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FINDINGS

Summer/Fall 2022

FEATURES

THE PUZZLE OF COVID AND AUTOIMMUNITY

Can Covid-19 infections lead to lifelong disorders?

CHANGING THE COMPLEXION OF SCIENCE

A partnership with Langston University aims to draw more Black students to biomedical research

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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LETTERING Anna Heigh
INSIDE FRONT COVER Sabrina Gabrielli
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PRESIDENT'S LETTER

I'VE KNOWN ABOUT THE Oklahoma Medical Research Foundation since the 1990s, when, as a young scientist, I began collaborating with OMRF's Dr. Rod McEver. Rod was an emerging star in cardiovascular biology, a field where I quickly learned of OMRF's stellar reputation. That reputation was based on a series of key discoveries, three of which led to lifesaving drugs now available in the U.S. and around the world.

The research I did with Rod and OMRF was rewarding, both scientifically and on a personal level. But my real education about OMRF started last year, when I began interviewing to become president of the foundation.

Throughout the process, the thing that stood out most was how everyone I talked with – donors, board members, community members, legislators, administrative staff, scientists – seemed deeply connected to the organization. They took great pride in every aspect of OMRF and wanted to do everything they could to ensure its ongoing success.

In short, they treated OMRF like it belonged to them. And it does.

Well, technically, as a nonprofit, OMRF doesn't have an owner. But the sense of ownership everyone displayed was one of the big reasons I decided to join OMRF. The other was the excellence I observed throughout the organization.

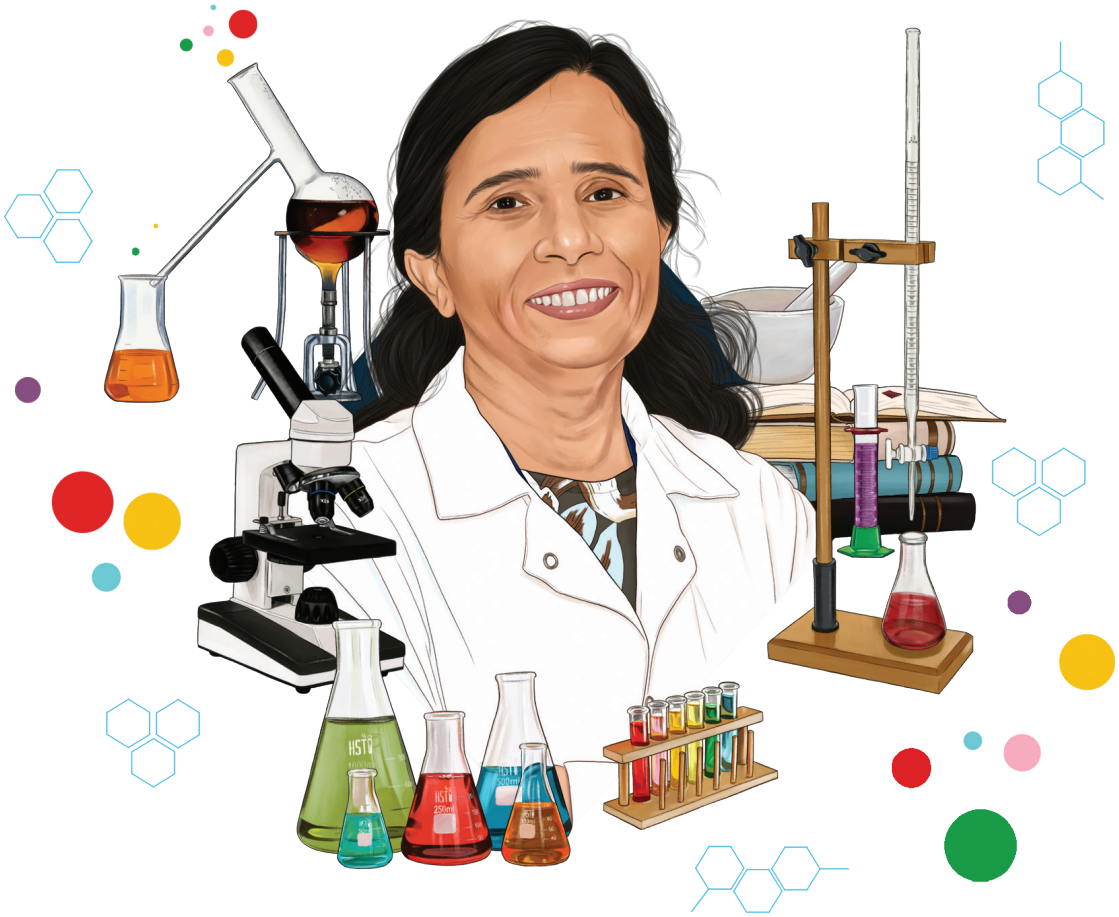
In this issue of Findings, I hope you'll see ample evidence of both that excellence and enthusiasm. You can read about our scientists' efforts to unravel the mystery of whether Covid-19 can trigger autoimmune diseases like lupus. You'll learn how they've found new clues that could help prevent relapses in multiple sclerosis and about OMRF's partnership with Langston University to introduce more students from underrepresented groups to biomedical research.

You'll also meet some of the foundation's researchers: OMRF's "lab couples," our attending veterinarian, and a physician-scientist who got her start in theater. And we'll introduce you to Kent and Jeanette Young, two of the many donors who make what we do possible.

It's been less than a year since I started at OMRF, but I already feel that personal bond to the institution I saw in so many others during the interview process. I hope you do, too. Because we're not just the Oklahoma Medical Research Foundation. We're Oklahoma's medical research foundation.

Andrew S. Weyrich

I love my work. I love the people I work with. I've built friendships with individuals from so many different cultures I never would have conceived meeting elsewhere. It's a matter of pride when I tell someone I work at OMRF.



Dr. Padmaja Mehta-D'souza

OMRF staff scientist and donor

After completing her Ph.D. in biochemistry at Bombay University in 1992, Dr. Padmaja Mehta-D'souza received fellowship offers from Paris to Quebec, but she said yes to OMRF. She's called the foundation home ever since.

Mouse Doctor

It's not unusual that, as a caregiver, Dr. Jennie Criley likes to talk to her patients. What's unusual is that those patients are mice.

"I think my staff finds that amusing," says Criley.

She joined OMRF in 2019 as the foundation's director of comparative medicine and attending veterinarian. In that role, Criley is responsible for the care of all of the foundation's experimental animals. By her count, that includes roughly 10 rats, 150 frogs and 20,000 tiny zebrafish.

However, she and her staff spend most of their time ministering to the animals involved in the bulk of OMRF's experiments: mice. At any given time, she estimates that's about 25,000 mice.

When a young Criley set her sights on becoming a veterinarian, she had no idea the world of laboratory research existed – or that she'd become a vital part of it. "But if you'd told me I'd be taking care of dolphins, I would have bought that!" she says.

After graduating from veterinary school, she completed a residency and postdoctoral fellowship in laboratory animal medicine, then embarked on a career as a lab animal vet. The work, she says, suits her. "I like the problem-solving, and I like being exposed to the cutting-edge research."

Criley came to OMRF from the University of Illinois, where, says the university's Executive Vice Chancellor for Research Dr. Lyndon Goodly, she

Dr. Jennie Criley has 25,000 pink-tailed, whiskered patients under her care

was "a rock star. She has a gift for balancing the needs of the animals and the needs of the researchers." He credits her with helping to rebuild the university's animal care program and establishing a facility where scientists could do mouse experiments in a germ-free environment.

It turned out OMRF had just established a similar germ-free mouse facility, and that proved key in recruiting Criley to Oklahoma. "It's a fascinating research tool," she says.

Dr. Matlock Jeffries, an OMRF investigator who uses the facility to study osteoarthritis, says that "we couldn't do what we do without Jennie. I can come to her with an idea, and it's not just, 'Yes, we can do this, or, no, we can't do that.' It's, 'Here's how we can make it better.'"

At OMRF, Criley says she's found a Goldilocks-like fit. "It's big enough to have all this exciting research, but not so big that you get lost in the fray."

Outside work, Criley and her husband, Tom, dote on their dogs, Tony and Noah. "Tony is a sweet, sweet boy who never does anything wrong," Criley says, "and Noah is a naughty, lovable imp." They're currently training the pair, both retired show dogs, for agility competitions.

Criley's papillon pair, Tony and Noah

With tens of thousands of mice to look after, the time has long passed since Criley individually named the little creatures in her care. Still, if there's any doubt about her feelings for her whiskered charges, look no further than the sign on her office door. It reads, "I ❤ Mice."

Coffee Conundrum

Dear Dr. McEver,

I'm usually not a coffee drinker, but on a recent vacation, I fell into the habit of starting my days off with a cappuccino. As I get back into the groove of regular life, I'm wondering whether the morning cup of java should go away. From a health perspective, what do you think?

Adam Cohen, Findings editor and curious person
Norman, OK

Dr. McEver Prescribes

Although you'd never take your coffee with a grain of salt, take research regarding coffee's health benefits with one. That's because almost all we know in this realm is based on observational studies.

In observational studies, scientists do not design an experiment and control the variables. Instead, they ask subjects to report their behaviors and then draw inferences from those reports. As you might imagine, this approach can lead to a pair of big problems: misreporting of behaviors and hidden factors (known as confounding variables) that might go unaccounted for but nevertheless influence the outcome of the study.

That said, these studies have generally shown that coffee drinkers tend to live longer than those who don't partake. It may come as a bit of a surprise that this seems to hold up even when people add a little bit of sugar to their coffee.

In numerous studies, drinking several cups of coffee a day has been associated with reduced death rates. In one, researchers tracked more than 200,000 people for up to 30 years and found that those who consumed three to five cups of coffee each day were 15% less likely to die from all causes than those who went java-free. Interestingly, the biggest risk reduction was for suicide, with moderate coffee drinkers showing 50% lower suicide rates than non-coffee drinkers.

On a physiological level, small studies have suggested that certain coffee components could have beneficial effects on lifespan. So, while not definitive evidence, they support the observational research.

Given the number of studies out there, I feel relatively confident that consuming moderate levels of coffee isn't harmful. A few cups a day, as long as they're not loaded with cream and sugar, might even be beneficial. But don't start drinking coffee just because of the potential health benefits. That's a bridge – okay, a cup – too far.

A physician-scientist, Dr. Rod McEver is OMRF's vice president of research.

Good Chemistry

OMRF's scientific couples balance love, life and the lab

As with countless other working couples, OMRF scientists Drs. Chris and Courtney Sansam typically discuss their day at the dinner table. Never mind that they spent that day separated by only a few feet and one interior wall.

Sweethearts since grad school at Vanderbilt University, the Sansams married in 2003. After completing their postdoctoral studies in Boston, they arrived at OMRF together: Chris as a principal investigator and Courtney as manager of his new lab.

In their lab, the Sansams study the genes, molecules and mechanisms needed to replicate DNA and how errors in this process contribute to cancer and other diseases.

Their typical dinner conversation frequently revolves around the day's experiments and revelations, sometimes to their 13-year-old son Mitchell's chagrin. "He tells us we're always talking about work," Courtney says.

With complementary training and a focus on similar segments of cancer biology, the Sansams' decision to join forces rather than open separate labs was met with mixed reviews from Chris' faculty advisors at the Massachusetts Institute of Technology. "One said, 'That's so wonderful. You'll make discoveries together.' The other said, 'That's a terrible idea. You'll get a divorce,'" Chris remembers.

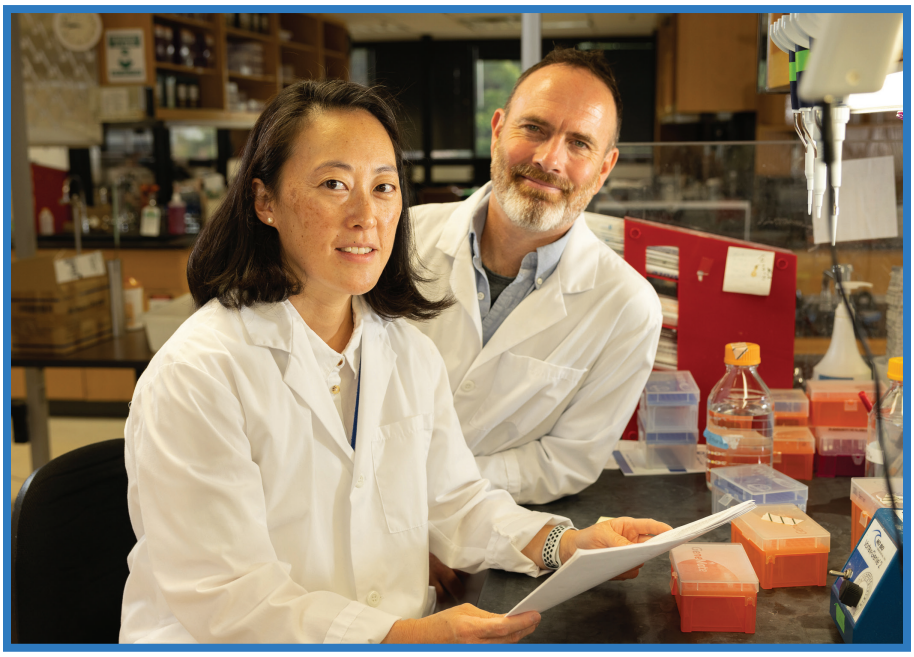
The Sansams are among roughly 30 married couples at OMRF. Together, they comprise more than 10% of the foundation's workforce, and in most cases, they work as a team in the same lab.

This phenomenon isn't unique to OMRF, nor is it new. More than a century has passed since the marriage of Marie and Pierre Curie, physicists and scientific collaborators who discovered the radioactive elements radium and polonium. They were the first married couple to win a joint Nobel Prize, and four others – including their daughter and son-in-law – have done it since.

In 2008, a Stanford University study of 9,000 faculty members

Drs. Chris and Courtney Sansam are among the more than two dozen married couples at OMRF.

Drs. Rose Ko and Bob Axtell have been together for two decades. They became scientific collaborators in 2014 when Axtell opened his OMRF lab.



at more than a dozen universities found 36% to be part of an academic couple, with 38% of those working in the same department as their partner. The numbers were even higher among scientists: Of those in relationships, 83% of women and 54% of men had a fellow scientist as a significant other.

OMRF staff scientist Dr. Rose Ko, half of another scientific couple, sees work-life balance as a key reason researchers choose one another as partners in life.

"There's no guilt involved when work calls," says Ko, who has been married to OMRF's Dr. Bob Axtell since 2008. "It's like, 'I know we said we're going to do a movie, but I've got this lab result I need to go check out.' Another scientist is going to say, 'I totally understand.'"

Axtell and Ko work in tandem, and their research centers around multiple sclerosis. Axtell says Ko, whose responsibilities range from conducting complex experiments to sharp-eyed editing of his writing for scientific papers and federal grants, is critical to their lab's success. "She's really, really good."

The pressure of science might follow them home, the couple agrees, if it weren't for their 4-year-old sons, John and Oliver. "Having twins kind of makes it simple," says Axtell. "At home, we're focused on our guys' needs – and that they're not, you know, injuring themselves."

The Sansams, with their son's toddler years long past, say there's no compartmentalizing work and home. "I ask science questions all the time," says Chris. The couple jokes that despite collaborating for the last decade, they're still making up for lost time. With rigorous schedules during their graduate studies in Nashville and the postdoctoral years at different institutions, "We never saw each other," says Courtney. Plus, being on the same team as her spouse has bolstered their ability to recruit graduate students and postdoctoral researchers to the lab: junior scientists, she says, see the duo as "like getting two mentors."

Most importantly, Courtney says, their partnership creates a deep, personal commitment to their science. "If you have to come back to the lab late at night, or if I'm working on weekends, I feel good knowing I'm going in and making a difference for our lab, not doing an experiment for somebody else."

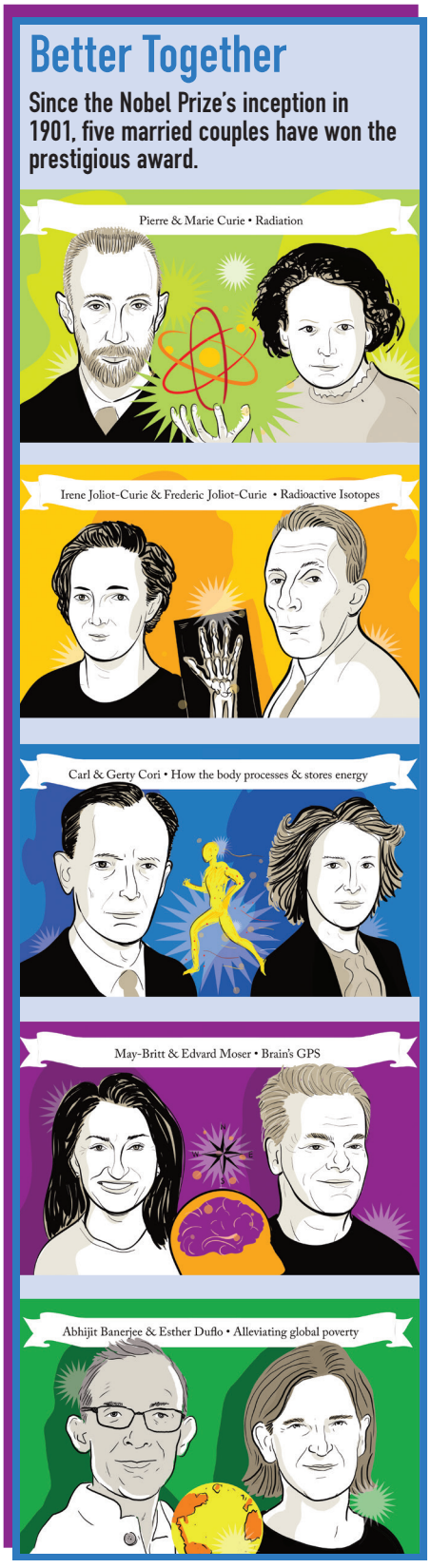


Illustration by Brian Taylor

For Kent and Jeanette Young, OMRF's work hits "right at home"

A Legacy of Giving

High school sweethearts Kent and Jeanette Young didn't start out with much. "Neither of us expected to have the opportunity to make the kinds of charitable contributions we're making now," says Kent. "Or what we're going to leave behind when we're both gone."

Born and raised in eastern Oklahoma's Wewoka, the pair landed in Tulsa in the 1960s and have called it home ever since. They've been supporting OMRF for almost as long.

Early in his career, Kent, a public relations specialist, was responsible for guiding his employer's charitable giving. This work led to a partnership with the Muscular Dystrophy Association, and "that was where we became acquainted with medical research," he says.

Around that time, Jeanette, volunteering at their church, noted how overwhelming floral arrangements could become following a funeral. Well-meaning mourners left scores of bouquets behind, which "confirmed our decision that we could put our memorial gift money to better use elsewhere," Kent says. "That elsewhere is OMRF."

The Youngs made their first memorial donation to the foundation more than 30 years ago, and it kindled a longtime connection. "Scientists at OMRF research diseases that a lot of our friends – and us – suffer from. It hits us right at home," says Kent, who had a near-fatal heart attack at age 58. Jeanette has lived with rheumatoid arthritis for nearly four decades.

Recently, after meeting OMRF scientists and learning more about the work done in the foundation's laboratories, the couple also decided to include OMRF in their estate plans.

"We've gotten to know the Youngs, had meaningful conversations about their intentions, and have been able to share our scientists' progress with them," says OMRF Senior Director of Development Sonny Wilkinson. "They have chosen to marry their legacy to OMRF forever, and we're committed to ensuring their generosity will fund meaningful research."

The Youngs' legacy also continues with their daughter, Leslie, who is following in Jeanette and Kent's charitable footsteps. "I've started making memorial donations to OMRF," she says. "I learned from my parents, and I love the idea of making a difference in this way."

The Youngs know that medical advances take time. Jeanette lost her grandfather to cancer at the age of 48 and her father to a heart attack at 57. But, she says, "These days, a diagnosis doesn't have to be a death sentence. And that's because of research."

Paying Tribute

For many years, Kent and Jeanette Young have been members of OMRF's Tribute Circle, a giving society designed to help individuals and organizations honor and celebrate friends, family and clients. Like all gifts to OMRF, 100% of Tribute Circle donations go directly to medical research.

To learn more about OMRF's Tribute Circle, visit omrf.org/TributeCircle or contact Caroline-Allen@omrf.org.

Predicting MS Relapses

Researchers look to the blood to spot – and stop – disease activity

For most of the nearly 1 million Americans living with multiple sclerosis, life is a teeter-totter.

The autoimmune disease causes the body's immune system to attack its own healthy tissues, resulting in inflammation that can cause vision issues, muscle spasms, tremors and paralysis. In the most common form of the disease, there are periods of stability and relapse.

In relapse, old symptoms worsen, new ones appear, or in some cases, both. And to prevent irreversible damage to the brain, quick diagnosis and treatment are critical.

Today, MS relapse is diagnosed with an MRI or by interpreting symptoms, says Dr. Gabriel Pardo, who leads OMRF's Multiple Sclerosis Center of Excellence. But diagnosis isn't foolproof. Sometimes the inflammation-related neurological damage precedes the onset of symptoms. Other times, symptoms can disappear within 24 hours or result from an infection or unrelated medical condition.

"We call this a 'pseudo-relapse,'" says Pardo. In a disease with limited medication options and where both swift action and avoiding unnecessary intervention are equally important, "making sure a true relapse is taking place is critical," he says.

Thanks to new research from OMRF's Dr. Bob Axtell, that certainty may soon be just a vial of blood away.

Recently, a blood protein called sNfl has emerged as a biomarker, or strong indication, of an MS relapse. Scientists can detect this protein in a small blood sample. But, says Axtell, monitoring MS activity with a single protein "has limitations." Age, sex and other neurological conditions could affect the protein's levels. And it may not behave the same way in all patients.

To increase diagnostic precision, Axtell's team searched for other biomarkers. The scientists examined blood samples of about 100 patients at OMRF and Stanford University, all experiencing an MS relapse.

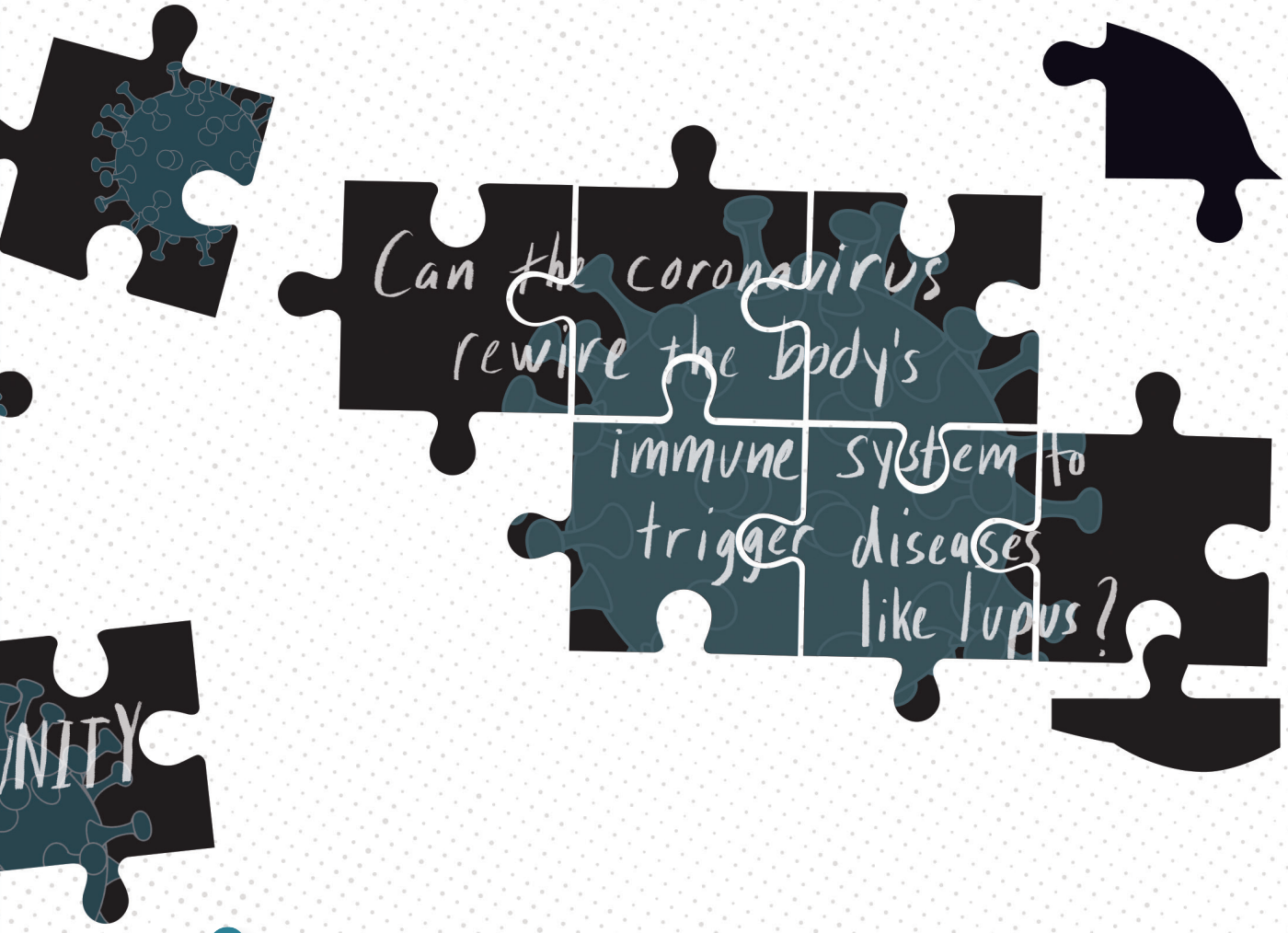
What the researchers found surprised them. In the donated samples, along with sNfl, they identified significantly different levels of a trio of other proteins. While a spike in sNfl correctly reflected a relapse in 69% of patients, the four-protein panel increased the accuracy to 87%.

Although scientists will need to verify the results with a more extensive study, Axtell hopes this insight will make a difference for people with MS sooner rather than later. One possible outcome is a home test that would use a finger prick to detect blood biomarkers. This would potentially spare rural patients from traveling great distances only to be diagnosed with pseudo-relapse and help others catch a true relapse before it can harm them.

> "If we could use these biomarkers for early identification of a relapse, we might be able to prevent long-term disability in patients."

"If we could use these biomarkers for early identification of a relapse, we might be able to prevent long-term disability in patients," says Axtell. For the more than 3,000 patients with MS receiving care at OMRF, that would provide some much-needed balance in lives too often made unstable by an unpredictable disease.


THE
PUZZLE
OF
COVID
AND
By
Adam Cohen
Illustrations by
Daniel Hertzberg



When Covid-19 started its inexorable march around the globe in early 2020, Dr. Linda Thompson knew what she had to do.

An immunologist, Thompson had joined the Oklahoma Medical Research Foundation in 1989 from Scripps Research, where she'd been a faculty member. In the ensuing three decades, she'd investigated the immune system in a variety of ways. She'd studied a form of severe combined immunodeficiency known as "bubble boy" disease. She'd created laboratory mice that lacked an enzyme key to immune responses and shared them with scientific collaborators on four continents.

In a project for the National Institutes of Health, she'd examined how patients with lupus responded to flu shots. That led to a collaboration with other OMRF scientists to study another illness that, like lupus, causes the body to turn its immune system against itself.

As Covid-19 spread, Thompson set her sights on helping to fight the virus. "How could you not?" she says.

With cases mushrooming and time in short supply, scientists understood that developing the most effective strategies against a virus that hadn't existed even a year ago meant building not from scratch but, rather, from existing research. For Thompson and her colleagues at OMRF, that pointed to a pair of beachheads.

"Because of the work we did in the flu vaccine, we had the infrastructure to measure the body's immune response," says Thompson, who holds the Putnam City Schools Distinguished Chair in Cancer Research at OMRF. "And because of our experience working with patients with lupus and other autoimmune diseases, it made sense for us to focus there."

Teaming with Dr. Mark Coggeshall and other scientists at OMRF, she submitted a proposal to the NIH to expand upon immunology projects Coggeshall had led for many years. When OMRF received the funding, along with a gift from a group of local philanthropists intended to jump-start Covid-19 research in Oklahoma City, labs across OMRF kicked into action.

Overnight, immunologists, cell biologists and rheumatologists all became Covid researchers. Their projects varied, but as time passed, the most successful ones coalesced around a theme: the relationship between this novel virus and autoimmunity.

The phenomenon of autoimmunity occurs when the body confuses its own cells for invaders like viruses and bacteria. The immune system then unleashes powerful countermeasures against itself. Depending on the cells targeted, this can result in a variety of diseases, including lupus, multiple sclerosis and Type 1 diabetes. All told, these and roughly 75 other autoimmune illnesses affect an estimated 25 million Americans.

Like so many other conditions, the origins of these disorders are not precisely known. However, scientists have increasingly found evidence that viral infection can trigger their onset.

As Covid-19 cases swept across the country and world again and again, scientists at OMRF and elsewhere looked at the interplay between the virus and autoimmune diseases. In the course of their work, the researchers grappled with the obvious tolls of the virus: acute illness, death in some, lingering effects in others. But as their understanding has taken more precise shape, they've also begun to ask another question.

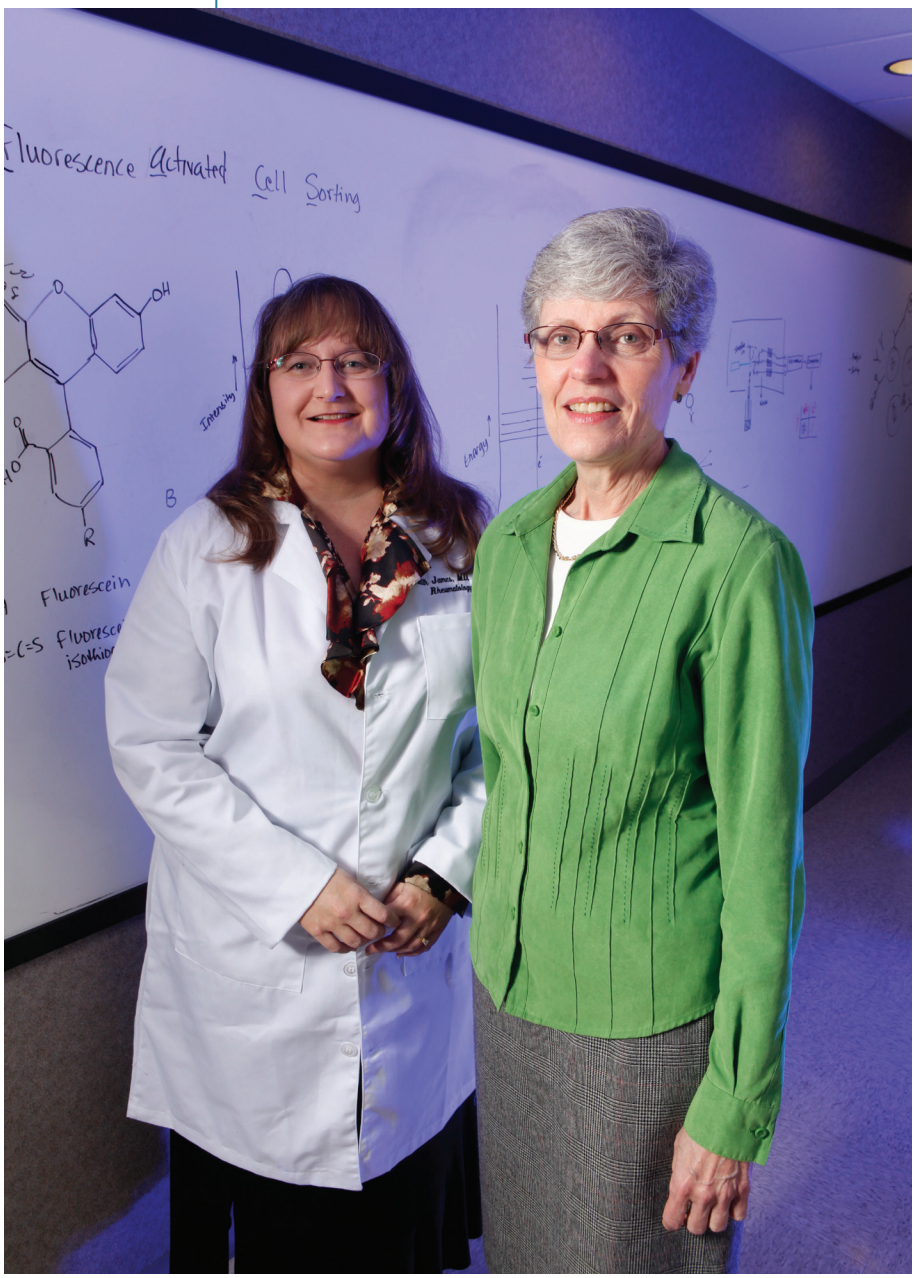
Can Covid-19 *cause* autoimmune disease?

Twenty-five years ago, OMRF's Dr. Judith James helped pioneer the idea that a virus might serve as the trigger for a chronic autoimmune disease. Trained both as a rheumatologist and an immunologist, James began her research career by looking at the causes of lupus, a disorder that's notoriously difficult to diagnose due to the many different ways it presents in patients. Although the illness can cause the body's immune system to lash out at numerous organs and systems, it most commonly strikes the joints and skin, and its dermatological symptoms most likely gave the illness its name: A 13th-century physician is reputed to have assigned the label "lupus" – Latin for wolf – to the condition because the facial lesions it caused reminded him of a wolf's bite.

Beginning in the 1970s, scientists identified multiple genes that seemed to predispose people to the disease. However, they also suspected that some unknown environmental agent was operating as a sort of "on" switch for those genes, causing them to activate in certain people. In 1997, James, who is now OMRF's vice president of clinical affairs and holds the foundation's Lou C. Kerr Endowed Chair in Biomedical Research, led a study that identified a potential culprit.

Using blood samples donated by children and young adults, James and her then-OMRF colleague Dr. John Harley found that 99% of young patients with lupus had at some point in their lives been infected with Epstein-Barr virus, which is known to cause common colds in most and mononucleosis in some. But among healthy matched controls from the same age group, the researchers discovered that a much smaller percentage tested positive for the virus. When the scientists looked for a similar correlation with other cold viruses, they found none.

"These data are consistent with, but do not in themselves establish, Epstein-Barr virus infection as an etiologic" – causal – "factor in lupus," James and Harley wrote when they published the results of their work in The Journal of Clinical Investigation, an influential scientific publication.



Drs. Judith James and Linda Thompson are leading OMRF efforts to understand the body's immune response to Covid-19.

Even a quarter-century later, the study stands out among the hundreds and hundreds James has since done in her career. She recalls driving to a small city in southeastern Oklahoma to enroll a girl with pediatric lupus. When the girl's softball teammates learned about the study, they all wanted to help their friend, so every one of them asked to enroll, too – as healthy controls. "Those are the kinds of papers," says James, "you don't forget."

The work also proved unforgettable from a scientific perspective. "Judith James and John Harley did seminal work showing that Epstein-Barr virus plays a causative role in lupus," says Dr. P.J. Utz, a professor of immunology and rheumatology at Stanford University. "That changed how we thought about autoimmunity in general."

In the ensuing years, James continued to amass evidence that the virus represented a crucial piece in the puzzle that is lupus. She gathered new clues both in the clinic and at the cellular level, which pointed to links between Epstein-Barr infection and the subsequent onset of the autoimmune disease.

She hypothesized that in a certain subset of people, most likely due to their genetic profiles as well as other factors in their lives, "the body makes the wrong immune response to Epstein-Barr virus." This confusion causes the immune system to create antibodies that target not only viral invaders but also the body's own cells. In landmark research in The New England Journal of Medicine, James, Harley and OMRF colleague Dr. Hal Scofield demonstrated that these "autoantibodies" often appeared in the blood of seemingly healthy people who would later go on to develop lupus.

That landmark revelation, says Stanford's Utz, made the study "one of the most impactful papers in autoimmunity." The work offered the strongest proof yet that lupus and other autoimmune disorders don't simply crop up overnight; those who develop the conditions often have preexisting autoantibodies that are like dominoes waiting to fall. "They've been percolating them for months or years," Utz says.

As Covid-19 cases became widespread, James, Utz and other experts saw hints that infection with the novel coronavirus might be exactly the sort of nudge this group did not need. "With people who are predisposed to autoimmunity," says Utz, "the virus might just push them over the edge."

When James and other researchers studied Covid-19 patients, they observed what she characterizes as "an overzealous immune response." Much of the data, she says, "looked very similar to what we see in lupus." Patients' blood showed a low concentration of white blood cells, which is atypical of infections but consistent with lupus. On a molecular level, some of the same immune pathways that overreact in lupus and rheumatoid arthritis, another autoimmune disorder, were also overreacting with SARS-CoV-2 infection.

"If you get sick enough from Covid-19 to end up in the hospital, you may not be out of the woods even after you recover."

Covid-19 can elicit a dizzying array of symptoms. But many – rashes, joint pain, severe fatigue, fever, swollen lymph nodes – mirror those found in lupus.

Joining with Utz's team at Stanford as well as researchers in Germany and the University of Pennsylvania, James dug deeper into the roots of those similarities. Specifically, the scientists examined the blood of patients who'd been hospitalized with Covid-19. They found that, compared with people who hadn't been infected, the patients were much more likely to harbor autoantibodies.

Those autoantibodies were some of the same ones James had first demonstrated can serve as harbingers of autoimmune disease. So, says Utz, "If you get sick enough from Covid-19 to end up in the hospital, you may not be out of the woods even after you recover."

The work offered a tantalizing clue that severe Covid-19 could ultimately trigger autoimmune disease. But it represented only a fraction of the work she'd launched into to explore the overlap between these two conditions.

As part of the effort to expand on the long-term immunology project led by OMRF's Coggeshall, she looked at the immune responses of autoimmune disease patients who'd recovered from Covid-19. "We wanted to understand how individuals who did poorly after infection compared to those who did very well," she says. She hoped she could "learn from the people who did well to see what part of the immune system needed to be shored up."

In the clinic, she led an arm of an NIH trial testing various vaccination strategies in autoimmune patients. The trial focused on how to maximize the effect of boosters in people whose immune systems are compromised. "Should we switch to a different vaccine? And does it help to stop their medicines?"

In the course of her work, James expected to see that people with autoimmune disease had higher levels of severe Covid-19 than those without comorbidities. This didn't turn out to be the case: Both groups showed similar levels of severe illness. However, in autoimmune patients, their symptoms lasted longer. And as reports emerged of long Covid – prolonged symptoms that linger or develop after the initial acute phase of infection – the syndrome once again echoed what she saw in her patients. "Fatigue, joint pain, rash. These are typical of autoimmune diseases

Understanding Autoimmune Disease

Lupus, rheumatoid arthritis and Type 1 diabetes are among the more than 80 known autoimmune disorders that develop when the body's immune system goes haywire and attacks its own organs, tissues and cells. The National Institutes of Health estimates the conditions impact more than 25 million Americans, most of whom are women.

"We are in a very challenging situation."

we take care of as rheumatologists," conditions such as fibromyalgia, lupus and rheumatoid arthritis.

She joined a national consortium led by New York University called RECOVER, which is studying multiple aspects of long Covid in patients over a four-year period. "Our goals are to identify treatments and other interventions to help patients who have long Covid symptoms. We also want to be able to predict people who are at the highest risk of developing long Covid," she says.

With RECOVER, she'll also stay alert for clues about how long Covid overlaps with autoimmunity. Already, a study from researchers at the Institute for Systems Biology has produced a pair of intriguing leads.

The work identified four factors that appear to place people at high risk for the syndrome. One is viral load, and another is having Type 2 diabetes. But it's the last two that are of particular interest to James and her colleagues.

The scientists determined that patients were at greater risk for long-term symptoms if they had autoantibodies in their blood early in their coronavirus infection. Ditto if their bodies showed reactivation of a common pathogen: Epstein-Barr virus.

Autoantibodies, Epstein-Barr virus. As James has shown, both are also likely culprits, or at least accomplices, in autoimmune disease. Now, it's up to her and other autoimmunity researchers to decipher their role in Covid-19. And then, of course, to use this information to blunt the impact of the virus and improve outcomes for patients worldwide.

"We are," says James, "in a very challenging situation."

James will continue to study Covid-19 through the lens of autoimmune disease. She'll focus on how she can ensure the well-being of her patients with lupus and rheumatoid arthritis in the teeth of a viral pandemic that is becoming endemic.

But like others in her field, she also has her eye on the autoimmune implications of widespread coronavirus infection for the hundreds of millions of Americans who don't have autoimmune conditions. Or at least not yet.

In the clinic, following coronavirus infections, she's seen one patient develop lupus, another rheumatoid arthritis. As a scientist, she knows this is "clinical observation, not research." Both might already have been on the road to autoimmune disease.

Still, that's how research begins: with an observation. That observation becomes research when scientists put it through rigorous testing and analysis.

Moving forward, James is interested in finding people with autoantibodies – but not full-blown autoimmune disease – and following them clinically for the next few years. She wants to see what happens to those who get Covid-19 and those who don't.

A study by Stanford University and OMRF found that people hospitalized with Covid-19 were much more likely to harbor autoantibodies linked to diseases like lupus.

Will hospitalized patients, who disproportionately tested positive for autoantibodies in James' study with Stanford's Utz, go on to develop autoimmune disease at higher levels than the general population? How will the severity of a person's illness factor into the equation? And what about long Covid, with the condition's eerie resemblance to autoimmune disorders?

Finding answers to these and a host of other related questions will not be simple, says James. "We need hundreds of thousands of people who've been infected with the coronavirus and tens of thousands of people who have long Covid to understand whose autoantibodies go away, who progresses to autoimmune disease, and what the underlying mechanisms are." There are, she says, "a lot of different clinical syndromes that get lumped together, so we have to have enough patients to tease out the many different pieces."

While James searches, variants of Covid-19 will continue to run through the population. And with those infections, she predicts, will come more patients with joint problems, more with prolonged fatigue – "symptoms that look like what we see in autoimmune disease patients."

Solving the puzzle of Covid-19 and autoimmunity will not be easy. But if the pandemic has taught us anything, it's that the virus won't stand still. That means neither can we.

CHANGING THE COMPLEXION OF SCIENCE

OMRF's partnership with Langston University, the state's only historically Black college or university, aims to prepare underrepresented students for careers in biomedical research.

By Lindsay Thomas | Photos by Brett Deering and Rob Ferguson | Illustration by Antoine Doré

Of the thousands of questions researchers posed at OMRF in 2020, one took an unusually public stage. Amid the surge of attention on racism in the U.S., scientists across the country and at OMRF placed their labs under the microscope.

"It got a lot of us thinking about how we didn't have a lot of Black scientists or other underrepresented groups at the faculty level, and why was that?" says Dr. Susan Kovats, an immunologist who'd led a lab at the foundation since 2005. In the conversations that followed, researchers wondered whether the underrepresentation was direct discrimination, an absence of opportunity, lack of outreach, a combination of those factors, or something else entirely. And apart from the root cause, says Kovats, a second question followed: "What can we do to fill the pipeline?"

In a June 2020 editorial that appeared in The Oklahoman newspaper, the late Dr. Stephen Prescott, then OMRF's president, addressed the lack of diversity in high-level scientific roles head-on. "Above all else, science relies on facts and data," Prescott wrote. "When it comes to bringing minorities into our ranks, those facts and data are clear: We're failing."

The commentary prompted Kovats to reach out. If OMRF was going to do something about the issue, she told Prescott in an email, she wanted to help. "He wrote back and said, 'Would you like to chair the committee?'"

The path to faculty-level positions in biomedical research is arduous and highly competitive. And narrow. According to a 2019 National Science Foundation survey, of students earning a Ph.D. in life sciences at a U.S. university, only 23% will go on to a faculty-level position.

In an independent research institute like OMRF, the principal investigators, or PIs, are its faculty. They are the leaders of the foundation's individual laboratories, senior researchers who chart the organization's scientific course. OMRF has more than 50 PIs.

"In the sciences, principal investigators set the tone for an institution," says Dr. Andrew Weyrich, OMRF's president and a principal investigator at the University of Utah for more than 25 years. "They not only direct the research, but they inform its culture. They also train the next generation of scientists."

The first step to becoming a PI is to earn a bachelor's degree, usually in the biological sciences. The NSF survey found that only about a quarter of undergraduate science and engineering degrees were earned by underrepresented minorities, which the NSF defines as Black or African American, Hispanic or Latino, and Native American or Alaska Native people.

The next stop is graduate school for a doctorate. For doctoral degrees among the same groups, the number shrank to 16%. And while both figures are up significantly over the last two decades, representation lags the country's general population. According to the U.S. Census Bureau's latest statistics, these groups now make up more than 1 in 3 Americans.

A multi-year postdoctoral fellowship follows, the equivalent of a clinical residency for physicians. A study released this year found that for those scientists who finished their fellowships after 2013, only 30% had become PIs five years later.

The numbers are particularly stark when it comes to Black scientists and biomedical research. Fewer than 2% of PIs receiving research project grants from the National Institutes of Health are Black.

Dr. Susan Kovats and 2021 Langston Scholar Yamiah Mitchell

Trejon James was eager to "see what the field of biology had to offer."

OMRF is not homogeneous. A third of the foundation's employees identify as people of color, and staff hail from close to 40 countries. Still, in the foundation's more than three-quarter-century history, and especially at its highest levels, researchers from underrepresented groups are notably absent.

This reality is not unique to OMRF. Universities and research institutes across the U.S. are confronting it. And with good reason: Time and again, research has shown that diverse teams outperform uniform groups when it comes to problem-solving and innovation. And in science, different approaches yield different results.

In the summer of 2020, with backing from Prescott and other OMRF administrators, Kovats led the creation of a new outreach committee at OMRF. The group's first meetings, says Kovats, involved "a lot of brainstorming." Members discussed how the foundation might reach historically underrepresented groups in science, ranging from Black and Native American to Hispanic and Latino students. They considered field trips, hands-on programming for elementary and secondary schools, and summer internships for college students in the model of the foundation's longtime Fleming Scholar program.

Dr. Valerie Lewis, a postdoctoral researcher studying autoimmune illnesses like lupus and Sjögren's disease, served on the committee. Before she chose a career in science, though, she worked in the career placement office at Langston University, Oklahoma's only historically Black college or university. She knew the school had an impressive science program, top-notch students who came to the state from around the U.S., and a faculty with research partnerships with federal agencies like NASA.

"When it comes to bringing minorities into our ranks, we're failing."

"Langston sends their students throughout the country to do research during the summer," says Lewis. She wondered aloud whether OMRF, just 40 minutes from Langston's campus, might be a destination for some of them. "OMRF is an amazing environment with amazing scientists, and students are leaving the state to do research? It was insanity to me."

Lewis connected OMRF's leadership with key faculty at Langston. Soon, talks were underway. During the OMRF committee's first visit to Langston, Dr. Byron Quinn, chair of the university's biology department, described the same issue Lewis raised.

"We see a lot of our top students apply to out-of-state internships," he explained. Once they spend a summer at Stanford or Yale, he said, they almost always end up leaving Oklahoma upon graduation. "It would be nice to keep some of the students here."

In the months that followed, leaders from the two institutions put their heads together to create a new program. It's one they hope will spur change, both for Langston students and OMRF.

Ask Trejon James about his first impression of OMRF, and he laughs. "I just remember thinking, 'Dang, this building is huge.'" And then, "'You can tell a lot of important things go on here.'"

The 19-year-old biology major from Topeka, Kansas, had just wrapped his freshman year at LU. In summer 2021, he and five other students arrived at the foundation and made up the inaugural class of the OMRF-Langston Biomedical Research Scholars Program.

For eight weeks, James worked under the mentorship of OMRF's Dr. Tim Griffin. With Griffin's guidance, he studied how osteoarthritis gets a foothold in the body and investigated strategies to better treat people living with the painful condition.

James enrolled at Langston as an honors student with a full scholarship, his sights set on pharmacy school. He's loved science since he was a child and cites a sixth-grade experience as the spark that ignited an interest in biology in particular. "We dissected a cow heart," James says. "It was my first chance to actually get in the lab."

After spending his first year of college learning via Zoom due to the Covid-19 pandemic, James was eager to be around people and to "see what the field of biology had to offer." In Griffin's lab, he embraced a steep learning curve.

"It was a lot of newness for me," says James. "Working in the lab, the scientific terms, the machines, the tools. And I'd never worked with mice. It was pretty fun."

The two-month paid internship opened James' eyes to lab life. In a traditional summer program, the experience would have ended there. But with the new program, OMRF and Langston took a different approach. "We wanted to create something more meaningful and long-lasting," says Langston's Quinn.

"The point is to grow and develop these kids," says OMRF's Lewis. Rather than sending them on their way after a brief experience, "we want to guide them on the path of science."

OMRF-LANGSTON BIOMEDICAL RESEARCH SCHOLARS PROGRAM

Inaugurated in 2021, the program begins with an eight-week, paid summer internship for Langston University undergraduate students in one of OMRF's labs. Students work full-time on individual research projects under the guidance of OMRF scientific mentors. They also attend weekly seminars, write scientific papers and give formal presentations summarizing their research.

After the summer, students can opt to continue their work into the school year and throughout their undergraduate careers, either in Langston's Science Research Institute or at OMRF. They may also return to OMRF for subsequent summers.

With studies consistently showing that underrepresented students are more likely to drop out of STEM majors than their white peers, the program aims to provide long-term mentorship to aspiring scientists of color. That way, says program liaison Dr. Valerie Lewis, when students encounter roadblocks or need guidance, "they will have a mentor who can help and support them."

After the summer, students could elect to continue their OMRF research over the school year. Some work could take place in Langston's Science Research Institute; other projects would continue at OMRF. And the following summer, students could return for another eight weeks. Ultimately, their research projects and mentorships could extend throughout their undergraduate careers. If the students elected to apply to graduate school, their mentors could help guide them through the process.

Down the road, some students might do graduate or postdoctoral work at OMRF. One day, one might even become a PI at OMRF.

"This is the only program like this that I know of in STEM," says Quinn. "It is a true collaboration that can create real research and real opportunities."

Like most experiments, this one looked great on paper. But after the first summer, the institutions realized their approach needed a bit of tweaking.

When school resumed, James was eager to return to OMRF to continue his research. But with a full load of classes, plus GPA and volunteer hour requirements to retain his scholarship, finding time to devote to OMRF proved difficult. Several other students from the inaugural class were working part- or full-time jobs while in school, sometimes with overnight shifts, leaving no time for outside research.

"We have to balance all these pieces," says Quinn.

OMRF's Kovats, along with colleague Dr. Susannah Rankin and Quinn, have applied for an NSF grant to support that balance. The trio believes a key ingredient will be Lewis and fellow OMRF scientist Dr. Chris Schafer, who will work onsite at Langston part time as a bridge between OMRF mentors and students, providing hands-on training and guidance in the lab. They also want to reduce the financial pressure on Langston students by paying them a stipend to conduct research during the academic year, eliminating the need for outside employment.

As the scientists await a decision on the grant application, the second class of Langston Scholars has now completed a summer at OMRF. James returned for a second internship, and eight other students joined him as first-time program participants.

Aijalon Underwood, a 22-year-old chemistry major from Mansfield, Texas, was one. She spent her summer in Dr. Jake Kirkland's lab working to understand why alterations in certain genes drive cancer.

Now entering her senior year, she'd planned on a job at Walmart this fall to help pay for school and expenses. Instead, she'll be working in Kirkland's lab.

Until the summer, she says, she told anyone who asked that she was going into forensic science. "It was just easy for people to understand, even though I wasn't sure."

But after two months at OMRF, she says, a new career goal has come into focus: "Biomedical research." Grad school is in her sights, and she needs the lab experience as she sets out for her Ph.D.

After spending a summer at OMRF, Aijalon Underwood is charting a career in biomedical research.

Starring Role

Before lupus research, **Dr. Joan Merrill** tried her hand at stage and screen

When the Lupus Foundation of America named OMRF's Dr. Joan Merrill as the recipient of its highest honor, the Evelyn V. Hess Award, the president of the LFA saluted Merrill's "unwavering commitment to improving approaches to lupus research and clinical trials." He recognized her dedication to science and the role she has played in bringing safer and more effective treatments to patients with lupus worldwide.

Nowhere, though, did he mention her role in the film "The Super Cops."

At Vassar College, Merrill majored in drama. After graduation, she took the path trodden by many a youngster with a degree in theater: to Broadway. Or, more accurately, off-Broadway.

"I had parts in a number of plays in Greenwich Village and [Manhattan's] Upper West Side," she remembers. One particular high point came when legendary playwright Tennessee Williams paid a visit to a production of his "Battle of Angels," which Merrill was working on.

Merrill eventually secured membership in the actors' union, which led to bit parts in several movies. She still laughs about her non-speaking role in a now-forgotten 1974 crime drama. "I was supposed to be a go-go dancer wearing a little outfit with fringes on it, dancing up on a stage in a bar," she says. "The super cops walked past me, and one of them pointed at me and said, 'That one has a Ph.D.'"

The line might have been intended as snarky, but it turned out to be prophetic. At 29, after completing some basic science classes that hadn't seemed necessary for the career she mapped in acting, Merrill applied to medical school.

"She's from New York, she's loud, she's full of energy."

She soon received a call from Cornell University Medical College. "They wanted to interview me before admission because they weren't sure how I was going to cope with school at my 'old age.' I said, 'Not gracefully, but I will do it,'" Merrill remembers.

The answer satisfied the admissions committee, and in her final year at Cornell, a rotation at the National Institutes of Health led Merrill to specialize in rheumatology. In particular, she focused on lupus, an autoimmune disease that primarily affects women and that can present with a confusing array of symptoms.

She accepted a faculty position at Columbia University and split her time between the laboratory and treating patients. But when OMRF offered Merrill the chance to build her own specialized clinical research program in 2001, she jumped at the new opportunity.

"We were a calm little clinic before Dr. Merrill," says Fredonna Carthen, who manages clinical trials at the foundation's Rheumatology Research Center of Excellence. "She was an explosion. She's from New York, she's loud, she's full of energy." Merrill also realigned the clinic, which had previously targeted cardiovascular studies, to specialize in lupus care.

For people with lupus like Phyllis Perry, Merrill's care proved transformative. When the Lawton resident came to OMRF, she says, "I was really, really sick, and I was hurting all over." Merrill identified one particular drug that, it turns out, was causing devastating side effects. She stopped the treatment immediately. "Dr. Merrill saved my life," says Perry.

That approach – fewer drugs rather than more – has become a hallmark of Merrill's. In addition to patient care, she's used it as the backbone of designing clinical trials for new lupus drugs, a specialty for which she's become world-renowned. Recently, she's also spearheaded efforts to recruit more underrepresented patients to trials and to restructure trials to increase collaboration and communication between patients and caregivers.

The same openness that led Merrill to acting marked her interactions with patients. Often, she'd build rapport by sharing her own experiences with illness, including a bout with breast cancer. "I could tell them, 'It's horrible, but it gets better,'" Merrill says.

With patient care now in the hands of a junior OMRF colleague she describes as "fabulous," Merrill is excited to collaborate with researchers and pharmaceutical companies to develop new and more effective therapies for lupus. In at least one way, she says, the work hearkens back to her days as an aspiring actor.

"It's like an episode of your favorite mystery show," the physician-scientist says. "And we're detectives picking up clues."

Illustration by Evgeny Parfenov

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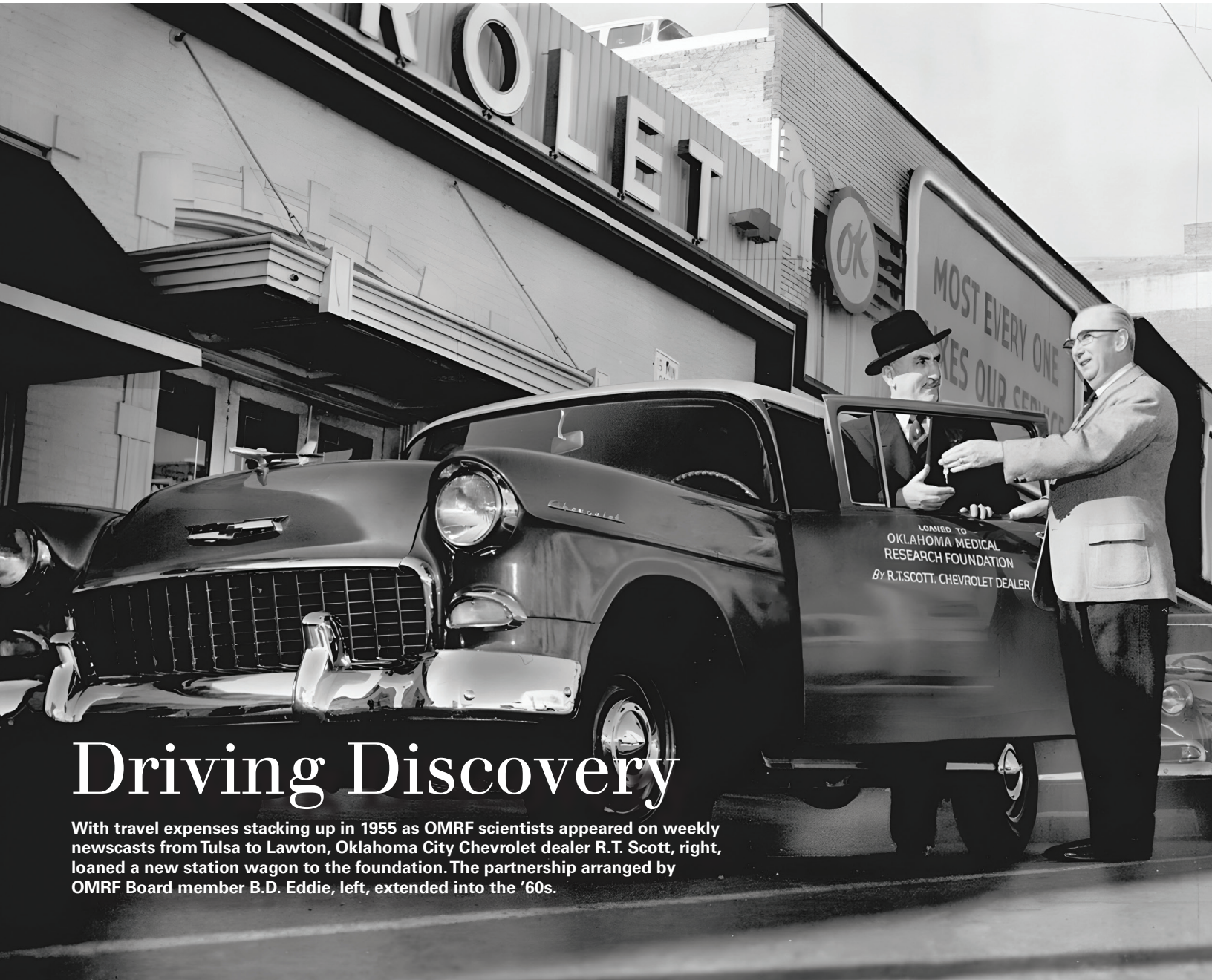

Driving Discovery

With travel expenses stacking up in 1955 as OMRF scientists appeared on weekly newscasts from Tulsa to Lawton, Oklahoma City Chevrolet dealer R.T. Scott, right, loaned a new station wagon to the foundation. The partnership arranged by OMRF Board member B.D. Eddie, left, extended into the '60s.