Immune MATTERS

LA JOLLA INSTITUTE
FOR IMMUNOLOGY
SPRING 2024

DATA IN THE REAL WORLD

THE ART OF FOLDING "BIG DATA" TOGETHER TO CURE DISEASE.

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Immune MATTERS

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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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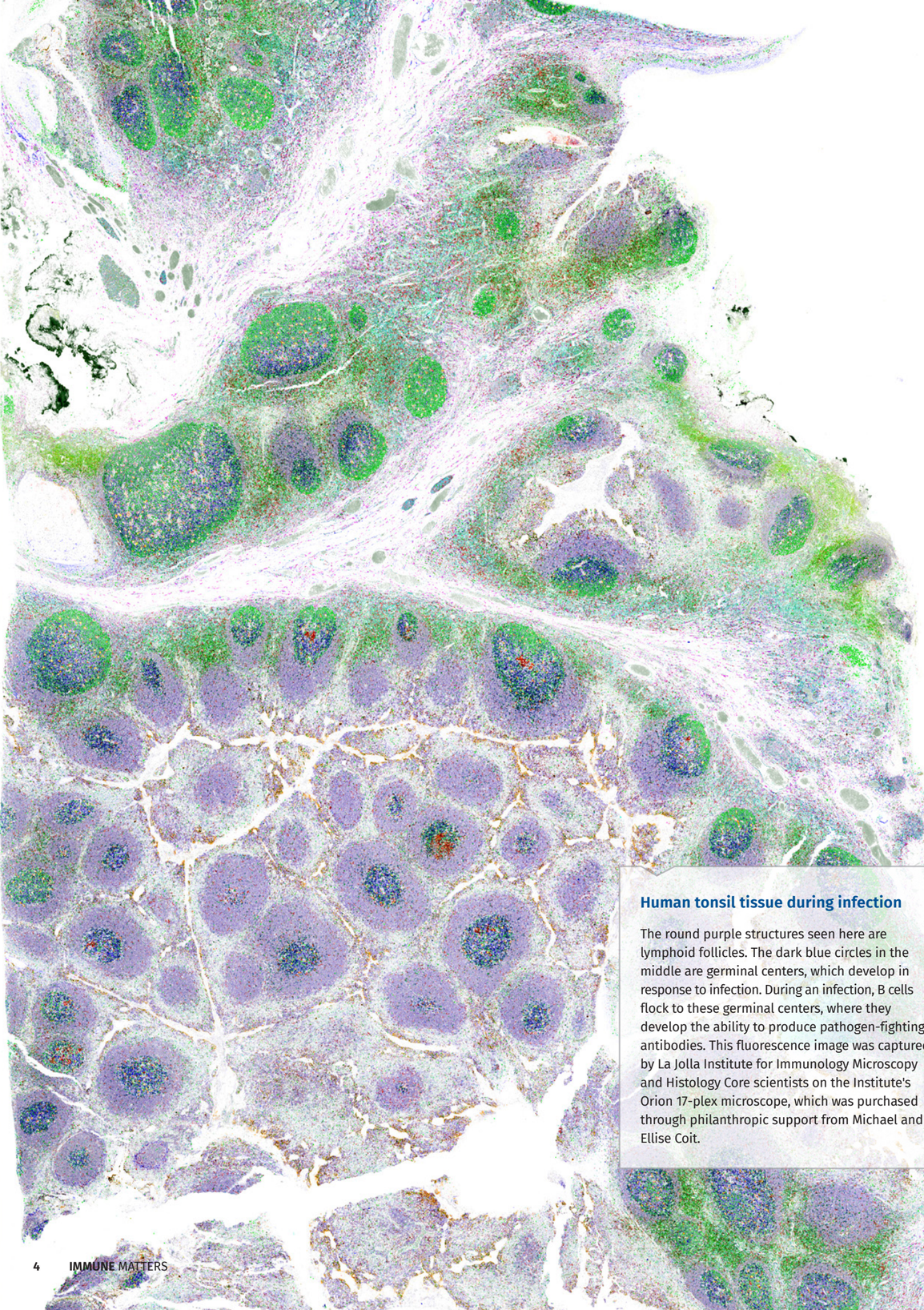


Human tonsil tissue during infection

The round purple structures seen here are lymphoid follicles. The dark blue circles in the middle are germinal centers, which develop in response to infection. During an infection, B cells flock to these germinal centers, where they develop the ability to produce pathogen-fighting antibodies. This fluorescence image was captured by La Jolla Institute for Immunology Microscopy and Histology Core scientists on the Institute's Orion 17-plex microscope, which was purchased through philanthropic support from Michael and Ellise Coit.

Data science detectives

Here's a scientific mystery for you: How is it that two people can receive a carefully controlled, identical dose of the same vaccine—and yet have a 100-fold difference in their immune response to that vaccine?

We see differences in individual immune responses in study after study, and on topic after topic. Think of cases in which a promising cancer immunotherapy helps only a fraction of patients, or cases where an entire household catches COVID-19. They are infected with the same strain, but some family members are severely ill while others barely notice.

To truly understand—and combat—all diseases, we need to understand the complicated interplay of age, sex, genetics, vaccination history, and other variables that affect the immune system. That is why scientists at La Jolla Institute for Immunology (LJI) are on a mission to gather and analyze valuable immune system data to crystallize new ways forward.

This issue of ***Immune Matters*** highlights the brilliant scientists who make LJI a data science and bioinformatics powerhouse. Thanks to their hard work, researchers can quickly comb through mountains of experimental data, uncover hidden trends, and predict individual immune responses to vaccines, therapies, and emerging diseases.

In fact, by harnessing data science, scientists in LJI's Center for Sex-Based Differences in the Immune System have already discovered clues to why men and women experience many diseases, such as asthma, differently. We're now coordinating with Women's Health Access Matters (WHAM), founded by LJI Board Member Carolee Lee, to contribute our findings to the new White House Initiative on Women's Health Research.

LJI supporters have made much of this work possible. You have donated funding, resources, time—and sometimes even blood—so we can study the smallest details of the immune system. Every experiment and every dataset brings us closer to ***Life Without Disease***.

Sincerely,

Erica Ollmann Saphire, Ph.D., MBA
Professor, President & CEO
La Jolla Institute for Immunology

Special T cells gather in the salivary gland to fight cytomegalovirus

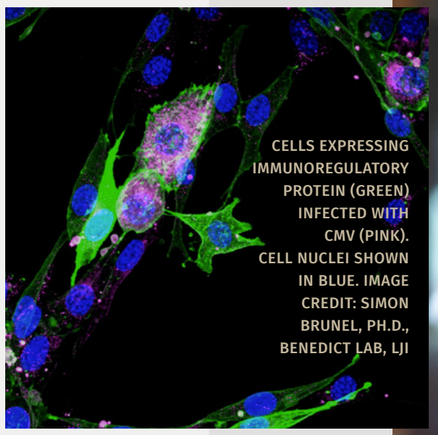
La Jolla Institute for Immunology (LJI) Associate Professor Christopher Benedict, Ph.D., and his colleagues are investigating how the body's immune cells combat a common pathogen called cytomegalovirus (CMV). Their latest study, published recently in ***PLOS Pathogens***, reveals how a subset of CD4+ "helper" T cells may help a person fight CMV and reduce the chances of the virus spreading from person to person.

These T cells gather in the salivary glands around 40 days after CMV infection. This location is important because the salivary gland is a hub of CMV replication and a key source of viral transmission. In the study, LJI Postdoctoral Fellow Simon Brunel, Ph.D., found that the T cells help fight CMV by expressing powerful antiviral immune molecules called IFNγ and IL-2.

This new insight into the body's response to CMV infection may help guide CMV vaccine development. As Dr. Benedict explains, many people carry CMV and experience no symptoms, but the virus can cause birth defects if a person catches it for the first time while pregnant. Babies born with congenital CMV disease can develop deafness and life-long health problems. "That's why there's such a push to develop a vaccine against this virus," says Dr. Benedict.

This new research was conducted with mice, and the scientists say the next step is to identify similar cells in humans.

> **"We now have the footprint of these cells and can say, 'Here is the type of cell we'd want to induce through a vaccine approach.'"**
>
> LJI ASSOCIATE PROFESSOR
> CHRISTOPHER BENEDICT, PH.D.



CELLS EXPRESSING IMMUNOREGULATORY PROTEIN (GREEN) INFECTED WITH CMV (PINK). CELL NUCLEI SHOWN IN BLUE. IMAGE CREDIT: SIMON BRUNEL, PH.D., BENEDICT LAB, LJI

STUDY CO-LEADER, LJI ANTIBODY CENTER DIRECTOR KATHRYN HASTIE, PH.D.

LJI scientists join national pandemic preparedness initiative

LJI researchers, led by LJI Professor, President & CEO Erica Ollmann Saphire, Ph.D., MBA, recently received funding through the U.S. Department of Energy's Biopreparedness Research Virtual Environment (BRaVE) initiative to accelerate research into emerging infectious diseases.

With this new funding, LJI scientists will collaborate with other institutions to develop faster methods for capturing detailed images of human antibodies and viral structures through an imaging technique called X-ray crystallography. Streamlining this process may help scientists develop effective vaccines and antibody therapies for pathogens with pandemic potential.

The work at LJI is part of a larger BRaVE project led by Aina Cohen, Ph.D., Division Director of Structural Molecular Biology at the Stanford Synchrotron Radiation Lightsource at SLAC National Accelerator Laboratory.

> **"This is a fantastic collaboration that we are really excited to be a part of."**
>
> LJI ANTIBODY CENTER DIRECTOR
> KATHRYN HASTIE, PH.D.

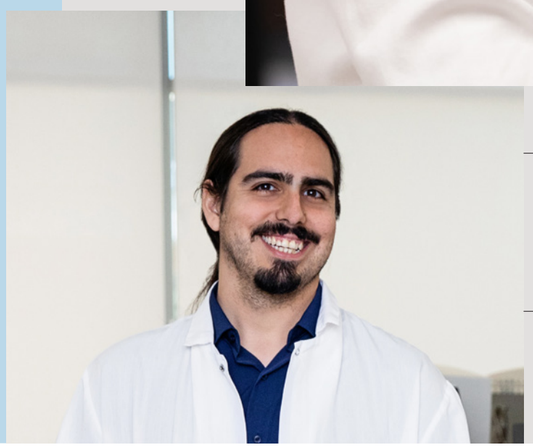
MAIT cells break the rules to stop disease

LJI scientists are getting closer to harnessing a unique group of T cells, called mucosal-associated invariant T (MAIT) cells, to better treat infectious diseases and improve cancer immunotherapies.

In a new study, published in ***Science Immunology***, LJI Professor and President Emeritus Mitchell Kronenberg, Ph.D., and his colleagues provide a closer look at how MAIT cells operate differently than typical T cells. As Dr. Kronenberg explains, most T cells are not interchangeable—they only work in the person who made them. But MAIT cells don't follow that rule.

In their investigation, the scientists found that MAIT cells can actually recognize the same tell-tale markers of disease, whether those markers come from different people, or even from mice. This means MAIT cells might serve as key players in cell-based therapies.

> **"Because MAIT cells are the same across individuals, they could more easily be used in cell therapies, where, in principle, my MAIT cells could be given to you."**
>
> LJI PROFESSOR & PRESIDENT EMERITUS
> MITCHELL KRONENBERG, PH.D.



MAIT CELL STUDY CO-FIRST AUTHOR & MEMBER OF KRONENBERG LAB, UC SAN DIEGO GRADUATE STUDENT GABRIEL ASCUI-GAC

DATA IN THE REAL WORLD

THE ART OF FOLDING "BIG DATA" TOGETHER TO CURE DISEASE.

At La Jolla Institute for Immunology (LJI), researchers sort through massive datasets to answer questions no one has ever considered before. By bringing diverse data points into the fold, hidden trends begin to take shape and form something entirely new and unexpected. This advances our understanding of human health.

A big question swirled through the scientific world last year: Was the highly mutated SARS-CoV-2 "Pirola" variant going to be a problem? Could it rip through immune cell defenses to trigger severe cases of COVID-19?

LJI researchers worked quickly to solve these puzzles. Doctors in Israel and Denmark had already reported cases of infections with the Pirola variant, and the virus appeared to be spreading to new regions. Speed was critical. The problem was that no one had collected comprehensive data yet showing how immune cells actually responded to the Pirola variant. The variant was just too new.

That hurdle didn't stop LJI Professor Alessandro Sette, Dr.Biol.Sci., and LJI Research Assistant Professor Alba Grifoni, Ph.D. The researchers had access to a massive, well-organized collection of SARS-CoV-2 data. This resource, known as the Immune Epitope Database (IEDB) holds key findings on how the immune system's T cells have combatted previous SARS-CoV-2 variants.

Dr. Grifoni quickly devised a bioinformatics approach to comb through the IEDB and uncover clues to how T cells might respond to Pirola. "SARS-CoV-2 keeps evolving, and it's hard for experimental researchers to keep up with how fast the virus changes," says Dr. Grifoni.

Thanks to the IEDB, the researchers were on their way to finding patterns, fast.

> **"We wanted to know—can we design a data-analysis pipeline to essentially predict the effects of new SARS-CoV-2 variants?"**
>
> LJI RESEARCH ASSISTANT PROFESSOR ALBA GRIFONI, PH.D.

About the artist:

Christine Ott is an origami artist based in Southern California. See her work online at **@oco_origami**

continued ▶

ON THE COVER

LEADERS SHAPING DATA SCIENCE

LJI scientists use data science and bioinformatics to make the world a healthier place. Every study requires some data analysis, of course, but LJI scientists have created resources that fold huge datasets together so researchers can easily share findings and launch new projects.

These efforts have helped guide vaccine development and fuel public health efforts around the world. For example, in March 2020, Drs. Grifoni and Sette published the first study suggesting that human T cells could recognize SARS-CoV-2 infection. This prediction was based on coronavirus data from the IEDB, and it gave many hope that a COVID-19 vaccine was possible. Later, once scientists had analyzed data from actual COVID-19 patients, they found the exact T cell activity Drs. Grifoni and Sette had predicted.

LJI's role as a world leader in immune system data science began with the IEDB. Dr. Sette and LJI Professor Bjoern Peters, Ph.D., established the IEDB in 2003 with funding from the National Institute of Allergy and Infectious Diseases. At that time, important data were scattered across manuscripts in dozens of different scientific journals. Scientists needed to view these discoveries in one place.

> "We were pioneers in making data accessible to the wider scientific community."
>
> LJI PROFESSOR BJOERN PETERS, PH.D.

"Every lab generates a wealth of data. We make these data more useful by capturing it, not in some kind of lab notebook, but in a database, and making it available to internal or outside users," says Dr. Peters.

Managing the IEDB is a surprisingly hands-on process—even an artform. IEDB Senior Project Manager Nina Blazeska leads the team of curators who comb through scientific studies for epitope data. "These LJI curators are Ph.D.-level immunologists who extract epitope data from scientific publications," says Blazeska. "It takes a detailed understanding and a lot of time."

The IEDB isn't just a database: It's a tool. LJI Bioinformatics Core Director Jason Greenbaum, Ph.D., was instrumental in building the IEDB in the mid-2000s. Today he works closely with Blazeska and manages a team of web developers who handle requests from the IEDB's user base. "We do a lot of problem-solving, and we're always reviewing user feedback to see which features we should add," says Dr. Greenbaum. One fascinating new IEDB feature is the 3D structure viewer, which gives scientists a glimpse of the actual molecular structures that immune cells "see" when they encounter pathogens.

A look at the numbers shows the importance of the IEDB within the research community. "Over the course of the IEDB's life, we have been cited more than 25,000 times," says Dr. Sette. "We can also look at the impact of the IEDB in stimulating applications in the pharmacological and biotech industry. Over the last 20 years we have been quoted in 665 patents. Of those, 225 are patents submitted between 2021 and 2022. The impact of the IEDB is accelerating."

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HOW ARE IMMUNOLOGISTS USING AI?

Artificial intelligence (AI) and machine learning describe ways of getting computers to sift through data to make predictions.

For example, a popular AI engine called ChatGPT can comb through articles online to come up with answers for just about anything. ChatGPT says it is "reasonable to expect" that Stephen King will continue writing horror novels, and "likely" that Taylor Swift will perform another Super Bowl halftime show.

The stakes are much higher when it comes to using AI and machine learning in medical research. LJI Assistant Professor Tal Einav, Ph.D., and colleagues are working to make sure these cutting-edge tools actually work—that predictions are as accurate as possible.

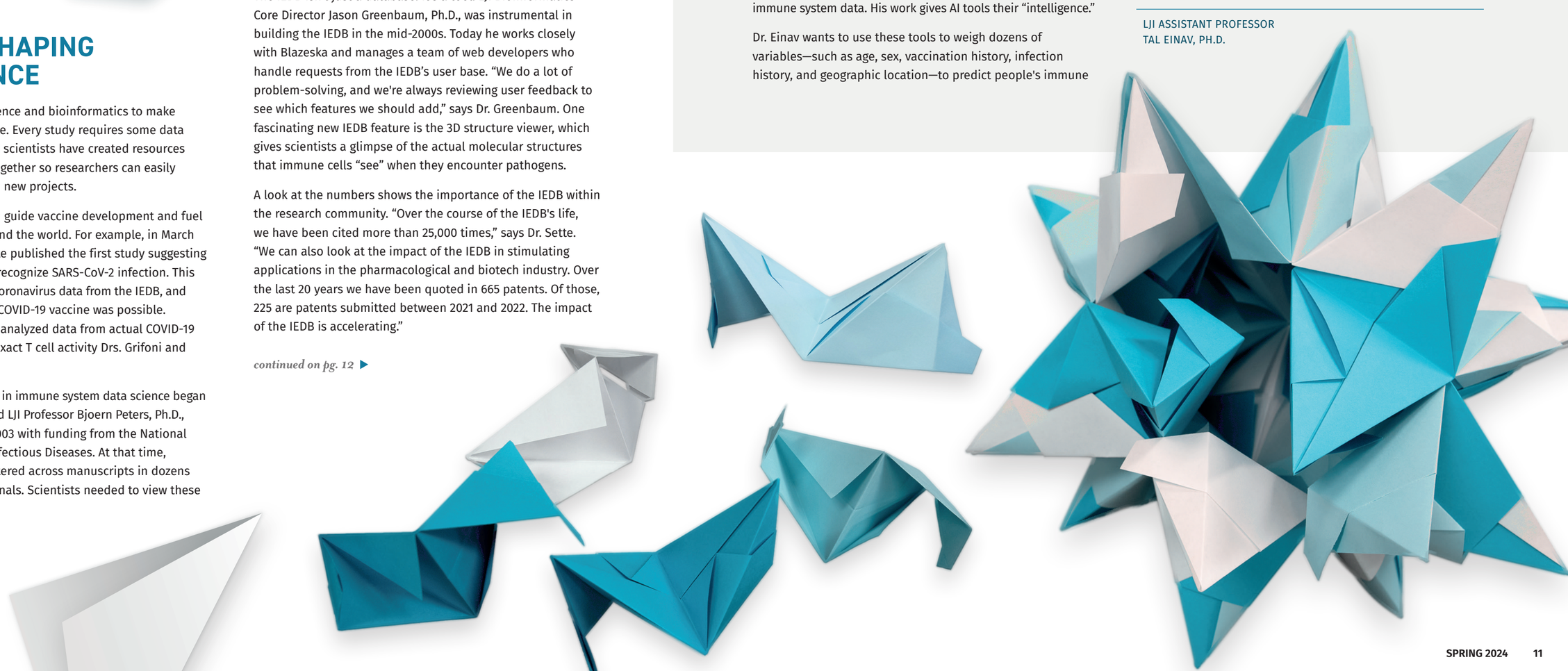
Dr. Einav uses datasets from studies around the world to build computational models and develop new algorithms to analyze immune system data. His work gives AI tools their "intelligence."

Dr. Einav wants to use these tools to weigh dozens of variables—such as age, sex, vaccination history, infection history, and geographic location—to predict people's immune responses to the many types of vaccines we could create. Right now, Dr. Einav's laboratory is especially interested in predicting each individual's response to the influenza vaccine in order to provide personalized vaccine recommendations.

How might a specific influenza vaccine affect a young mom in Minnesota versus an older adult in Sri Lanka? The questions (and the flow of data) seem endless, but Dr. Einav knows the answers are out there.

"Every person is special, and we want to be able to give patients their best medicine interventions," says Dr. Einav.

> "With these tools, we can handle larger and more diverse datasets to make sharper predictions."
>
> LJI ASSISTANT PROFESSOR TAL EINAV, PH.D.



NEW DATABASES UNFOLD

In 2021, the National Cancer Institute granted Drs. Peters and Sette funding to build a similar epitope database to fuel cancer research. This new database is called the Cancer Epitope Database and Analysis Resource (CEDAR). Scientists can use CEDAR to study—and even predict—how T cells and antibodies target different types of cancer cells. Understanding these responses to cancer is a key step in developing cancer immunotherapies that rely on the immune system to kill cancer cells.

“We're giving the cancer community what they're after—a one-stop resource for experimentally-validated cancer epitopes,” says Blazeska.

A DEEP DIVE INTO PATIENT HEALTH

LJI's Database of Immune Cell Epigenomics (DICE) addresses a different critical need: to understand exactly how genetic variations regulate gene expression and drive disease risk.

This database, directed by LJI William K. Bowes Distinguished Professor Pandurangan Vijayanand, M.D., Ph.D., launched in 2014 with funding from the National Institutes of Health. Dr. Vijayanand and his colleagues are on a mission to learn everything they possibly can about immune cells from a unique cohort of donors recruited from the San Diego area.

“We started by collecting and freezing blood cells from 91 donors,” says LJI Research Assistant Professor Benjamin Schmiedel, Ph.D., who worked on DICE with Dr. Vijayanand and LJI Research Assistant Professor and Director of Immunogenomics Gregory Seumois, Ph.D. “Over eight months, we accumulated more than 19,000 vials in our nitrogen tanks. Then, over the years, in multiple batches, we isolated about 30 different kinds of immune cells from each of these donors.”

The DICE team then used high-throughput sequencing tools to look at gene expression in immune cells from each individual donor. This told them what kinds of genes are expressed in different cells and which proteins the cells are making. At last, the researchers could see how different immune cells functioned and spot striking differences in cells from donors with different genetic backgrounds and of different sexes.

Today, scientists around the world can search the DICE dataset to figure out how small genetic variations, called polymorphisms, affect how certain immune cells do their jobs. Researchers have used DICE to investigate gene expression and the function of immune cells connected to Alzheimer's disease, asthma, inflammatory bowel disease, and many other diseases.

In 2021, Dr. Vijayanand, Dr. Schmiedel, and their colleagues turned to DICE to better understand why some people develop more severe cases of COVID-19. Their research revealed polymorphisms that may change how immune cells use important signaling pathways to sense infections and transmit danger signals—which could help explain why some people fail to mount an immune response to control SARS-CoV-2 infection.

“Building DICE was hard work, but now we can easily look at the data to identify interesting genetic associations between immune cell function and disease risk—for any disease of interest,” says Dr. Schmiedel. “And we find new things everywhere we look.”

FROM DATA TO DISCOVERY

As Dr. Grifoni worked to shed light on the Pirola variant, she and Dr. Sette came to an encouraging conclusion. Her bioinformatics approach suggested that T cells could see right through Pirola’s mutations and find their targets. “It appears previous exposure to Omicron—or vaccination with the newer bivalent vaccines—may arm a person with new T cells that can ‘catch up’ and generate responses that can also recognize Pirola or new upcoming variants,” says Dr. Grifoni.

Dr. Grifoni was eager to see if this prediction was supported by data from actual patients. In fact, she and Dr. Sette had established several overseas collaborations with scientists studying whether SARS-CoV-2 infections or vaccinations could prompt T cells to recognize novel SARS-CoV-2 variants.

It didn't take long for real-world data to start coming in. By January 2024, two different research groups (one based in South Africa and one based in Sweden) published strong evidence that T cells induced by previous vaccination and infection could indeed cross-recognize the Pirola variant.

The LJI team had been on the right track. Their prediction, based on a deep understanding of immunology and data science, had been corroborated.

LJI scientists set the standard for how to organize and analyze immune system data, making it possible for researchers such as Dr. Grifoni to ask tough questions about human health. Every day, LJI scientists add valuable findings to these databases—and they continue to take on new projects that strengthen data science and collaboration in immunology.

In 2023, Dr. Peters was named co-director of the Human Immunology Project Consortium (HIPC) Data Coordinating Center. The HIPC project connects experts in immunoprofiling—the effort to capture complex immune system data to better understand a person's disease risk or predict their reaction to a particular drug treatment.

LJI scientists have transformed disparate data points into something revolutionary. Their work powers immunology—and the world is taking note.

Last fall, IEDB users met virtually for their annual workshop. The occasion marked 20 years since the IEDB had launched, and Dr. Sette reflected on how researchers have come to rely on the IEDB. “We read scientific manuscripts and go online to query findings in the IEDB—almost like Googling,” said Dr. Sette. ◆

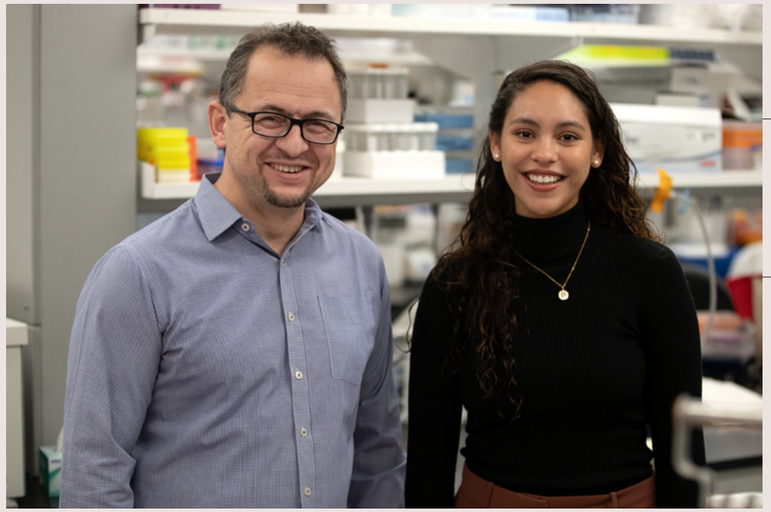
The true story of IKAROS

Art by **Ann Kiernan**, commissioned by the Ay Lab at LJI. You can find Kiernan's work online at **annkiernan.com**

As poet Jack Gilbert wrote,

"Everyone forgets that Icarus also flew."

In the human body, a protein called IKAROS also performs wonders. Scientists at La Jolla Institute for Immunology (LJI) recently co-led a study showing how IKAROS controls B cell development and makes it possible for B cells to produce life-saving antibodies.



LJI ASSOCIATE PROFESSOR FERHAT AY, PH.D., (LEFT) AND UC SAN DIEGO GRADUATE STUDENT & MEMBER OF THE AY LAB DANIELA SALGADO FIGUEROA (RIGHT)

"Without IKAROS, you cannot make a functioning B cell," says LJI Associate Professor Ferhat Ay, Ph.D.

Dr. Ay uses computational approaches to develop 3D maps of the genome. For the new research, Dr. Ay's laboratory partnered with Katia Georgopoulos, Ph.D., of Massachusetts General Hospital at Harvard Medical School. Dr. Georgopoulos led previous studies showing that IKAROS is critical for immune cell development—and her team discovered an association between loss-of-function mutations in IKAROS and a poor prognosis in children and young adults with B cell-precursor leukemias.

The Ay Lab at LJI and the Georgopoulos Lab at Harvard joined forces to figure out why IKAROS is so important. Yeguang Hu, Ph.D., an Instructor in the Georgopoulos Lab, spearheaded the experiments to study IKAROS in a mouse genetic model. Meanwhile, UC San Diego Graduate Student Daniela Salgado Figueroa, a member of the Ay Lab, led the bioinformatics approach to analyze the massive experimental datasets.

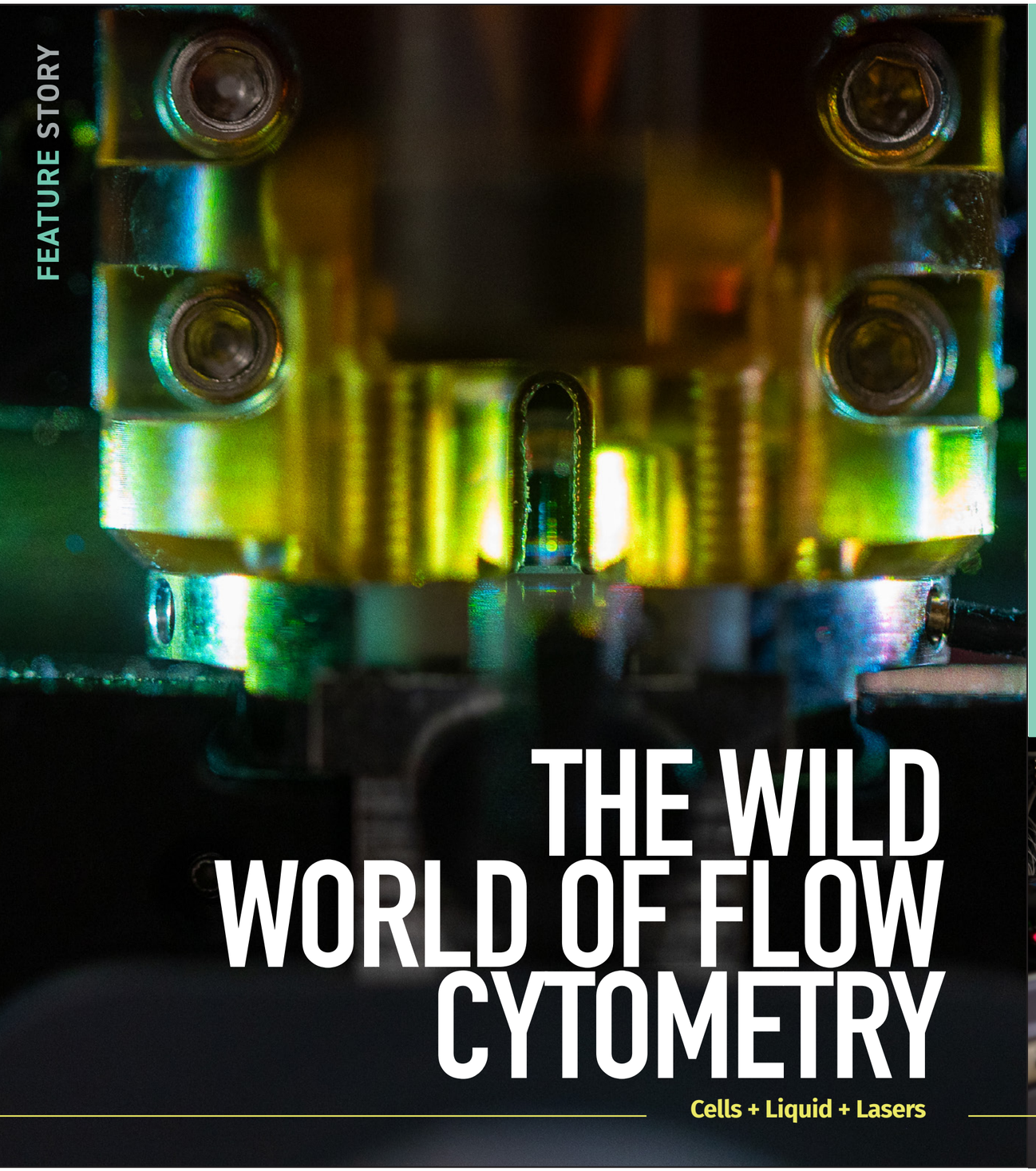
The researchers found that IKAROS helps B cells by directing important genome choreography. To detect pathogens, B cells need to assemble receptor "arms." These arms have a "light chain" region and a "heavy chain" region. Assembling the light chain regions can be tricky because the genes encoding light chain development sit pretty far apart on the DNA.

Fortunately, IKAROS can spur the genome to form loops that bring far-away genes together with their control elements. With those pieces in place, a B cell can express the genes needed for proper light chain assembly and future antibody production.

IKAROS is a talented protein, indeed.

Dr. Ay says this research can help us understand how healthy cells develop—and how an improperly folded genome can cause diseases such as immunodeficiencies and cancers. ◆

IMPORTANT GENES (GREEN DOTS) OFTEN SIT FAR AWAY FROM EACH OTHER IN THE GENOME (BLUE LINES). IKAROS FORCES THE GENOME TO FORM LOOPS, TURNING FAR-AWAY GENES INTO NEIGHBORS.



THE WILD WORLD OF FLOW CYTOMETRY

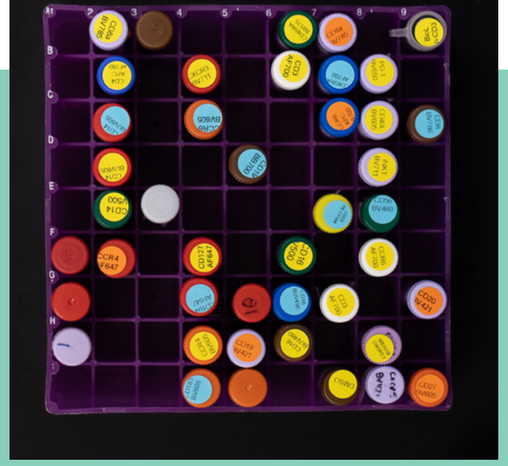
Cells + Liquid + Lasers

No one knows how many types of immune cells are out there. Experts in the Flow Cytometry Core at La Jolla Institute for Immunology (LJI) are on their way to finding out.

"Most textbooks say there are around 80 to 100 immune cell types," says LJI Flow Cytometry Senior Core Director Cheryl Kim. "But scientists use flow cytometry to discover new immune cell types all the time. So there must be hundreds and hundreds."

Flow cytometry is an important technique in immunology because it can reveal exactly which kinds of immune cells jump into action against different diseases. "Cytometry" translates to "measurement of a cell." The "flow" part just means that the process takes place in a stream of fluid.

LJI's Flow Core is one of the best facilities of its kind in California. The Flow Core is home to an impressive range of machines—machines so precise they can detect incredibly rare immune cells. Kim's team can literally separate one cell from a million.



The Flow Core staff starts with a sample—perhaps a vial of blood from a clinical study volunteer or a bit of spleen from a mouse model of disease. They isolate immune cells from the sample by mixing them with some very useful antibodies. These antibodies are tagged with fluorescent dyes, called fluorophores, and they are engineered to seek out and bind to specific immune cells. When the right antibodies recognize proteins on the right immune cell, they bind to that immune cell and light it up.

Flow Core staff use a whole rainbow of fluorophores to tag many different cell types in a single sample. "We work in colors here," says LJI Flow Cytometry Core Scientific Lead, Denise Hinz, Ph.D. "The technology is evolving so quickly, and new dyes are constantly being released."

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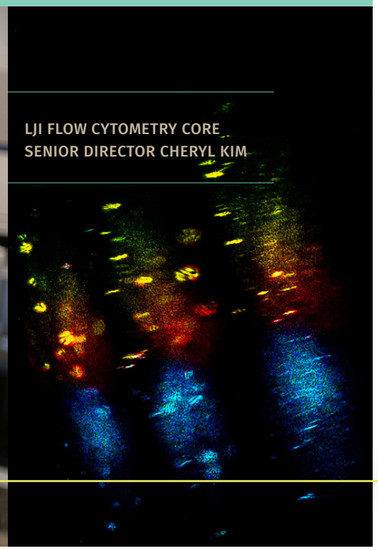


LJI FLOW CYTOMETRY CORE SENIOR DIRECTOR CHERYL KIM

LJI FLOW CYTOMETRY SPECIALIST KIRBY INOCENTE (LEFT) ANALYZES SAMPLES PROVIDED BY LJI POSTDOCTORAL FELLOW FELIX NETTERSHEIM, M.D. (RIGHT)

Lasers are next. The Flow Core staff put the cells into machines called flow cytometers, or "analyzers," where the cells flow along in a saline stream. Each cell passes through lasers of different wavelengths, which "excite" the different fluorophores. On a nearby computer screen, Kim's team can see—in real time—whenever a fluorophore is detected.

> **"You can see it instantaneously. This is a high-throughput technique. We can go through at least 20 million cells an hour, which is huge."**
>
> LJI FLOW CYTOMETRY CORE SENIOR DIRECTOR CHERYL KIM

From these data, scientists can figure out which immune cells are most active in a sample. For example, they could compare immune cell responses between different patient age groups—or between women and men.

Then the cell sorters do their magic. "The sorter component is kind of wild," says Kim. Once the cells pass through the laser, the machine vibrates the stream of liquid and traps cells in individual droplets. The sorter adds an electric charge to each droplet and divides the immune cells by type.

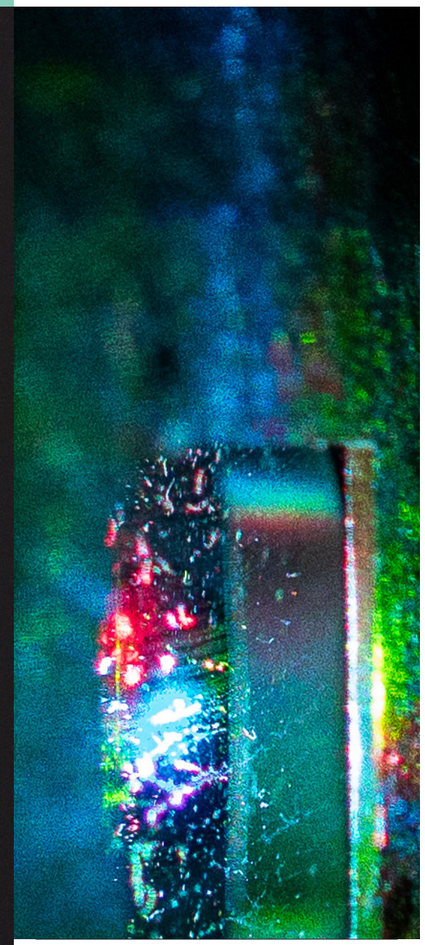
These flow cytometers are astonishingly precise. For a recent investigation into drivers of cardiovascular disease, the Flow Core staff worked with LJI scientists to detect immune cells called ex-T regulatory cells in human samples for the first time ever. The Flow Core's speed also makes a big difference. In early 2020, Flow Core staff worked around the clock to uncover key data showing the importance of T cells in fighting off SARS-CoV-2.

The Flow Core continues to grow thanks to new grants and generous philanthropic support, including large purchases made possible by The Conrad Prebys Foundation and an anonymous foundation. In 2019, LJI purchased an advanced type of cell sorter called the BD FACSymphony S6—the first one ever installed in a U.S. facility, and the fourth ever installed in the world. Philanthropic support allowed the Institute to purchase a second one soon after. And the Flow Core team recently brought in a machine called the Cytek Aurora CS, which has lasers that distinguish between 40 different colors.

In March 2024, the Flow Core earned a rare distinction when it was named a BD Biosciences Center of Excellence.

"We want to be right on the bleeding edge," Kim says. ◆

Learn more:
Scan this QR code to view a behind-the-scenes video of the Flow Core in action!



LJI FLOW CYTOMETRY CORE SENIOR DIRECTOR CHERYL KIM (LEFT) & LJI FLOW CYTOMETRY CORE SCIENTIFIC LEAD DENISE HINZ, PH.D. (RIGHT)

TRAINING THE BEST

La Jolla Institute for Immunology (LJI) has an important responsibility: to train the next generation of world-changing immunologists. Every year, early career Postdoctoral Researchers and Instructors come from around the globe to train under LJI faculty.

These scientists work closely with LJI faculty to lead important immune system studies. Their time at LJI is also a chance to learn new research skills and establish strong collaborations.

Many of LJI's Postdoctoral Researchers and Instructors go on to start their own academic laboratories or to direct cutting-edge research in the pharmaceutical industry. Here are the stories of four scientists who launched their careers at LJI.

"To be able to learn from him—on one of the world's best microscopes—was a game-changer for my career."

MICHAEL NORRIS, PH.D.

Michael Norris, Ph.D.

Assistant Professor at the University of Toronto

In 2017, Michael Norris, Ph.D., and his husband packed their lives—and their 70-pound Husky—into a small Toyota Yaris. They headed to Interstate 80 and began the long drive from Toronto, Canada, to La Jolla, California.

Dr. Norris had just been hired to complete his postdoctoral training under then-Professor Erica Ollmann Saphire, Ph.D., MBA. "I had to uproot my entire life," says Dr. Norris. "It was a really big change, but Erica was very welcoming, and she created almost a family environment in her lab."

As a member of the Saphire Lab, Dr. Norris led research into paramyxoviruses, a viral family which includes measles and the deadly Nipah virus. To better understand these viruses, Dr. Norris worked closely with LJI Cryo-Electron Microscopy Core Director Ruben Diaz Avalos, Ph.D., who trained him to use an advanced, donor-funded cryo-electron microscope called the Titan Krios.

Meanwhile, Dr. Saphire emphasized scientific communication and collaboration. Dr. Norris watched as the Saphire Lab became the hub of the international Coronavirus Immunotherapy Consortium. "Erica brought in perspectives from different areas and different people," says Dr. Norris.

In 2021, Dr. Norris won $30,000 in funding from the Tullie Family Foundation through LJI's Tullie and Rickey Families SPARK Awards for Innovations in Immunology to identify potential drug candidates to treat measles and Nipah virus infections.

> By 2022, Dr. Norris had published key findings on how paramyxoviruses replicate and spread throughout the body. His findings may prove important as scientists design new therapies to block these viruses.

Dr. Norris soon began looking for job opportunities where he could apply his new skills. Today, Dr. Norris serves as an Assistant Professor at the University of Toronto—he's happy to be back in his hometown—and he is a member of the University's Emerging & Pandemic Infections Consortium. Dr. Norris continues to collaborate with Dr. Saphire, who now serves as LJI Professor, President & CEO.

Dr. Norris says his time at LJI taught him the importance of establishing strong collaborations. "If you really want to make groundbreaking, world-changing discoveries, you do it as part of a massive multidisciplinary team," he says.

"Coming to LJI was the best decision I ever made. The level of science is so high, and Shane was a tremendous mentor."

CAMILA COELHO, PH.D., MBA

Camila Coelho, Ph.D., MBA

Assistant Professor at the Icahn School of Medicine at Mount Sinai

Camila Coelho, Ph.D., MBA, came to LJI with a clear goal: to someday run her own lab. Dr. Coelho had just completed a postdoctoral position studying B cell responses to malaria vaccines at the National Institutes of Health, but she still had a lot to learn.

"I knew that if I were to become a PI [Principal Investigator] it would be very important for me to have an extramural experience with people doing important science, relevant science, and to learn how to acquire my own funding," says Dr. Coelho.

Dr. Coelho had come to the right place. She joined the laboratory of LJI Chief Scientific Officer Shane Crotty, Ph.D., in the summer of 2021—a time when the entire world was focused on COVID-19 vaccine research.

As a new LJI Instructor, Dr. Coelho helped spearhead this cutting-edge vaccine research. Dr. Coelho's accomplishments included co-authoring the first-ever head-to-head comparison of four COVID-19 vaccines, published by ***Cell*** in May 2022.

At the same time, she learned important lessons from Dr. Crotty about how to manage a lab and motivate young scientists. "With his support, I was able to publish four high-impact studies as first author," Dr. Coelho says. "He also helped me get grant funding and get feedback from other LJI faculty as I was preparing to apply for my PI position."

> In late 2022, Dr. Coelho became an Assistant Professor and PI in the Icahn School of Medicine at Mount Sinai. As a PI, she leads her own research team and has acquired funding to investigate B cell responses to mpox and novel COVID-19 vaccine boosters.

Dr. Coelho continues to collaborate with LJI scientists, and she recently authored a ***Lancet Infectious Diseases*** article with LJI Research Assistant Professor Alba Grifoni, Ph.D., and LJI Professor Alessandro Sette, Dr.Biol.Sci.

continued ▶

Stephane Becart, Ph.D.

Scientific Director of Prometheus Biosciences

Stephane Becart, Ph.D., grew up with an unusual family tradition. His father, grandfather, and great-grandfather had all been gastroenterologists. “So science has always been really in our blood, in a way,” he says.

But when it came time for university, Dr. Becart bucked the gastroenterology tradition to study immunology. “I was really intrigued by how different cells interact to defend us from disease,” he says. He went on to earn his Ph.D. in Immunology from France's National Institute of Health and Medical Research (Inserm).

In 2004, Dr. Becart came to LJI to work as a Postdoctoral Researcher in the laboratory of LJI Professor (now Professor Emeritus) Amnon Altman, Ph.D. There, Dr. Becart helped lead research into a molecule called SWAP-70-like adapter of T cells (SLAT). He studied the role of SLAT in immune cells in mice, and he showed that SLAT is important for T cell function and has therapeutic potential to treat autoimmune diseases and fight infection.

Dr. Becart stayed at LJI for nine years, where he was promoted to LJI Instructor. He says the research environment was incredibly motivating.

> **“There was not one PI who wasn't at the top of their scientific field. And I could collaborate with them and publish with them.”**
>
> STEPHANE BECART, PH.D.

Dr. Becart began looking for ways to help patients more directly. “I wanted to be a little closer to human healthcare,” he says. In 2013, Dr. Becart became a Project Leader for the Janssen Pharmaceutical Companies of Johnson & Johnson. The company hired Dr. Becart to study key proteins he knew well from his research at LJI—and see if they could serve as drug targets to treat certain autoimmune diseases.

> In 2021, Dr. Becart left Johnson & Johnson to serve as Scientific Director for a San Diego-based biotech company called Prometheus Biosciences, which initially focused on precision medicine for inflammatory bowel syndrome. With his family's background in gastroenterology, perhaps this was “meant to be,” Dr. Becart says.

Prometheus Biosciences was acquired by Merck in 2023. This development may help Dr. Becart's work move closer to clinical testing. “When you work in pharma, these companies can scale up what you are doing,” he says.

Dr. Becart sees academia and industry as complementary, with academic researchers leading in-depth investigations and industry scientists focused on applying findings to help patients. “Healthcare systems need researchers in both areas,” he says. “Both sides are valuable, fulfilling, impactful, and fun.”

Rosa Isela Gálvez, Ph.D.

Postdoctoral Researcher at the Bernhard Nocht Institute for Tropical Medicine

Rosa Isela Gálvez, Ph.D., always loved insects. In college, she fell in love with medical entomology. Still, she wasn't sure how to turn that passion into a career. “My ex-husband was also making fun of it—he said, ‘You're going to be the master of mosquitoes,’” says Dr. Gálvez.

It turns out the world needs masters of mosquitoes. Dr. Gálvez grew up in Peru and moved to Germany as a teenager. She had seen how mosquito-borne diseases, such as dengue fever and Zika fever, affect people. Thanks to climate change, disease-carrying mosquitoes are moving farther and farther away from their habitats near the equator. “These pathogens are not just in the tropics anymore,” says Dr. Gálvez.

After working at a German biotech company, Dr. Gálvez studied immunology at Hamburg's Bernhard Nocht Institute for Tropical Medicine. By 2021, Dr. Gálvez had earned her Ph.D. and had started applying for postdoctoral positions. She was excited when LJI Professor Alessandro Sette, Dr.Biol.Sci., offered her a Postdoctoral Fellow position in his laboratory. “This is a very famous place,” says Dr. Gálvez.

> **“Where I grew up, you are primed to believe you have a task in life—that we're each given a responsibility. I can't fix the world, but it's my responsibility to do something of value.”**
>
> ROSA ISELA GÁLVEZ, PH.D.

As a member of the Sette Lab, Dr. Gálvez learned to develop “epitope megapools” to study how the body's T cells target different types of infection. In 2023, Dr. Gálvez won $25,000 in Tullie and Rickey Families SPARK Awards funding to use these epitope megapools to investigate T cell activity during malaria and dengue virus infections. In collaboration with the Bernhard Nocht Institute, Dr. Gálvez studied samples from a cohort of Ghanaian children and found that children who survived childhood malaria infections had less severe dengue virus infections, likely due to a shift in T cell function. Dr. Gálvez hopes these findings can guide the development of new dengue vaccines or treatments.

Along the way, Dr. Gálvez formed a strong partnership with LJI Research Assistant Professor Daniela Weiskopf, Ph.D., a former Tullie and Rickey Families SPARK Award winner herself. Dr. Gálvez credits Dr. Weiskopf's mentorship for preparing—and inspiring—her to lead her own lab one day.

> In November 2023, Dr. Gálvez left LJI for a Postdoctoral Researcher position back at the Bernhard Nocht Institute. In a few years, she'll be qualified to work as a full Professor in Germany.

Right now, Dr. Gálvez is working with an international team to study immune cell activation during pregnancy. “We want to understand what happens when women are exposed to infectious diseases, mainly malaria, during pregnancy, and how that affects the immunity of their children in utero,” says Dr. Gálvez. ◆

A legacy of groundbreaking allergy research

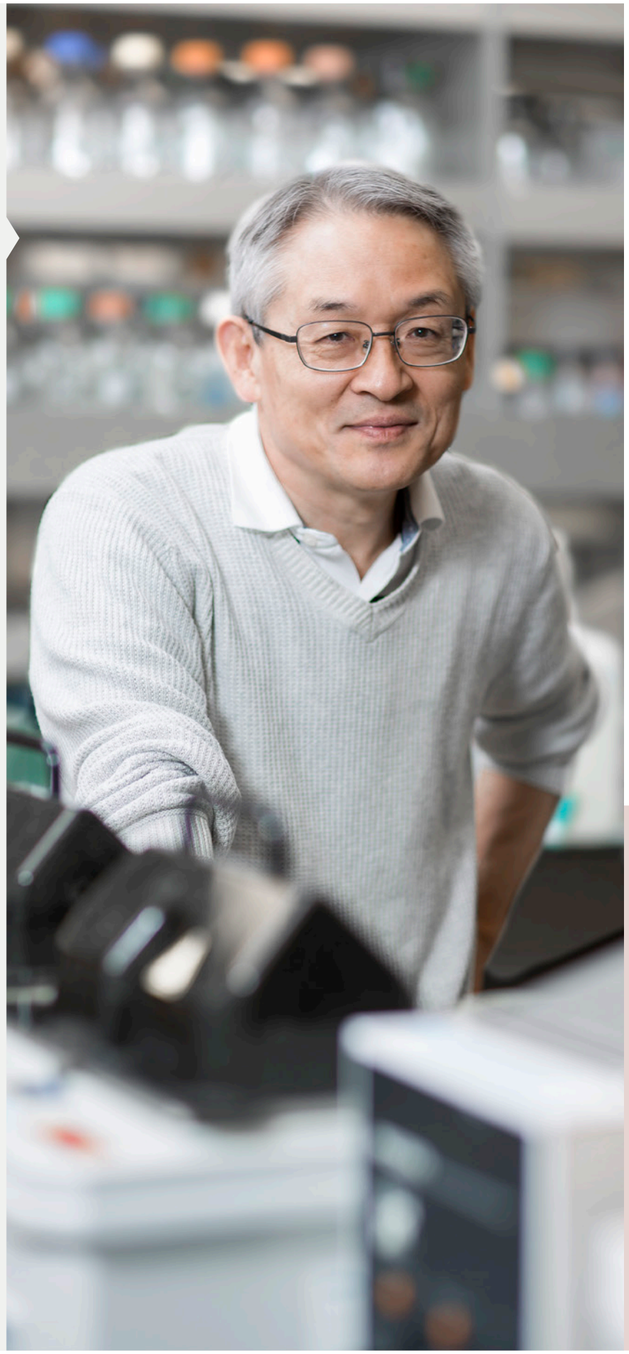
LJI Professor Emeritus Toshiaki Kawakami, M.D., Ph.D., uncovered the molecular underpinnings of allergies, tumor suppression, and more.

Pioneering immunologist Toshiaki Kawakami, M.D., Ph.D., has retired and is now a La Jolla Institute for Immunology (LJI) Professor Emeritus. Dr. Kawakami joined LJI in 1990, where he led critical research into immune cell activation and the roles of signaling molecules in allergic responses and tumor suppression.

Much of Dr. Kawakami's research focused on a process called FcεRI signaling—a crucial step in activating immune cells called eosinophils and mast cells. By investigating FcεRI signaling, Dr. Kawakami and his colleagues revealed new opportunities to treat allergic diseases such as atopic dermatitis and asthma.

One of his key discoveries was the role of a protein called Btk in triggering allergic responses. Dr. Kawakami and his colleagues went on to show that Btk inhibitors can block allergic reactions in mouse models of asthma and food allergies. “Our basic research now has led to the use of a Btk inhibitor in human trials,” says Dr. Kawakami.

Dr. Kawakami shares credit for these findings with his research partner and wife, LJI Staff Scientist Yuko Kawakami, M.D., Ph.D. “We found each other in the same classroom at the University of Tokyo, and it's been wonderful,” says Dr. Toshiaki Kawakami. The couple now plans to travel in retirement and focus on exploring the sights—and local sushi varieties—of Japan.



Dr. Erica Ollmann Saphire receives Pantheon Award

California Life Sciences, the state’s life sciences trade association, has awarded LJI Professor, President & CEO Erica Ollmann Saphire, Ph.D., MBA, the 2023 Pantheon Academia, Non-Profit, & Research Award. The award recognizes Dr. Saphire’s leadership and innovative research toward addressing the urgent need for effective antibody therapeutics for viral threats such as SARS-CoV-2, Ebola virus, and Lassa virus.

In her Pantheon Award acceptance speech, Dr. Saphire lauded the hard work and innovative thinking that put many LJI laboratories at the forefront of SARS-CoV-2 research.

“I am immensely proud of what we were able to accomplish by coming together and getting to work for the greater public good during a time of need.”

LJI PROFESSOR, PRESIDENT & CEO
ERICA OLLMANN SAPHIRE, PH.D., MBA

In the community: Suzie Alarcón honored by Girl Scouts San Diego

LJI Next Generation Sequencing Core Director Suzie Alarcón was named a 2024 Cool Women honoree by Girl Scouts San Diego. This award, given to five San Diego women each year, recognizes Alarcón's leadership in the field of genetic sequencing and immune system research. The award also celebrates Alarcón's dedication to diversity, equity, and inclusion (DEI) programs at LJI and in the community—as well as Alarcón's role as a Girl Scout Troop Leader.

OCT 4, 2023

Life Without Disease Event Series

La Jolla Institute for Immunology (LJI) welcomed visitors to the Institute for a special "Life Without Disease" presentation, delivered by new LJI Assistant Professor Tal Einav, Ph.D., on Oct. 4, 2023. Dr. Einav shared how his laboratory harnesses computational biology and physics to study the ways the body fights disease. The presentation was followed by a Q&A with Dr. Einav and a reception for LJI guests and scientists.

FEATURED SPEAKER TAL EINAV

GUESTS GATHER TO HEAR FROM 2020 AND 2024 SPARK AWARD WINNER THOMAS RIFFELMACHER (FAR RIGHT)

AARON DYER & PADMA NANDURI

DEC 14, 2023

Donor Holiday Luncheon

LJI welcomed Bonsai Legacy Society and Vanguard Giving Society members to a special holiday luncheon on Dec. 14, 2023. LJI Professor, President & CEO Erica Ollmann Saphire, Ph.D., MBA, shared the extraordinary progress achieved by LJI researchers over the past year and provided glimpses into her vision for the Institute for 2024 and beyond.

JOHN & SUE MAJOR

ERICA OLLMANN SAPHIRE, SYLVIA LIWERANT, & BETH SIRULL

ERICA OLLMANN SAPHIRE MAKES REMARKS

JAN 30, 2024

Tremblay-Jacobs Symposium

Leading immunologists shared their recent findings on the causes of and treatment options for autoimmune diseases at the Jan. 30 Tremblay-Jacobs Symposium on Human Autoimmunity: Novel Approaches at LJI. Attendees learned from a series of fascinating scientific talks and gathered for an evening panel discussion and reception.

PAUL JACOBS & GENEVIÈVE TREMBLAY JACOBS

PAIGE & ROBERT VANOSKY

ROSSEN & YULIYA VALKANOV

ERICA OLLMANN SAPHIRE (FAR RIGHT) MODERATES THE TREMBLAY-JACOBS SYMPOSIUM PANEL

LEFT TO RIGHT: BINGFEI YU, MAUREEN SU, MITCHELL KRONENBERG, MONTSERRAT ANGUERA, MARIA-LUISA ALEGRE, SHANE CROTTY, GENEVIÈVE TREMBLAY JACOBS, ERICA OLLMANN SAPHIRE, ANNE DAVIDSON, MICHAEL CROFT, SONIA SHARMA, & HILDE CHEROUTRE

The Arvin Gottlieb Charitable Foundation makes breakthroughs possible

ARVIN GOTTLIEB CHARITABLE FOUNDATION TRUSTEE BARTON COHEN, MBA

When Missouri business leader Arvin Gottlieb passed away, he left generous funding—and a group of dedicated friends—to support causes close to his heart.

"Arvin and I were very close friends," says Barton Cohen, MBA, a trustee of the Arvin Gottlieb Charitable Foundation. "We had a serendipitous meeting in the early 1980s and became tight friends, and eventually even became business partners."

Sadly, Gottlieb suffered from a congenital heart condition that necessitated a heart transplant. Gottlieb's body rejected the first transplant, and then a second transplant. As he got sicker, Gottlieb made his wishes clear: He wanted his financial success to benefit the arts, the sciences, and health and human services efforts for years to come. He passed away in 1992, but his legacy lives on through the generosity of the Arvin Gottlieb Charitable Foundation.

Cohen and his fellow trustees have grown the foundation through prudent investment, and they've worked to identify important philanthropic causes. Their projects include funding the construction of the world-class Arvin Gottlieb Planetarium in Kansas City, Missouri, and establishing the Arvin Gottlieb Endowed Chair for Advanced Heart Failure and Cardiac Transplant at Saint Luke's Mid America Heart Institute.

The Arvin Gottlieb Charitable Foundation first began supporting La Jolla Institute for Immunology (LJI) with donations toward heart disease research at the Institute. In 2020, Cohen, a former LJI Board Member, learned of LJI scientists working around the clock to study COVID-19 and the body's response to SARS-CoV-2. To accelerate this research, the scientists needed a laboratory with special safeguards against viral contamination—they needed a Biosafety Level 3 (BSL-3) laboratory. The Arvin Gottlieb Charitable Foundation wanted to give it to them.

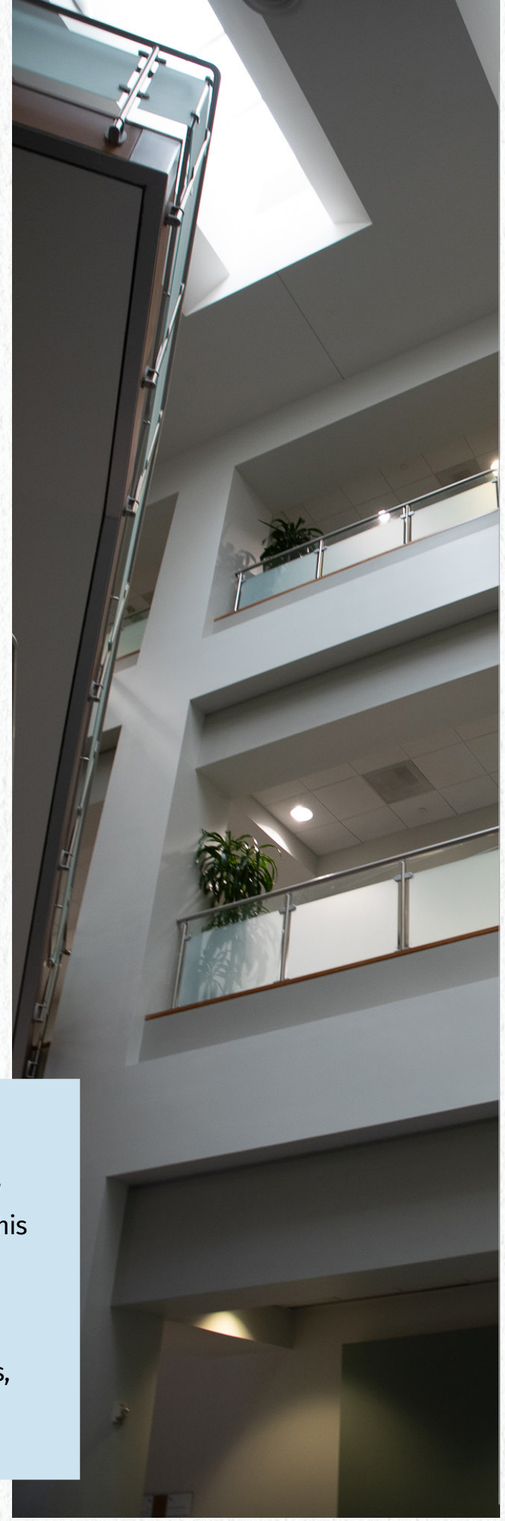
> **"We understood that LJI scientists were working on the outer frontier of immunology, in a very good sense."**
>
> ARVIN GOTTLIEB CHARITABLE FOUNDATION TRUSTEE BARTON COHEN, MBA

With philanthropic support from the Arvin Gottlieb Charitable Foundation, the GHR Foundation, the London Stock Exchange Foundation, and individual donors, LJI opened the Infectious Disease Exploration and Abatement (IDEA) Facility just one year later. This BSL-3 facility has already proven incredibly valuable for LJI scientists.

In January 2024, Cohen visited the Institute and toured the BSL-3 facility while it was closed for its annual recertification. While there, he met with researchers who rely on the facility. The researchers had some news for Cohen—they were about to publish an exciting T cell discovery. They had uncovered the first direct evidence that T cells that fight common-cold coronaviruses can "cross-react" to the closely related SARS-CoV-2 virus. This research is an encouraging step toward devising a "pan-coronavirus" vaccine that trains T cells to protect the body from many kinds of coronaviruses.

Cohen calls the development "heartwarming." He says the Arvin Gottlieb Charitable Foundation continues to support LJI because of the unique projects led by scientists who use the BSL-3. "Important research is being done in that facility," says Cohen. "We feel like—from a foundation standpoint—that we're making a significant contribution to science."

The Arvin Gottlieb Charitable Foundation has doubled down on its support, providing a new multiyear grant to support the operations of this critical facility for the next several years. The BSL-3 will support investigations into a variety of contagious zoonotic pathogens, including chikungunya virus, Japanese encephalitis virus, and Powassan virus. ◆



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 substantial contributions to the field of immunology research and his leadership at 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. Bonsai symbolize wealth and abundance, harmony, and balance.

LJI's Bonsai Society is named in honor of this evergreen gift. The Dixon family's vision for LJI is represented by the generous act of leaving a legacy gift.

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

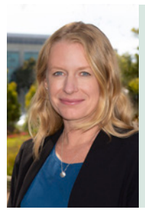
Planned gifts in any amount are deeply appreciated and qualify for membership in LJI's Bonsai Legacy Society.

Bonsai Legacy Society members enjoy a variety of benefits, including:

- Invitation to annual exclusive events for Vanguard Giving Society and Bonsai Legacy Society members
- Invitations to 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
Estate of Kim Ash*
B. Jack and Dorie DeFranco
Frank J.* and Marion* Dixon
Barbara Donnell
Glennie Ginder*
James B. Isaacs, Jr.
Jaime *z"l** and Sylvia Liwerant
John and Susan Major
Judith L. Bradley and David L. Mitchell
Eleanor Mosca
Joani Nelson*
The Roberto Family Trust*
Paulette Roberts
Shelley Rowland*
The Sandor Shapery Testamentary Trust
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, MBA, CSPG
Advancement Officer
(858) 752-6872 | clare@lji.org

La Jolla Institute | BONSAI LEGACY SOCIETY

Learn more:
Scan this QR code for more information about planned gifts or visit **lji.org/plannedgiving**

SPARK | THE TULLIE AND RICKEY FAMILIES SPARK AWARDS FOR INNOVATIONS IN IMMUNOLOGY

Support the next breakthrough in immunology!

A meaningful investment

The Tullie and Rickey Families SPARK Awards for Innovations in Immunology program at La Jolla Institute for Immunology is a sophisticated philanthropic investment. Since launching in 2017, this program has provided $25,000 in flexible start-up funding to LJI's early career investigators to act on their promising projects for bold new approaches to diagnoses, treatments, and possibly even cures for diseases that afflict us today. It has filled the gap between scientists' imagination and that first solid set of data that has allowed them to attract additional funding to further their research and ultimately make life-saving discoveries.

A program impact snapshot

$11M+
Received in follow-on funding

11
SPARK winners have started independent labs

20
SPARK winners have advanced their careers with a promotion or new position

*Based on 39 completed SPARK projects, fully funded between 2018 and 2023

A path to discovery

Through the recognition and cultivation of talented researchers, the Tullie and Rickey Families SPARK Awards have fostered a collaborative environment that encourages bold experimentation and facilitates the development of novel therapeutic approaches. As a result, the program has advanced scientific knowledge and paved the way for significant medical advancements. The enduring legacy of the SPARK program underscores the invaluable role of philanthropy in driving scientific progress and improving global health outcomes.

Read more:
Scan this QR code to learn more about the Tullie and Rickey Families SPARK Awards and the 2024 SPARK Winners or visit **lji.org./spark**

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