

LA JOLLA INSTITUTE FOR ALLERGY AND IMMUNOLOGY

Immune

FALL 2016

MATTERS

Chronic Inflammation

Unraveling its mysteries

PAGE 4

Zika's Global Reach

Understanding the virus' impact

PAGE 12

Donor Honor Roll 2016

PAGE 19

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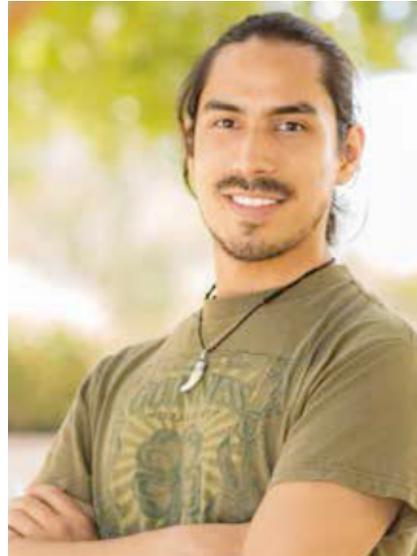
FALL 2016



4 ON THE COVER

Chronic Infl

Unraveling its mysteries



12 Zika's Global Reach

Understanding the virus' impact

14 Q&A

with Hilde Cheroutre

17 Up & Coming

Edahi Gonzalez-Avalos

18 Board of Directors

San Diego investor Tom Tullie joins LJI Board of Directors

19 Philanthropy

Donor Honor Roll 2016

23 New Team Members

IMMUNE MATTERS CONTRIBUTORS

Nick Abadilla
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ON THE COVER

DNA sequence of sickle cell gene superimposed onto the interior of a blood vessel.

Letter from the President

In 2007, La Jolla Institute created the Division of Inflammation Biology to study an area of immunology we believed was having an increasingly critical—and frequently debilitating—impact on human health. Specifically, we wanted to mount a major effort against chronic inflammation, the often out-of-control process that fuels some of our most serious diseases.

After recruiting a group of talented scientists from the University of Virginia to launch the effort, we steadily built the division into the potent research force that it is today, one that complements and supports all of the other aspects of immune system research we pursue at the Institute.

Looking back nearly a decade later, we can report that creating the division was one of the most important decisions we've made in the nearly 30-year history of the Institute. The wide-ranging research that is now emerging regularly from the labs of our principal investigators is nothing short of remarkable, with the potential for a vaccine against heart disease being just one exciting example. Our cover story in this issue of *Immune Matters* highlights that study as well as the work of several other dedicated outstanding researchers whose groundbreaking advances in the battle against chronic inflammation, both in and out of the division, have the real potential to transform human health.

In our Q&A section, you'll meet Dr. Hilde Cheroutre, Head of our Division of Developmental Immunology, who is breaking new ground in her study of the development, function, and regulation of T lymphocytes, a type of white blood cell. Dr. Cheroutre is one of the most innovative scientists in the country, and I'm not just saying that because we recently celebrated our 30th wedding anniversary. A few years ago Dr. Cheroutre received the prestigious NIH Director's Pioneer Award from Francis Collins himself, funding designed to support "individual scientists of exceptional creativity who propose pioneering and transforming approaches to major challenges in biomedical research."

You'll also read about an outstanding young scientist from Mexico in our "Up and Coming" series. Edahi Gonzalez-Avalos, a graduate student in Dr. Anjana Rao's lab, comes to us from the Genomic Sciences Program at the National Autonomous



University of Mexico, one of the world's most selective and demanding undergraduate programs. Edahi's expertise is in bioinformatics and computational biology, and we look forward to his contribution in this emerging field that is revolutionizing immunology.

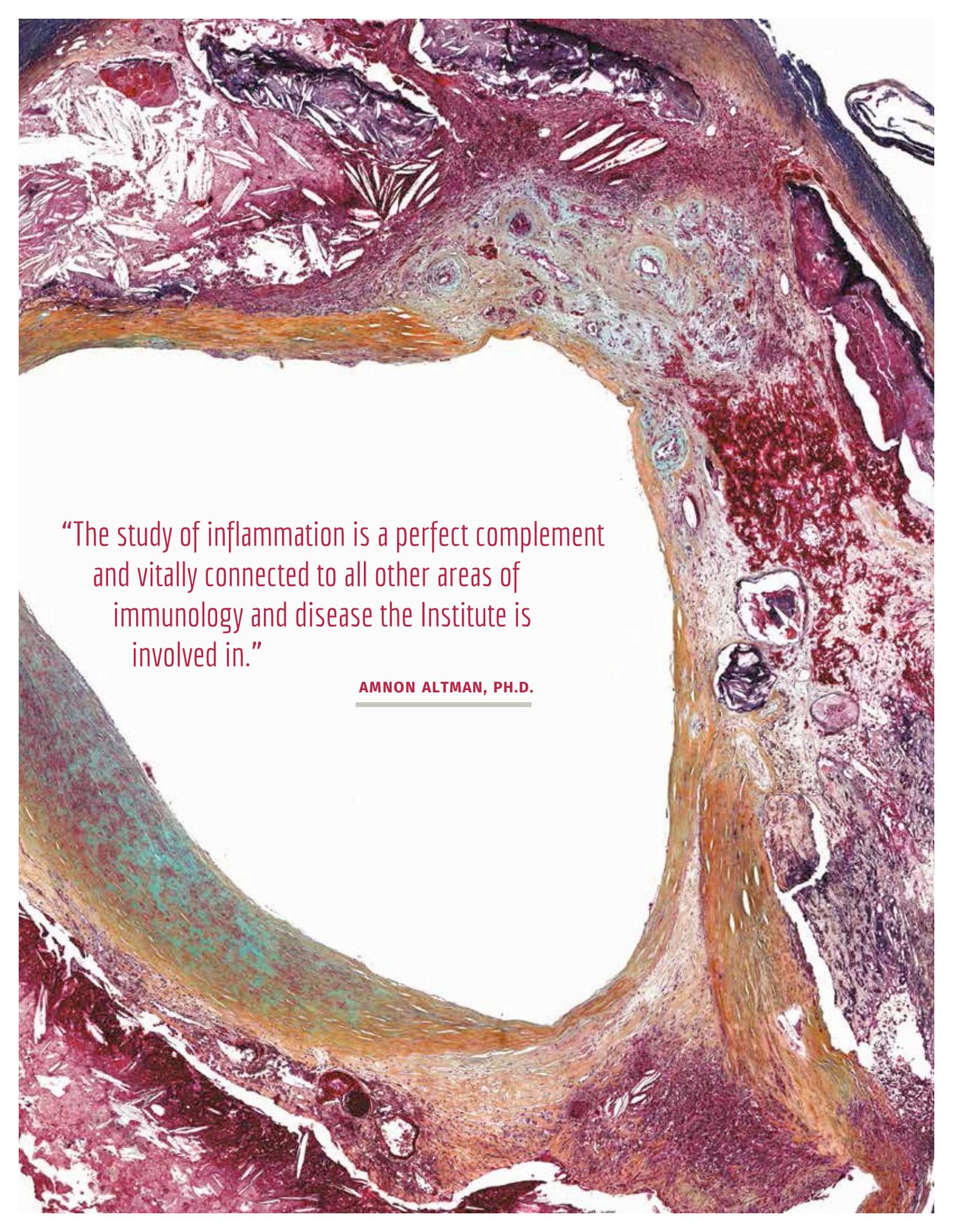
Finally, we welcome the newest member of our Board of Directors: Tom Tullie, a Del Mar resident who is Executive Chairman of Everyone Counts, Inc., the world's leading provider of cutting edge software for election administration and voting systems. Tom's family has faced challenges with autoimmune and chronic inflammatory diseases and that has ignited a desire within him to assist the Institute with his many capabilities, including his deep experience both in technology and investment sectors.

La Jolla Institute is truly honored to be associated with people like Tom and all of our amazing partners—including individual donors, foundations, and federal funding sources—all joining forces to support the critical research we know one day will lead us closer to *Life Without Disease*®.

Sincerely,

A handwritten signature in dark ink that reads "Mitchell Kronenberg". The signature is written in a cursive, flowing style.

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

A histological section of tissue, likely from a joint, showing significant inflammation. The tissue is stained with hematoxylin and eosin (H&E). The image displays a dense infiltrate of inflammatory cells, including neutrophils and mononuclear cells, within the synovial lining and surrounding connective tissue. There is also evidence of fibrin deposition and some cartilage damage. The overall appearance is consistent with a chronic inflammatory process.

“The study of inflammation is a perfect complement and vitally connected to all other areas of immunology and disease the Institute is involved in.”

AMNON ALTMAN, PH.D.

CHRONIC INFLAMMATION

La Jolla Institute's chronic inflammation research creates pathways to understanding and treating debilitating diseases.

Calor, dolor, rubor, and tumor . . . those were the words 1st Century A.D. Roman scholar Celsus used to describe the classical signs of inflammation: heat, pain, redness, and swelling. Remarkably, it would take more than two thousand years for science to recognize that this process was only a small part of a much greater medical story.

For deep inside the molecular functioning of virtually everyone's body, is a different and insidious process wreaking havoc. Silently at first, and almost always unnoticed, it ravages cells and tissues leading to debilitating and sometimes lethal consequences. No, it's not cancer or heart disease, but it fuels both of these leading killers—and tragically, a host of other serious diseases—that plague humanity.

The villain is chronic inflammation. Within the immune system, chronic inflammation is the evil Cain to its good brother Abel, acute inflammation. As described by Celsus, acute inflammation acts early and quickly to effectively attack and eliminate infections (a cold or the flu) and heal injuries (a sprained ankle or splinter), then subsides when its job is done. However, when inflammation continues to simmer and becomes chronic, it contributes to a wide range of diseases: type 2 diabetes, obesity, multiple sclerosis, asthma, rheumatoid arthritis, inflammatory bowel disease, and even neurodegenerative diseases such as Alzheimer's and Parkinson's disease.

The full extent of chronic inflammation's destructive effect has only been recognized for about the last two decades. Even though it has now entered public awareness as a major health risk, progress has been slow in understanding its mechanisms, let alone figuring out how to address it.



Inflammation causes the build-up of plaques in blood vessels. Image: Andreas Schober, Ph.D., University of Munich, Germany

“Our vaccine teaches the immune system to tolerate certain molecules in our own bodies that it mistakenly attacks, which leads to inflammation.”

KLAUS LEY, M.D.

Thanks to the groundbreaking research of scientists at La Jolla Institute that’s all changing. These pioneering researchers have been probing chronic inflammation’s inner workings for nearly a decade since the Institute’s board and scientific leaders had the foresight to recruit several top researchers in the field to create a separate Division of Inflammation Biology (see President’s letter, page 3).

“That investment is now paying significant scientific dividends, including a number of discoveries here at the Institute that have the potential to transform treatment of chronic inflammation and, in some cases, restore health to those who suffer from it,” says Amnon Altman, Ph.D., Institute Director of Scientific Affairs, and Head of the Division of Cellular Biology.

“The study of inflammation is a perfect complement and vitally connected to all areas of immunology and disease the Institute is involved in,” Dr. Altman adds. “So we’re especially thrilled about several specific breakthroughs we’ve made recently that we believe will lead to significant advances in the fight against heart disease, cancer, and sickle cell disease.”

One of those discoveries is due to the groundbreaking work of Institute Principal Investigator Klaus Ley, M.D., Professor and Head of the Division of Inflammation Biology. Dr. Ley was a nationally recognized pioneer in vascular biology at the University of Virginia when he was recruited to start the inflammation division in 2007. He is responsible for one of the most exciting of these breakthroughs: a potential vaccine against atherosclerosis, the primary cause of heart attacks and strokes.

It has been known for decades that excess cholesterol is a major factor in the development of artery-clogging plaques. Only recently investigators have realized that it is actually the inflammation that emerges at sites of vessel tissue damage that helps catalyze the first build up of arterial plaques. This suggests that reducing chronic inflammation might be equally effective at reducing atherosclerosis as dietary or pharmaceutical interventions, such as statins.

Dr. Ley’s belief that an atherosclerosis vaccine might work is due in part to his groundbreaking research

Dennis Jolly, M.D. and Klaus Ley, M.D.





Atherosclerotic plaques in a mouse carotid artery.

published in 2012 in the *Journal of Clinical Investigation*. The study revealed that a specific type of immune cell (CD4 T cells) orchestrates the inflammatory assault on the artery wall by recognizing one of our own proteins as being foreign, like a virus or bacteria, and mounting an inadvertent self-attack.

With that knowledge, Dr. Ley developed a vaccine to target and interrupt those inflammatory factors to reduce atherosclerotic plaque formation. In mouse models of the disease, Dr. Ley's theory has proved remarkably successful. Animals inoculated with the vaccine developed up to 50 percent less plaque in their arteries. Working in collaboration with Alessandro Sette, Dr. Biol.Sc., Professor and Head of the Institute's Center

for Infectious Disease, Dr. Ley has now identified several peptides suitable for vaccinating humans and he will test those in mice engineered to harbor a humanized immune system. Human clinical trials could begin within a couple of years.

"Instead of a vaccine that teaches your immune system to launch an attack if it encounters bacteria or virus, our vaccine works more like the desensitization process used in allergy shots to instruct the immune system to tolerate certain allergens," Dr. Ley says. "Our vaccine teaches the immune system to tolerate certain molecules in our own bodies that it mistakenly attacks, which leads to inflammation."

Dr. Ley's research has drawn praise from a number of luminaries in the medical and scientific world, including Stanley Hazen, M.D., Ph.D., Section Head of Preventive Cardiology at the Cleveland Clinic, who called the research "elegant and tremendously exciting," and "truly, a remarkably important advance."

Dr. Ley appreciates the accolades but cautions there is more research and hard work ahead before the vaccine ever reaches the clinic.

"We're always cautious in extrapolating from animal models to humans, but we are extremely optimistic we're on the threshold of developing a powerful new medical tool we believe one day soon will extend and save lives by delaying or preventing the onset of chronic inflammation that underlies the development of atherosclerosis."



Left to right: Dalia Gaddis, Ph.D., Thomas Graham, Ph.D., Catherine “Lynn” Hedrick, Ph.D.

Another Institute scientist conducting breakthrough research on chronic inflammation is Catherine “Lynn” Hedrick, Ph.D., Professor and a colleague of Dr. Ley’s in the Division of Inflammation Biology. One of Dr. Hedrick’s core studies looks at how immune cells, such as T cells and a specific type of white blood cell called monocytes, are changed by high cholesterol and may contribute to atherosclerosis and cancer.

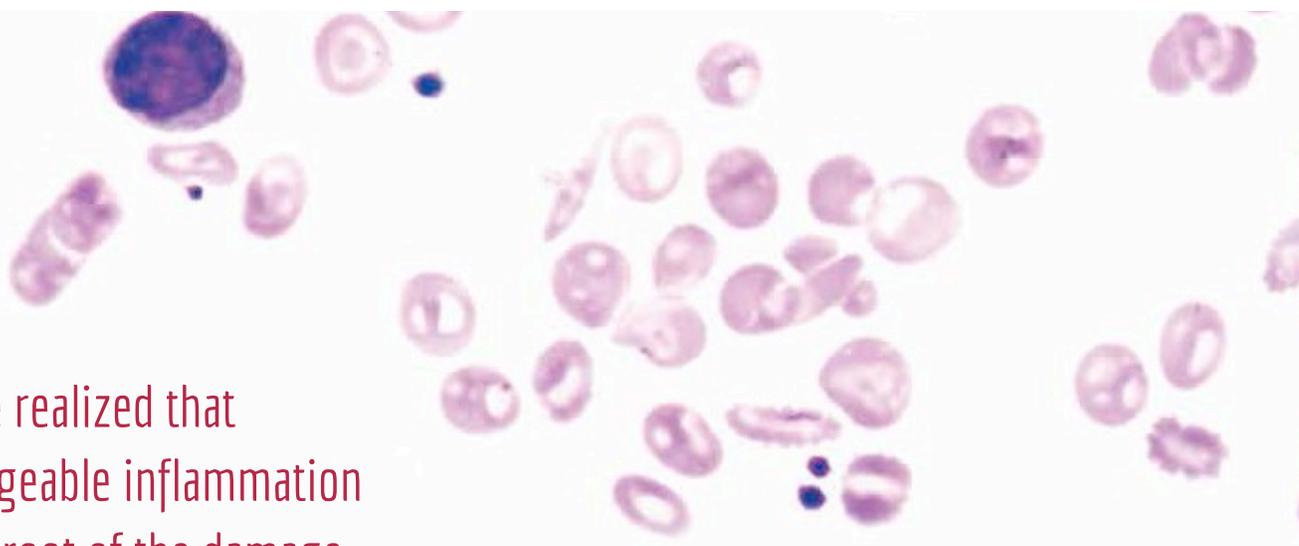
Some of the fundamental questions Dr. Hedrick is trying to answer are: How does the presence of atherosclerotic lipids alter the responding immune cells, does this impact their function, and does this result in more or less inflammation and disease? Dr. Hedrick got a partial answer recently through an interesting experiment in her lab in which her team took two groups of mice and fed one normal mouse chow and the other a diet that simulated a high calorie, high cholesterol, and pro-inflammatory “Western” diet.

“We were fascinated to observe that the regulatory T cells in the mice on the fatty diet gradually began to

disappear,” Dr. Hedrick says. “As immunologists, we can usually identify these cells by the markers they express, but all of a sudden we couldn’t find those markers. Did the cells die or did they change and become something else?”

“Fortunately, we use a really cool mouse model in which we can fluorescently tag these cells so even if they don’t express their markers we can find them. And what we found was that the T cells weren’t dead. They were alive and functioning quite well. But instead of working as suppressive, protective immune cells, due to the high cholesterol environment they changed their phenotype and became unmanageable activated T-cells that produced inordinately high levels of pro-inflammatory cytokines. We believe this cholesterol overload may prompt cells to overproduce inflammatory factors that lead to even more plaque formation.”

A completely different approach in the battle against inflammation—one that may offer hope to those with the painful and life-shortening sickle cell disease that afflicts 100,000 Americans—has emerged from the lab of



“Once we realized that unmanageable inflammation was the root of the damage caused in both processes, we turned our attention to finding a compound that could interrupt that sequence.”

JOEL LINDEN, PH.D.

Joel Linden, Ph.D., Professor in the Division of Developmental Immunology. Dr. Linden is eagerly awaiting the results late this fall of a phase II clinical trial based on his research, which predicted that sickle cell patients should benefit from the existing prescription drug Lexiscan.

In its traditional medical use, Lexiscan is given as a rapid IV injection to increase the blood flow through the arteries of a patient’s heart during a cardiac nuclear stress test. However, in mouse studies, Dr. Linden discovered the drug also worked as a short-acting anti-inflammatory agent. It seemed to inhibit an unwanted inflammatory response where white blood cells are activated after sensing sickle cells that begin to clog the blood vessels during patients’ periodic sickle cell crises. During a crisis, these activated immune cells actually further restrict blood flow.

“We’re hopeful we’ll see the same kind of results in the human trials that we saw in the animal studies,” says Dr. Linden. “If we do, we’ll go to a much larger scale phase III patient study. I believe we’ll have a chance to really make a difference in the lives of sickle cell patients through inhibiting the inflammation, reducing organ damage, and dramatically shortening the duration and intensity of their painful episodes.”

The foundation of Dr. Linden’s research was a brilliant connection he made one day a few years ago after reading an article in a scientific journal. It described what happens in the blood of sickle cell patients and how the damage is caused.

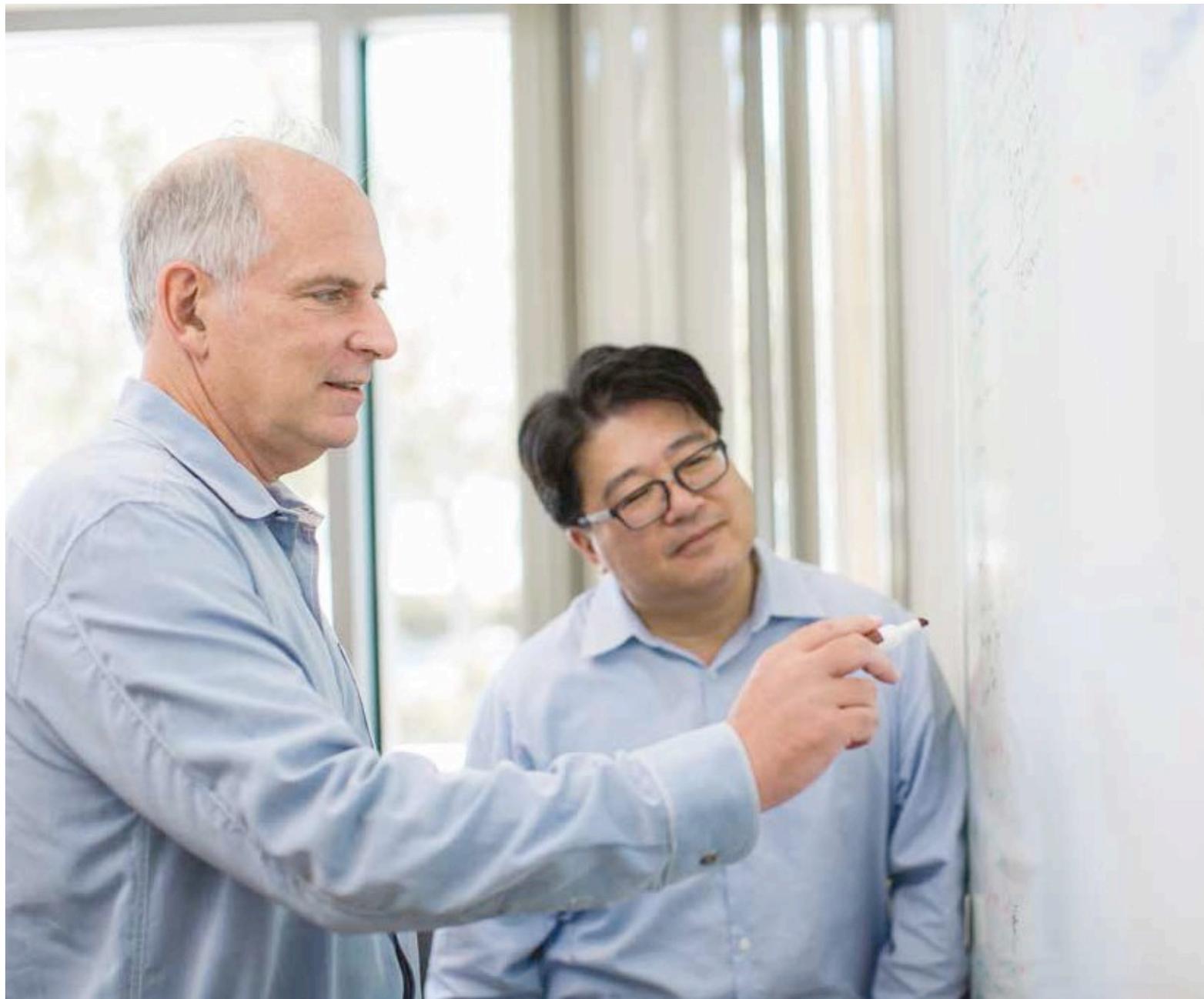
He suddenly realized the inflammation-caused damage was virtually the same process that occurs during ischemia reperfusion injury when the blood supply to a tissue is cut off, for example during a heart attack, stroke, or when blood vessels are clamped for organ transplantation. In these cases, the damage not only occurs from the injury itself, but also when the blood supply returns to the tissue and triggers the immune system to mount an unwanted inflammatory response.

“Once we realized that unmanageable inflammation was the root of the damage caused in both processes, we turned our attention to finding a compound that could interrupt that sequence,” Dr. Linden says.

He didn’t have to look far. Dr. Linden is a world-renowned expert on cell surface receptor molecules that recognize the natural chemical adenosine. The production of adenosine shoots up when the cells are stressed, activated, or lack enough oxygen.

Dr. Linden discovered that the adenosine receptor is a powerful inhibitor of many immune cells, and activating these receptors can inhibit many inflammatory disease processes. In Lexiscan, he found the perfect substance to activate adenosine receptors and thereby dampen the inflammation in the blood of sickle cell patients.

In an interesting twist, Dr. Linden’s research has shown that blocking instead of activating adenosine receptors could soon become a powerful weapon in cancer immunotherapy. Solid tumors escape detection by our immune system, in part



Joel Linden, Ph.D. and Gene Lin, Ph.D.

by generating large amounts of adenosine, and therefore adenosine receptor blocking drugs could be used to enhance the effectiveness of tumor vaccines.

“I’m excited every day because the field that uses the immune system to kill tumors is moving at blazing speed right now,” Dr. Linden says. “I think adenosine is a big part of the story and has great potential for becoming a bigger therapeutic target. If you talk to people in the field of cancer immunotherapy, adenosine is seen as a Johnny-come-lately but it’s gaining ground rapidly. Adenosine receptor blockers aren’t very big right now, but just wait a few years and I think we’ll see them become a critically important tool in our immunological arsenal for killing tumors and saving lives.”

For Dr. Altman and his colleagues, the latter is the Holy Grail that drives the Institute’s intense focus on inflammation.

“Given that it took centuries for science to even become aware of the existence and danger of chronic inflammation, the Institute’s rapid progress in unraveling some of the mysteries of the process in a relatively short span of time is remarkable,” Dr. Altman says. “And since we’ve only scratched the surface of what needs to be done to fully address the challenge, the potential for the Institute to transform human health by neutralizing chronic inflammation is truly immense.” ●

Prestigious grants will help Institute scientists probe complexities of mucosal immunity

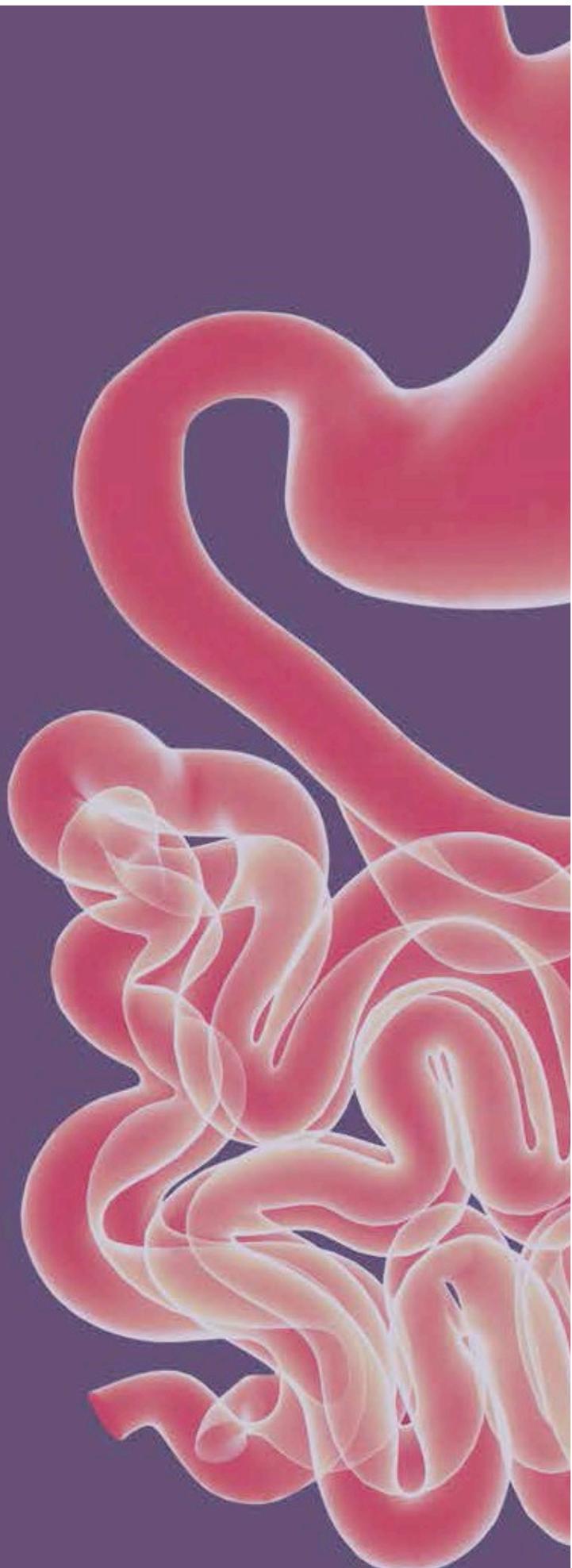
When you think of the immune system, the intestinal tract is not the first area of the body that comes to mind. Amazingly, however, the gut contributes almost 80 percent of the immune cells within the body. The problem is that it is a delicately balanced system vulnerable to being disrupted by chronic inflammation and pathogens.

The challenge for scientists is that little is actually known about this system so critical to human health. That's about to change, thanks to two prestigious grants awarded last summer to the La Jolla Institute's Mitchell Kronenberg, Ph.D., President and Chief Scientific Officer, and Hilde Cheroutre, Ph.D., Professor and Head of the Division of Developmental Immunology (see Q&A with Dr. Cheroutre on page 14).

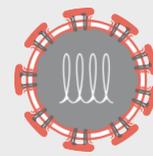
On the basis of their innovative research, these two principal investigators have been independently selected to join the Mucosal Immunology Studies Team, a cooperative research group funded by the National Institute of Allergy and Immunology. It brings together 11 of the nation's most innovative immunologists to break new ground in the understanding of mucosal immunity. The two participating LJI labs will receive a total of more than \$5 million over the next five years to study immune defense mechanisms with the body's largest "interface" to the outside world, the intestines.

"We're fascinated by the prospect of learning how the mucosal immune system balances its job of defending against pathogens while carrying out its other function of avoiding responses to beneficial components of the microbiome as well as collateral damage to the gastrointestinal system," Dr. Kronenberg says.

Adds Dr. Cheroutre, "Our two studies will use different approaches to get at the core of how this critical immune system recognizes and adapts to changes in its environment. We're excited about the opportunity to shed a light on this complex process because we know it will have far-reaching implications for treating inflammatory bowel diseases, strengthening the immune system, and enhancing human health." •



Zika's global reach



1947

Virus discovered in monkeys in Uganda

1960

First human case in Nigeria

1970s

Cases in Malaysia, Indonesia, India, and Pakistan

2007

Micronesian Epidemic

2013

French Polynesian Epidemic



Modes of Transmission



Although Zika is primarily thought of as a mosquito-borne illness, sexual transmission plays an important role in the spread of the virus. Weeks or even months after the virus has been cleared from the bloodstream, virus can still be found in semen and transmitted through sexual contact. Women can pass Zika to their unborn babies during pregnancy and there is a strong possibility the virus can spread through blood transfusions.

Zika and the Brain

DEVELOPING BRAIN

Zika can cause microcephaly, a severe birth defect where babies are born with abnormally small heads. It may also cause a wider range of more subtle brain disorders. The virus infects and kills neural progenitor cells, a type of stem cell that develops into different types of brain cells, leading to incomplete or faulty brain development. Zika infection seems to do the most harm during the first trimester.

ADULT BRAIN

Experiments by LJI scientist Sujan Shresta and her collaborators have shown that Zika can also infect neural progenitor cells in adult brains. Adult brains retain a stash of neural progenitor cells that spawn new brain cells. The integration of new neurons is important for learning and memory and interrupting this process may lead to cognitive decline, depression and contribute to the development of Alzheimer's disease.

2014-16

Virus emerges in northern Brazil and spreads across the Americas



Zika has been declared an international health emergency by the World Health Organization citing concerns that as many as four million people could be infected by the end of 2016. Several LJI labs have joined the worldwide effort to combat Zika.

Zika virus causes mild symptoms in most people, including fever, headache, rash, and possibly pink eye. In fact, most individuals never realize they have been infected. That is especially concerning for pregnant women as they unknowingly may pass on the virus to their unborn babies where it can cause severe developmental disorders and even death. As the epidemic progresses, more complications related to Zika infection are emerging. We now know that in addition to causing eye damage in babies, adults' vision can be affected as well. Babies that appear healthy at birth are sometimes coming down with microcephaly and other brain-related disorders months after birth.

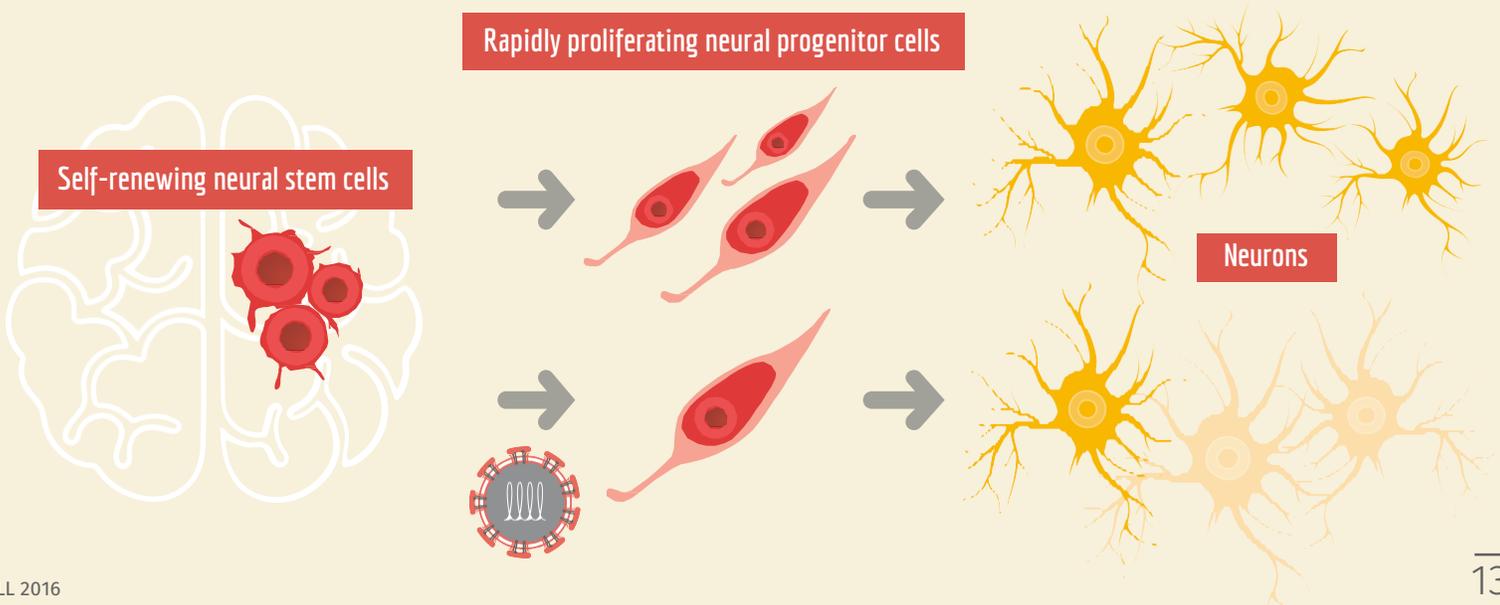
In response to the recent Zika outbreak, several LJI scientists recently shifted their focus to Zika research. Their efforts involve a network of scientists from Florida, North Carolina, Nicaragua, Colombia, and Brazil and tie in with a large Zika research project sponsored by the European Union.

Dr. Sujan Shresta, who is internationally recognized for her pioneering work on dengue virus, developed a Zika mouse model that can mimic the virus infection in the lab. She is particularly interested in learning

how the virus spreads and evades the immune system as well as in screening vaccine candidates and compounds that can treat Zika infections. The mouse model also formed the basis for studying the virus' effect on adult brain cells (see "Zika and the brain").

Dr. Alessandro Sette, known for his work studying the role of T cells in the immune response to other flaviviruses, such as dengue and yellow fever, is also expanding the scope of his research to include Zika. He is particularly interested in whether dengue infections or yellow fever vaccinations crossreact with Zika infections.

In collaboration with Dr. Bjoern Peters' lab, his team is identifying those parts of the virus particle that are recognized by the immune system. It is an extension of Dr. Peters' most recent study, which used machine-learning tools to predict which parts of Zika are likely to elicit an immune response. Together with experimental data, this research not only provides the basis to map how the human immune system responds to Zika and what makes some people more resistant to disease but also how to best measure the efficacy of vaccine candidates.●





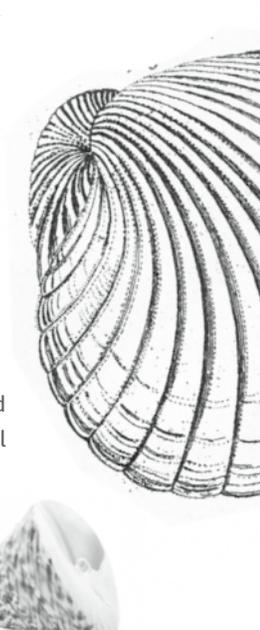
Hilde Cheroutre

A pioneering scientist

Hilde Cheroutre, Ph.D., Professor and Head of the Division of Developmental Immunology, always felt drawn to nature. Growing up in Belgium, she spent a lot of time combing Belgium's coastline for shells. "I knew there were 89 different species that you could find," Cheroutre recalls. "My brother and I spent days and days just walking along the beach to find the last missing species. It took us years but we found them all." When it was time to enroll at the university, Dr. Cheroutre briefly considered engineering and medicine but ultimately settled on biology. However, she wanted more than just an undergraduate degree and decided to pursue a Ph.D.

Initially simply a means to be independent, Dr. Cheroutre's doctoral thesis would forever change the trajectory of her life and career. As a graduate student, she was part of a team that isolated the gene encoding human gamma interferon, one of the first known proteins with antiviral activity. When she presented her work at an international conference, it made a big splash and she had her pick of offers from renowned scientists to join their labs for postdoctoral training. At a time when most of her colleagues chose to stay closer to home, Dr. Cheroutre went abroad to join Dr. Lee Hood's lab at Caltech in Pasadena, Calif. She only planned to stay for a few years in the U.S., but things changed.

Today, she runs a very successful lab at La Jolla Institute and has received the prestigious National Institutes of Health (NIH) Pioneer Award, the highest-ranking award given by the NIH to "support individual scientists of exceptional creativity who propose pioneering and highly innovative approaches." Recently she was also chosen as one of 11 members of the Mucosal Immunology Studies Team, a cooperative research group funded by the National Institute of Allergy and Immunology to break new ground in the understanding of the mucosal immune system (see page 11).

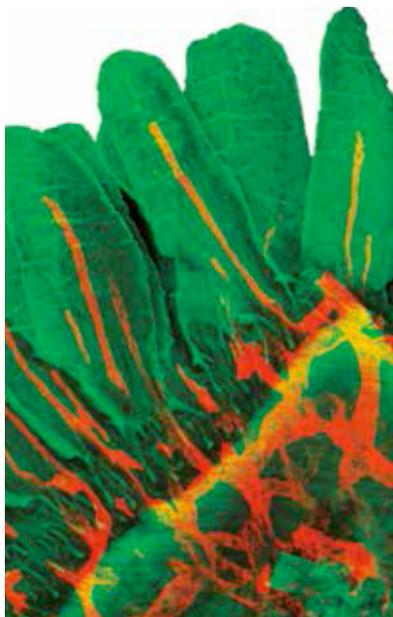


WHAT IS THE MUCOSAL IMMUNE SYSTEM?

The mucosal immune system is our built-in defense system that operates at the borders of the body, such as the epithelial barrier of the intestine. We are constantly exposed to pathogens but most of the pathogens around us never get a chance to gain entry through these mucosal borders because every second and every moment of the day, the mucosal immune system that operates there prevents the invasion of pathogens. Once pathogens break through that first line of defense, the systemic immune system takes over.

WHY DID YOU DECIDE TO WORK ON THE MUCOSAL IMMUNE SYSTEM WHEN MOST IMMUNOLOGISTS ARE FOCUSED ON THE SYSTEMIC IMMUNE SYSTEM?

During my post-doctoral training I studied a molecule that is important for the immune system and that turned out to be highly expressed in the intestine. This prompted me to further investigate this molecule and led me to start working on the intestinal immune system. All of sudden a whole world opened up for me because the immune system in the gut is so fascinating and fairly unexplored. If you think about it, the intestine is the largest contact surface



“All of a sudden a whole world opened up for me because the immune system in the gut is so fascinating and fairly unexplored.”

with the outside environment and most infectious pathogens enter the body through the intestinal epithelium. The immune defense at that border is enormous and very sophisticated. But not only that, compared to the systemic immune system, which functions in a basically sterile environment, the mucosal immune system has to operate in the context of a very dirty environment.

HOW DOES THE MUCOSAL IMMUNE SYSTEM KNOW WHO IS FRIEND AND WHO IS FOE?

The systemic immune system operates in a sterile environment and the moment something comes in that’s “non-self,” it knows it is bad. The mucosal immune system cannot operate that way and often, in fact, the mucosal immune system provides protection based on recognizing self-molecules.

CAN YOU EXPLAIN?

The epithelium in the gut consists of a single layer of epithelial cells and the cells are designed to absorb “foreign” molecules such as broken-down food. The mucosal immune system that patrols the mucosal border is not “alarmed” by the uptake of these foreign molecules. However, if a pathogen infects the epithelial cell, then it will become stressed and it will induce stress or “danger” proteins. In addition, cellular proteins will become misfolded and all together these dietary proteins and “danger” self-molecules will generate a completely different repertoire of antigens on the surface of the infected epithelial cell. This will alarm the mucosal immune system, which then eliminates that infected epithelial cell regardless of the nature of the pathogen. In that way, the mucosal immune system is able to prevent invasion of a large variety of pathogens because it does not need to recognize each specific pathogen separately.

AS A GRADUATE STUDENT YOU IDENTIFIED HUMAN GAMMA INTERFERON. WHAT LED TO THAT DISCOVERY?

The goal for my Ph.D. study was to find and identify a protein that had antiviral activity. Back then we knew the body had the capacity to identify and destroy virus-infected cells, but it wasn’t clear how and immunology as we know it today didn’t exist. I would isolate RNA from human spleen cells and divide it into separate pools. Then I would inject them separately into frog eggs, which functioned as an incubator to translate that human RNA into proteins. I then took those proteins and put them on infected cells to see which pool of RNA molecules encoded proteins that protected the cells and cleared the virus. I then split that pool of RNAs and did the same assay until I had isolated a single RNA that encoded a protein with antiviral activity. And that’s how we found human gamma interferon.

HOW DID IT FEEL TO MAKE SUCH A MOMENTOUS DISCOVERY?

I never thought about the finding itself. I was more interested in understanding how the molecule worked and its application.

WHAT’S YOUR ADVICE TO KEEP YOUR IMMUNE SYSTEM IN SHAPE?

Be happy! If you are unhappy, stressed, or tired it impacts the condition of your immune system enormously. Do things that make you happy, that give you peace and satisfaction, things that relax you whatever they may be. Enjoy life, tend to your garden, enjoy art and music, eat healthy food, get enough sleep, and be active. If you do these things, you help your immune system stay fit. If you want to maintain good health, it is very important to keep your immune system in the best condition.

WHEN DID YOU DISCOVER YOUR INTEREST IN ARCHITECTURE?

I guess it had always been in me, but I wasn’t aware of it. As a scientist I always have to envision the whole picture, to see where this or that system, mechanism, or cell fits in, ask why would it be, and why would you have self-reactivity as part of mucosal immunity. It requires very three-dimensional thinking and also thinking ahead.

It’s the same with architecture. With architecture you always have to envision what it will look like, how the sunlight will travel across the room throughout the day, what the shadows will look like when the light falls this way or that way. You’re constantly imagining the whole picture and that’s exactly what we do in science. We’re constructing things in our mind to figure out how they work.●

UP & COMING

Edahi Gonzalez-Avalos

ALWAYS UP FOR A CHALLENGE

Whether it is beating his opponents at a videogame or getting accepted into one of the world's most exclusive undergraduate programs, graduate student Edahi Gonzalez-Avalos enjoys a good challenge.

“What distinguishes human beings from other species is our ability to think, to be conscientious about how to influence and modify our world,” says Gonzalez-Avalos, “and that’s why I decided to dedicate myself to sciences.” But not just any program would do.

Gonzalez-Avalos had set his sights high: on the Genomic Sciences Program at the National Autonomous University of Mexico, one of the world’s most selective and demanding undergraduate programs.

It emphasizes genetics and bioinformatics over botany and zoology, and students host international scientists who challenge their critical thinking during scientific discussions instead of only attending traditional lectures.

Each year hundreds of applicants vie in a series of exams and interviews for one of two dozen coveted spots. Gonzalez-Avalos aced the entrance exam and impressed the interviewers with his intense interest in science and easygoing charm.

“I knew I would be working day and night and would have no social life but the last part turned out not to be true,” he says. “I found many like-minded friends and we discussed science all day long.”

After three years of intense theoretical instructions and intimate workshops with world-renowned scientists, it was time for what Gonzalez-Avalos calls the magical fourth year: “You are free to do real research,” he says.

Students can choose any lab in the world—as long as the lab accepts them. “I decided on Anjana Rao’s lab because I wanted to apply bioinformatics to the field of epigenetics and her research was a perfect match,” he says.

After Gonzalez-Avalos convinced Dr. Rao with a glowing letter of recommendation to invite him to join her lab at La Jolla Institute, she assigned him to a bioinformatics project. “The project was much bigger than I ever expected,” Gonzalez-Avalos recalls. “It was a real challenge for me but I fell in love.” He rose to the occasion and the study was published in the scientific journal *Nature Communications* late last year. This past August he graduated from the Genomics Sciences Program and earlier this fall he joined Dr. Rao’s lab as a graduate student.

Now the real magic is about to start. ●



San Diego investor Tom Tullie joins LJI Board of Directors

Tom Tullie created a successful career building high tech companies by making sure whatever moves he made in business had a “triple bottom line” that not only ensured financial reward, but also provided products that were invaluable to customers and improved the world at large.

Tullie, a resident of Del Mar, Calif., accepted an invitation to become the newest member of the La Jolla Institute Board of Directors because he believes his multi-benefit philosophy meshes perfectly with the Institute’s mission.

Trained as an electrical engineer, Tullie’s first job was designing semiconductors. But he also had an MBA and a real passion to move into sales and management. His first major success came after he joined Applied Micro Circuits Corporation (AMCC) as vice president of sales in 1996. Four years later, his team had transformed a company worth

\$20 million into a high tech giant with a \$35 billion market cap. By the time he left AMCC, Tullie had risen to chief operating officer.

As Tullie’s career unfolded, he began a pattern of joining companies as CEO and turning them around so successfully they were soon acquired by other firms. After leaving AMCC, he did that with two different high tech firms—Path 1 Network Technologies and Vativ Technologies.

Tullie also began to focus on companies he could not only improve financially, but which contribute to improving the world. In 2009, he helped launch ecoATM as chairman and CEO of the automated electronics recycling company, which has since recycled millions of cell phones. Just a little over three years later, ecoATM was sold for \$350 million. He is also executive chairman of Everyone Counts, a high tech voting systems firm he believes will improve and expand democracy by enabling millions to vote online. Tullie is particularly proud of his support as vice chairman of the non-profit EvoNexus, a startup technology incubator that has helped launch dozens of high tech firms in San Diego and Irvine.

It’s clear Tullie’s focus these days as an “angel investor” is as much about giving back as it is on business success, and it’s why he was so interested in joining the Institute’s board of directors.

“La Jolla Institute is a true game changer in human health. I hope to help them achieve their triple bottom line by utilizing my expertise to advise them financially, whether it’s licensing their technologies or creating separate commercial ventures to deliver their discoveries to the world. It’s a truly exciting combination of potential commercial success, the delivery of cutting-edge research, which relieves the suffering of people with autoimmune diseases—like my father who struggles with Crohn’s disease—and the real potential to transform medicine and save millions of lives around the world. To play a role in helping the Institute achieve that kind of global impact would be one of the most satisfying highlights of my career.”●

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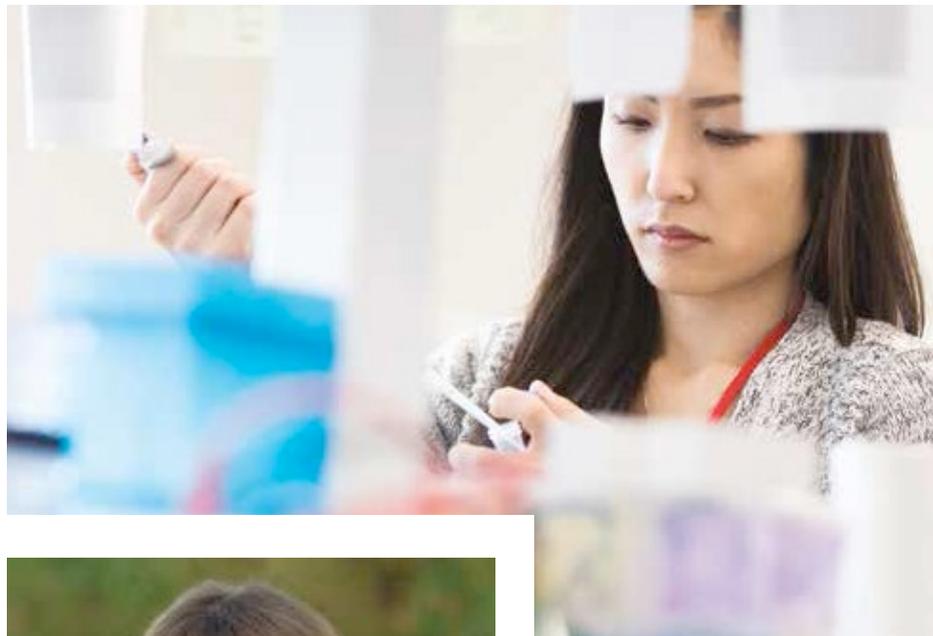


Pam Blakely

BOARD MEMBER AND
CHAIRMAN'S CIRCLE MEMBER

Many years ago I watched helplessly as my father's strength and vitality was depleted by the autoimmune disease multiple sclerosis. I decided to honor his brave struggle with this devastating disease by assisting the research of groundbreaking scientists like those we have at La Jolla Institute. Their use of innovative scientific technologies to understand the immune system is simply breathtaking. I'm truly optimistic that the Institute's cutting-edge style in understanding and empowering our own immune system to heal will help them reach their goal of *Life Without Disease*, including cures for a number of diseases like MS.





Nancy Vaughan

PRESIDENT'S COUNCIL MEMBER

In my opinion, La Jolla Institute is one of the most important research institutions, not just in San Diego, but the world. Their work is truly fascinating. I'm impressed with the comprehensive areas of the immune system the Institute is involved in and how their scientists are able to focus on the smallest matters without losing the big picture. I feel certain that the research done there will influence changes in the way we evaluate and prevent disease, which will lead to groundbreaking changes in the way medicine is practiced in the future.



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PRESIDENT'S COUNCIL MEMBERS

As scientists, we value the quality and breadth of research being done at La Jolla Institute. Its focus on trying to understand the role of the immune system in disease processes is extremely promising. Recent medical advances continue to validate the importance of what is being learned. We are impressed by the far-reaching fields of medicine that are being studied, the talent of the staff, and the facilities at La Jolla Institute. We look forward to the Institute remaining at the forefront of translational medicine, bringing therapies from the lab to the clinic.





Joani Nelson

DONOR

When I became involved with the Institute a few years ago, I was immediately impressed with the caliber of the researchers and the fact that they're working to understand the immune system's role in disease instead of trying to create more pills and medications. Having two children who developed type 1 diabetes in their 30s, I'm especially pleased to see that the Institute focuses so much of its research on understanding this disease. Diabetes is such a debilitating disease, both emotionally and physically, the very real potential the Institute will be able to develop new treatments is really exciting.



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The information listed above represents contributions as of **August 31, 2016**.



Christopher A. Lee



Kelsey Dale

La Jolla Institute names new development leadership team

Christopher A. Lee has been named Chief Advancement Officer at La Jolla Institute for Allergy and Immunology. He is joined by Kelsey Dale, who has been appointed Deputy Director of Advancement.

“We are delighted to welcome Chris and Kelsey to La Jolla Institute,” says Dr. Mitchell Kronenberg, President and Chief Scientific Officer. “Their passion, professional credentials and deep roots in the San Diego community are invaluable for strengthening philanthropic support of our research.”

Lee has a long history of bringing his experience and strategic vision to non-profit organizations in the San Diego area. He most recently served as Director of Philanthropy at The Scripps Research Institute (TSRI). Prior to TSRI he held fundraising leadership roles as Vice President of Development at PCI (Project Concern International), a global health and development organization internationally headquartered in San Diego and as Vice President of External Relations at Sanford/Burnham/Prebys Medical Discovery Institute in La Jolla, Calif.

He also held the position of Director of Development with Catholic Relief Services based in Baltimore and of Director of Leadership Gifts for Villanova University, outside Philadelphia and worked as staff member of former United States House of

Representative Member Alan B. Mollohan. Lee graduated from West Virginia University with a bachelor’s degree in political science and from Villanova University with a master of business administration.

“There is such enthusiasm and clarity of mission at the La Jolla Institute,” Lee says. “I am thrilled to join their team and work toward a common goal.”

Dale is a seasoned development professional who emphasizes the use of data to build successful fundraising campaigns. Before joining La Jolla Institute, she held the position of Philanthropy Officer at The Scripps Research Institute and served in a variety of development roles at San Diego non-profits, including Senior Development Officer at PCI, where she built a robust annual giving program; Project Manager for Event Innovations; and Development Coordinator at MiraCosta College, among others.

Dale holds a bachelor’s degree in History from Whitman College and serves on the Board of the San Diego Chapter of the Association of Fundraising Professional.

“I’m pleased to work for such a dynamic and impactful organization, and I look forward to helping raise awareness and support for the vital work underway here at the La Jolla Institute,” Dale says. •

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Our Mission

La Jolla Institute for Allergy and Immunology is dedicated to understanding the intricacies and power of the immune system so that we may apply that knowledge to promote human health and prevent a wide range of diseases. Since its founding in 1988 as an independent, nonprofit research organization, the Institute has made numerous advances leading toward its goal:



Life Without Disease®.

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