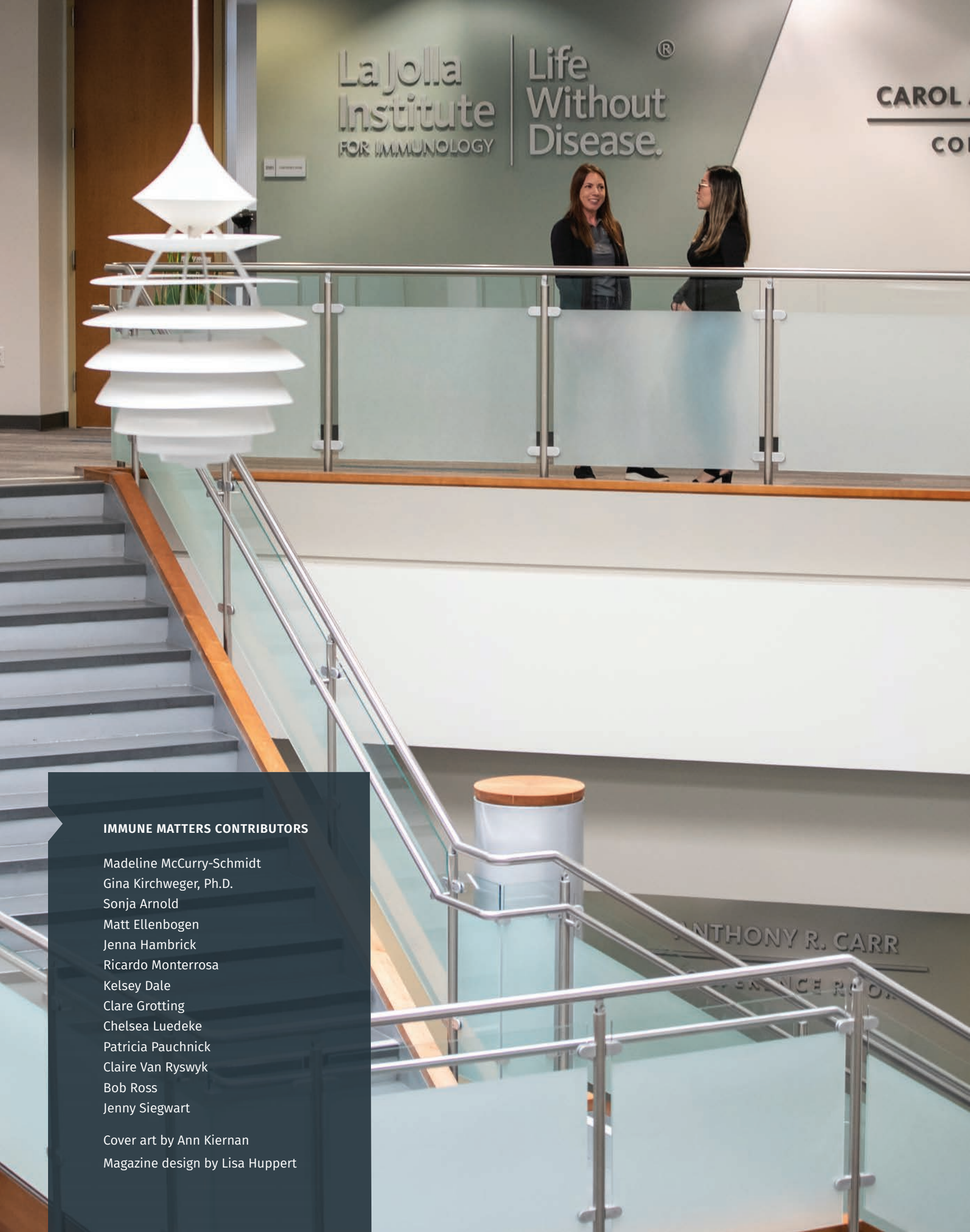
Immune MATTERS

LA JOLLA INSTITUTE
FOR IMMUNOLOGY

SPRING 2023

Neuroimmunology

RESEARCH ON THE EDGE
OF THE IMMUNE SYSTEM



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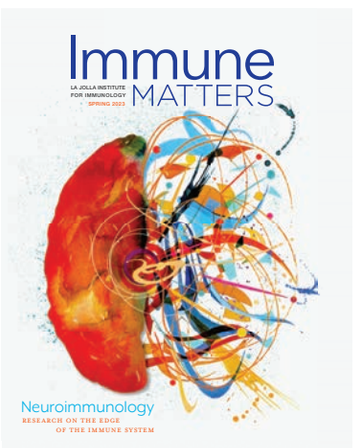
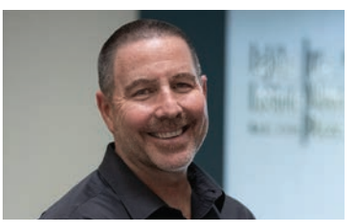
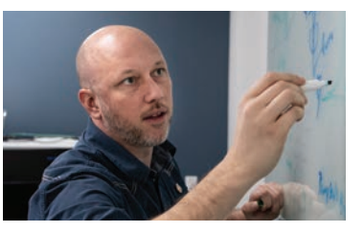


Researchers at La Jolla Institute for Immunology have found the brain and the immune system interact in fascinating ways. Here's the latest on how the growing field of "neuroimmunology" could lead to new therapies for Parkinson's disease, type 1 diabetes, and more.





OUR MISSION

The Institute will engage in a world-class biomedical research program with a focus on the immune system. It will conduct, share, and partner such that the results of its discovery program will make outsized contributions to the betterment of human health.

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FOR IMMUNOLOGY

Of brains and brain trusts

Immunologists have to think connections and networks. To stop disease, we need to understand the interplay of molecules and influences, genetic quirks, and cellular circuitry that power the immune system. When your work invites you to think about the body as a series of networks and circuits, it's remarkable to realize there's a central processing organ where the very basics of immune circuitry are still relatively unknown: the brain.

In just the last few years, researchers at LJI and around the world have discovered unexpected interactions between the immune system and the nervous system. I am confident this growing field of neuroimmunology will lead to new treatments for brain tumors, neurodegenerative diseases, infectious diseases, and even autoimmune diseases. Much of the brain is still undiscovered country for immunologists, so we're excited to share our latest findings in *Immune Matters.*

This issue also offers an inside look at the launch of a new lab. LJI Assistant Professor Samuel Myers, Ph.D., shares the story of how his laboratory came together after he was hired by the Institute in 2021. I know from experience that starting a new laboratory means a lot of heavy lifting, late-night shopping—and trips to the hardware store. I want to thank Sam for bringing his chemistry expertise to LJI and for sharing a behind-the-scenes view of what it takes to launch a career in science. I also want to thank my colleague John Keegan, Chief Operating Officer (and subject of this issue's Q&A article), for stepping into his new role and using his strong analytical skills and resourcefulness to ensure smooth day-to-day operations of the Institute.

LJI supporters like yourself play a direct role in keeping our agile Institute at the forefront of biomedical research. You shine the light so that LJI scientists can uncover still-shaded secrets of the human body. With donor support, new LJI faculty members can swiftly launch discovery programs and break new ground in fields like neuroimmunology.

I hope you enjoy this issue of *Immune Matters.* Let us share with you the new ground we've covered and remaining uncharted territories that keep immunology exhilarating. Walk with us into terra nova.

Sincerely,

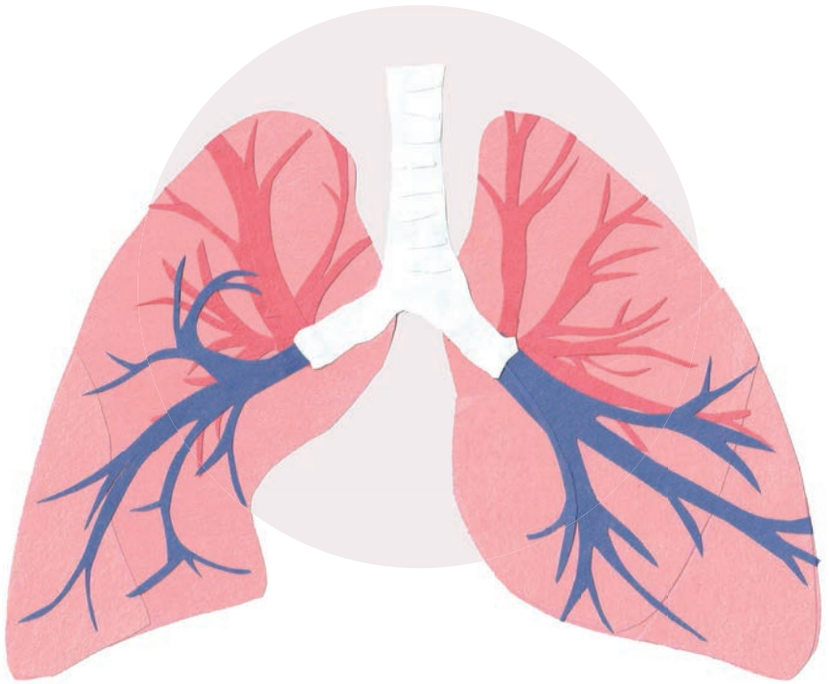
Erica Ollmann Saphire, Ph.D.
President and CEO
La Jolla Institute for Immunology

LJI researchers find a potentially long-term answer to asthma

An inflammatory molecule called LIGHT appears to be the cause of life-threatening airway damage in patients with severe asthma. According to new research from La Jolla Institute for Immunology (LJI) scientists, therapeutics to stop LIGHT (which is related to tumor necrosis factor) could reverse airway and lung damage in patients—and potentially offer a long-term treatment for asthma.

"This is a very, very significant finding," says LJI Professor Michael Croft, Ph.D., senior author of the new study. "This research gives us a better understanding of the potential of therapeutic targeting of LIGHT and what we might do to relieve some of the symptoms and inflammatory features seen in patients with severe asthma."

The research, published recently in the *Journal of Allergy and Clinical Immunology*, included experiments with both mouse and human tissues and was spearheaded by LJI Instructor Haruka Miki, M.D., Ph.D. •



> "This research gives us a better understanding of the potential of therapeutic targeting of LIGHT and what we might do to relieve some of the symptoms and inflammatory features seen in patients with severe asthma."
>
> LJI Professor Michael Croft, Ph.D.

Opening a new window into cancer development

LJI researchers have made a major breakthrough in understanding how deletion of the genes that encode TET proteins can lead to cancer growth. Their new study, published in *Nature Communications*, is the first to show the immediate consequences of deleting all three genes from the TET family in mouse embryonic stem cells.

By using this mouse model, the researchers discovered that TET proteins are critical for keeping the process of cell and DNA replication running smoothly. Without TET proteins, important genes go missing, leading to mutations, or aneuploidies. Aneuploidies are cases where genetic material is added or deleted on a massive scale. "Aneuploidies are a common feature of cancer cells," says LJI Postdoctoral Researcher Hugo Sepulveda, Ph.D.

Uncovering this direct connection between TET loss of function and aneuploidies is a major discovery in the field of cell biology, and gives researchers a clue to finding genes that underpin cancer development.

Dr. Sepulveda co-led the research with former LJI Postdoctoral Researcher Romain Georges, Ph.D., who generated the mouse model and derived the stem cells for the project. LJI Professor Anjana Rao, Ph.D., served as the study's senior author. •

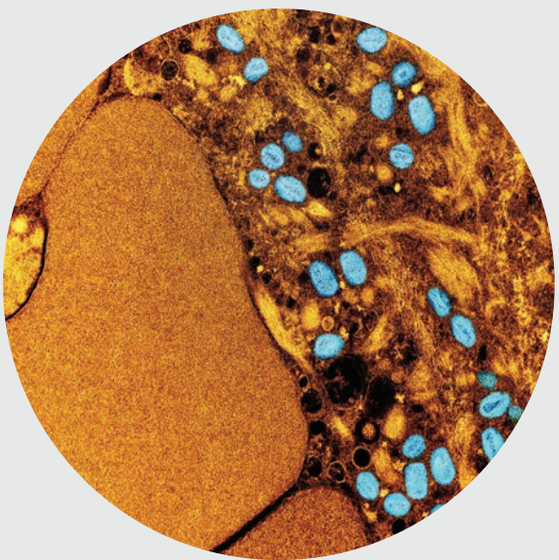
Aneuploidies are cases where genetic material is added or deleted on a massive scale. Aneuploidies are a common feature of cancer cells.

Existing vaccine may teach T cells to fight mpox

A recent LJI study, published in *Cell Host & Microbe*, is the first to provide evidence the vaccinia vaccine MVA-BN (brand name JYNNEOS) may also train virus-fighting T cells to recognize mpox sequences.

JYNNEOS works by prompting immune cells to recognize viral molecules, called antigens, from an orthopoxvirus called vaccinia (VACV). The vaccine was developed with the goal of training the immune system to also fight the virus that causes smallpox (called variola virus). These two viruses are similar enough that the immune system should recognize smallpox antigens alongside VACV antigens.

Mpox (termed monkeypox until recently) is also an orthopoxvirus. For the new study, LJI Professor Alessandro Sette, Dr.Biol.Sci., and LJI Research Assistant Professor Alba Grifoni, Ph.D., demonstrated that the known targets of T cell responses against VACV are also found in JYNNEOS and mpox, suggesting the JYNNEOS vaccine can indeed trigger an effective T cell response against mpox infection. “This study gives us confidence that T cell response induced by the JYNNEOS vaccine should be able to also recognize mpox virus,” says Dr. Sette.



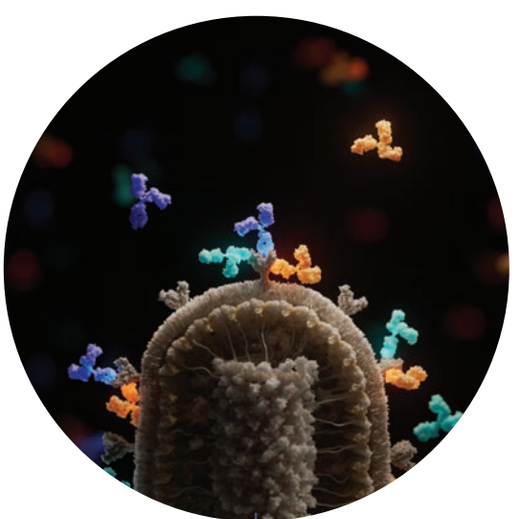
Colorized transmission electron micrograph of mpox virus particles (teal) found within an infected cell (orange). Image cedit: NIAID

A closer look at the new Ebola virus treatment

LJI scientists have uncovered the structure and function of the first FDA-approved treatment for *Zaire ebolavirus* (commonly referred to as Ebola virus). Inmazeb (REGN-EB3), developed by Regeneron, is a three-antibody cocktail designed to target the Ebola virus glycoprotein. The drug was first approved for clinical use in October 2020, but its exact mechanism of action had remained unclear.

In a recent cover story for *Cell Host & Microbe*, LJI researchers present a high-resolution, 3D structure of the three antibodies as they bind to the Ebola virus glycoprotein (the viral protein that launches Ebola virus infection). The new research also shows the potential for Inmazeb in treating additional species of other closely related viruses.

“Before this, we had a general idea of what the drug was doing, but we didn’t know exactly how,” says LJI President and CEO Erica Ollmann Saphire, Ph.D., who served as senior author of the study. “We now know which specific amino acids the antibodies are latching onto and how their binding affects the viral glycoprotein.”



The new study shows how three antibodies (light blue, dark blue, and yellow) used in Inmazeb (REGN-EB3) bind to different regions of the Ebola virus glycoprotein (grey) to combat infection. Image credit: Ethan MacKenzie (Phospho Biomedical Animation)

Neuro

"NEUROIMMUNOLOGY IS REALLY GAINING MOMENTUM NOW. THERE ARE THERAPEUTIC OPPORTUNITIES HERE."

MATTHIAS VON HERRATH, M.D.,
VISITING SCIENTIST

immunology

RESEARCH ON THE EDGE OF THE IMMUNE SYSTEM

For years, many scientists thought of the brain as "immunologically privileged." Few microbes can penetrate the brain, thanks to a layer of cells called the blood-brain barrier. This barrier also stops some immune cells and antibodies. In their place, specialized immune cells called microglia and astrocytes patrol the brain for danger.

It's comforting to imagine the all-powerful brain cloistered away in the skull, bathed in a special immune cell soup.

Yet many diseases do strike the brain. Aggressive tumors, such as glioblastomas, aren't shy about growing there. Alzheimer's disease and Parkinson's disease damage brain cells and steal memories. The wider nervous system isn't safe either. Viruses can camp out in the nervous system for years, and many autoimmune diseases exclusively target nerves.

To stop these diseases, scientists at La Jolla Institute for Immunology (LJI) have embraced the growing field of "neuroimmunology." By taking a closer look at how pathogens, immune cells, and the nervous system interact, these scientists have shown the brain is far from isolated.

In fact, researchers at LJI have uncovered clues that the nervous system and the immune system are in constant communication. LJI scientists have found that signals from the brain may influence the development of type 1 diabetes, and they've linked immune cell activity to Parkinson's disease. They've also launched new research to understand the role of immune cells in Alzheimer's.

"Neuroimmunology is really gaining momentum now," says Matthias von Herrath, M.D., a visiting professor at LJI. "There are therapeutic opportunities here."

THE WEIRD VIRUSES THAT LIVE IN YOUR NERVOUS SYSTEM

LJI Professor Chris Benedict, Ph.D., is interested in how viruses infect the nervous system—and why the body often fails to fight back. His laboratory focuses on a type of herpesvirus called cytomegalovirus (CMV). An estimated 70 percent of the population has CMV, and nearly 100 percent of the population has a similar herpesvirus called Epstein-Barr virus (EBV).

CHRIS BENEDICT, PH.D.

"This is a family of DNA viruses that once you're infected with them, you're infected for life. Your immune system can't clear them," says Dr. Benedict.

Dr. Benedict's work has shed light on how these viruses evade the immune system. Using mouse models and next-generation sequencing tools, he has shown that herpesviruses actually produce proteins that look very similar to human proteins. Immune cells try to fight back, but herpesviruses use these clever doppelgangers to trick the immune system into a cease fire. "They're able to throw up these smokescreens and thwart your immune system," says Dr. Benedict. Once the initial battle is over, certain types of herpesviruses move into the nervous system, only occasionally reactivating to cause a rash or canker sore (depending on the type of herpesvirus). CMV doesn't usually haunt the nervous system in adults. Instead, herpesviruses HSV-1 and HSV-2 are the lurkers.

At least that's the case in healthy people. A fetus can get CMV too, and this kind of infection in utero is the leading cause of congenital deafness. Even a latent CMV infection can turn dangerous in someone with a weak immune system—as seen in cases where CMV reactivates in someone with AIDS. "When your immune system is suppressed, all of these herpesviruses come out of hiding," Dr. Benedict explains.

These are the rare cases where scientists know CMV is to blame. Because so many people have CMV and virtually everyone has EBV, it's often hard to know whether a herpesvirus is driving a neurological disease or if it's just along for the ride. A 2022 study in *Science* showed a connection between EBV infection and the development of multiple sclerosis. Some studies have linked CMV to chronic fatigue syndrome. Cancer researchers studying brain tumors called glioblastomas have detected the CMV genome within the tumors.

"CMV is associated with glioblastoma, but most likely infection of the tumor cells (or tumor stem cells) happens at a very early stage in the womb (congenital infection). But does that mean cytomegalovirus is driving glioblastoma?" asks Dr. Benedict. "It's always been a sort of a chicken-and-egg argument. Are these viruses causative or are they associative?

Dr. Benedict suspects these viruses are part of the cause in cases where someone is already genetically predisposed to a disease. Herpesviruses are, after all, experts at manipulating human cells. "A person might have a gene linked to a higher susceptibility for getting a disease such as multiple sclerosis," he says. "Then EBV might further sensitize them for developing that disease."

SECRET MESSAGES FROM YOUR BRAIN

Dr. von Herrath is very interested in how the brain talks to immune cells. "The central nervous system controls the whole body, right?" says Dr. von Herrath. "So why wouldn't the nervous system set the inflammatory immune 'tone' in certain organs?"

Tracking messages from the brain to the pancreas is key to Dr. von Herrath's work to understand the origins of type 1 diabetes. Researchers know that type 1 diabetes occurs when self-reactive T cells start attacking the insulin-producing beta cells in the pancreas. In a 2020 study, Dr. von Herrath showed that everyone—not just people with type 1 diabetes—has these potentially harmful T cells.

These T cells linger near the beta cells but don't attack until they get some kind of signal. Dr. von Herrath thinks this signal may be coming from the nervous system. Using mouse models, his laboratory has shown that blocking nerve signals to the pancreas can stop the onset of type 1 diabetes.

One clue that Dr. von Herrath is on the right track is that beta cells in the pancreas tend to die off in patches that correspond to the presence of nerves in the pancreas. He suspects the nervous system may be communicating with immune cells called macrophages, since macrophages have the right kinds of molecular receptors to receive certain signals from the nervous system.

"Figuring out whether the nervous system regulates immune function is really a new frontier," says Dr. von Herrath.

GENETIC SEQUENCING GUIDES THE WAY

Sometimes the brain itself gets sick. Thanks to advances in neuroimmunology, LJI researchers are closer to understanding why.

In a series of pivotal studies, LJI Professor Alessandro Sette, Dr.Biol.Sci., and Research Assistant Professor Cecilia Lindestam Arlehamn, Ph.D., have shown a clear connection between harmful T cells and Parkinson's disease. In a collaboration with partners at Columbia University Irving Medical Center, the LJI team showed that dangerous, "self-reactive" T cells can be found in the brains of people with Parkinson's disease.

CECILIA LINDESTAM ARLEHAMN, PH.D.

These T cells are most active at the onset of Parkinson's disease, and they are on a mission to find and attack misfolded alpha-synuclein proteins. Unfortunately, these misfolded proteins are found on dopamine-producing neurons—the very cells that die as Parkinson's disease progresses.

ALESSANDRO SETTE, DR.BIOL.SCI.

ARE SELF-REACTIVE T CELLS TO BLAME?

There's still a lot to learn about these cells, but there's mounting evidence that Parkinson's disease onset may be an autoimmune process.

In a 2022 study in the journal *npj Parkinson's Disease*, Drs. Sette and Lindestam Arlehamn showed that the T cells involved in Parkinson's can express LRRK2, a gene associated with the genetic, or familial, type of Parkinson's disease. This gene expression had never been seen in T cells before—and the surprises continued. Many of the genes expressed in these T cells were completely unexpected and not previously linked to Parkinson's disease. "This finding suggests we found novel targets for potential therapeutics," says Dr. Sette.

Dr. Benedict says recent advances in genetic sequencing are key to connecting the dots between many more diseases and the nervous system. Across the Institute, many LJI laboratories are harnessing deep sequencing tools to understand how different genes are expressed in different types of immune cells. This research gives scientists a window into how the body fights—or surrenders to—different pathogens or diseases.

Just last year, Dr. Benedict collaborated with Dr. Sette to uncover exactly how T cells respond to CMV infection—work that is critical for future CMV vaccine design. Dr. Benedict has also partnered with LJI Professor Pandurangan "Vijay" Vijayanand, M.D., Ph.D., to use deep sequencing methods to tease apart the interplay of viral and immune cell gene expression.

"We are getting closer to understanding how genetics add to a person's susceptibility to these diseases," says Dr. Benedict. "That's really the cutting edge."•

Neuroimmunology in men vs. women

Myasthenia gravis is a neuromuscular disease that often begins with one drooping eyelid. The culprits?

Antibodies.

For most patients with myasthenia gravis, the body's own antibodies target muscle cells and mistakenly block or destroy the receptors for a neurotransmitter called acetylcholine. Without these receptors, nerves cannot properly communicate with muscles, and patients begin to suffer muscle weakness and may struggle to eat, speak, and even breathe. Even though scientists have uncovered the antibodies behind this rare disease, they still don't know what triggers immune cells to start making these self-targeting antibodies in the first place.

Another puzzling mystery: why does myasthenia gravis tend to target women under 40 and men over 60?

Many neurological diseases affect the sexes differently. Parkinson's disease is more common in men, but Alzheimer's disease is more common in women. ALS is 20 percent more common in men, but multiple sclerosis is 100 to 150 percent more common in women.

At LJI, researchers have launched several important projects to examine sex-based differences in the immune system. This initiative, led by LJI Associate Professor Sonia Sharma, Ph.D., is important for understanding why immune cells may behave differently in women and men—and how we might better diagnose and treat all patients. The Institute has also partnered with **Women's Health Access Matters (WHAM)**, led by LJI Board Member Carolee Lee, to accelerate autoimmune research focused on women.•

Get to know John Keegan

How LJI's new Chief Operating Officer defines "mission success"

Since 2005, John Keegan has been responsible for every piece of La Jolla Institute for Immunology (LJI) anatomy. If a scientist needs a new room for a multi-million dollar piece of equipment? His team builds it on time and within budget. Keegan and his team manage everything from the real estate lease to LJI's insurance coverages.

Keegan was here when LJI's current Research Park building was nothing more than a dirt lot studded with steel girders. And he was here when COVID-19 hit. Under his leadership, LJI continued to operate and thrive, opening new facilities to accelerate critical studies on SARS-CoV-2 infections and later COVID-19 vaccines.

Keegan was recently promoted to the position of LJI Chief Operating Officer (COO). As COO, he oversees and manages the day-to-day operations of the Institute while continually looking for ways to improve operational efficiency and anticipate future needs.

In this Q&A, he shares what it's like to create an environment for world-changing research.

How does your team keep research running smoothly?

A. Our first priority is always to not interrupt the science, but to support and promote it. Research is not a 9 to 5 operation and it is very important to be present and available for the researchers when needed. There is usually activity and support happening around the clock, many times behind the scenes so that lab operations are not impacted.

We have a very large and dedicated team and we all embrace providing the highest level of service. We communicate closely within groups and cast a "Service Net" across different departments that provides a full service methodology to everything we do, often involving every single department.

Wow. You have to think so many steps ahead.

A. I try to operate by a method called "plus five," where we try to be five steps ahead in every possible scenario. Obviously you can't hit them all, but that's our mindset. It really forces you to address the "what ifs" and it's always eye-opening what you find!

How does your team help new LJI faculty members get settled in?

A. The best way to get new PIs set up is to meet them, get to know them, walk around the building, and show them other researchers' labs. We want to know what they envision as their dream set up, and then we try to get as close to that as possible.

We just started a new on-boarding process that is exciting and highly functional. It is something that Erica Ollmann Saphire brainstormed and successfully tested with Sam Myers. We have now adopted that process, modeled it, and are using it to get new faculty members acquainted with all aspects of the Institute. I am thrilled to be part of the process. It is a series of 30-minute meetings between the new faculty and every department and scientific core here at LJI, and they have been incredibly informative. This allows faculty to function efficiently and alerts the administration to what is important to them and what they need.

> "When everyone feels heard and welcome, ideas can flow freely, and maybe even plant the seed for the next breakthrough.

You led the construction of the John and Susan Major Center for Clinical Investigation, which opened in Spring 2021. You built that center extremely quickly—in the middle of a pandemic, no less. What was that like?

A. That was a whole new level of involvement for us. We had a vision of what we wanted, but the space was a very crowded storage area and we needed to poke a hole through the exterior of the building for a new dedicated entry door. We also had a fixed budget, and this was the middle of COVID.

LJI convinced UC San Diego to allow us to take on the role of general contractor, which had never been done on the university's campus before. This bold step immediately cut 20 to 25 percent of the construction costs and four months off the schedule. This also allowed us to deal directly with the architects and the engineers, streamlining changes. We had to run construction meetings the university attended and pay for all the subcontractors directly. We included our contractors in our COVID testing program to help with site safety and keep the teams working. This was a massive undertaking and I couldn't have done it without the operations and facilities teams. They are incredibly committed and handled the majority of the heavy lifting.

We finished in just over six months, and it turned out to be a great project. Getting that up and running in time really propelled LJI's COVID-19 research.

You've had a front row seat at a research organization operating at a very high level for many years. How have operations evolved?

A. The Institute has grown over the years, and new technologies have become available and will continue to do so. As a result, the infrastructure needs keep changing. Microscopes have evolved into ultrasensitive machines, and we had to figure out how to control vibrations and humidity. Over the last few years we also took a hard look at how we can save energy and operate in the most environmentally conscious way possible. There have been a lot of changes along the way but one operating principle never changed: Science is the reason we are all here, and it has and always will come first.

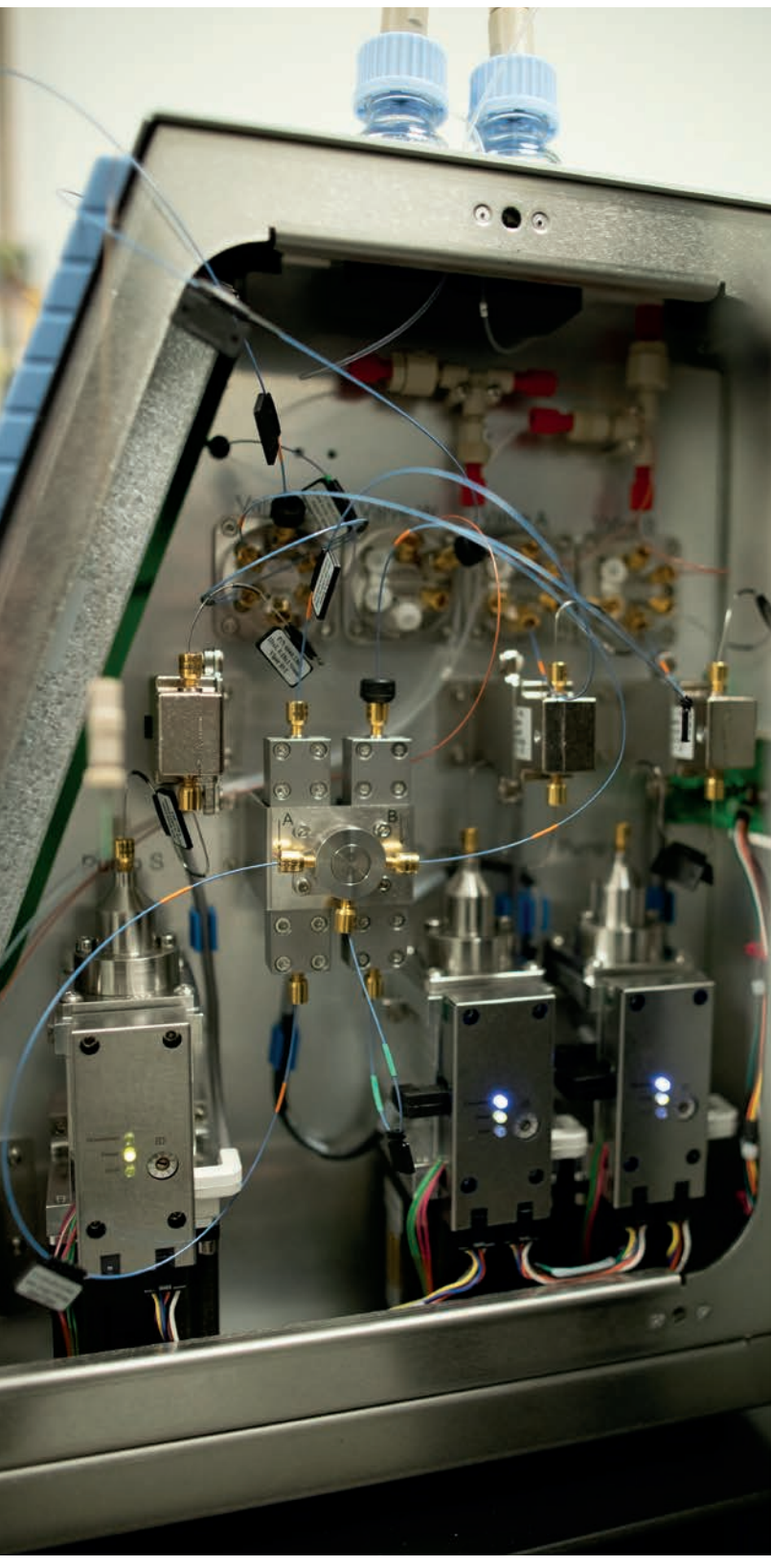
Going forward, how do you define mission success?

A. We succeed when we give scientists the space—physically and mentally—to do their best work. For me, it all comes down to creating an efficient environment so they can spend their time thinking about and doing research and are not slowed down by administrative obstacles or inefficient systems. Just as important is nurturing a climate of mutual respect and trust. When everyone feels heard and welcome, ideas can flow freely, and maybe even plant the seed for the next breakthrough.

LJI Postdoctoral Fellow Maria Matias, Ph.D., meets with Dr. Myers in his LJI office.

HOW TO BUILD A LAB

Scientists often compare starting a new lab to starting a small business. It takes finding the right people and solid funding to make the dream work. Assistant Professor Samuel Myers, Ph.D., shares an honest look at what it's like to start a new lab at La Jolla Institute for Immunology (LJI).



The Myers Lab uses a technique called nano-liquid chromotography to help process samples. Here, nano-liquid chromotography pumps allow for dual in-line flow before solvent mixing, a key step in the analysis process.

Dr. Myers speaks with the drawn-out vowels of someone who came of age in 1990s SoCal. He's the kind of scientist who rides a bicycle to work. He marks milestones not with plaques on the wall but with tattoos. "My lab members know my offer—when they publish a paper, I will pay for a scientific tattoo if they want it," he explains. His move back to Southern California was a homecoming.

After completing postdoctoral training at the Broad Institute of MIT and Harvard in Cambridge, Mass., Dr. Myers joined LJI as an Assistant Professor in April 2021 and launched the Laboratory for Immunochemical Circuits.

Dr. Myers says a person needs to have an "ambitious but realistic" outlook to try to start a new laboratory. He's also grappled with the shift from hands-on scientist to lab leader and administrator. "I trained to move microscopic amounts of liquid around for 15 years. Now I'm a small business owner," he says.

His team studies how protein signaling can change a cell's behavior in a matter of minutes. This research is important for understanding the very mechanisms behind cell survival and how the body responds to cancers, autoimmune diseases, and more.

"I'm trying to build and map these very complex signaling-to-transcription networks—so basically how cells interpret their environment and process that information to turn on or off the genes they need to respond correctly," says Dr. Myers.

Dr. Myers has been part of LJI for two years now. He's organized his lab space, gotten new machinery up and running, and hired a crew of lab members. None of that has been easy, especially amid global supply chain problems.

STEP ONE: MOVING IN. Dr. Myers' laboratory is sandwiched between the laboratories of LJI Professors Anjana Rao, Ph.D., and Patrick Hogan, Ph.D. From one side of the long room you can see how several sections of lab benches are split between the three faculty members. Dr. Myers appreciates the chance to work alongside Drs. Rao and Hogan. Both scientists are experts in protein signaling and have welcomed new collaborations with Dr. Myers.

Staff in LJI's Facilities Department helped Dr. Myers make the space his own. "This office actually used to be the break room, so I was making friends right from the start," he jokes. Besides the new desk and white boards, it still kind of resembles one. It's a surprisingly large room with a couch along the wall.

To prevent downtime, Dr. Myers keeps extra tubes at the ready for use in the mass spectrometer.

Dr. Myers keeps bottles of hot sauce and salad dressing on his desk and a mini fridge in the corner by the window.

Research isn't just a vocation for Dr. Myers. Twenty years ago, he was an art student at a community college. Then he took a human biology course and discovered he loved science—and he was good at it. He loved learning about the complexity and the chemistry behind the ways cells signal each other.

"I'm very passionate about this. I feel like it's my job and my hobby," he says. "I love thinking about it. I wish it didn't keep me up at night, but I love the fact that there's always something new and exciting, and I don't mind being a little obsessive."

STEP TWO: GETTING THE GEAR. Mass spectrometers are workhorses of protein signaling and biochemistry. These complex instruments allow researchers to identify unknown proteins in a sample. Just as a bird watcher needs binoculars, a biochemist needs a mass spectrometer.

To do any proteomics research in his new space, Dr. Myers needed a mass spectrometer that costs about $1.4 million. Thanks to the generosity of an anonymous donor, Dr. Myers made this key purchase fairly early on. "I am so grateful to this donor," he says. "This funding allowed me to build the mass spectrometry facility of my dreams from scratch, with everything we need. And it's arguably one of the most sophisticated mass spectrometry and proteomics platforms on the Mesa."

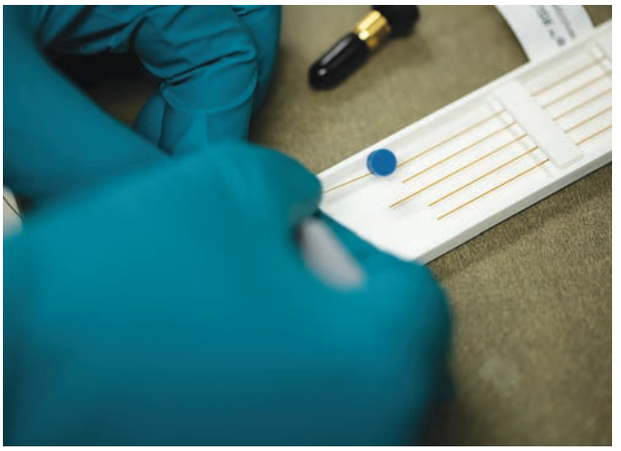
PUSHING THE LIMITS OF MASS SPEC

Scan this QR code for a behind-the-scenes video of Dr. Myers' work with the mass spectrometer.

Dr. Myers and his lab members are experts at troubleshooting the mass spectrometer when something goes wrong. As Dr. Myers explains, this equipment is often out of commission due to the intense nature of his work. "We don't have to be running at this high level of sensitivity but to answer the questions we want to, we do," he says. Running at the limits of what the mass spec can do means new insights but also more challenges in the process.

From there, he needed to order the accessories (special columns, tiny glass capillary tubes, etc.) to actually use the machine—things an immunology institute typically does not have. As the Institute's facilities team worked to assemble the lab infrastructure, Dr. Myers was stuck in limbo. Basic lab supplies have been in short supply due to the pandemic, and his orders took months to arrive at the Institute.

"I was waiting on this last piece of the system, a speed vac, which is this centrifuge that applies a vacuum so we can remove acids and solvents from samples," says Dr. Myers. "Every month the company told me it would come the next month. Finally, it came in after seven months, and then it didn't even have the tube I needed. I had to go to a hardware store in Carmel Valley to get the right tube. In fact, we only recently got the right part number for proper tubing. "But once that last piece was here, we were sailing."



Certain specialized components for the mass spectrometer are crafted in house by members of the Myers Lab.

The black box behind Dr. Myers is the $1.4 million mass spectrometer his laboratory uses to better understand how immune cells function and respond to pathogens.

STEP THREE: ASSEMBLING THE TEAM. "The risks of starting a new lab are manifold and stressful," says Dr. Myers. "Not only do I have to be good enough to do the work, I have to be good enough to train people who aren't experts yet," he says. "Their careers are kind of in my hands."

The first person to take the leap was an undergraduate student named Patrick Kennedy. Kennedy impressed Dr. Myers with his persistence and patience in the lab's early days. "He got a lot done over that first summer when we only had a set of half-broken pipettes," says Dr. Myers, who ended up hiring Kennedy to stay on as a full-time research technician. The full set of pipettes also took seven months to arrive, he notes. Dr. Myers also feels lucky to have found Research Technician Cindy Manriquez Rodriguez. "She's great!" he says. "I think she learned maybe three mass spectrometry data analysis software programs in one week."

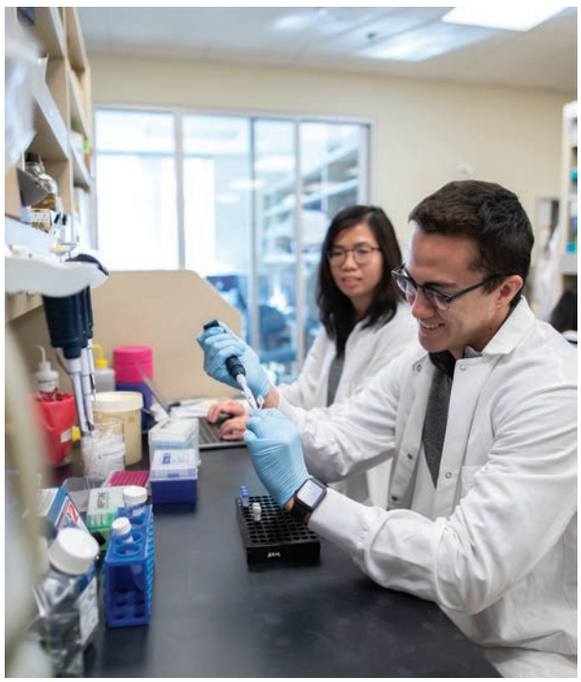
His laboratory now has five full-time members, with one on the way, and hosts several students and interns. His trainees include Postdoctoral Fellows Khanh Nguyen, Ph.D., and Maria Matias, Ph.D. "Khanh has done a fantastic job keeping the mass spectrometer running at a high level," he says. "And Maria has done a great job setting up our mouse work and immune cell purification protocols. She's a T cell biologist, so she has a lot of experience that I don't have."

The last two years of work are starting to pay off. In 2022, Dr. Myers received a grant of over a million dollars from the NIH's National Institute of General Medical Sciences that funds part of his laboratory's vision. This grant is a major milestone in the life of a new lab, and the funding supported research that led to a major paper for the Laboratory for Immunochemical Circuits. Dr. Myers is also listed as last author among the study contributors, which designates him as a study leader.

The research, co-led by Dr. Rao, helps solve the mystery of why an enzyme called OGT is critical for cell survival. This study came out in a top scientific journal, *Proceedings of the National Academy of Sciences*, and has implications for treating cancers, metabolic diseases, and more.

For his *first*, first author paper of his career, Dr. Myers got a tattoo of a boxing baby with a piece of mass spectrometry equipment for its head. His next tattoo will commemorate his move from Boston to San Diego.

"There are these old sailor tattoos where you got a clipper ship on your chest," says Dr. Myers. "I was going to pick the fastest clipper ship that sailed from Boston to San Diego. It was actually called the Eclipse, the HMS Eclipse, and the name of our mass spectrometer is also the Eclipse. So that's the plan." •



Research Technician Patrick Kennedy pipettes while Postdoc Fellow Khan Nguyen, Ph.D., observes.

Research Technician Cindy Manriquez Rodriguez prepares samples for mass spectrometry analysis.

A thick skin

How a very exposed organ fights disease

Humans are just so naked. Where many creatures have scales or spines—or even a shell—humans have a soft, sweaty, stretchy layer of skin standing between the world and our internal organs.

Thank goodness the skin also has an army of immune cells. The main players are keratinocytes, which make up 90 percent of skin cells. These cells produce the proteins (such as keratin) and lipids that make your skin such an effective barrier to the outside world. Keratinocytes make us waterproof. They help us heal from cuts, scrapes, sunburns, and tattoo guns. Keratinocytes offer immune protection: they can produce antimicrobial peptides, and they can make inflammatory molecules signal other immune cells to defend the skin.

Dotted amongst the keratinocytes are Langerhans cells. These are really just dendritic cells, a kind of innate immune cell (or first line of defense). Then there are "intradermal" immune cells. These intradermal cells include a large population of T cells, which specialize in detecting foreign molecules, and memory T cells, which remember past infections. Anyone who's itched a bug bite or touched poison oak has experienced the speed and sensitivity of the skin's immune system.

Unfortunately, reactions in the skin also can lead to inflammatory and autoimmune diseases. La Jolla Institute for Immunology (LJI) Professor Michael Croft, Ph.D., studies skin diseases such as atopic dermatitis, the most common type of eczema. His laboratory has discovered important molecules that drive skin inflammation—and helped demystify the immune system of the skin.

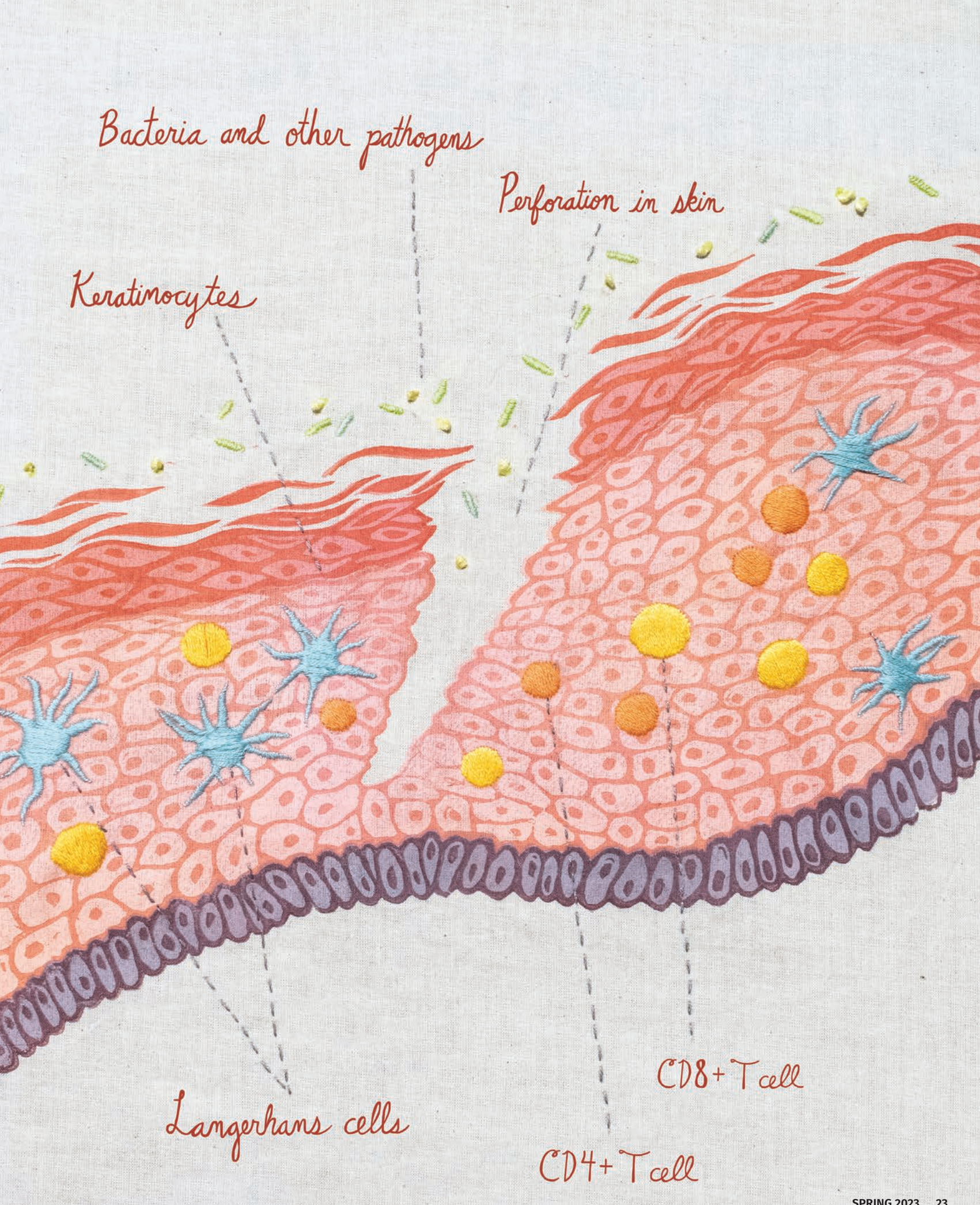
"You could argue that some of the immune molecules we study really evolved to help the skin heal itself," says Dr. Croft. "This system activates any time you get a disruption of the skin, like a scratch. Part of the response that may occur in people with skin inflammatory diseases like atopic dermatitis, psoriasis, scleroderma, and similar diseases is really an aberrant or exaggerated wound healing response."

In atopic dermatitis, for example, the immune system of the skin starts to overreact to innocent molecules, such as milk proteins or laundry detergents. Keratinocytes are triggered to react to these inflammatory stimuli and become overactive, just as they would when trying to close a wound. "Keratinocytes divide more than they normally should," says Dr. Croft. "And you start to build up a much thicker epidermis." This keratinocyte activity is why patches of skin affected by atopic dermatitis, psoriasis, or scleroderma feel thicker or rougher than unaffected areas. A very similar process happens in the airways when an allergen triggers an asthma attack: cells in the airways thicken, worsening breathing issues.

ker·a·tin·o·cyte

Keratinocytes make up **90 percent** of skin cells.

» **About the artist:** Patricia Pauchnick is a mixed media artist living and working in San Diego County. Her focus is exploring the natural world through art. She also produced the motif for this issue's back cover.


Bacteria and other pathogens
Perforation in skin
Keratinocytes
CD8+ T cell
Langerhans cells
CD4+ T cell

We think of skin as a shield or a barrier, but skin can also be a window into the immune system.

Dr. Croft's laboratory has shown we might bring balance back to the skin by targeting a pair of immune system proinflammatory proteins called TWEAK and LIGHT. These proteins belong to a family of molecules known for causing inflammation throughout the body, and Dr. Croft's research with mouse models of disease as well as human keratinocytes shows they can drive the deregulated keratinocyte activity that is common in most inflammatory and autoimmune diseases of the skin. Dr. Croft and his colleague, LJI Instructor Rinkesh Gupta, Ph.D., have found that deleting the genes for the receptors of TWEAK or LIGHT found on keratinocytes can protect mice from getting psoriasis and atopic dermatitis. Blocking the activity of TWEAK or LIGHT in mice with neutralizing antibodies also appears to stop psoriasis and atopic dermatitis after the inflammation has started. "We think both of these molecules are essential to all skin diseases and represent more universal targets for therapeutic treatment in humans," Dr. Croft says.

Dr. Croft points out that keratinocytes aren't very different from the epithelial cells, or barrier cells, that line the airways. "A lot of the barrier surfaces actually have somewhat the same structure and potentially the same mechanisms for healing, as well as producing damage," he says. That means shedding light on inflammation in diseases like asthma may advance skin disease research too—and vice versa. In a recent asthma study, Dr. Croft and his LJI colleagues showed that blocking the activity of LIGHT can stop the kind of tissue thickening seen in the airways of people with severe asthma. So there's good reason to think a similar strategy could lead to healthier skin.

We think of skin as a shield or a barrier, but skin can also be a window into the immune system. Look down at your hands. They've been through cuts and burns, snowball fights and sun damage. Yet keratinocytes close the wounds, immune cells remember past threats, and your skin stands ready for the next challenge. •

What is **zit?**

Pimples aren't fun, but they are an excellent chance to see the immune system in action. Acne happens when a hair follicle or pore gets clogged by dead keratinocytes and oils (sebum) produced under the skin. The normally harmless bacteria living on the skin then move into the clogged pore and start multiplying like crazy.

The skin knows exactly how to deal with this kind of invasion. Keratinocytes and nearby immune cells begin to produce inflammatory molecules called cytokines, which turn the clogged pore into a hot, red, puffy pimple. Other immune cells, such as monocytes and neutrophils, are called into battle, leading to more and more pressure and redness around the clogged pore. Sometimes a white layer appears on the surface of a pimple. This liquid is mostly made up of dead immune cells and keratinocytes. By bringing this debris to the surface, the body can heal without pushing an infection into deeper layers of the skin.

Many people also get "cystic" acne, which feels like a hard, hot lump under the skin. This kind of cyst means keratinocytes and immune cells have walled off an infected pore. The body has enveloped the infected area and formed a cyst.

Both processes tend to be fairly painful, due to the abundance of nerves in the skin, but pimples do highlight how quickly and precisely the skin's immune system can react. •

Antibodies vs. Omicron

How well do your antibodies target Omicron and other SARS-CoV-2 variants?

It depends on their structure. By analyzing antibodies sent in from around the world, La Jolla Institute for Immunology (LJI) scientists have shown that the ideal antibodies against SARS-CoV-2 can hit two viral targets at once.

Current COVID-19 vaccines are designed to teach the body to recognize the SARS-CoV-2 Spike protein. Antibodies that bind to the Spike in the right spots can stop infections in their tracks.

The problem is that SARS-CoV-2 keeps mutating, and many once-powerful antibodies can't recognize their usual targets on key regions of the Spike protein. Building vaccines and therapies that will withstand future variation hinges on figuring out what surviving antibodies have in common.

Now we have a window into how these neutralizing antibodies do their jobs, thanks to recent research led by Kathryn Hastie, Ph.D., an LJI Instructor and the Director of the Antibody Discovery Center at LJI.

Dr. Hastie led the new *Cell Reports* study alongside LJI Postdoctoral Researcher Heather Callaway, Ph.D., Sharon Schendel, Ph.D., and LJI President and CEO Erica Ollmann Saphire, Ph.D. The new research was made possible through the Coronavirus Immunotherapy Consortium (CoVIC), a global effort with Dr. Saphire as Director and Dr. Schendel as Program Manager.

For this research, Drs. Callaway and Hastie analyzed nearly 400 antibodies sent by scientists around the world to the CoVIC, which is headquartered at LJI. They narrowed down this huge pool and found 66 potent antibodies that could neutralize Omicron lineage BA.1 and early sub-lineages such as BA.1.1 and BA.2. By the time they tested antibodies against Omicron lineages BA.4/5, only seven antibodies had neutralizing power.

Dr. Callaway then used an imaging technique called cryo-electron microscopy and conducted biochemical analyses to see exactly how this unique group of neutralizing antibodies was getting the job done. "It became clear there was a pattern," says Dr. Callaway. "The successful antibodies overcome loss of affinity for Omicron by simultaneously binding two receptor binding domains (key sites) in the Spike."

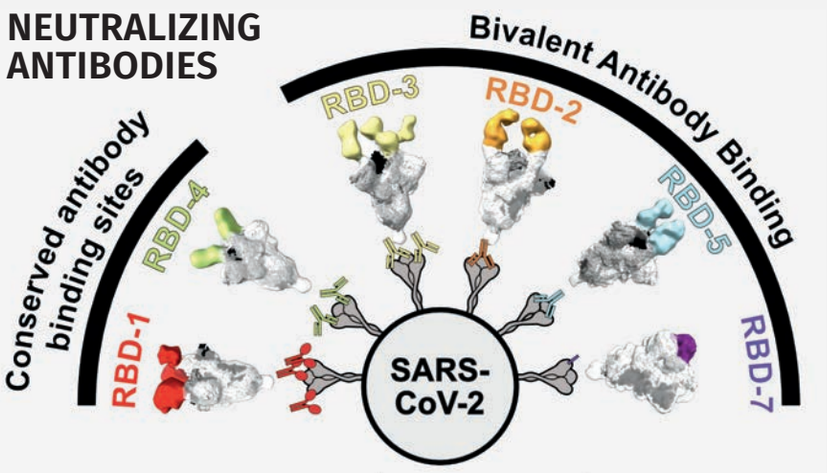
These "bivalent" antibodies hung on with both hands. With these antibodies locking together two adjacent receptor binding domains at once, both early SARS-CoV-2 variants and several later Omicron variants had a tough time escaping.

Scientists are now looking at how we might harness their power in new antibody therapeutics and even more effective COVID-19 vaccines. "The ideal antibodies exist," says Dr. Hastie. "Now the question is, how do we preferentially boost those?"

The very fact that researchers were able to analyze a broad pool of nearly 400 antibodies has been a major step forward for science. "The scale of the study allowed the team to study enough Omicron 'survivors' to find general rules about what made them successful," says Dr. Saphire.

Dr. Schendel says that having both the Salt Lake City-based biotech company Carterra and the laboratory of Duke University Professor Georgia Tomaras, Ph.D., as partner reference labs in the CoVIC was especially important for sorting the different neutralizing antibodies into epitope-binding "communities," based on where they target SARS-CoV-2.

"CoVIC demonstrated that collaboration allowing studies on a larger scale can lead to better insights," says Dr. Schendel. •



SIX NEW LJI BOARD MEMBERS BRING EXPERTISE TO ENHANCE LJI'S STANDING AS WORLD-CLASS RESEARCH ORGANIZATION

La Jolla Institute for Immunology (LJI) has welcomed six new members to the Institute's Board of Directors: venture capitalist and former AT&T executive Richard S. "Dick" Bodman, former Congresswoman Susan Davis, philanthropist and research advocate Barbara Donnell, business strategy expert and Chief Operating Officer at GHR Foundation Fred Miller, pioneering cellular and molecular biologist Sandra Schmid, Ph.D., and leading immunologist and science policy expert Linda Sherman, Ph.D.

Richard S. "Dick" Bodman is the Managing General Partner of VMS Group, which provides administrative and advisory services to more than 100 venture capital funds. He is also Chairman of TDF Ventures and co-founder and Chairman of PurThread Technologies, Inc. Bodman's past leadership positions include Assistant Secretary of the U.S. Department of the Interior and Assistant Director of the Office of Management and Budget during the Nixon administration. He later served as Senior Vice President of AT&T for Corporate Strategy & Development and Lead Director of Sandia National Laboratories. He founded AT&T Ventures, and went on to acquire the firm (renamed Venture Management Services) when he retired from AT&T, becoming its co-managing partner. Bodman is the former manager of Bodman Oil and Gas LLC., and he serves as an Emeritus Trustee at The Buck Institute for Research on Aging. Bodman and his wife Karna have also given significant philanthropic support to LJI through the years and recently endowed the Institute's Richard S. and Karna S. Bodman Leadership Fund. After serving a term on the LJI Board from 2015-2021, Bodman is rejoining the Board after a brief hiatus.

The Honorable **Susan Davis** is a former member of Congress who served as the U.S. representative for California's 53rd congressional district for 10 terms from 2001 to 2021. She holds a masters' degree in social work and has been an outspoken supporter of health equity and patients' rights. Davis first became active in politics through her membership in the local branch of the League of Women Voters, of which she became president in 1977. She was elected to the board of the San Diego Unified School District in 1983. In 1994, Davis was elected to the California State Assembly, where she chaired the Committee on Consumer Protection, Government Efficiency, and Economic Development. She was elected to Congress in 2000. As a member of Congress, provisions of an OB/GYN bill she authored were included in the health care reform bill enacted into law. Her roles in Congress include leadership as the Ranking Member of the Subcommittee on Higher Education and Workforce Development and as a member of the House Armed Services Committee.

Barbara Donnell is a San Diego-based philanthropist and type 1 diabetes patient parent advocate. Through her work on behalf of diabetes research, Donnell is an invaluable member of the San Diego biomedical sciences community. Her work includes coordination of the Juvenile Diabetes Research Foundation/LJI "Meet the Scientists Day" for type 1 patients and their families. She has also devoted her time and expertise to coaching early career researchers through the application process for The Tullie and Rickey Families SPARK Awards for Innovations in Immunology.

Fred Miller is a business strategy expert, Chief Operating Officer at GHR Foundation, and leader of GHR's Alzheimer's Initiative. Miller spent the majority of his career with McKinsey & Company, where he worked to guide business strategy, new product development, and commercial operations for Fortune 500 healthcare companies. He retired from McKinsey & Company in 2010. He then took a position with the GHR Foundation, an independent global philanthropic group as head of its Alzheimer's program, which seeks to support promising new ideas in the field. Miller has established a strong partnership with LJI on behalf of the GHR Foundation, which gave a generous $1 million gift to propel the efforts of the Coronavirus Immunotherapy Consortium (CoVIC), a global partnership headquartered at LJI. And since, GHR has given more than $3.12 million in total to LJI.

Sandra Schmid, Ph.D., is a renowned cellular and molecular biologist who has worked to uncover the molecular mechanisms and regulation of clathrin-mediated endocytosis, a process in cells that controls nutrient uptake, cell signaling, and the surface expression of membrane transporters. Dr. Schmid's work has been recognized by numerous awards, including a National Institutes of Health MERIT Award, the William C. Rose Award from the American Society for Biochemistry and Molecular Biology, the Women in Cell Biology Senior Career Award from the American Society for Cell Biology, and the Arthur Kornberg and Paul Berg Lifetime Achievement Award in Biomedical Sciences. Dr. Schmid was elected as a foreign member of the European Molecular Biology Organization in 2014, to the American Academy of Arts of Sciences in 2015, and to the National Academy of Sciences in 2020. Dr. Schmid has held many leadership roles at the national level, including as Co-founding Editor of the journal *Traffic*, as Editor-in-Chief of MBoC, and as President of the American Society for Cell Biology. In 2020, Dr. Schmid also became the inaugural Chief Scientific Officer of the Chan Zuckerberg Biohub Network.

Linda Sherman, Ph.D., is a former President of the American Academy of Immunology and Professor Emeritus at Scripps Research, where her laboratory shed light on how T cells respond to threats such as tumor cells. Dr. Sherman has served the national scientific community extensively as a member of numerous NIH committees and National Advisory Councils designed to review grant applications and write policy on federal funding priorities. Her leadership in the local community includes involvement in the early growth and direction of a successful San Diego charitable organization, Kids Included Together, which provides opportunities for inclusion of children with developmental disabilities in child care, after school, and recreational programs.

"I have watched LJI do such a great job in science and technology. It's such a collaborative place. I am thrilled to deepen my relationship with the Institute and to offer my skills to help."

Board Member Barbara Donnell

CECILIA LINDESTAM ARLEHAMN RECEIVES WHAM EDGE AWARD FUNDING TO STUDY SEX-BASED DIFFERENCES IN ALZHEIMER'S AND PARKINSON'S PATIENTS

LJI Research Assistant Professor Cecilia Lindestam Arlehamn, Ph.D., has been granted more than $25,000 through a Women's Health Access Matters (WHAM) Edge Award to support new research into Parkinson's and Alzheimer's disease. Dr. Lindestam Arlehamn aims to shed light on how sex-based immune system differences may affect the development and progression of these neurodegenerative diseases in men versus women.

Dr. Lindestam Arlehamn will work closely with the LJI Bioinformatics Core to analyze male vs. female gene signatures. She'll also collaborate with LJI's Flow Cytometry Core for sample analysis and LJI's John and Susan Major Center for Clinical Investigation for additional study volunteer recruitment and blood processing.

The project will be a team effort, and a personal one for Dr. Lindestam Arlehamn. "I have a personal connection to the research—my dad has Parkinson's," says Dr. Lindestam Arlehamn. "The WHAM Edge Award will bolster my understanding of this disease as I look for a solution."

ERICA OLLMANN SAPHIRE RECEIVES ASBMB AWARD IN HONOR OF BASIC BIOMEDICAL RESEARCH

LJI President and CEO Erica Ollmann Saphire, Ph.D., has been awarded the 2023 Bert and Natalie Vallee Award in Biomedical Science from the American Society for Biochemistry and Molecular Biology (ASBMB). The award recognizes Dr. Saphire's work in structural biology, as well as her leadership of global consortia focused on finding, discovering, and advancing antibody therapeutics against diseases such as COVID-19 and Ebola virus infection.

ANNIE ELONG NGONO WINS GVN SUPPORT TO ADVANCE INFECTIOUS DISEASE RESEARCH

Instructor Annie Elong Ngono, Ph.D., has been accepted into the Global Virus Network's (GVN) highly selective Rising Star Mentorship Program.

GVN is a coalition of human and animal virologists from 68 Centers of Excellence and 11 Affiliates in 39 countries. Dr. Elong Ngono is the first LJI scientist to be accepted into the GVN Rising Star Mentorship Program, which offers early career virologists unique opportunities for close collaboration with senior GVN scientists and clinicians. Through the program, Dr. Elong Ngono will also participate in exclusive GVN meetings and other professional development opportunities in virology.

"It's an honor," says Dr. Elong Ngono. "Collaboration is critical for answering questions in emerging disease research, so I really appreciate this opportunity."

Dr. Elong Ngono was nominated for the program by LJI President and CEO Erica Ollmann Saphire, Ph.D., a member of the GVN. "Annie's research highlights the fascinating dynamics between viruses and host cells, to explain how we can get immune cells to ramp up their protection," says Dr. Saphire. "Annie is also a strong supporter for international collaboration in the field of emerging disease, so I know she'll make important advances through the GVN."

"It's an honor. Collaboration is critical for answering questions in emerging disease research, so I really appreciate this opportunity."

SHANE CROTTY HONORED WITH AAI-BIOLEGEND HERZENBERG AWARD FOR B CELL RESEARCH

LJI Professor Shane Crotty, Ph.D., has been named winner of the 2023 AAI-BioLegend Herzenberg Award from the American Association of Immunologists. The award recognizes Dr. Crotty's groundbreaking work in the field of B cell research, which has advanced our understanding of SARS-CoV-2 immunity, HIV vaccine strategies, and more.

"AAI is the preeminent immunology association in the United States, so to be honored by them is wonderful," says Dr. Crotty.

Dr. Crotty leads research in LJI's Center for Infectious Disease and Vaccine Research. His laboratory is dedicated to advancing vaccine and immune system research by shedding light on the roles of B cells, and highlighting which B cells are responsible for producing potent antibodies to fight disease. Dr. Crotty's work has shown how to boost antibody production through new vaccine ingredients and the timing of immunizations.

THE POWER OF FRIENDSHIP

Remembering Shelley Rowland

WE ARE SO GRATEFUL FOR HER VISIONARY SUPPORT OF A FUTURE THAT ADVANCES *LIFE WITHOUT DISEASE®.*

In the summer of 2022, Shelley Rowland of La Jolla lost her life to cancer. A couple of weeks following her passing, we learned Shelley made a charitable bequest by naming La Jolla Institute for Immunology (LJI) as beneficiary of her retirement account.

While Shelley attended a handful of LJI events, we didn't have an opportunity to get to know her well and wish we had. We were struck by her generosity, and that one of her final acts was to push immunology research forward for the benefit of future generations.

We wanted to learn more about who Shelley was during her lifetime. So, we reached out to her friends and they were eager to share stories about Shelley. We quickly came to understand from this devoted and loving group of people that beyond being a loyal friend, two of Shelley's most prominent characteristics were selflessness and generosity. Indeed, both attributes shine through in this charitable act.

Shelley's life was enriched by close friendships she held dear. She did everything with her friends, including volunteering, adopting and caring for stray cats, participating in activities and events at church, planting community gardens and rallying support for the issues and programs about which she was passionate. Shelley even roomed with her friend Eleanor Mosca, who was right by her side when she was diagnosed with ovarian cancer. (Eleanor and Shelley are pictured together on page 29.)

Eleanor is a retired nurse with a keen interest in biomedical research. Together, Shelley and Eleanor learned about the disease, possible treatments, and monitored the latest research breakthroughs by watching webinars and searching for clinical trials. As Shelley's medical team grew, and her treatment became increasingly complicated, Eleanor stayed by Shelley's side as her medical care advocate.

The important role Shelley's friends played in her life is evident. So, it is no surprise to learn Shelley was introduced to LJI through her friend Eleanor. They attended LJI events together where they made new friends and learned about cutting-edge research in immunology. In her final months, Shelley decided to update her retirement account, adding LJI as a charitable beneficiary. While we didn't have the opportunity to thank her in her lifetime, we want to honor Shelley and the wonderful friend she was to people, to animals, and to her favorite charities. We are so grateful for her visionary support of a future that advances *Life Without Disease.*

To honor her legacy and generosity, the team at LJI is carefully ensuring Shelley's gift will achieve just what she intended. Recently, the Schoenberger Lab at LJI, led by Professor Stephen Schoenberger, Ph.D., was awarded a grant from Curebound to pursue novel cancer immunotherapy research that could lead to new treatments for ovarian cancer. While this grant provides the majority of funding needed for the project, additional funds are required to complete the budget and enable the work to begin. Shelley's gift will fill this gap and enable Dr. Schoenberger and his team to move full steam ahead. •

If you have named LJI as a beneficiary in your will or retirement plan, please let us know. We would appreciate the opportunity to thank you, welcome you to our Bonsai Legacy Society, and keep you informed about the research that's important to you. Please reach out to Clare Grotting at clare@lji.org with any questions.

NOVEMBER 3 . 2022

Shailendra K. Verma, Ph.D., with Ambassador Diana Lady Dougan and Susan Major

Life WITHOUT DISEASE EVENT SERIES

A special evening celebrating the return of LJI's *Life Without Disease* event series

The LJI *Life Without Disease* event series this fall highlighted groundbreaking heart disease research by LJI Instructor Marco Orecchioni, Ph.D. Dr. Orecchioni presented new research related to heart disease, showing that immune cells in your arteries can "sniff" out their surroundings and cause inflammation. After the presentation, guests connected with peers and Institute leadership during a lively reception on LJI's back patio.

LJI's community lecture series *Life Without Disease* provides guests with an opportunity to hear about the latest advances in immune research and learn first-hand about the exciting research conducted at the Institute. The seminars are delivered by leading figures in immunology and are offered at no charge to the public several times each year.

Marco Orecchioni, Ph.D.

DECEMBER 12 . 2022

La Jolla Institute | VANGUARD
GIVING SOCIETY

We were grateful to have had several Vanguard Giving Society and Bonsai Legacy Society members in attendance for our special holiday luncheon at The Lodge at Torrey Pines. It was wonderful to close out the year with so many familiar faces, and to have had the opportunity to give thanks for the support members have provided to La Jolla Institute for Immunology over the years.

LJI President and CEO Erica Ollmann Saphire, Ph.D.

Susan Major, LJI Board Chair Emeritus John Major, and LJI Board Member François Ferré, Ph.D.

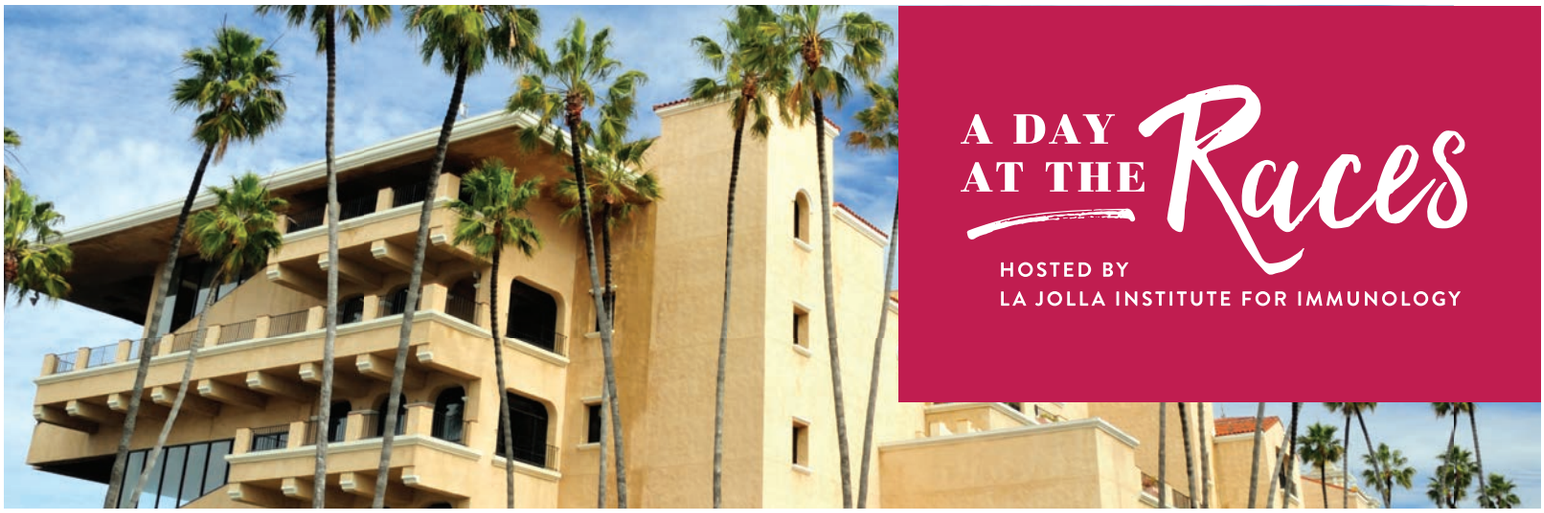
Back row: Gina Kirchweger, Ph.D., Suzie Alarcón
Front row: Connie Sourapas, Rebecca Wright, LJI Board Member Barbara Donnell

FEBRUARY 2 . 2023

LIVE FROM THE LAB

World-renowned immunologist and LJI Professor and Chief Scientific Officer Mitchell Kronenberg, Ph.D., discussed the immune cells on the front lines of infection and their role in inflammatory bowel disease and cancer immunotherapy during a live webinar as part of our ongoing *Live from the Lab* webinar series. He was joined by LJI's Imaging Core Director Zbigniew Mikulski, Ph.D., who demonstrated how he and his team use cutting-edge tools to investigate how immune cells defending our bodies on the frontlines move us closer to *Life Without Disease®*.

Scan QR code to watch past webinars.



A DAY AT THE Races

HOSTED BY
LA JOLLA INSTITUTE FOR IMMUNOLOGY

Save the Date 18

FRIDAY | AUGUST 18, 2023

Del Mar Thoroughbred Club

2260 JIMMY DURANTE BLVD. | DEL MAR, CA 92014

Join us to participate in the ultimate horse racing experience.

Guests will enjoy the races from the exclusive Turf Club's Il Palio Restaurant and Patio known for its panoramic views of the famous Del Mar racetrack and coastline.

Place your bets in style and meet LJI researchers while enjoying premium food, beverages, and entertainment in private VIP accommodations.

- For event information please contact Chelsea Luedeke at cluedeke@lji.org or 858.752.6896.

lji.org/races

Make *Life Without Disease* part of your legacy!

Consider joining La Jolla Institute for Immunology's

BONSAI LEGACY SOCIETY

There is a special space set aside at La Jolla Institute for Immunology (LJI) where our beloved olive bonsai lives. It was a gift from the family of Frank J. Dixon, M.D., to commemorate his outsized contributions to the field of immunology research and LJI, as a member of our Board of Directors.

The bonsai art form has been practiced in Chinese and Japanese cultures for many centuries. A bonsai tree is seen as a living, growing entity that brings joy and a sense of accomplishment to your life; it will likely outlive you and continue to bring joy to others. Bonsais symbolize wealth and abundance, harmony and balance.

LJI's Bonsai Legacy Society is named in honor of this gift and the family that gave it, as both are represented in the visionary and generous act of leaving a legacy gift to LJI.

Bonsai Legacy Society members have named LJI as a charitable beneficiary of one of the following:

- Will or living trust
- Charitable remainder trust or charitable lead trust
- Qualified retirement plan
- Life insurance policy

Planned gifts in any amount are deeply appreciated and qualify for membership in LJI's Bonsai Legacy Society.

Members of LJI's Bonsai Legacy Society enjoy a variety of benefits, including:

- Invitation to annual exclusive events for Vanguard and Legacy Society members
- Invitations to various private events throughout the year
- Breaking research updates from the labs at LJI
- Special recognition at events and in Institute materials
- An appreciation gift from LJI

We are pleased and honored to thank the members of our Bonsai Legacy Society, who have chosen to invest in the future of research and *Life Without Disease*:

Anonymous
Anonymous
Estate of Kim Ash*
Judith L. Bradley and David L. Mitchell
B. Jack and Dorie DeFranco
Frank J.* and Marion* Dixon
Glennie Ginder*
James B. Isaacs, Jr.
John and Susan Major
Joani Nelson
The Roberto Family Trust*
Paulette Roberts
Shelley Rowland*
Nancy L. Vaughan

**deceased*

If you have a question about LJI's **Bonsai Legacy Society** or your gift plans, please reach out to:

Clare Grotting,
Advancement Officer
(858) 752-6872 | clare@lji.org

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