Immune MATTERS

LA JOLLA INSTITUTE
FOR IMMUNOLOGY
SPRING 2021

Learning from
men.
Learning from
women.

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Immune MATTERS SPRING 2021

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.

STAY UPDATED! If you would like to receive email updates from La Jolla Institute, please contact us at: communications@lji.org or 858.752.6645.

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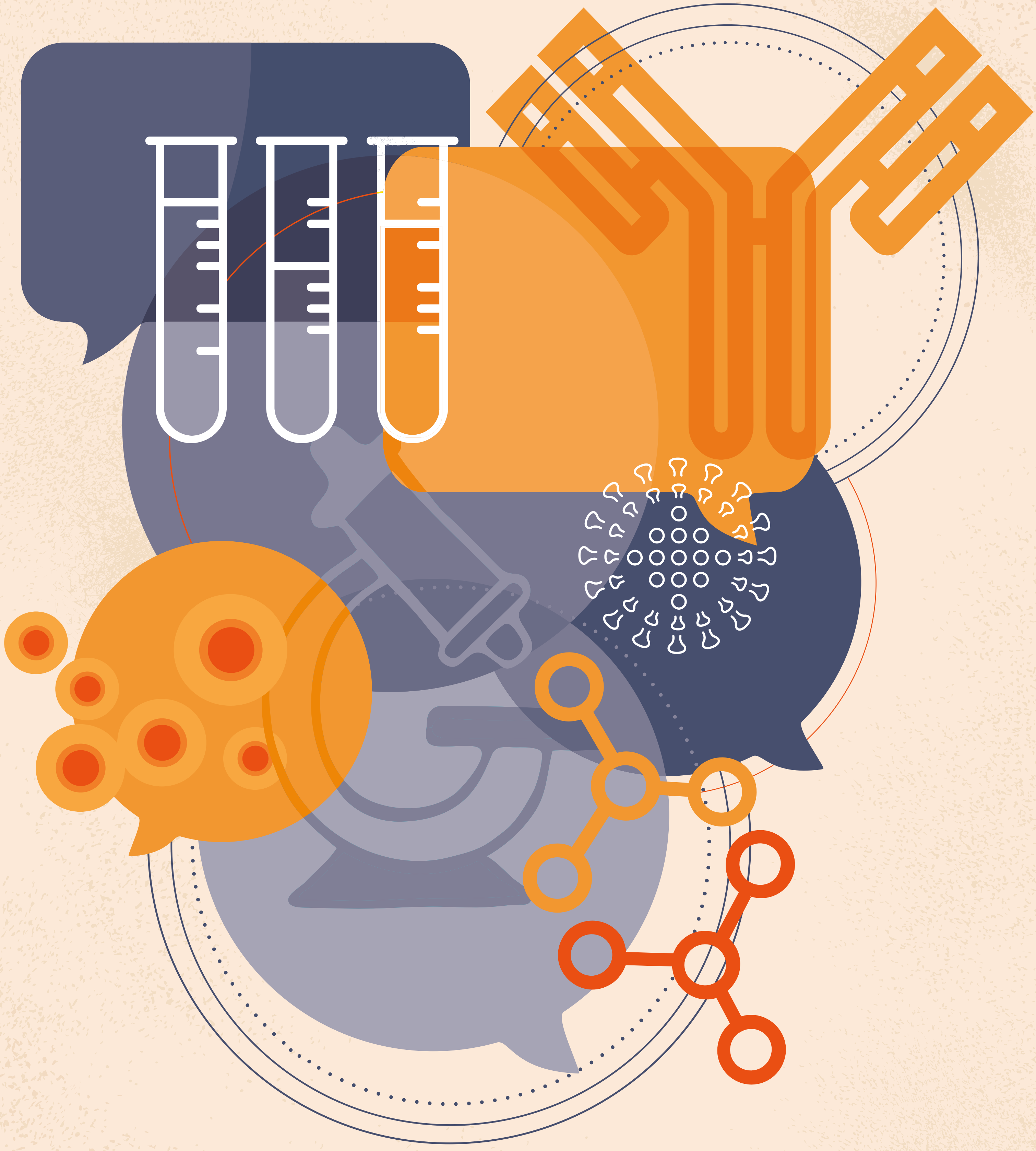


On immunology and gratitude

These days, going into work at La Jolla Institute for Immunology means submitting a saliva sample in a tube, and after RNA analysis, the SARS-CoV-2 virus (COVID-19 disease) screening results are posted online within a few hours. Like many changes since 2020, this strange ritual has come to feel routine.

It's now been more than a year since the first pandemic shut-downs in the United States. As we reflect on this milestone, I'm proud of how much LJI scientists and staff have accomplished in learning about anti-viral immunity in patients exposed to the coronavirus.

Our saliva screening program for viral genes in LJI employees is an additional breakthrough. That system was developed at LJI by the staff of the Next Generation Sequencing Core, led by Suzanne Alarcon. Her team worked day and night for months to get the screening up and running. In this issue of *Immune Matters*, you'll learn how this effort led to Alarcon and her colleagues winning the ultra-competitive XPRIZE.

I'm also in awe of what scientists like Dr. Alba Grifoni, featured in this issue's "Up and Coming" article, have accomplished in communicating the importance of immunology to the public. Researchers here have spoken to global conferences, newspaper reporters, local clubs, Twitter followers—and many other groups—to explain the importance of our COVID-19 studies and vaccines.

The next step is to help more people to understand that immunology is the way to combat other health threats, from cancers to autoimmune diseases. Sharing the latest insights from our labs will be especially important as LJI researchers take on studies in new areas.

We don't yet know why men and women face different health issues. Men are more vulnerable to some infectious diseases, including COVID-19, while women are more prone to autoimmune diseases—and these trends can't just be chalked up to hormonal differences. In our cover story, you'll learn about the fascinating new world of research on the influence of sex on the immune response.

This issue's Q&A with Dr. Bjoern Peters explores the challenges of launching a global project, the Immune Epitope Database (IEDB), which requires computational and experimental scientists around the world to work together to report their findings in a way that can inform vaccine development and immune therapies.

As we've shared our science in the last year of social isolation, we've appreciated the chance to hear back from supporters. In this issue, long-time LJI advocates and donors, the dynamic couple of François Ferré (a member of the LJI Board) and Magda Marquet, explain why LJI stands out to them. As Magda says, "Everyone at LJI is very approachable and very good at explaining what they do—and immunology is not the easiest thing to explain." As researchers here take on new challenges, we'll continue to speak up and share our science.

On September 1st, after 18 years at the helm, I will step down from the role of LJI President. We have planned for this transition for some time, working with the Board of Directors, administrative leaders, and faculty members. I am very pleased to announce that after an extensive search, LJI Professor Dr. Erica Ollmann Saphire has been chosen to be the President and CEO. Erica is an award-winning scientist with expertise on immune recognition of viruses, the ability to galvanize groups of scientists around the world to work together, and a most engaging and effective communication style. You will learn more soon, as Erica will be featured in the next issue of *Immune Matters*. I will continue research in my laboratory and will participate in helping Erica in leadership as Chief Scientific Officer. This is an exciting era with the spotlight shining on immunology and LJI. With much gratitude, I thank you for being part of our journey.

Sincerely,

Mitchell Kronenberg

Mitchell Kronenberg, Ph.D.
President & Chief Scientific Officer
La Jolla Institute for Immunology

WITH NEW CLINICAL CORE, LJI EXPANDS CRUCIAL DRUG AND VACCINE CANDIDATE RESEARCH

Photo: Artist's rendering of the new John and Susan Major Center for Clinical Investigation. The clinical center will be located in the current LJI building at University of California, San Diego's Science Research Park, with an entrance adjacent to the main entryway of the building

More and more scientists rely on human blood samples to study how the immune system responds to diseases such as COVID-19, cardiovascular disease, cancers, and other conditions.

Now La Jolla Institute for Immunology (LJI) scientists will be able to accelerate this research thanks to a generous gift from John Major, Chair Emeritus of LJI's Board of Directors, and his wife, Susan. Their philanthropy is driving the construction of the new John and Susan Major Center for Clinical Investigation, which will consolidate scattered rooms to streamline the sample donation process and increase capacity.

This critical infrastructure will aid LJI investigations through subject recruitment and consent, donor blood draws, and the processing of donor samples for analysis for analysis. The John and Susan Major Center for Clinical Investigation will initially fuel LJI research into COVID-19 and then support studies into other infectious diseases, cancer, and autoimmune diseases.

"Expanding these services at LJI will allow us to study more individuals and more diseases, opening the door to increased understanding so we can find new drug and vaccine candidates for some of the world's deadliest diseases," says LJI President Mitchell Kronenberg, Ph.D.

John and Susan Major have long supported critical LJI initiatives. An LJI board member since 2009, John Major served as Board Chair from 2010 to 2019. In 2016, the Majors gave a landmark gift to support the merging of precision medicine and immunotherapy at LJI. Their support was instrumental in recruiting Ferhat Ay, Ph.D., a renowned bioinformatics expert, to LJI. •

> "We're proud, to, in a small way, contribute to the wonderful work that La Jolla Institute does."
>
> – John Major, LJI Board Chair Emeritus

SAM MYERS JOINS LJI FACULTY, AIMS TO PUT NEW FOCUS ON THE IMPORTANCE OF PROTEINS IN DISEASE

Dr. Myers stands in front of paintings by Broad Institute Artist-in-Residence Lucy Kim. Myers worked closely with Kim to help her grow the pigments used in these images from melanin-producing bacteria.

Cells make very small amounts of the proteins they need—and they make those proteins quickly! This efficiency is great for cells, but not so great for the researchers who want to understand how changes in proteins drive the development of autoimmune diseases, cancers, and much more.

For these researchers, detecting small amounts of critical proteins in a cell's vast "proteome" is like hunting for a needle in a landslide.

This spring, La Jolla Institute for Immunology (LJI) appointed Sam Myers, Ph.D., to the position of Assistant Professor. Dr. Myers is an expert in the emerging field of proteomics, and he is developing cutting-edge methods to see protein expression in action.

These advances have allowed scientists to better detect and study proteins that are made by cells in very small quantities. With a better understanding of how and when cells make key proteins, scientists can study the complex series of events in cells that lead to disease.

"We can now do a whole new suite of experiments and ask the right questions," says Dr. Myers.

Dr. Myers is especially interested in how proteomics can shed light on the development of autoimmune diseases. In these diseases, T cells mistakenly attack the body's own tissues. Dr. Myers wants to study how cellular signaling—conveyed by proteins—could drive these T cells to "go berserk."

Dr. Myers also has cancer in his sights. While cancers can be triggered by genetic mutations, changes in protein signaling pathways can also play a role. "It's really the proteins in a cell that do all the work," he says.

Proteins can acquire small chemical modifications that change how well they work or how long they last, Dr. Myers says. These changes can contribute to many diseases, including cancers and inflammatory disorders.

"If we can start looking directly at the machinery of a cell, what's being modified with small molecules and small chemicals, we'll get a better understanding of what the cell is doing and where we can intervene therapeutically."

Outside the laboratory, Dr. Myers is an avid motorcycle rider and an artist. In fact, he's found ways to merge science with the art world. Recently, he worked with Broad Institute Artist-in-Residence Lucy Kim to grow melanin-producing bacteria, and Kim then used the melanin for pigment in paintings.

"I showed her how to do all the microbiology and molecular biology to make the bacteria and induce the generation of melanin in large quantities," says Dr. Myers. "She's now got undergraduates working with her to develop it further."

As he launches his new lab, Dr. Myers is excited to collaborate with other LJI researchers and the wider San Diego science community. "The faculty at LJI are doing really fantastic work," he says. "I see myself being able to fit into a really good niche here." •

Learning from men. Learning from women.

Men and women have different immune systems. With a better understanding of sex-specific immune differences, scientists can more effectively fight infections, cancers, heart disease, and even pregnancy complications.

The blood still holds secrets. In the complex soup of cells and molecules of the bloodstream, La Jolla Institute for Immunology (LJI) Associate Professor Sonia Sharma, Ph.D., has found something odd.

Her laboratory has uncovered a specific group of bioactive lipids that show up in dramatically different numbers in men and women with inflammatory diseases. These lipids may be representative of the hidden factors that explain sex-specific differences in how men and women develop heart disease, Alzheimer's, COVID-19, and autoimmune vasculitis.

"It's become clear that sex-specific differences in the immune system are intimately tied to certain disease outcomes," says Dr. Sharma.

For many years, researchers downplayed health differences between men and women. "Researchers believed that in general we should observe similar results in male and female mice, and if you didn't, that was an 'artifact' as opposed to a bona fide biological phenomenon," says Dr. Sharma. Clinical trials often enrolled only men.

Then, around the time more women began working in the sciences, researchers started asking new questions. What if we actually tried to learn from sex-specific differences? In 1986, the National Institutes of Health required grant applicants to include women in clinical studies. Once scientists started comparing cases, the sex-specific health differences were glaring. Women are better at fighting off infection but are more likely to develop autoimmune diseases. Men are more prone to heart disease and neurodegenerative diseases such as Parkinson's.

"In some diseases, the difference is huge, so much so that you could basically say the disease is almost sex-specific," says LJI Professor Klaus Ley, M.D. "For example, ankylosing spondylitis is basically only found in men, and lupus is five times more common in women. That teaches us that the immunology is different in men and women. There are many, many examples of this."

> "It's become clear that sex-specific differences in the immune system are intimately tied to certain disease outcomes."
>
> **Dr. Sonia Sharma**

Researchers at LJI are now working to understand why these trends exist. Some of it may come down to hormonal differences, but there's more going on.

This new research into fundamental immune differences between men and women could have life-saving implications and lead to better medicine for all.

Science beyond the binary

We use "men" and "women" in this article to describe people assigned male or female at birth. This is a narrow way to describe sex and gender, and it leaves out transgender and non-binary people. By looking beyond assigned sex, we can learn even more about how individual immune systems combat disease. For example, new tools for sequencing single immune cell genomes are one way we can shed light on the diversity within what we call "sex."

Gender and sex-based discrimination affects disease risk too. Transgender men and women and people who identify as non-binary often lack access to safe medical care. To learn more, we recommend visiting transequality.org.

Sonia Sharma, Ph.D.

Klaus Ley, M.D.

Back to the beginning

This is a field with more questions than answers. A big one: When do sex-specific immune differences first show up in the human body? LJI Professor Lynn Hedrick, Ph.D., has found evidence that differences in male and female immune responses could begin very early on—when immune cells called monocytes first develop in the bone marrow.

The bone marrow is home to the stem cells that mature into monocytes. Researchers have found differences in the numbers and types of these stem cells between men and women.

Dr. Hedrick and her lab are working to tell these young cells apart. What early differences could change how future monocytes fight disease in men and women? "We can probe these questions in a really detailed, meaningful way," says Dr. Hedrick.

Monocytes help with vascular health, so Drs. Hedrick and Ley are curious about their roles in heart disease, which tends to affect more men than women.

Dr. Ley is also looking closely at demographic data to identify a telltale molecular "signature" for heart disease risk. Through work with the NIH-funded Women's Interagency HIV Study, he's discovered women with HIV are especially vulnerable to heart disease, compared with HIV-negative women. His lab has uncovered several genes that may explain this difference. He hopes to analyze more samples from men to better understand sex as a factor for heart disease.

Lynn Hedrick, Ph.D.

For all women, the risk of a heart attack goes up even more when they hit menopause—and no one knows why.

“Estrogen plays a role, of course, but it’s not the whole story,” says Dr. Ley.

Dr. Sharma agrees. Sex-specific health differences don’t just come down to estrogen versus testosterone. “It’s time to look beyond sex hormones,” she says. “There are other fundamental differences that we are only beginning to appreciate.”

More than hormones

Dr. Sharma recently joined forces with scientists at Cedars-Sinai Medical Center, the University of California, Los Angeles, and the University of Southern California to form the new Women’s Evaluation of Systemic Aging Tenacity (MAE-WEST, “You’re Never Too Old To Become Young”) Specialized Center of Research Excellence on Sex Differences (funded through a National Institutes of Health U54 Consortium grant).

Through her new collaboration, Dr. Sharma has the resources to look at sex-specific differences in early-onset dementia and Alzheimer’s, as well as vasculitis and COVID-19. She’s focusing on innate immune cells called stromal cells or endothelial cells.

Dr. Sharma is testing whether vascular endothelial cells fuel inflammation when they receive certain signals from bioactive lipids, called eicosanoids, a unique and incompletely understood class of inflammatory mediators in the blood. “Our hypothesis is that there are profound differences in the ways these stromal cells produce and respond to bioactive lipids in males versus females,” says Dr. Sharma. “Many immunologists focus on inflammatory cytokines and immune cell subsets, which are important, without realizing that eicosanoids and other bioactive lipids regulate both of these things.”

Meanwhile, LJI scientists are shedding light on the roles of an entirely different group of immune cells.

When T cells strike

In 1588, Queen Elizabeth I gave a famous speech to inspire her troops as they prepared to face the Spanish Armada. “I know I have the body of a weak and feeble woman, but I have the heart and stomach of a king,” she said, telling her men to imagine her fighting alongside them.

Elizabeth didn’t really think of herself as weak, but she also knew her reign came as a surprise to many. For years, scientists underestimated women’s power too. Especially their ability to fight disease. For infectious disease after infectious disease, women show a better ability to fight off pathogens. This is the case for influenza and for COVID-19.

“In general, females have a better immune system—it’s more reactive,” says LJI Professor Alessandro Sette, Dr. Biol. Sci.

“The X chromosome contains the largest number of immune genes. Females have two copies of that X chromosome,” explains LJI Professor Erica Ollmann Saphire, Ph.D. “Maybe that diversity gives the female immune system more options or greater strength.”

Women appear to have stronger adaptive immune systems. Their T and B cells are better equipped to fight pathogens and destroy infected cells. The downside is that their stronger T cell response might also unleash more “autoreactive” T cells that mistakenly attack the body’s own tissues. That could be why women are much more likely to suffer from autoimmune diseases such as multiple sclerosis and lupus.

Alessandro Sette, Dr. Biol. Sci.

Erica Ollmann Saphire, Ph.D.

Men, women, and COVID-19

More men than women have died of COVID-19. Some of these deaths are tied to differences in biology. For example, men are more likely to suffer from heart disease, which can contribute to severe COVID-19 cases. Other deaths can be tied to societal expectations, such as a reluctance in men to seek treatment. (In the United States at least, fewer men than women reported they proactively sought medical help.)

Biology and society can come together to increase disease risk. That is why LJI scientists are looking at COVID-19 infections from many angles.

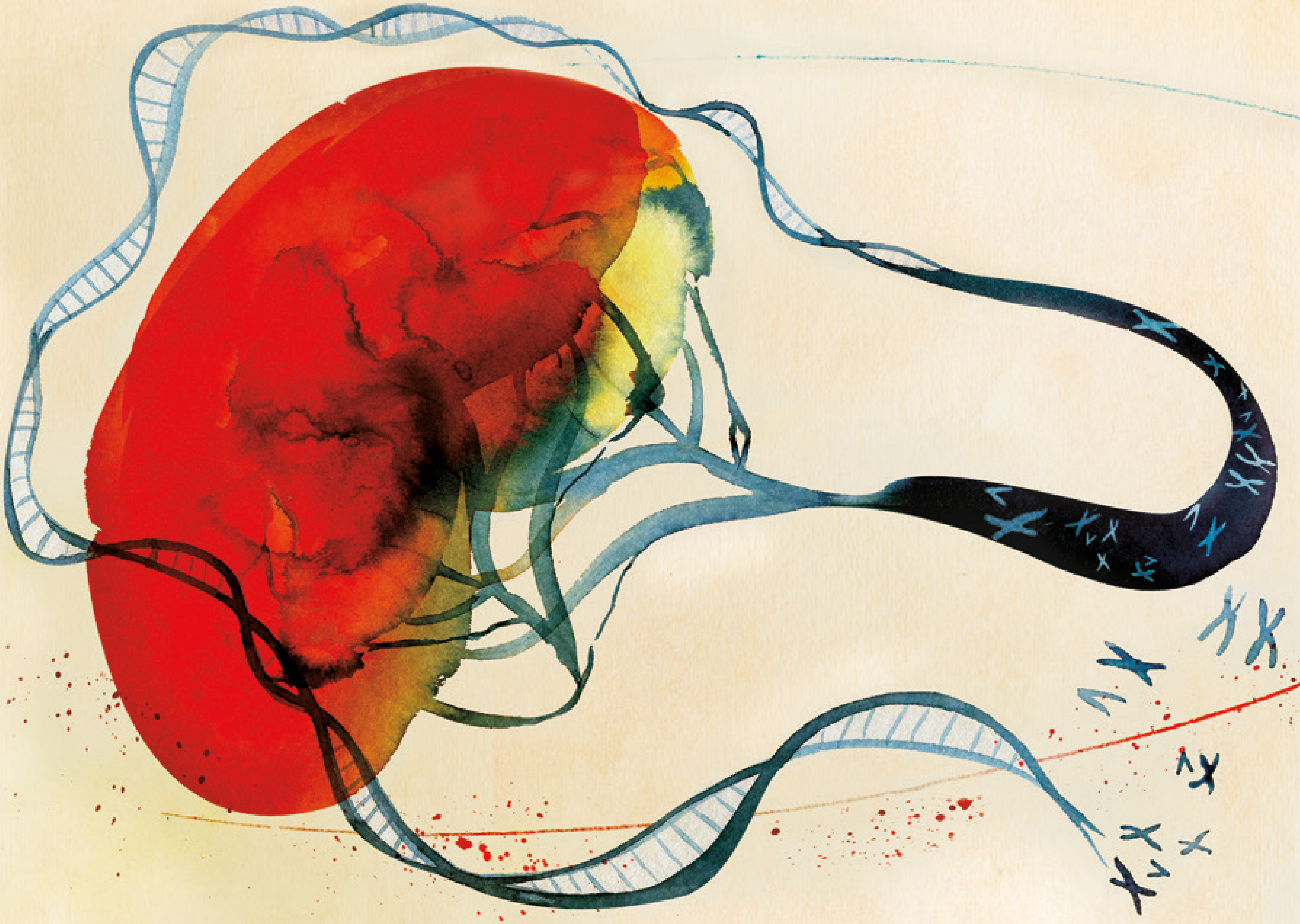
We know men tend to be more susceptible in general to acute viral diseases. To help figure out why, LJI Professors Alessandro Sette, Dr. Biol. Sci., and Shane Crotty, Ph.D., have been looking for differences in immune responses to SARS-CoV-2 in men and women.

Meanwhile, LJI Professor Sonia Sharma, Ph.D., is interested in the long-term inflammation affecting COVID "long haulers." She says vascular inflammation and the lingering multi-organ damage seen in COVID-19 cases is similar to vasculitis, an autoimmune disease that affects more women than men.

"I think female patients will be more predisposed to the long-term inflammatory complications of COVID, in a similar way they are more susceptible to chronic inflammatory diseases that can affectmany organs—heart, brain, lung, and kidney," says Dr. Sharma.

LJI scientists also weigh how ethnic background, cultural practices, and the environment affect disease risk. For example, Professor Sujan Shresta, Ph.D., is studying the immune response of COVID-19 patients in countries such as Vietnam, Thailand, and Nepal, where she has close research partnerships. Such studies are expected to provide valuable insights on how to better control the global pandemic.

Science is a lot like detective work, and COVID-19 is revealing crucial clues about how immune system differences and societal differences intersect for men and women around the world.



Scientists don't know what triggers these T cells to attack. One theory is that the female immune system needs to be flexible to sustain a pregnancy without having immune cells harm the fetus. These immune system fluctuations could make the T cells in women more likely to become overactive and potentially dangerous.

Or not. Something complicated is going on in the female immune system. After all, not all autoimmune diseases affect women more.

Autoimmunity in men

LJI Research Assistant Professor Cecilia Lindestam Arlehamn, Ph.D., is studying T cells to shed light on why men are more likely to develop Parkinson's disease.

Dr. Arlehamn has worked closely with Dr. Sette to show that T cells can mistakenly attack misfolded proteins, called alpha-synuclein, that form clumps around the brain cells that die in Parkinson's disease. This T cell activity is a sign that Parkinson's disease may be an autoimmune disease at its core. The team is now studying the numbers of T cells and their reactivity in men versus women.

"We've found there may be a difference, but we need to repeat this and do a more in-depth analysis," says Dr. Arlehamn.

"There must be some basic difference between men and women. It might have nothing to do with immune reactivity, but at least we are in a position to start asking those questions," adds Dr. Sette.

Secrets of the placenta

Back to pregnancy. A weaker immune system during pregnancy can leave a woman more vulnerable to infectious diseases.

Dr. Saphire has studied Lassa virus for many years. This hemorrhagic fever virus normally causes mild, flu-like symptoms, but the virus has proven 90 percent fatal in pregnant women. “The viruses my lab works on can disproportionately affect women,” says Dr. Saphire.

This dramatic difference has motivated Dr. Saphire to look for sex-based differences in how future antibody treatments for Lassa could help women most at risk.

A pregnant woman’s immune system is also intriguing because it interacts with an unusual, transient organ: the placenta. The placenta has defenses to keep pathogens from getting through—and it normally does a fantastic job.

Zika virus is an exception. The virus can get through the placenta and cause developmental problems, such as microcephaly, in infants. LJI Professor Sujan Shresta, Ph.D., is investigating how. She’s published several studies showing how T cells in pregnant mice react to Zika virus—and how their young have fared.

“Researchers are used to being humbled by experimental results. Even so, our work with Zika has been a constant reminder of how little anybody really knows about the immune response at the maternal-fetal interface, and how important it is to better understand it,” says Dr. Shresta.

Cecilia Lindestam Arlehamn, Ph.D.

Sujan Shresta, Ph.D.

Dr. Shresta is now using mouse models to study how the “killer” CD8+ T cells that fight Zika in pregnant mice react to related viruses, such as dengue. This research could guide Zika and dengue vaccine design and help pregnant women deliver healthier newborns, even in areas where it is very common for mosquitoes to spread both diseases.

Dr. Shresta thinks a better understanding of the placenta and the maternal immune system could shed light on a huge range of pregnancy complications and autoimmune diseases.

> “The viruses my lab works on can disproportionately affect women.”
>
> Dr. Erica Ollmann Saphire

As the new field of sex-specific immune research takes off, there’s a sense scientists need to make up for lost time. “You kick yourself for not focusing on it before,” says Dr. Sharma.

LJI will soon be training a new generation of researchers to consider sex-specific differences in immunology. As a council member for the NIH’s Specialized Centers of Research Excellence (SCORE) initiative to study sex differences in biology, Dr. Sharma will be leading the charge.

“We’ve just started,” she says. •

Alba Grifoni, Ph.D.

Speaking Up for Science

Most scientists don't expect to end up in the news. Alba Grifoni, Ph.D., certainly didn't. As a postdoctoral researcher (later promoted to instructor) at La Jolla Institute for Immunology (LJI), Dr. Grifoni had always worked on diseases that were global killers—but not headline news.

Then came COVID-19. In the early months of 2020, Dr. Grifoni worked closely with LJI Professor Alessandro Sette, Dr. Bio. Sci., to publish the first clues to how T cells target SARS-CoV-2. Their work inspired scientists around the world to consider how T cells, and not just antibodies, could drive immunity to the virus.

For many, the work gave hope that a COVID-19 vaccine would be possible. *The New York Times*, *Washington Post*, and many others began publishing updates from the research team.

"I just kept blinking my eyes. Am I reading this? Am I dreaming this? It was a shock," says Dr. Grifoni. "They were acknowledging that our field of study was important in the fight against COVID."

Dr. Grifoni comes from a family of medical doctors. As a girl growing up in Italy, she assumed she would go into medicine too. Yet as she took college courses, she started to wonder if a career as a doctor, where she'd see patients one by one, was the right fit. She started to consider studying immunology instead.

"What if I could do research that doesn't just help one person in the moment but could help way more people—even after I'm not around anymore?" she says. "That was the path I wanted to follow."

Dr. Grifoni had also grown up with several role models in the sciences. One was Rita Levi-Montalcini, M.D., the Italian neurobiologist who received a Nobel Prize in 1986 for the co-discovery of important nerve growth factors. "She showed me that being a woman should not hinder my aspirations," says Dr. Grifoni.

The others were Dr. Sette and LJI Professor Bjoern Peters, Ph.D. The pair leads cutting-edge research in epitope identification. Put simply,

they pinpoint the parts of a pathogen that provoke an immune response. “Everyone in immunology knows about Sette and Peters,” she says.

Dr. Grifoni earned her Ph.D. in immunology in 2014. Then she saw a job listing for a postdoctoral position in the Sette and Peters labs. “I thought, ‘You know what—I’m just going to apply for the postdoc. I’m going to give it a shot.’”

At LJI, Dr. Grifoni spearheads research that combines immunology and genetics. She uses bioinformatics tools to analyze viral genomes. This research can reveal which viral epitopes might be targeted by the immune system. Dr. Grifoni can then work with clinical samples to see exactly which potential targets are most important for fighting off the virus.

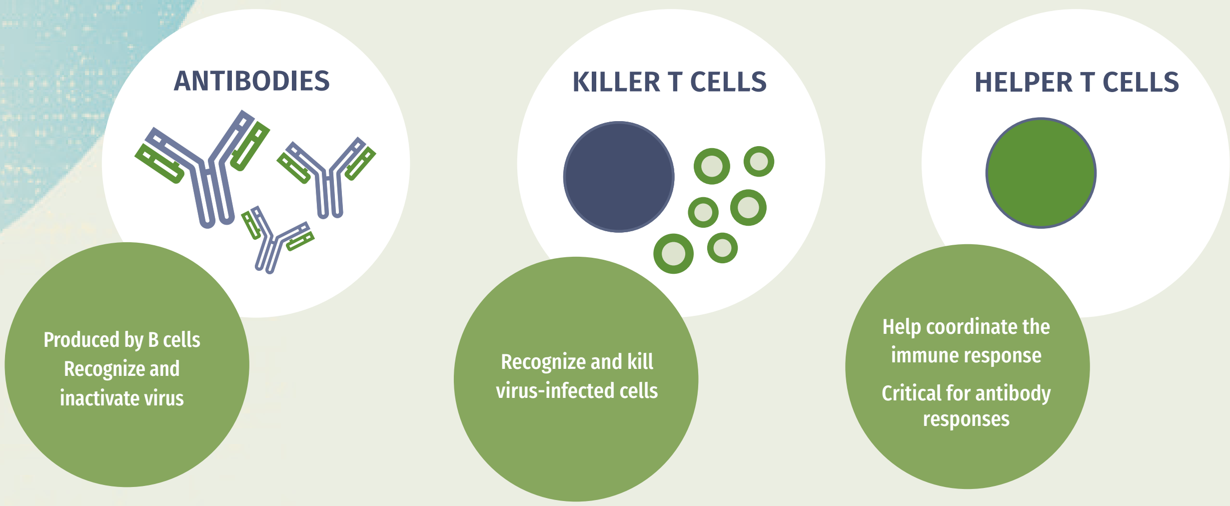
Her work has shed light on HIV, hepatitis B and C, Ebola virus, Zika, dengue, yellow fever, and many other pathogens. “I’ve lost count,” says Dr. Grifoni. “But the focus is always the same. I want to know how human T cells respond to viral infections.”

The hardest part of the job? “That I need to wait to see the data!” she says with a laugh.

“Some steps of my research require patience,” she adds. “You need to get the technical steps figured out. But once that’s set up, I want to go fast because I want to see the results.”

“What if I could do research that doesn’t just help one person in the moment but could help way more people—even after I’m not around anymore?”

WHAT KIND OF IMMUNITY IS IMPORTANT AGAINST COVID-19?



Dr. Grifoni's persistence in figuring out key SARS-CoV-2 T cell epitopes was recognized last fall when she received the Embassy of Italy Award to Honor Young Italian Researchers for Research to Fight COVID-19 from the Italian Scientists and Scholars in North America Foundation (ISSNAF).

As an ISSNAF winner, Dr. Grifoni had the chance to present her work virtually to leading Italian scientists and speak with the Italian media.

"It meant a lot to have my science recognized in the U.S. and Italy," says Dr. Grifoni. "It gave me the opportunity to share my research not only with other scientists in the field but with the general Italian population, in my own language, and deliver important information for them to understand the impact of SARS-CoV-2 and the importance of vaccination."

Dr. Grifoni is the kind of researcher who can easily explain her work to a non-scientific crowd, and that task has gotten even easier during the pandemic. "Now, when you talk to the average person about T cells, they know what those are," says Dr. Grifoni.

Going forward, Dr. Grifoni wants to help people understand the same cutting-edge research techniques and sense of urgency we've had with COVID-19 are needed to fight other global threats, such as dengue and chikungunya. She says researchers need to better understand how T cells recognize these viruses. They need to know how to balance T cell responses with antibody responses, and how to spark the right kind of immune responses with a vaccine.

"I find the need to simplify the science when speaking with a wide audience, but sometimes it would be good for people to really understand the complexity of the research," says Dr. Grifoni.

While much more work is to be done, Dr. Grifoni has already achieved what she'd hoped for. Her research has affected many other people and inspired new lines of research.

"I've had a great passion to guide me," she says. Thinking back to her university days, she remembers feeling discouraged, that she wouldn't make big contributions to science. Dr. Grifoni has advice for young scientists today.

"To them I'd say, 'Be brave. Throw yourself into the sky. No matter where you end up, you will definitely enjoy the journey—and if your work can also help others, that will be the best reward you can aim for.'"

Unmasking the pancreas

It's easy to overlook the pancreas. It doesn't have the beautiful symmetry of the brain or the muscular curves of the heart. Instead, the pinkish-yellow pancreas is shaped a bit like a squashed sweet potato.

Yet, the pancreas is a hidden gem. From its perch behind the stomach, the pancreas spends its days churning out the life-giving enzymes that break down the sugars, fats, and starches in your food. Zooming in, small cell clusters called islets come into view. Special beta cells live nestled within the islets, busily making the insulin the body uses to regulate blood sugar.

Unless there's trouble—with a capital T.

The body's own T cells target and destroy these beta cells in people with type 1 diabetes. Without beta cells, blood sugar levels go haywire. Blood thickens, causing strokes, heart disease, blindness, kidney damage, even death.

No one knows what causes these "autoreactive" T cells to attack, but researchers at La Jolla Institute for Immunology (LJI) have uncovered some fascinating clues.

In a recent study, LJI Professor Matthias von Herrath, M.D., and LJI Postdoctoral Researcher Christine Bender, Ph.D., tracked the movements of T cells that attack beta cells. These T cells find the beta cells by targeting preproinsulin, the precursor molecule to insulin.

To their surprise, the researchers discovered these T cells gather in the pancreas in nearly everyone, not just people with type 1 diabetes. Then the T cells wait. The T cells should move into the islets like hyenas, but for some reason, they can't see their prey until some unknown event forces the islets or beta cells to "unmask" themselves.

"These cells, which are supposed to be the bad guys, are actually present in healthy people," says Dr. Bender. "They are already there, and then in type 1 diabetes, something triggers them to recognize the islets or the beta cells and attack them—and destroy them."

"There has to be a component where the beta cells play an active role in revealing themselves to the immune system," adds Dr. von Herrath.

> "Organs are innervated—the skin is innervated—and it might just be that the innervation of a given target organ or area plays a role in sensitizing that organ for immune destruction or unmasking."

With a watchful eye on these predatory cells, Dr. von Herrath is tracking down what triggers them to attack the beta cells. In a recent collaboration with Gustaf Christoffersson, Ph.D., a former LJI postdoctoral researcher, Dr. von Herrath exposed a possible culprit: nerves.

Using a mouse model of type 1 diabetes, the researchers found that beta cells die off in patches that match up with where the cells are "innervated," meaning sensitized by nerves that branch out to the pancreas. The team found that blocking the nerve signals protected mice from beta cell death. "If the innervation is not occurring—like if you cut the nerves—then the organ remains invisible," says Dr. von Herrath.

This discovery has led Dr. von Herrath to consider nerves as the triggers for other organ-specific autoimmune diseases. He points out that other autoimmune diseases show patterns of patchy cell death that may be linked to innervation.

One example is vitiligo, a skin condition in which pigment-producing cells die off, leading to pale areas of skin. These pale areas often show up around the mouth and hands in symmetrical patterns that may reflect the symmetry of the underlying nerves.

"Organs are innervated—the skin is innervated—and it might just be that the innervation of a given target organ or area plays a role in sensitizing that organ for immune destruction or unmasking," says Dr. von Herrath. "If we could understand that, we could treat these diseases by modulating the nerves, which would be really cool."

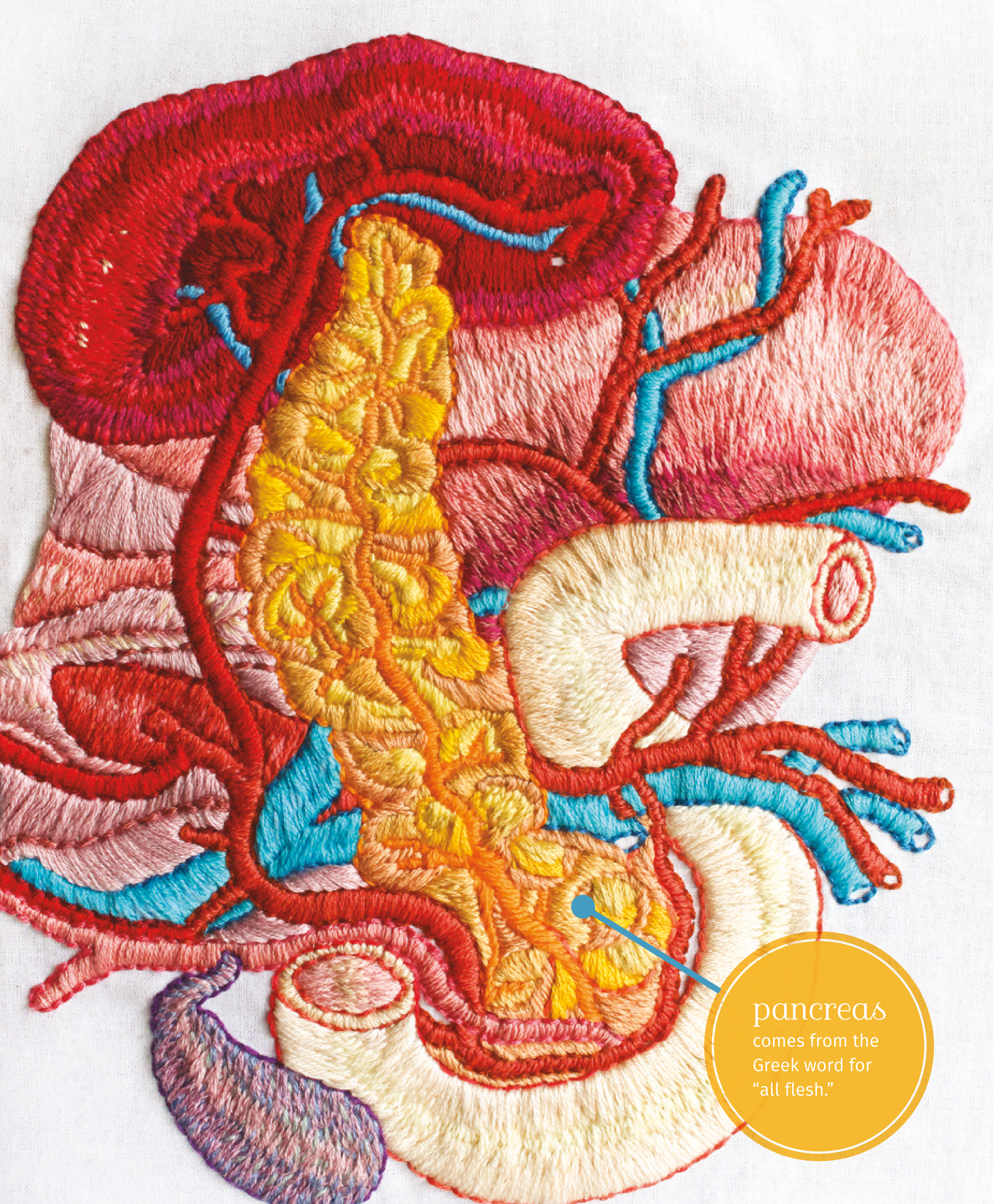
We're in the early days of understanding the role of innervation in type 1 diabetes. Meanwhile, Dr. Bender is still on the hunt for T cells that may attack other targets on beta cells. The researchers hope that by finding the most vulnerable targets, they might be able to block specific T cell attacks and treat type 1 diabetes. Their goal is to protect the pancreas without affecting how the immune system does its job overall.

To do this, Dr. Bender is working with scientists in the LJI Microscopy Core to track how T cells move around the organ. "We can scan whole tissue sections to see the bigger picture," says Dr. Bender.

The researchers are also working closely with tissue biobanks, making them one of the few teams with access to rare human pancreas samples. This is important because—while mouse models are very helpful—the islets of a human pancreas have a different architecture than a mouse pancreas.

"Having these human pancreas samples is unique," Dr. Bender says. "The window they provide into the inner workings of the pancreas gives LJI researchers another powerful tool in understanding this critically important organ."

The pancreas, that precious organ. •



pancreas comes from the Greek word for "all flesh."

Q&A with

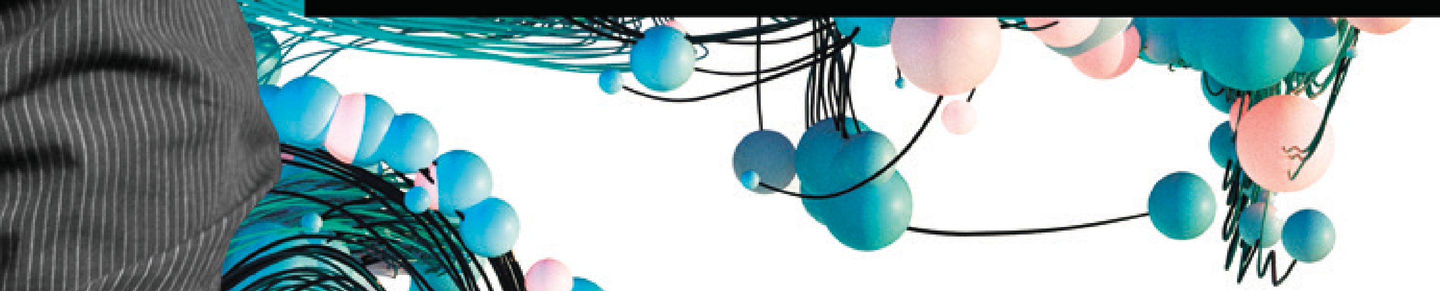
Professor Bjoern Peters, Ph.D.

When La Jolla Institute for Immunology (LJI) Professor Bjoern Peters, Ph.D., was a college student in the 1990s, no one knew the term “bioinformatics.” Most immunologists weren’t dealing with huge datasets. Then came the reams of data generated by efforts like the Human Genome Project.

Researchers needed new tools to sort through data and help answer crucial questions about the human body. At the same time, immunologists needed better models for understanding the inner workings of immune cells.

That’s when Dr. Peters stepped in. Early in his bioinformatics career, Dr. Peters published the first combined model showing the detailed steps cells take to expose specific invaders or mutated cells to the immune system. In 2004, Dr. Peters joined LJI, where he continues to push bioinformatics forward.

The tools Dr. Peters has developed are invaluable for immunologists worldwide. Thanks to his expertise and collaboration with LJI Professor Alessandro Sette, Dr.Biol.Sci., the Institute is home to the Immune Epitope Database (IEDB), a resource for immunologists studying how the immune system targets viruses, bacteria, and other threats.



Immune Matters asked Dr. Peters what it's been like to bring bioinformatics to immune system research.

What came first for you—an interest in bioinformatics or immunology?

Actually, my first love was physics! But when I did my Physics Diploma work in Germany, as my minor, I was doing biophysics training, and there was no lack of open questions in that field. We were asking "why do these cells die?" and other questions. And the answer was always "no one knows." That made me want to work on the biology side.

So I decided to pursue a Ph.D. in an area of physics that was then called theoretical biophysics. At that time, there was no such thing as bioinformatics, that word did not exist. But there's a long history of physicists exploring subject areas that are new, that require the same sorts of methodologies and approaches used in physics—heavy use of computers, math, and stats. Then in biology, with the advent of large data generation as part of genetic sequencing, that became a growth area. So many of the founders of bioinformatics have a physics background.

My Ph.D. advisor was studying the generation of epitopes by the MHC class 1 presentation pathway—a key step in getting the immune system to recognize a threat—and he was the first to develop a model of a phenomenon called proteasomal cleavage. That became the basis of my thesis topic, and I found it extremely interesting to learn how the immune system can recognize there's something wrong going on inside a cell.

When you were starting out, what kinds of tools did the field really need?

First of all, there wasn't really much of a field. There were maybe 100 people or so worldwide working in bioinformatics applied to immunology. So given the lack of people working in the field, every little bit helped. I essentially started work on a combined model—showing, stepwise, how the immune system goes from chopping up a protein from a pathogen to presenting that protein on the surface of a cell. These processes, called TAP transport and MHC binding, are key to getting other immune cells to recognize and fight disease.

During my Ph.D. study, this was a wide-open field. You could do the obvious things and people hadn't done them. Now that's changed, and there is a wealth of people working in bioinformatics in immunology.

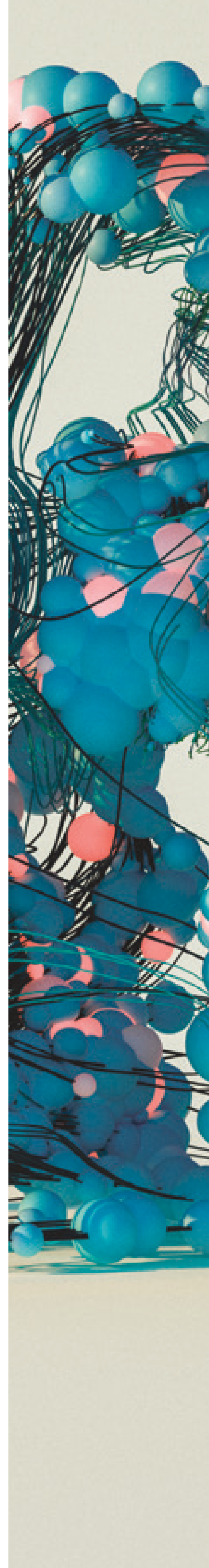
Collaboration has always been one of your strong suits. How do you go about bringing together immunologists with different backgrounds?

When I was working on my Ph.D., I realized the computational scientists didn't talk to the experimentalists in other labs. We were just taking data from them and thinking we understood them. We'd throw some models at the scientists in the lab, but we didn't understand the data, and they didn't understand the models. This led to some early mistakes I could have avoided. That made me want to understand the experimental parts better: how the datasets were being generated and how to work with them.

I've kept doing that, talking to experimentalists and learning their language—and at the same time communicating what I am doing in a way that experimentalists can understand. Now my lab has both computational and experimental scientists, and collaboration comes naturally.

What are the challenges of directing a global resource like the IEDB?

It's a very complex project. It was really initiated and led by my colleague Dr. Alessandro Sette, and I've learned a lot from him. Alex brings in his expertise from the biotech industry to manage big projects like the IEDB. One challenge is to manage these very different user groups. There are people who just want to use the



database, and then there are the NIH funders who have very specific goals in mind. And then there are the bioinformaticians, who are just interested in downloading the data. We're trying to understand what the different needs are.

Then there's a big risk of becoming complacent. We've been constantly trying to reinvent ourselves since the IEDB started. The database was originally designed to be a rapid anti-bioterror knowledge generator, and then we shifted to asking questions about important diseases. What are the real threats and big health problems, and can we work on those? And now we're working in the emerging field of cancer neoepitopes.

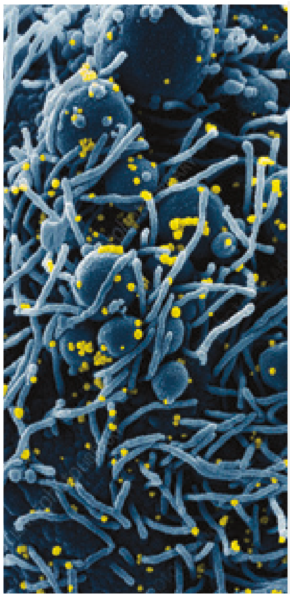
Do you have any advice for scientists just starting out in the field who want to combine bioinformatics with immunology?

I would highly recommend everyone studying immunology or experimental biology do some basic data analysis and programming—because this is not going away. For example, in physics, where I come from, it's taken for granted that everyone can write computer programs. But that work is not called "computational physics," it's just called "physics." In the same way, I think what we're doing right now will be called just "immunology" or "biology." The field is going to evolve, and if you have a bit of a quantitative background, it's going to help you.

Did you always picture yourself becoming a scientist?

No, I think I decided I wanted to become a scientist when I started university and I saw professors teaching. I saw how much they loved their subject, even after working on it for decades—they still had passion for it. That really excited me. •

The field is going to evolve, and if you have a bit of quantitative background, it's going to help you.



A closer look at T cells reveals big differences in mild vs. severe COVID-19 cases

A research team from LJI, The University of Liverpool, and the University of Southampton has found that people with severe COVID-19 cases may be left with more of the protective "memory" T cells needed to fight reinfection.

"The data from this study suggest people with severe COVID-19 cases may have stronger long-term immunity," says study co-leader LJI Professor Pandurangan Vijayanand, M.D., Ph.D.

The research, published in *Science Immunology*, is the first to describe the T cells that fight SARS-CoV-2 in "high resolution" detail. "This study highlights the enormous variability in how human beings react to a viral challenge," adds co-leader Christian Ottensmeier, M.D., Ph.D., FRCP, Professor at the University of Liverpool and adjunct professor at LJI.

A better way to ward off asthma triggers

When a person with allergies encounters an asthma trigger, harmful T cells boost their numbers in the lungs and release molecules that cause inflammation. A new LJI study shows how to throw a wrench in this process.

According to findings published recently in *The Journal of Allergy and Clinical Immunology*, blocking two immune molecules—called OX40L and CD30L—at the same time is key to preventing asthma attacks in a mouse model.

"We have found a way to block the acute asthmatic inflammatory response—and we saw a strong, long-lasting reduction in asthma exacerbations," says LJI Professor Michael Croft, Ph.D., senior author of the new study.

These findings suggest that dual antibodies or a "bi-specific" reagent could work to block OX40L and CD30L signaling together in a single treatment, but more research is needed.

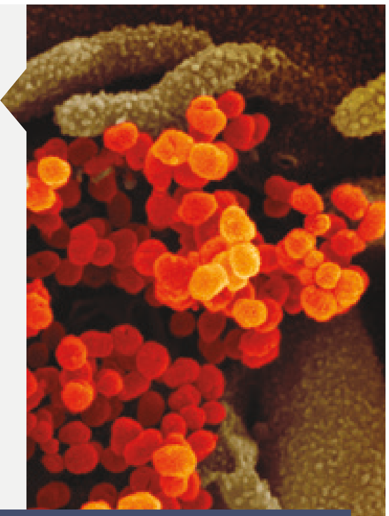
Top: Lung tissue of untreated mice. Bottom: Lung tissue of mice treated with antibodies blocking OX40L and CD30L.

Protective immunity against SARS-CoV-2 could last eight months or more

Recent findings at La Jolla Institute for Immunology (LJI) suggest that nearly all COVID-19 survivors have the immune cells necessary to fight re-infection. This research, based on analyses of blood samples from 188 COVID-19 patients, suggest that responses to the novel coronavirus, SARS-CoV-2, from all major players in the "adaptive" immune system, which learns to fight specific pathogens, can last for at least eight months after the onset of symptoms from the initial infection.

"Our data suggest that the immune response is there—and it stays," LJI Professor Alessandro Sette, Dr.Biol.Sci., who co-led the *Science* study with LJI Professor Shane Crotty, Ph.D., and LJI Research Assistant Professor Daniela Weiskopf, Ph.D.

"We measured antibodies, memory B cells, helper T cells, and killer T cells all at the same time," says Dr. Crotty. "As far as we know, this is the largest study ever for any acute infection that has measured all four of those components of immune memory."



> "Our data suggest that the immune response is there—and it stays."
>
> *– Alessandro Sette, Dr. Biol. Sci.*

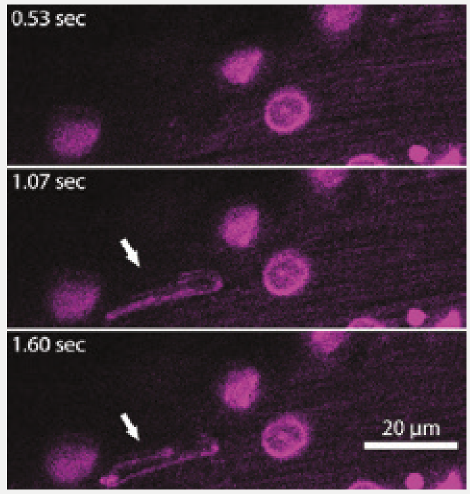
Researchers discover new particle in the blood of septic patients

"LJI scientists have found never-before-seen particles in the blood of people with sepsis. The researchers are the first to show these particles, called elongated neutrophil-derived structure (ENDS). Their work reveals that ENDS break off immune cells and change their shape as they course through the body.

"We actually found a new particle in the human body that had never been described before," says LJI Instructor Alex Marki, M.D., who served as first author of the study. "That's not something that happens every day."

The research, published in the *Journal of Experimental Medicine*, shows the importance of understanding how immune cells change over the course of a disease.

"ENDS are not normal—they are not detectable in healthy people or mice," says LJI Professor Klaus Ley, M.D., who served as senior author of the study. "But ENDS are very high in sepsis, and I would not be surprised if they were high in other inflammatory diseases."



This timelapse image shows the appearance of an ENDS and how it curls over time.

> "We actually found a new particle in the human body that had never been described before, That's not something that happens every day."
>
> *– Alex Marki, M.D.*

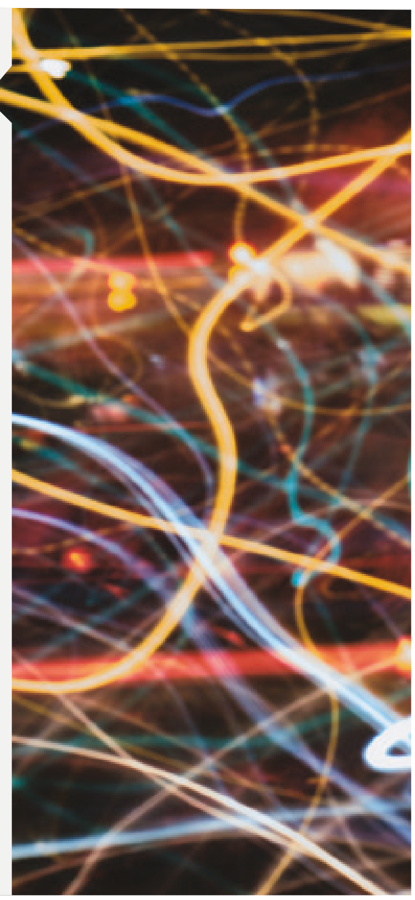
3D maps reveal inner workings of immune cell gene expression

To truly understand how genes affect health, LJI researchers have tracked down the switches (also called "enhancers") that control when and where a gene is expressed in the body. These 3D maps reveal how enhancer sequences and genes interact in several types of immune cells.

Importantly, these maps, published in *Nature Genetics,* have opened the door to understanding individual risk for diseases—from asthma to cancer.

"Nobody has done this mapping, either technically or analytically, to this precision in immune cells," says LJI Professor Pandurangan Vijayanand, M.D., Ph.D., co-senior author of the study.

"Going forward, we can apply this framework to understand cell types involved in many different diseases," says study co-senior author Ferhat Ay, Ph.D., the Institute Leadership Assistant Professor of Computational Biology at LJI and an assistant adjunct professor at the UC San Diego School of Medicine.



DONOR PROFILE

Tempus dare
A time to give

"How can I help?" That was the life-saving question this year, as people around the world stepped up to volunteer for clinical trials and staff vaccination sites.

"How can I help?" That was the question supporters of La Jolla Institute for Immunology (LJI) asked as the Institute took on COVID-19 research.

"The extraordinary progress our researchers made in addressing the global pandemic was a direct result of private philanthropy," says Christopher Lee, LJI's Chief Advancement Officer. "Critical early funding from individuals and foundations, both locally and nationally, allowed for immediate work in studying the virus at LJI—as federal funding was being organized and eventually distributed."

"Without our donors, our highly impactful work—now cited and used around the globe—would have been limited if not impossible," says Lee.

San Diego biotech entrepreneurs François Ferré, Ph.D., and Magda Marquet, Ph.D., knew supporting LJI would be critical for advancing

> "Philanthropy can help researchers jump into more adventurous science. That's really the core of why we need strong philanthropy at LJI at all times."
> – François Ferré, Ph.D.

our understanding of COVID-19. Scientists at LJI dedicated themselves early on to long days and nights studying how immune cells and antibodies could fight SARS-CoV-2.

"We really connected with the fact that LJI was in the weeds, trying to make new COVID-19 research happen," says Dr. Ferré, who also serves on LJI's Board of Directors.

Drs. Ferré and Marquet knew scientists would be hard-pressed to find funding for such rapid shifts in research. After listening to a presentation from LJI Professor Erica Ollmann Saphire, Ph.D., the couple made a gift to LJI that allowed the Saphire Lab to purchase two incubators essential for COVID-19 antibody therapeutic research.

"François and Magda are real difference makers here at LJI," Lee says. "We know that when urgent action is required, LJI can always count on these two remarkable philanthropists. We are deeply honored to be associated with them."

As LJI continues to shed light on COVID-19, many are now wondering how to build on the public's new grasp of medical research. LJI has been a leader in immune system research for more than 30 years, and now the public is in a position to understand how insights into immune cells can open the door to better vaccines, cancer therapies, autoimmune disease treatments, and more.

"People have realized what LJI is doing—in a much more practical way," says Dr. Marquet.

"We're at a point in medicine right now where it is so important to truly understand the functioning of the immune system," Dr. Ferré adds. "I cannot think of a better cause right now."

Drs. Ferré and Marquet took an interest in LJI long before the pandemic. Dr. Ferré joined the LJI board in 2017, and the two have funded early career research projects through the Tullie and Rickey Families SPARK Awards for Innovations in Immunology.

The couple appreciates that LJI is open about how gifts are used. Following their donation in 2020, they received a personal letter from Dr. Saphire. "She explained in detail where the money was going, describing why this incubator was so important for the research she was doing," says Dr. Ferré.

"LJI recognizes the importance of donors, and that goes a long way," says Dr. Marquet.

They also recognize the importance of efficiency at LJI. "Being an entrepreneur myself, I really like the Institute's approach," says Dr. Ferré. "It's not encumbered by layers of bureaucracy."

Dr. Ferré says he's looking forward to where the Institute goes from here, especially in the area of autoimmune disease. "One of the big crises of our immune system is inflammation going berserk," he says, adding that with donor support, researchers at LJI will be in a good position to quickly follow up on promising findings—for any disease.

"Philanthropy can help researchers jump into more adventurous science," Dr. Ferré says. "That's really the core of why we need strong philanthropy at LJI at all times." •

Shane Crotty, Ph.D.

Bjoern Peters, Ph.D.

Alessandro Sette, Dr. Biol. Sci.

THREE LJI FACULTY NAMED "HIGHLY CITED" RESEARCHERS

LJI Professors Shane Crotty, Ph.D., Bjoern Peters, Ph.D., and Alessandro Sette, Dr. Biol. Sci., were recently named "Highly Cited Researchers" by Clarivate. The honor recognizes researchers whose peer-reviewed studies have been cited most often by their scientific peers. This means Drs. Crotty, Peters and Sette have been in the top 1% of citations for their field of study between 2009 and 2019.

"The La Jolla Institute is a champion of providing reliable scientific facts," says Dr. Sette. "And being Highly Cited means scientists at LJI are being cited in the scientific literature."

All three researchers were on the list in previous years, and their work continues to garner international attention. In 2020, the three researchers joined forces to conduct crucial research into how immune cells respond to SARS-CoV-2, the virus that causes COVID-19. "One reason we've been so successful is because LJI is a really collaborative place, so it's set up for doing immunological research quickly," says Dr. Crotty.

An example of strong collaboration is how experimental work in these labs has benefited from Dr. Peters' expertise in bioinformatics (more on page 22). The Peters Lab is leveraging experimental data to better predict vaccine outcomes. "We are trying to learn from what happens immediately after vaccination to then predict what will happen long-term after," says Peters.

In the end, the "highly cited" work from all three labs is valuable for guiding research efforts worldwide.

ASTHMA RESEARCHER JERMAINE KHUMALO RECEIVES AAI INTERSECT FELLOWSHIP

LJI postdoctoral researcher Jermaine Khumalo, Ph.D., has been named a 2021 Intersect Fellow by the American Association of Immunologists (AAI). With this fellowship, Dr. Khumalo will bring together immunology and computational science training to fuel new research into allergic asthma.

"It's really important to have the new fields merge," says Dr. Khumalo.

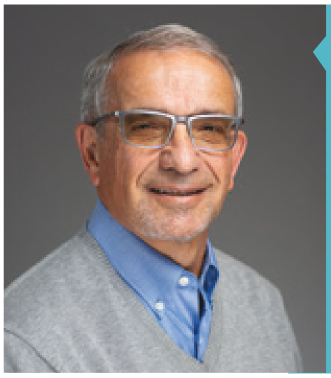
Dr. Khumalo will be working with LJI Professor Pandurangan Vijayanand, M.D., Ph.D., a physician-scientist with expertise in clinical disease and the development of genomics tools, and LJI Associate Professor Ferhat Ay, Ph.D., a computational scientist and leader in the fields of genomic and epigenetic analysis.

ARCS SAN DIEGO NAMES ERICA OLLMANN SAPHIRE "SCIENTIST OF THE YEAR"

LJI Professor Erica Ollmann Saphire, Ph.D., has been named Scientist of the Year by ARCS San Diego, a chapter of the Achievement Rewards for College Scientists (ARCS) Foundation. The award recognizes Dr. Saphire's breakthroughs in structural virology and her leadership of the Coronavirus Immunotherapy Consortium (CoVIC) in 2020.

"This is the first time LJI has been recognized," says Dr. Saphire. "Emerging recognition of the Institute as a whole this year has been important to me—our depth and focus on human immunity provide a rich opportunity for human health."

"I have been watching Dr. Saphire via the La Jolla Institute for Immunology webinars recently as she provides global leadership in understanding host-virus interactions, which will be key to responding to COVID-19 today and for future pandemics," says Holly Heaton, ARCS San Diego President. "She is a remarkable scientist and leader."



Amnon Altman: Leading immunologist and educator retires

After 31 years of leading groundbreaking studies at La Jolla Institute for Immunology (LJI), Professor Amnon Altman, Ph.D., is retiring and transitioning to the role of professor emeritus. Over those years, Dr. Altman's research into T cell activation opened the door to new therapies for inflammation, autoimmune diseases, cancers, and more.

Dr. Altman was born in Israel and came to the United States in 1975 to complete postdoctoral studies at the National Institutes of Health. After serving on the faculty at Scripps Research, Dr. Altman joined LJI in 1990, just a year after the Institute was founded.

At the time, LJI had strong backing from the pharmaceutical division of Kirin Brewery in Japan, but it had yet to prove that it could compete for federal funding. "It was a small institute taking its first steps, and there was no guarantee that LJI would be successful, so there was some risk involved" says Dr. Altman.

Dr. Altman took the leap and launched LJI's Division of Cell Biology. Since then, he's seen the Institute grow from about 40 employees to nearly 500. "I've lived through essentially the whole life of the Institute," says Dr. Altman.

When Dr. Altman began his independent research career in the 1980s, the field of T cell activation was in its early days. "There were many open questions," he says.

Then in 1990, his laboratory published a pivotal study in *Science* showing that, when T cells are triggered through their antigen-specific T cell receptor, the earliest biochemical event in T cell activation was a process of phosphorylation of proteins on tyrosine residues. This process was mediated by enzymes called protein tyrosine kinases, and it turned out to be a key signaling event for many cell types.

The Altman Lab then worked to characterize other types of protein kinase enzymes. This effort led to the discovery and biological characterization of an enzyme called protein kinase C-theta (PKCθ). "We demonstrated that this enzyme is essential for the proper activation of T cells," says Dr. Altman.

Over time several drug companies have taken on projects to develop small molecule inhibitors of this enzyme. "The idea is that inhibition of this enzyme would inhibit autoimmune diseases or rejection of organ transplants," Dr. Altman says.

In recent years, Dr. Altman has focused on improving the immune system's ability to fight cancers. His work has focused on a subset of T lymphocytes called regulatory T cells (Tregs), which normally act to dampen excessively active immune responses that can cause autoimmune diseases and inflammation. However, in the context of cancer, these same cells act to suppress desirable antitumor immunity—and promote cancer progression. Dr. Altman's work in mouse models showed that deleting an enzyme called protein kinase C-eta (related to, but distinct from, PKCθ) in a critical signaling pathway operating uniquely in Tregs reduces the suppressive activity of these cells and, hence, improves the immune system's antitumor activity to slow tumor growth.

Outside of the science itself, Dr. Altman is most proud of his efforts to mentor the next generation of researchers. He has trained an estimated 65 postdoctoral fellows in his career, and many of these trainees have gone on to establish their own laboratories at universities around the world and serve as leaders at pharmaceutical companies.

Dr. Altman says learning can go both ways, and he encourages trainees to speak up. "I count on their opinions and their thinking," says Dr. Altman. "I don't have a monopoly on great ideas, and I expect to hear from them."

As he transitions to retirement, Dr. Altman is looking forward to spending more time with his four grandchildren. He'll also continue supporting LJI's work in different ways, including, for example, assisting postdoctoral researchers with fellowship applications. Still, he says he will miss being a part of LJI on a daily basis.

"It's a place where I was happy to come to work every day," says Dr. Altman. "I'll especially miss the daily contacts with young trainees coming to LJI from all over the world, who have enriched my life; they make me feel a lot younger than I actually am." •

Ultra-competitive **XPRIZE** goes to LJI team

Left to right: Arturo Hernandez, Suzanne Alarcon, Hannah Dose, Kyle Tanguay, and Rosalinda Diaz.

When the COVID-19 pandemic shut down laboratories around the world, four researchers at La Jolla Institute for Immunology (LJI) developed a rapid, saliva-based screen to get the Institute back up and running safely.

Their innovative work has won them the XPRIZE Rapid COVID Testing Competition. The team will receive $500,000 in guaranteed winnings and is eligible to receive $1 million total as they take steps to make their screening protocol widely available.

The LJI team was led by Suzanne Alarcon, manager of the LJI Next Generation Sequencing Core. Her team members were Hannah Dose, Arturo Hernandez, Kyle Tanguay and Rosalinda Diaz.

"We are all super excited," says Alarcon. "We want to get our protocol out there because it's reliable, it's quick and it doesn't require extremely specialized equipment or technical skills."

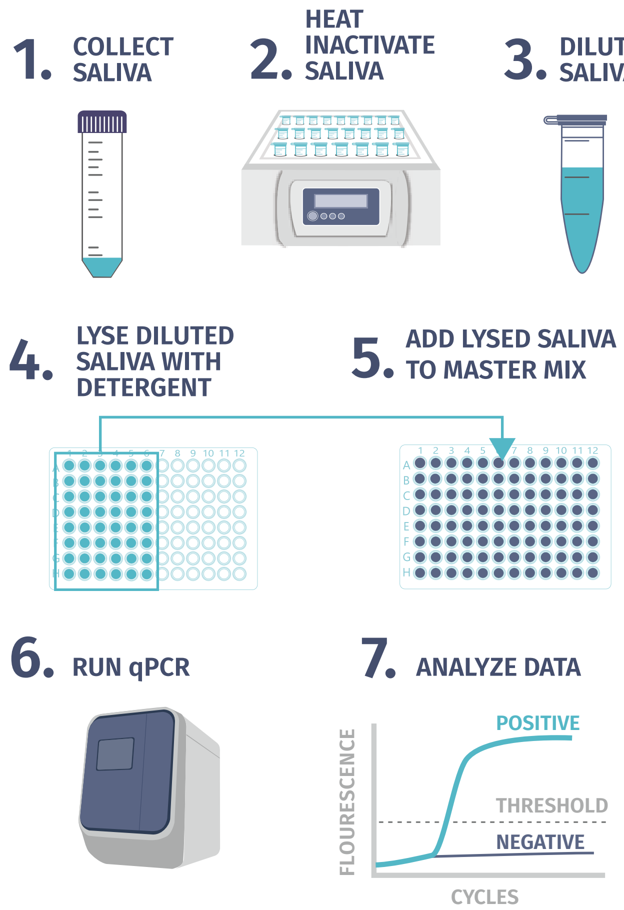
The competition was fierce, with more than 700 teams in the running, but the LJI screening protocol stood out for being fast, inexpensive, and reliable. As a bonus, the saliva-based screen proved easy for LJI employees to participate in. Employees simple spit in a tube that comes with a take-home kit. Employees then drop off their samples in a cooled collection bin, and Alarcon and her staff take it from there.

"The team worked so hard," says Stephen Wilson, Ph.D., executive vice president and chief operating officer at LJI. "This was an everyday, all-day effort to go from concept to assay to a system we could actually use."

WHY SPIT?

"At the time, when we first started talking about this, workplaces were just beginning to face the idea that they may need to screen their employees to keep the workplace as safe as possible," says Alarcon.

The Institute needed a COVID-19 screen that would be easier to administer than a blood test or deep nasal swab. Ideally, employees would be able to quickly collect samples themselves with a take-home kit. Saliva samples were the answer, and Alarcon was just the person to make it happen.



> "We want to get our protocol out there because it's reliable, it's quick and it doesn't require extremely specialized equipment or technical skills."
>
> – Suzanne Alarcon

"At the time, there were only a few papers out with small numbers of samples and no approved tests based on saliva, so it was a bit of a gamble," says Alarcon. Luckily, Alarcon started her career working in labs that studied taste and smell. "I have done lots of different field tests and saliva collections, so it was something I was totally comfortable with," she says.

HOW THE SCREENING WORKS

COVID-19 screen looks for very tiny pieces of SARS-CoV-2 virus in saliva. The researchers found that looking for the viral particles, as opposed to looking for other signs of infection (such as antibodies), can allow for early detection.

To accomplish this, Alarcon's team performs a one-step RT-qPCR assay to detect genetic material from SARS-CoV-2. The basic strategy is the same as the Centers for Disease Control's early SARS-CoV-2 test, but the LJI teamhas worked to make it faster, safer and cheaper.

Alarcon and her teammates use heat to inactivate the virus (before they uncap the sample) and a detergent to process the sample, eliminating the expensive and time-consuming need to extract or purify RNA from a raw sample. They then repeat each screen to double-check the accuracy of the result.

Because the reaction to detect the virus is done with only a low volume, the scientists can perform high-throughput screening at a low cost. The whole protocol can be carried out in less than a day and only costs $1.21 per sample.

GOING FOR THE XPRIZE

XPRIZE competitions challenge scientists to take on big, thorny problems. For example, Elon Musk is currently sponsoring an XPRIZE competition for scientists who can figure out how to pull massive amounts of carbon dioxide from the atmosphere and oceans.

When Alarcon heard about the XPRIZE Rapid COVID Testing competition, she knew the LJI protocol fit the bill.

The LJI team is still deciding what to do with the XPRIZE winnings. They are looking at additional funding opportunities to help make screening widely available and get sample collection kits to more people.

Overall, Alarcon says the prize will give her team members more resources to take on new scientific projects. Although it is still hard for them to meet in person, the XPRIZE team has become a tight-knit group.

"We encourage each other, commiserate, celebrate, cry, laugh, meme. I just can't say enough how grateful and proud I am of their hard work and persistence," Alarcon says. "In a time of absolute turmoil they have thrived." •

Immunologists share their work in "Live from the lab" dispatches

Webinar series continues with a fascinating behind-the-scenes look at LJI research and its impact

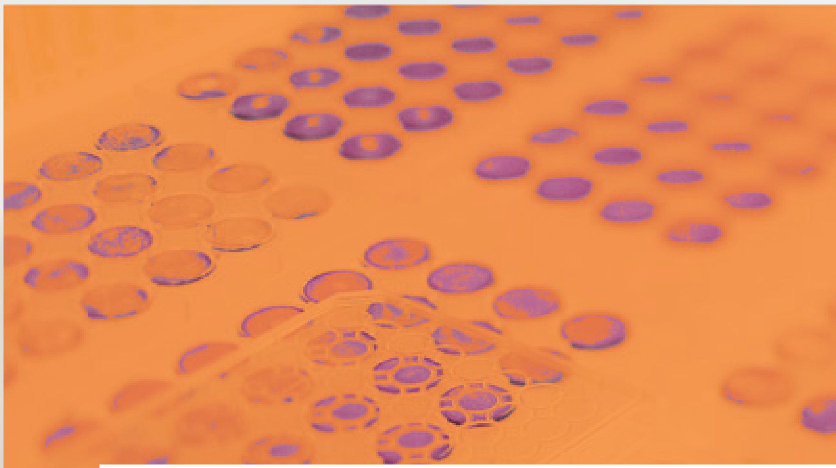
RECENT HIGHLIGHTS:

LIVE FROM THE LAB

Nov. 24: Infectious disease experts at LJI are tackling COVID-19 from many angles. In this webinar, Erica Ollmann Saphire, Ph.D., and Sujan Shresta, Ph.D., gave viewers an inside look at the latest COVID-19 findings. Both researchers are leading international efforts to study COVID-19, and they shared how global collaborations fuel this work.

Feb. 9: We've learned so much after a year of SARS-CoV-2. In this webinar, LJI Executive Vice President and Chief Operating Officer, Stephen Wilson, Ph.D., and immunology expert Alba Grifoni, Ph.D., shared how immunologists have shed light on the SARS-CoV-2 puzzle and the human immune response to the virus. They also highlighted the next steps as scientists continue to fight the pandemic and SARS-CoV-2 variants.

Join our next webinar:
lji.org/LFL



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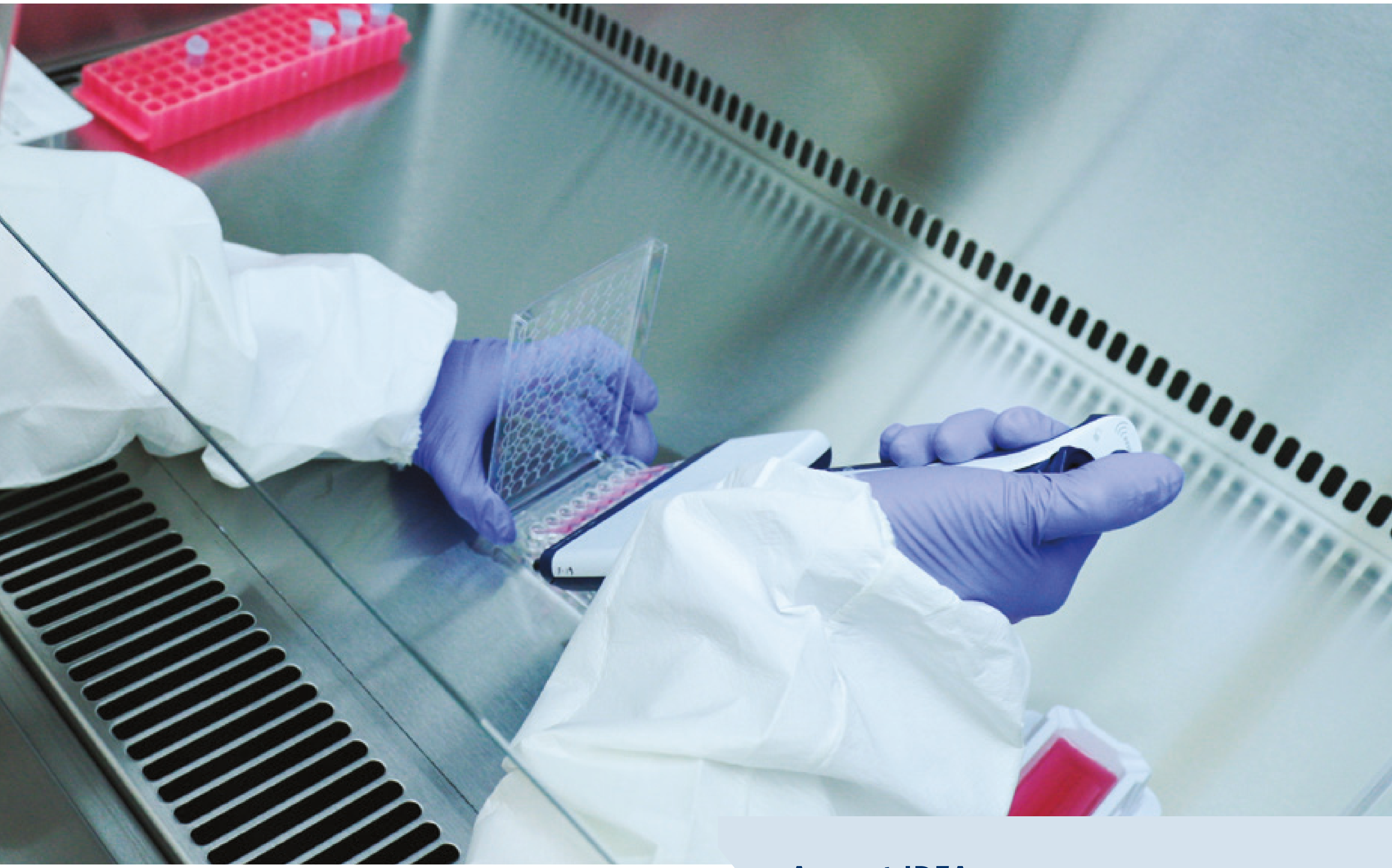

A great IDEA

Work continues in LJI's new, donor-funded Infectious Disease Exploration and Abatement (IDEA) Facility, a biosafety level 3 lab built to contain highly infectious agents. Scientists at LJI require this level of containment to safely study the virus that causes COVID-19, as well as other viral threats. This research could lead to better diagnostics and vaccine strategies for many diseases.