surgical site has resulted in numerous brain bleeds. He can't bend over or lift more than 10 pounds. Painful skin grafts, repeated staph infections, dozens of brain scans and daily medications are now part of his life. Ditto for a substantial hat collection.

None of this, Mike is quick to add, is because of OKN-007. "That drug saved my life."

Despite the challenges, the Schusters know the significance of the five-year mark. "We can't take a blessing like reaching this milestone for granted," says Teresa.

Biotechnology company Oblato has acquired the rights to OKN-007, which continues to undergo clinical testing. In addition to glioblastoma, the drug has shown promise in a rare form of pediatric brain cancer. In August, the FDA awarded OKN-007 a pair of designations that will provide special status and priority review for regulatory applications for the drug.

"Enthusiasm for OKN-007 is very high," says OMRF's Towner. "It's going to be a drug that can provide real hope to patients. I anticipate we'll see a lot more stories like Mike's in the future."

And the man from the waiting room? "I'm happy to say he's still alive and doing well," reports Mike.

Teresa and Mike Schuster

Photo by Brett Deering

Like a Boss

Len Cason marks two decades at the helm of OMRF's Board

When Len Cason received a call in 1988 asking him to join OMRF's Associate Board of Directors, the Oklahoma City attorney had one important question. "I asked, 'What does OMRF stand for?'" he recalls, chuckling.

In the years that followed, he'd learn the answer better than he ever imagined, serving first on the foundation's Associate Board and then, in 1991, becoming a member of OMRF's full Board when that group absorbed the Associate Board. Still, when Cason studied a roster of his new colleagues, he realized he didn't possess the same financial resources as other directors. So, he says, "I needed to find another way to help OMRF."

He joined the Board's Development Committee, where he helped spearhead fundraising initiatives to support OMRF science and rose to chair the committee. In 2001, a schism among the foundation's directors precipitated a search for new leadership for the full Board. "There were two factions, and they needed someone neutral as chair," remembers Cason. "I guess I was Switzerland." That year, he was elected Board chair.

The volunteer position comes with a one-year term. But since then, Cason has been unanimously reelected 19 consecutive times. On the heels of the most recent vote, he'll celebrate his 20th anniversary as Board chair when he begins his new term in 2021.

"You just don't see this continuity of leadership on nonprofit boards," says Bruce Benbrook, who chairs OMRF's Governance Committee and renominated Cason this past autumn. "It's a testament to Len's commitment to OMRF that he's willing to continue to devote his time and service to the foundation. And the fact that he keeps getting reelected – with 100% support – speaks volumes about what kind of leader he is."

Cason's tenure has been marked by tremendous growth at the foundation.

Photo by Brett Deering

He was instrumental in securing a pair of major grants from the state to build the Research Tower in 2011, the centerpiece of the largest campus expansion in OMRF's history. Under his leadership, the foundation's operating budget has more than doubled, and a combination of scientific success, philanthropic support and fiscal discipline has enabled the foundation to nearly triple its endowment. Three drugs born at OMRF have received FDA approval in this span, during which the National Institutes of Health has also repeatedly named the foundation one of the country's 10 Autoimmunity Centers of Excellence.

"OMRF has become an iconic institutional presence in our community and state," says retired Oklahoma Supreme Court Justice Steven Taylor, who joined the Associate Board in 1988 with Cason and has continued to serve with him on OMRF's full Board since 1991. "A lot of that has to do with what I'd call Len's inviting leadership style. He has created an atmosphere where people want to be involved with OMRF."

• • •

Leadership is nothing new to Cason. After a sports-filled youth in the Oklahoma town of Lindsay, where Cason played middle linebacker and defensive tackle on his state championship high school football team, he attended the University of Oklahoma. He served as president of the Beta Theta Pi fraternity, with pledge brothers who would go on to become not only lifelong friends but also fellow OMRF directors (Michael Cawley and Bill Johnstone) and a founding member of OMRF's National Advisory Council (Don Cogman).

In law school at OU, Cason made a few extra dollars playing the tenor saxophone in a band that had a regular Sunday night gig at the Hilton by Will

Rogers World Airport. (His favorite song was "Yakety Sax.") Upon graduation, he spent four years as a captain in the Air Force Judge Advocate General Corps, including a deployment in Southeast Asia defending soldiers in court-martial proceedings after the Vietnam War. While there, he and his fiancée, Donna, earned a spot in the Guinness Book of World Records for what was then the longest distance marriage ceremony (12,000 miles): He was in Thailand, she in Orlando. They said their vows over the phone, the groom with an entire raucous military base in attendance. "We have 14,000 people here!" Cason shouted into the phone at one point during the ceremony, which was conducted at midnight in Thailand and noon in Florida.

"Afterwards, the public information officer took Donna's picture off my desk and sent it to the wire services," says Cason. "Two days later, her photo was on the front page of The New York Times, the South China Morning Post and the Bangkok News." The couple, who now have three grown sons and share a passion for ballroom dancing, recently celebrated their 47th anniversary.

Following a stint at a major law firm in Dallas (where he also earned a master's degree in tax law from Southern Methodist University), Cason returned in 1979 to Oklahoma City to start a practice with a former mentor and another attorney. "I went from a 50th-floor office to a little space on Northwest Expressway with a brown shag carpet, a card table and four folding chairs," he recalls. With specialties in tax, estate planning and business law, Cason traveled the state to generate business. "If the Guymon Rotary Club needed someone to speak, I was there."

Over time, that approach paid off. Today, Hartzog Conger Cason is one of the state's most prestigious law firms, counting more than 35 attorneys and representing some of Oklahoma's leading businesses and individuals.

For Cason, practicing law is simply about solving problems. And the stickier the situation, the better. "That's the best part: to find a problem that looks like there's no way out and then to fix it."

Those same skills have served Cason well in helming OMRF's Board, where he's helped navigate the foundation through countless challenging situations. "Len is constantly applying his experience as a lawyer to every decision we make," says Taylor. "That has really benefited the foundation."

As chair, Cason has particularly enjoyed working with Dr. Stephen Prescott, whom he recruited from the University of Utah's Huntsman Cancer Institute to become OMRF's president in 2006. "We bonded immediately, and that was one of the primary factors that drew me here," says Prescott. But before he'd accept the position, Prescott asked Cason to commit to continuing to serve as chair, a promise Cason gave without hesitation.

In the 14-plus years since, says Cason, "We've never had an argument. We've never really disagreed about anything." The two, he says, "think alike" and are aligned when it comes to both goals and tactics. "And that's pretty special."

Cason has served on numerous other nonprofit boards in the city and state, but none have resonated with him like OMRF. "What OMRF does is so incredible – the science is amazing. I'm honored to be a part of it."

Of course, it never would have happened but for that out-of-the-blue phone call he received more than three decades ago.

"It's a coincidence I got here," says Cason, smiling. "But it's not a coincidence I've stayed."

Since 2001, Cason has overseen unparalleled progress at OMRF, ranging from the construction of the Research Tower to FDA approval of three drugs discovered in foundation labs.

> To a person of color, representation is essential. Seeing someone who looks like you doing the thing you aspire to do is very important.

Dr. Valerie Lewis

A postdoctoral researcher, Dr. Valerie Lewis studies lupus in the laboratory of OMRF's Dr. Hal Scofield. Last spring, she pressed pause on her research to be a part of the team from OMRF and the University of Oklahoma that established a Covid-19 testing lab at OU Health.

Vaccination Trepidation

Dear Dr. Prescott,

I trust vaccines. Nevertheless, I'm nervous about the Covid-19 vaccine. With all we still don't know about the virus, how can we be sure it will be safe? As a senior, I know I'm in the group that is at the greatest risk for a bad outcome from the coronavirus, but I worry that I may also suffer the most from vaccine side effects.

Teresa Moyeda, Kingfisher, OK

Dr. Prescott Prescribes

While the vaccines scientists are developing for the virus known as SARS-CoV-2 are new, the science behind them is not.

The roots of vaccination date back more than 500 years and, especially in the last century, we've developed a deep understanding of how the immune system functions – and doesn't. Vaccines work, and there's overwhelming evidence to support it. We've inoculated billions upon billions of people against a host of communicable diseases, so we know even the rarest of side effects.

The SARS-CoV-2 vaccines have moved through the development timeline at an accelerated rate, but scientists are not starting from scratch. Many vaccines had been in the works already in some form for other coronaviruses like SARS and MERS that never reached the global pandemic stage. That gave researchers a jump on a SARS-CoV-2 vaccine, and it helped make the rapid timetable more feasible.

When scientists develop drugs to treat a disease, there's a certain tolerance for side effects because you're weighing those against the harm that the condition (think cancer or lupus) might otherwise inflict. With vaccines, there's no active disease. You're vaccinating healthy people to prevent illness. As a result, scientists are much less willing to accept adverse consequences.

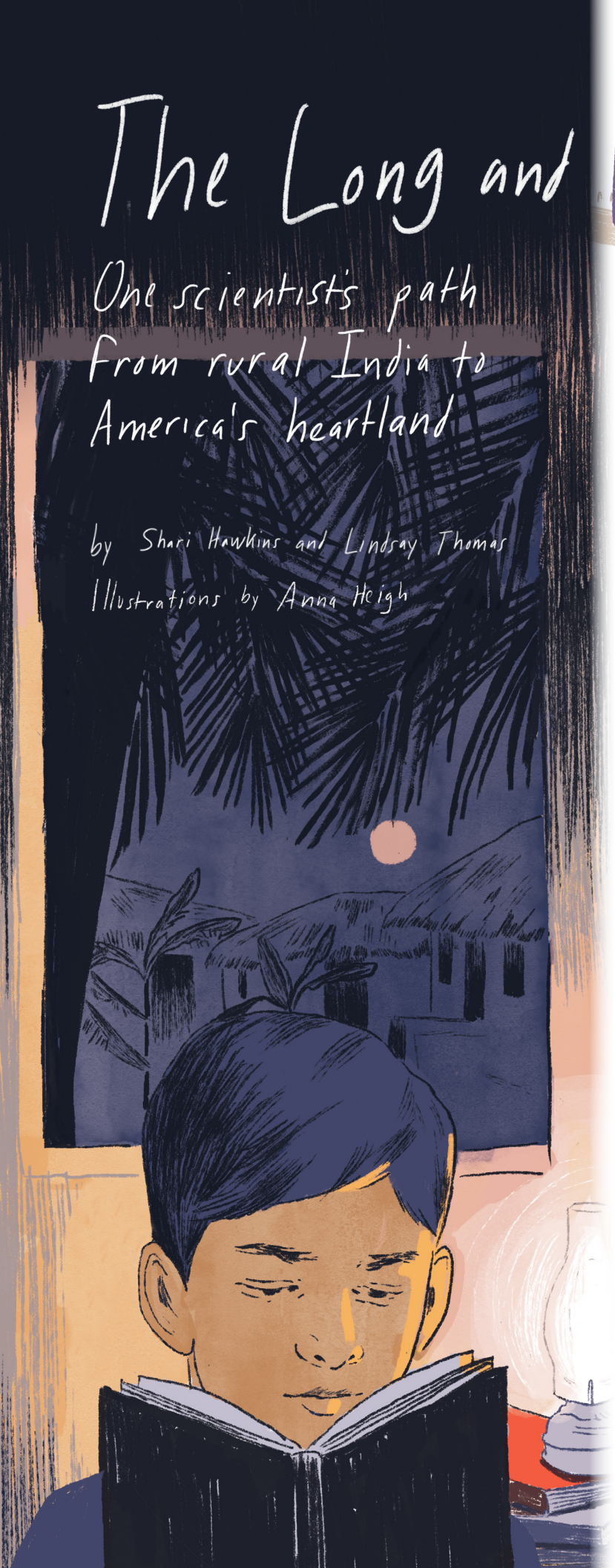
This extremely low tolerance for side effects, or even potential ones, is a big reason for the pauses we saw in some coronavirus vaccine trials. These shouldn't be viewed as negative developments; indeed, they are par for the course in the development of any vaccine. Rest assured that in these cases, data safety monitoring boards thoroughly investigate whether a side effect is related to the vaccine. If they find it is, they'll halt the trials, and that vaccine won't ever be available to the general public.

The bottom line: Trust the process. When there are SARS-CoV-2 vaccines available to take, you can feel good about getting them.

Vax Fact

The word "vaccine" comes from the Latin word "vacca," meaning cow. In the late 18th century, English physician Edward Jenner used a sample of cowpox to inoculate patients against smallpox, a deadly cousin of the milder cowpox. It was the first scientific demonstration that giving a person one virus could protect against another.

Illustration by Brad Gregg



As a young boy studying by the light of a kerosene lamp in his family's mud-and-straw home, Jasimuddin Ahamed imagined he might become a poet. Or perhaps he'd leave the remote farming village of Banti in West Bengal, India, to become a Bollywood movie idol or a cricket star.

But even in his wildest childhood dreams, he never envisioned a life as a scientist in America's heartland.

The eldest of six, Ahamed spent his formative years observing insects, animals and plants, particularly the migratory birds that visited his rural community. His childhood interest in fauna, says Ahamed, set him on a path to the sciences.

"Coming as I did from such a small village without even an elementary school, my parents doubted I would have the opportunities I needed to succeed in science," Ahamed says. "But I was fortunate to have an uncle who encouraged me to go after my dreams no matter how my prospects looked."

His uncle's village, some 30 miles away, did have a school. Ahamed moved there as a boy to pursue an education, trudging down unpaved roads often swollen by monsoons to attend classes, then returning home as frequently as he could to assist with the family's rice farm.

"I was an ordinary student in high school, barely passing the exams and, in fact, failed a level," Ahamed laughs. "But after completing high school, I was determined to focus on my first love: science."

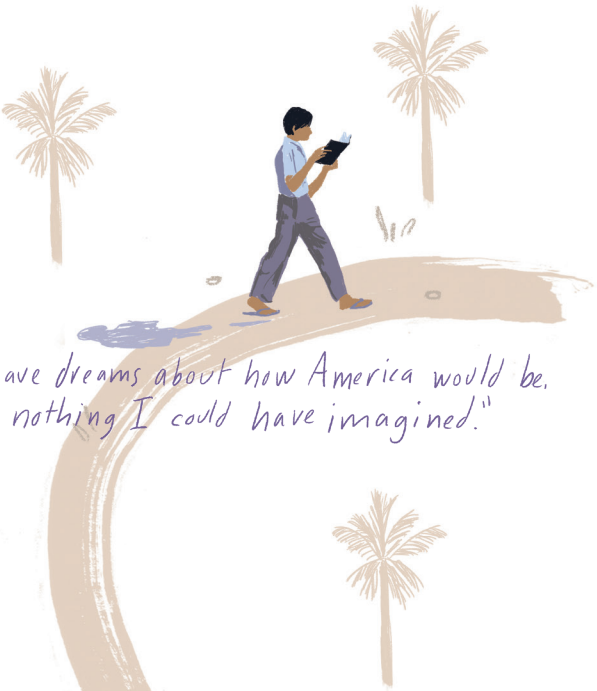
Ahamed's father, a successful farmer, wanted him to bypass college and take a job at a local coal mine. He even arranged a position there for his son at a salary of 1,500 rupees, or $20 a month. But Ahamed's mother helped persuade his father to let their son move to Kolkata to pursue his dream of higher education, specifically, how the human body works in health and disease.

"It cost my parents an entire year's profit from their rice crop to pay for my stay in a hostel while I went to college," says Ahamed, who was the first in his family to go beyond high school. "I realized it would be the only opportunity I would probably get, so I studied hard."

At the University of Calcutta, Ahamed's sharpened focus paid off. He was soon promoted to an honors program and earned his bachelor's and master's degrees in physiology, later going on to complete his doctoral studies in biochemistry and physiology.

He found his niche in cardiovascular research and was selected to complete a year of training at the University of Pennsylvania. It was hard to get a U.S. visa, he says, and he had to borrow money for plane fare from his parents (whom he later repaid).

The trip from the subcontinent to Philadelphia was Ahamed's first time on a plane, and when he discovered he had a fear of flying. But the jaw-clenching journey



proved worth it. His work at Penn earned him a prestigious postdoctoral position at Scripps Research in Southern California, followed by another at The Rockefeller University in New York.

When OMRF recruited him to join its Cardiovascular Biology Research Program in 2015, Ahamed says he found the foundation sort of a "mini Rockefeller," small in size but equal in intellectual and scientific pursuits. "OMRF is a place," he says, "where my work is valued and supported."

In his lab, Ahamed studies blood clots (thrombosis) that can lead to heart attack or stroke, and scarring (fibrosis) that can damage the heart muscle and other tissues. They are two of the leading causes of death in the U.S. in patients with cardiovascular disease and cancer.

With a new five-year grant from the National Heart, Lung, and Blood Institute, Ahamed is applying his knowledge of fibrosis to aortic stenosis, which occurs when the heart's main valve becomes stenotic or narrowed. The condition affects more than 200,000 Americans annually and can lead to serious heart problems.

Ahamed is building on his earlier discoveries to understand the mechanism that leads to the disease and, ultimately, to identify potential drugs for treating it. He also has his eye on Covid-19, devising experimental strategies to study the profound effects that the coronavirus has on the cardiovascular system.

His former mentor, Rockefeller professor and researcher Dr. Barry Coller, has watched admiringly as his protégé's research career has unfolded. "Jasim is an absolutely dedicated scientist who has an unquenchable thirst for new knowledge that can improve human health. At every step, he has devoted himself to obtaining the most rigorous training to prepare for an independent scientific career."

Ahamed's professional trajectory has carried him far from his native West Bengal, and he now considers himself an American. While he is proud of his Indian origins, he says his years here have helped him achieve much more than he could have in his homeland. "I used to have dreams about how America would be, but it was nothing I could have imagined." In 2017, with his wife, Anu, and his sons, Adil and Aaryan, there to share the moment, he became a U.S. citizen.

At the courthouse for the ceremony in downtown Oklahoma City, he was struck by the multitude of cultures represented by those who stood alongside him to take their oaths that day. "It was such a reflection of how diverse America is. I'm thrilled to be an American citizen."

These days, Ahamed doesn't think much about the life arcs he once mapped for himself in that mud-and-straw farmhouse in India. "I'm fortunate to be spending my career in a pursuit that has the potential to unravel the mysteries of human disease and, possibly, help all of humankind." And when that next discovery comes, it won't be by the light of a kerosene lamp.

Photo by Rob Ferguson

In Her Blo

Danielle Jamison's blood turned

Now, an OMRF drug is giving he

By Shari Hawkins and Lindsay Thomas • Photography by Kim Craven • Illustrations by Brad Gregg

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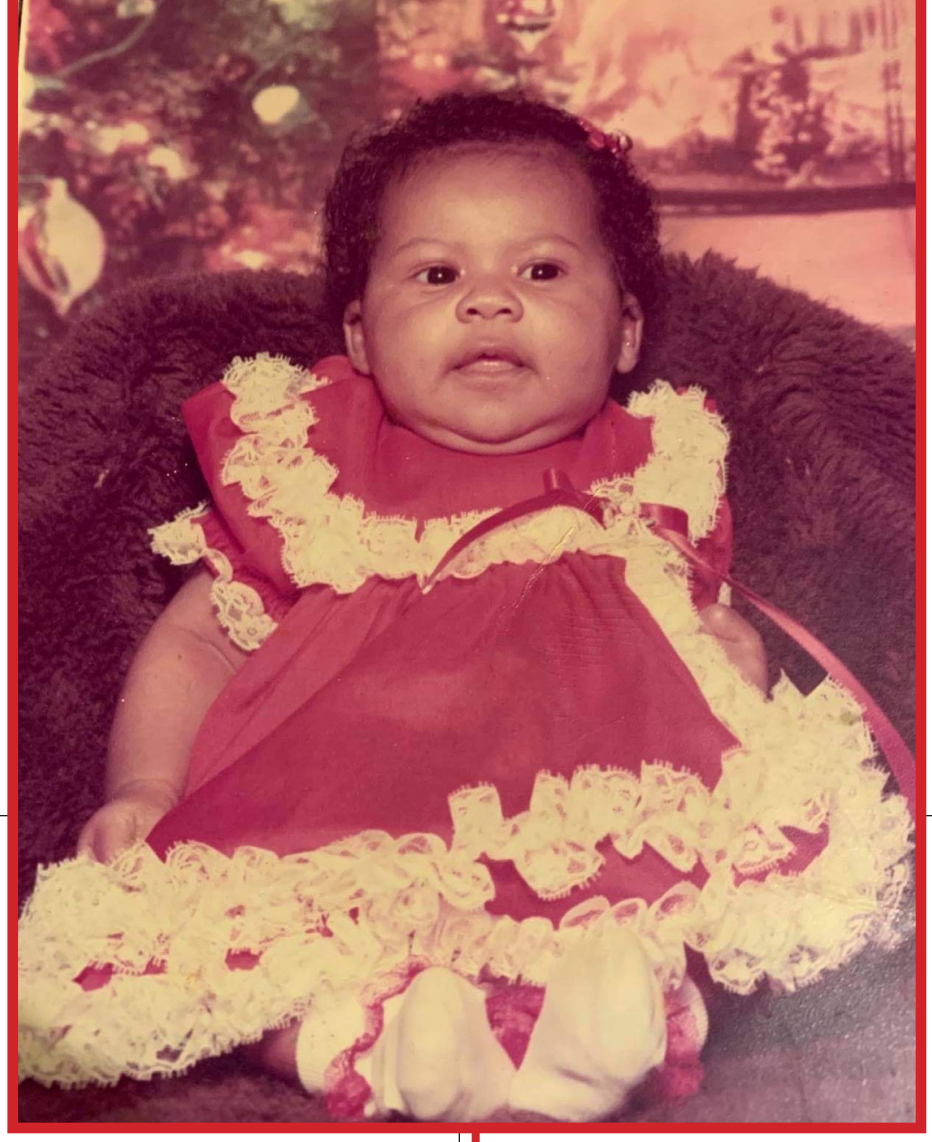


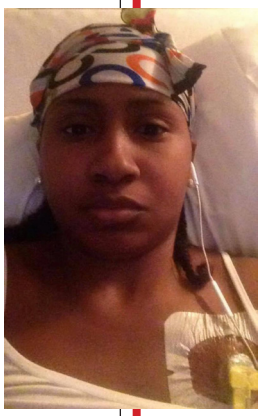
Danielle Jamison began experiencing pain crises from sickle cell disease as an infant.

Danielle Jamison was just a few months old when her parents realized something was wrong. All babies cry, but this was different. The incessant wailing was the first clue, her father tells her, but then he noticed her small body had begun to swell. "I was a chunky baby, but this was a lot more than normal," Danielle, now 36, says. "I have to commend my parents for not letting it go."

The Jamisons wrapped up their inconsolable child and rushed her to the best hospital available, an hour and a half away from their home in rural South Carolina. After a battery of tests, they learned their daughter had sickle cell disease, a rare, life-threatening genetic disorder that causes ongoing damage to blood vessels and organs.

"I count it as a blessing that we found out early. A lot of people born at that time found out way later," says Danielle, who has the most severe form of the disease, sickle cell anemia.

Because the condition stems from a chromosomal error passed from one generation to the next, Danielle's diagnosis prompted her parents to test her older sister. Happily, they discovered she had only one copy of the defective gene, thus dodging the disease. But when Adrienne Jamison was born two years later, she was not so fortunate; she carries twin copies of the miswired chromosome and also has sickle cell anemia.



The Jamisons are two of an estimated 100,000 Americans living with sickle cell disease. Like Danielle and Adrienne, most are of African descent.

The condition occurs when the body makes an abnormal form of hemoglobin, which carries oxygen throughout the body. Normally pliable and round, red blood cells become rigid and sticky in the presence of this rogue hemoglobin, taking on the shape of a C or "sickle." Instead of traveling smoothly through the bloodstream, they clump together in vessels, choking off blood supply to tissues and organs and causing long-term damage or even death.

The body responds to the problem by unleashing an arsenal of weapons to fight it. The extreme pain that results from the clustered cells, known as a crisis, can start anywhere in the body and last for weeks.

"You know what it is. It feels like you're getting hit, over and over and over and over," says Danielle. "And it never stops."

Dr. Rodger McEver is a hematologist, a physician who specializes in blood disorders. In a scientific career that's spanned five decades, his research has focused on blood cells.

As a medical student at the University of Chicago, McEver became fascinated with the abnormalities in blood cells that characterize many diseases. Peering at blood samples through a microscope, he wanted to know what caused these irregularities. When it came time for the young physician to choose a specialty, he picked hematology, the treatment and study of blood disorders. Since that time, his research in the laboratory has centered on blood cells.

In 1984, McEver led a team that discovered a protein now known as P-selectin. After joining OMRF three years later, McEver's lab uncovered P-selectin's function; namely, that it mobilizes white blood cells to hunt down and stop invaders such as bacteria in the body.

"Other investigators found that in laboratory mice engineered to develop a condition like sickle cell disease, P-selectin worsened symptoms," says McEver. That protein, McEver came to believe, might hold a key to unlocking new therapies for the illness.

As a physician, he understood the toll sickle cell exacted on the body. "I've treated patients with the disease, and their suffering is extreme," says McEver, who now serves as OMRF's vice president of research.

In time, McEver and his OMRF team developed an antibody that disabled P-selectin's effects. But he recognized the odds were long that his work would produce a treatment: The Pharmaceutical Research and Manufacturers of America estimates that only one in 5,000 compounds that begin preclinical testing prove safe and effective enough to reach pharmacies, clinics and hospitals. Still, he believed in the research and saw an opportunity to bring relief to people who were suffering. "It's the dream of every physician, and certainly every scientist, to do something that can make a difference for patients."

McEver helped create Selexys, an Oklahoma-based biotechnology company, to explore P-selectin's therapeutic potential. Selexys struggled for several years, pursuing scientific paths that proved to be blind alleys. But when McEver eventually recruited two former OMRF graduate research students to lead the company, everything changed.

Drs. Scott Rollins and Russell Rother left Oklahoma in the early 1990s to join Alexion Pharmaceuticals, a start-up company formed around another OMRF discovery. The pair helped transform the finding into an experimental drug, then shepherded it through development and clinical trials. In 2007, that medication, Soliris, became the first drug approved by the U.S. Food and Drug Administration to treat a rare blood disorder known as PNH.

Photo by Brett Deering

"It's the dream of every physician, and certainly every scientist, to do something that can make a difference for patients," says OMRF Vice President of Research Dr. Rodger McEver.

Upon the successful launch of Soliris, Alexion completed its evolution from scrappy upstart into one of the world's biotechnology leaders. Rollins and Rother had played key roles in the company's rise, but with the completion of the Soliris project, both saw a chance to return to their Oklahoma roots and to launch a new drug development project. When they came home – Rollins in 2008, Rother two years later – each joined Selexys.

With the pair at the helm, Selexys fine-tuned the antibody McEver had developed at OMRF, creating an experimental drug that bound to human P-selectin and blocked its function. In early-stage clinical trials, the treatment was shown to be safe and well tolerated. But the real test came in Phase II, where nearly 200 patients with sickle cell received the drug intravenously every four weeks for a year.

At the conclusion of the trial, the data showed nearly half of the patients had experienced a decrease in pain crises. When he saw the results, McEver "was so happy, but, honestly, I didn't know how to react." Rother, a biotech industry veteran, did. "We knew immediately that this was a home run."

So did Swiss drugmaker Novartis, which had been an investor in Selexys. It purchased the company and, with it, the drug that would come to be known as Adakveo. The Phase II results proved so convincing that Novartis bypassed the final stage of clinical trials and went directly to the FDA for approval, which the agency granted in November of 2019.

2020 has proved a challenging year in which to roll out a new drug. But because Adakveo is the first new medication for sickle cell disease approved in more than a quarter-century, it has already achieved close to 100% awareness among hematologists.

"We know this drug can decrease the frequency of sickle cell pain crises in a significant and meaningful way," says Dr. Kenneth Ataga, who led the Phase II trial for Adakveo and currently serves as director of the Center for Sickle Cell Disease at the University of Tennessee Health Science Center at Memphis. The medication, he says, "is an important advancement for people living with this very difficult condition."

Danielle Jamison couldn't agree more.

"I never thought I'd be here at 36 feeling how I feel. I'm not in and out of the hospital, going through the ups and downs of sickle cell so much," she says. "It's made a huge difference for me. A huge difference. It's a good feeling to know that somebody is paying attention to us."

What is Sickle Cell Disease?

In sickle cell disease, pliable and round red blood cells become hard and sticky and look like the C-shaped farm tool called a sickle. When these cells travel through small blood vessels, they can get stuck and clog blood flow.

These clogs deprive smaller vessels of oxygen and send people into crisis, resulting in inflammation and unbearable, unrelenting pain. Progressive damage from lack of blood flow can occur anywhere in the body. In some cases, long-term lack of oxygen can lead to organ damage, stroke or even death.

Sickle cell occurs when a child inherits a copy of the gene for the disease from each parent. If both parents are carriers, there's a 25% chance their child will be born with the condition. The disease can affect people of all races, but it's most prevalent in those of African or Hispanic heritage.

Approximately 100,000 Americans have sickle cell, but the exact number is unknown. Health authorities estimate more than 1 million people worldwide live with the illness, with 80% of patients found in sub-Saharan Africa. Stem cell transplants can reverse sickle cell in some cases, and clinical trials are also underway exploring the use of gene therapy to cure the disease.

Although two years apart, Adrienne and Danielle Jamison were like twins with their pain crises. When one entered the hospital, the other often followed; their mother slept in a rollaway bed between them.

Since that first night in the emergency room, Danielle's world has revolved around her condition. She has tried every pain medication available. She has undergone so many blood transfusions (which swap healthy red blood cells for Danielle's misshapen ones) that she can't get them any more; her body now attacks blood cells that aren't her own.

At the emergency room, her pain is rarely resolved in a few hours. More than once, her hospital stays have stretched beyond a month. As a child, Danielle's mom had to quit her job to care for her two chronically ill daughters.

"Growing up, we would be in the hospital: one in this bed, one in that bed, and my mom in the middle. And that was our childhood for a long time," Danielle says.

The hospital closest to her hometown of Islandton (population: 70) was not well-equipped to treat such a rare and poorly understood disease, but just as frustrating was the alternative: a three-hour round trip to the Medical University of South Carolina in Charleston.

A breakthrough finally came when her parents were introduced to a pediatric hematologist in Beaufort, cutting the journey by half. Still, it wasn't ideal, Danielle says. "Forty-five minutes is more like five hours when you're in pain — especially for a child."

Despite frequent hospitalizations, she enjoyed a happy upbringing. Crises grew less frequent in high school, where she joined the National Honor Society and cheerleading squad. College, a first for anyone in her family, was the next stop. But a medical emergency led to a transfer, followed by another. At the third school, she remembers, "I was there for about a year, constantly sick and in and out of the hospital," Danielle says. Finally, she'd had enough. She called her older sister, Tonya, who picked her up and shuttled her four hours to the hospital in Beaufort.

Danielle's long-time hematologist eventually got the pain under control, but each crisis deprives the body's cells of oxygen, causing a host of downstream effects. Spleen damage leaves patients more prone to illness and death from infections such as pneumonia and Covid-19. Sickle cells can plug up vessels in the eye, causing vision loss. There are recurrent leg ulcerations, the chance for kidney failure – and the ever-present risk of a deadly stroke.

For Danielle, the persistent lack of blood flow to her bones caused the bone tissue in her hips to die. Surgeons replaced her left hip, and now the right side is hurting. One of her shoulders bothers her, too.

Then there is the emotional toll.

"Going to the emergency room is a fight for your life," she says. "They look at you and say, 'You can't possibly be in that much pain.'"

Some women with sickle cell report feeling better while pregnant; for Danielle, who learned she would become a mother at 25, it was the opposite. "I almost didn't make it through," she says. To protect her baby from side effects, she stopped taking hydroxyurea, an anti-cancer agent

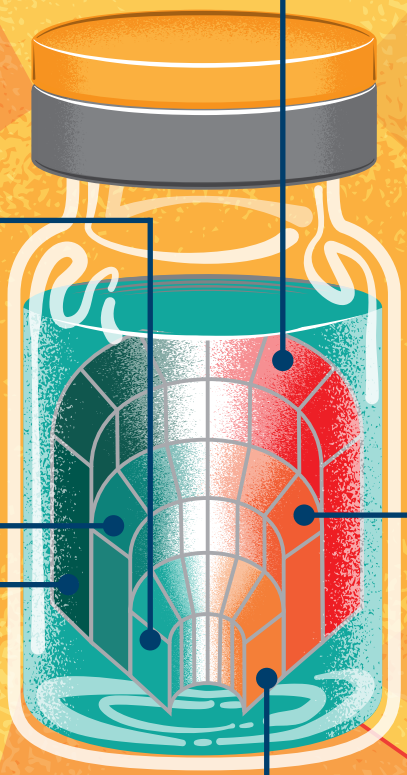
The Path to Patients

As a nonprofit biomedical research institute, OMRF doesn't manufacture drugs. But the work that takes place in the foundation's labs can lead to the creation of a drug such as Adakveo. Here's an example of how it commonly works:

Discovery
When an OMRF scientist makes a breakthrough that could lead to a new treatment for a disease, the foundation applies to the U.S. Patent and Trademark Office for a patent.

Phase 3
Hundreds or thousands of volunteers who have the disease or condition continue taking the medication for another one to four years, while organizers study efficacy and watch for adverse reactions.

Since Adakveo's FDA approval in November 2019, Novartis has continued to monitor its long-term effectiveness through ongoing surveillance trials. This step helps identify any possibility of unforeseen negative side effects that might occur over time.



Patent
Once the patent is granted, this gives OMRF the exclusive right to develop the discovery, which the foundation then licenses to a pharmaceutical company.

Phase 2
Up to several hundred people with the disease take the drug for anywhere from several months to two years to allow doctors to monitor efficacy and side effects.

Adakveo stopped here. Because data from Phases I and II was so positive, the drug received approval without need for Phase III.

Licensing
If the company succeeds in transforming the discovery into an experimental drug, it faces three levels of clinical trials before it can apply to the FDA for approval.

Phase 1
Twenty to 100 healthy volunteers or people with the disease take the drug to evaluate safety and standardize dosage. This stage usually takes months, although in rare diseases it can be longer.

used to prevent sickle cell crises. "I remember lying in the hospital bed, just crying out."

Eventually, she had an emergency C-section and delivered a baby girl, Jocelyn. Although Danielle knew her daughter's father didn't have sickle cell, it was three weeks before the by-then-standard newborn screening test for the disease showed that her daughter had only inherited the trait. "I was one happy new mom," she says.

When Jocelyn was a year old, Danielle went back to college, finally earning the degree she had set out for nine years earlier. She began engaging with the sickle cell community online, helping others with her knowledge of the disease. It was from a Facebook post that she learned about Dr. Julie Kanter, a hematologist at the Medical University of South Carolina who had recently established a network of clinics for people with sickle cell disease. Danielle jumped at the chance to establish care with a bona fide sickle cell specialist, the first in her adult life.

Under Kanter's care, Danielle joined a trial for Adakveo in 2014, but she couldn't complete it because of an unrelated hospitalization. When Kanter offered her a slot in a second Phase II trial with a higher dose of the drug in 2017, Danielle seized it.

"If I don't help do it, who will?" she says. "How else will we know if it works? They can't try it on people without sickle cell, so I'll take that risk."

Every four weeks since, Danielle has visited her sickle cell clinic for a 30-minute IV infusion. During those three years, she says, she hasn't been hospitalized for a crisis. "I never expected this could be possible."

Danielle no longer has to set an alarm to wake up and take pain medication, hoping the dose gets her through her morning routine. She's a newly-certified event planner, eager to launch a business. And before Covid-19 put a hold on in-person learning and activities, she was volunteering in Jocelyn's classroom and shuttling the budding dancer, now 10, to practice and competitions.

"I'm able to be much more active and have less pain. It's such a blessing."

"I'm able to be so much more active and have less pain. Three years ago, I couldn't have done any of this," Danielle says. "It's such a blessing."

Kanter has moved to the University of Alabama at Birmingham, where she now co-directs the university's Comprehensive Sickle Cell Center. But she continues to see Danielle through virtual visits. Since Danielle began receiving Adakveo, "she's clearly had many fewer crises," says Kanter. "She's more functional and able to do more things. She's more active." In Kanter's clinical practice, she now treats almost 40 patients with Adakveo.

This past October, the drug received approval for use in Europe. And in sub-Saharan Africa, where Novartis estimates that 80% of the world's sickle cell patients live, plans are underway for clinical trials in Ghana and Kenya.

For OMRF's McEver, who retired from the lab in June but continues to serve as OMRF's vice president of research, Adakveo represents the ideal capstone for a career devoted to medical research. "It's enormously satisfying to know you've developed a drug that helps patients. It's such a long process; you just try to do good science, do your job and look for how what you learn might be applied to human disease."

And while Danielle has never met McEver, she's grateful for all he and so many others did to make Adakveo a reality. "Life is so much better now," she says. "Every minute I have not dealing with pain is a miracle."

With her pain in check, Danielle can focus on what matters most to her. "I want to see my baby grow up," she says. "She's my little angel. She's my reason to fight, my will to live."

"I want to see my baby grow up," says Danielle. "She's my reason to fight, my will to live."

Goodbye, Dr. Tang

A proud "Okie" who embraced his adopted home, Jordan Tang's pioneering research changed fields ranging from HIV treatment to Alzheimer's

For many scientists, years may pass before they experience a true "Eureka!" moment. But Dr. Jordan J.N. Tang was no ordinary scientist. His discovery of a new stomach acid as an OMRF laboratory technician in 1958 launched a distinguished research career that spanned six decades and impacted diseases from HIV to Alzheimer's.

When cancer claimed Tang's life this past fall, remembrances poured in. And they spoke of a scientist who was not only a giant in his field, but also a man of extraordinary warmth and gentleness.

"I had the honor of moving into Jordan's former lab space in the Research Tower," says OMRF scientist Dr. Courtney Griffin. "I spent two weeks with my lab manager going through all of Jordan's remarkable lab equipment, notebooks, reagents and supplies. It was a treasure trove of scientific accomplishment and accumulation. What a kind, personable and thoughtful man. I will miss him very much."

Tang arrived in Oklahoma from Taiwan with just $300 in his pocket to achieve his dream of studying at an American university. At Oklahoma State (then A&M) University, he did just that, earning a master's degree in biochemistry and practicing his English with other Chinese students. To make ends meet, he washed dishes in the lab.

In 1957, he drove his beat-up Ford from Stillwater to Oklahoma City to interview for a job as a technician at OMRF, for a salary of $275 per month. When Tang soon identified gastricsin, a previously unknown protein in stomach acid, he became a research star practically overnight.

That work led to his Ph.D. and a position as a faculty member at OMRF. And for the ensuing half-

century, he called the foundation his scientific home.

From a lab that overlooked 13th Street in northeast Oklahoma City, he studied a family of cutting proteins known as proteases. Over time, he

"If somebody gave me one million dollars, it's not going to change my life a bit. But, if I discover something, then that would keep me happy for a long time."

pinpointed their roles in numerous diseases. Most notably he helped create the protease inhibition drugs that have saved the lives of countless people with AIDS, and he made a series of watershed discoveries about Alzheimer's disease.

But for Tang, the search for answers was much more than an abstracted scientific quest. "I understand the magnitude of tragedy that's involved when people find out their loved ones have a terrible disease," he told Findings in 2011. "I feel powerless to help. But what I can say is that we're trying to work at the best of our ability and knowledge."

For many years, Tang led OMRF's Protein Studies Research Program and held the J.G. Puterbaugh Chair in Medical Research. He published over 200 articles in the world's leading scientific journals and was an invited speaker at scores of national and international symposia and conferences. His work was recognized and honored by, among others, the National Institutes of Health, the Guggenheim Foundation, the Chinese Academy of Sciences and the United Nations. He was the only Oklahoman ever to receive the Alzheimer's Association's highest research prize, the $1 million Pioneer Award.

The first OMRF scientist inducted in the Oklahoma Hall of Fame, Tang loved his adopted home and proudly called himself an "Okie." He delighted in translating complicated scientific concepts into cartoons so non-scientists could understand his research. (A Pac-Man-like drawing explaining his Alzheimer's work was a favorite.) On occasion, he'd gather his lab staff and others to lead them in rousing choruses of "The Protein Song," a ditty he'd penned on a whim.

Upon his retirement from the laboratory in 2013, the OMRF Board of Directors named him an OMRF Distinguished Career Scientist.

"Jordan was a treasure, not only to OMRF but to all of Oklahoma," says OMRF President Dr. Stephen Prescott. "Anyone lucky enough to spend time with him knew he was that rarest of all creatures, a brilliant but humble person."

Tang is survived by his wife, Kuen, whom he married at OMRF in 1958; his sons, Albert and Joseph; and his grandson, Aaron. Like his family, we will miss him dearly.

Jordan J.N. Tang
March 23, 1931 - Sept. 29, 2020

Illustration by Brian Taylor

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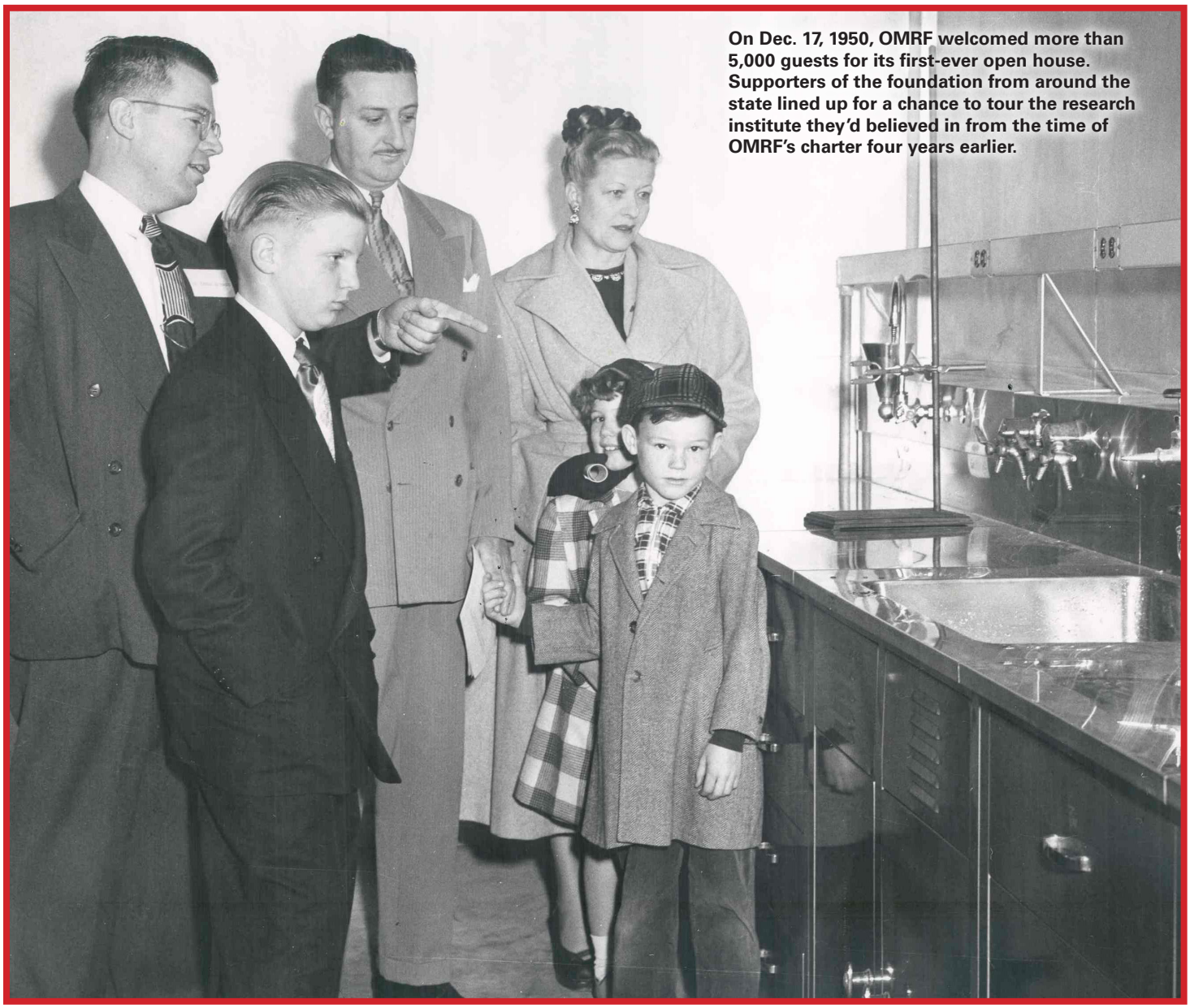
Open House for the Holidays



On Dec. 17, 1950, OMRF welcomed more than 5,000 guests for its first-ever open house. Supporters of the foundation from around the state lined up for a chance to tour the research institute they'd believed in from the time of OMRF's charter four years earlier.