

Immune Matters

FALL 2015



Physician-Scientists

Blending Research and Patient
Care for the Benefit of Both

Page 4

Clinical Studies Core

Research Volunteers Contribute
to Cutting-Edge Science

Page 8

9420 Athena Circle • La Jolla, CA 92037

Board of Directors

John E. Major, Chairman
Pamela W. Blakely
Anthony R. Carr
David Dominguez
Robert C. Dynes, Ph.D.
Leroy Hood, M.D., Ph.D.
Sergio Jinich
Richard K. Kornfeld
Mitchell Kronenberg, Ph.D.
Toshifumi Mikayama, Ph.D.
Gail K. Naughton, Ph.D.
David A. Perkins
Hunt Pettit
Rhonda F. Rhyne
Larry Spitcaufsky
Fred Wasserman, Dr.P.H.
David R. Webb, Ph.D.
Herbert A. Wertheim, OD, D.Sc.
Timothy J. Wollaeger
Eric Zwisler

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**®.

Immune Matters Contributors

Chris Benedict, Ph.D.
Ken Hansen
Lisa Huppert
Rachel Jonte
Gina Kirchweyer, Ph.D.
Daniel Moyer
Bob Ross
Joel Sotelo
Stephen Wilson, Ph.D.

STAY UPDATED! If you would like to receive email updates from the La Jolla Institute, please email us at: institute_relations@lji.org
858.752.6542

Letter from the President

The groundbreaking research on the immune system we conduct at La Jolla Institute (LJI) ultimately has one purpose: to prevent and cure disease. That's why connecting scientific inquiry to patient need is a constant source of motivation and inspiration for our investigators.

This crucial connection is particularly close for those with a medical (M.D.) degree—the physician-scientists working at the Institute. Whether they actually see patients in a clinical setting, as several do, or their medical training informs their research, physician-scientists have a unique perspective on human disease.

In this issue of *Immune Matters*, a number of our physician-scientists share personal stories of how they became scientific investigators. We'll also hear about the rewards and challenges experienced by those who choose to devote their careers to both lab and clinic.

LJI's connection to clinical medicine will be even stronger with the recent announcement that we've signed an official affiliation agreement with UC San Diego Health System and UC San Diego School of Medicine. The agreement codifies an informal, decades-old relationship built on shared research interests and a long history of successful scientific collaboration.

The future potential of this agreement is exciting because in leveraging the shared resources and expertise of two world-class organizations, it will promote much closer integration of basic immunology research here with our colleagues on the UCSD campus and also with clinical medicine to speed the development of treatments for diseases of the immune system.

In our Q&A section, you'll learn how Dirk Zajonc, Ph.D., an Associate Professor in the Division of Cell Biology, began his career in Germany studying fat metabolism and transitioned to become an important researcher in the field of structural biology. He uses x-ray crystallography to help determine the shape and function of proteins. His work will ultimately enable colleagues to develop drugs that interfere with proteins involved in causing disease.

In this issue we also highlight our new Clinical Studies Core. Not to be confused with clinical trials, the process of testing and proving drug efficacy, the Clinical Studies Core centralizes many of our genomic and other technology-driven efforts and helps us acquire material from patients with particular diseases we are studying.

Finally, I hope you'll enjoy the profiles of our newest board members, Mr. Hunt Pettit of Fort Worth, Texas, and Mr. Larry Spitcaufsky, of Rancho Santa Fe, Calif. These two successful entrepreneurs and business leaders are passionate about the Institute's mission to eradicate diseases related to the immune system and they've already become two of our most enthusiastic supporters and ambassadors.

We are truly fortunate to have a remarkable group of partners—including individual donors, foundations, and federal funding sources—all working together to support the critical research we believe one day will move us toward *life without disease*.

Sincerely,



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





“We are thrilled that we will be able to leverage shared resources and expertise to redouble our efforts to harness the power of the immune system to fight infection and disease.”

– Mitchell Kronenberg, Ph.D.

research and clinical medicine to speed the development of treatments for diseases of the immune system.

“For many years, we have enjoyed a cordial and mutually beneficial relationship with UC San Diego. The reinforcement of our longstanding relationship through a formal agreement is a transformative step for both institutions,” said Mitchell Kronenberg, Ph.D., President and Chief Scientific Officer of the La Jolla Institute. “We are thrilled that we will be able to leverage shared resources and expertise to redouble our efforts to harness the power of the immune system to fight infection and disease.”

The agreement with UC San Diego will bring the Institute’s cutting-edge, fundamental research in immunology to a world class, research-focused

medical school, which already has an outstanding program in immunology.

“Scientists at both institutions have been very adept at making connections through informal channels,” said David Brenner, M.D., Vice Chancellor, UC San Diego Health and Dean of the School of Medicine. “With a formal agreement in place, we can be strategic about strengthening immunology research on the Torrey Pines Mesa. Without doubt, the close integration of scientists at LJl and UCSD with UCSD clinicians will spark innovation and allow us to deliver pioneering immune-based treatments and therapeutics to patients in the clinic.” ●

La Jolla Institute Announces Affiliation with UC San Diego

La Jolla Institute for Allergy and Immunology (LJI) entered an official affiliation agreement with UC San Diego Health System and the UC San Diego School of Medicine this past summer. The alliance formalized an informal, decades-old relationship built on shared research interests and a long history of successful scientific collaboration.

The 12-year agreement with UC San Diego will facilitate joint faculty appointments, enhance the range and depth of collaboration between the two organizations, and promote closer integration between basic immunology



Physician-Scientists Lead the Way in Translating Research into Patient Care



Dr. Pandurangan Vijayanand, a trained pulmonologist, splits his time between the lab and the hospital.

It was a poignant moment for both patient and physician: Having just learned he had inoperable lung cancer, the man looked his doctor in the eye and said, “You’re a really smart person. Isn’t there anything you can do for me?”

Pandurangan Vijayanand, M.D., Ph.D., a trained clinical pulmonologist, remembers that conversation and many similar patient interactions extremely well, because they ultimately motivated him to become the groundbreaking research scientist he is today at La Jolla Institute.

“It was such a penetrating question, it forced me to realize that in fact I did not have anything to offer him, and that the only way I could deal with my growing frustration over this was to shift directions and pursue a career in biomedical research,” Dr. Vijayanand says. “I felt compelled to study the very diseases I was seeing in the clinic so I could discover ways to treat them and offer some hope to my patients.”

“I’ve always wanted to alleviate patients’ suffering, so that’s why in my translational research I never lose sight of their needs.”

– MATTHIAS VON HERRATH, M.D.



Dr. Matthias von Herrath gave up patient care to focus on research.

Dr. Vijayanand, who has since made a number of significant discoveries in his asthma and cancer research at the Institute, still continues to see patients because he says it keeps him in touch with why he’s a scientific investigator. Dr. Vijayanand is an example of a true “physician-scientist,” that unique breed of dedicated and multi-talented leaders of translational research, an increasingly important biomedical field that takes scientific discoveries from “bench to bedside” where they improve and protect the lives of patients.

The concept of physician-scientist is not new, according to Mitchell Kronenberg, Ph.D., Institute President and Chief Scientific Officer.

“Throughout medical history, there has always been a small number of physicians whose drive to understand and investigate disease beyond the clinic has played a crucial role in medical discovery,” Dr. Kronenberg says. “We’re fortunate to have quite a few of them here at our Institute—some who are M.D.s and some who are M.D./Ph.D.s, and several of them continue to see patients in addition to conducting advanced immunology research. Their deep commitment to both scientific inquiry and patient care is a constant reminder to all of our researchers that the ultimate and most important

objective for our investigations is to prevent, treat, and cure the diseases of patients.”

In addition to Dr. Vijayanand, other physician-scientists on the 22-member faculty include Toshiaki Kawakami, M.D., Ph.D., Klaus Ley, M.D., Matthias von Herrath, M.D., and Nunzio Bottini, M.D., Ph.D., who also sees patients in his joint position as an Associate Professor of Medicine at UC San Diego. A number of postdoctoral researchers are also physicians, bringing the total number of M.D.s doing research at the Institute to 25.

For the Love of Science

For those physicians who gave up patient care to pursue research full time, there were practical reasons behind their decision. Some felt the extreme mental and physical challenge of attempting both disciplines would prevent them from excelling at either. Others found they were more suited to the lab.

“When I was just out of medical school my girlfriend told me she didn’t think I would make a very good physician,” Dr. Ley says with a laugh. “She was probably right because I only practiced a year and research became my real passion.

continued on page 6

However, the mindset of physician and the desire to heal never left me. To this day, I only choose research projects I believe have a chance to be translated into significant patient benefit. I'm basically devoting the rest of my life, for example, to developing a way to prevent the inflammation that causes atherosclerosis, one of our most devastating diseases."

By contrast, Dr. von Herrath enjoyed his time in the clinic during the early part of his career. But since the reason he went into medicine in the first place was the premature death of his father and his resulting desire to understand the causes of disease, Dr. von Herrath gave up patient care to focus on research. It was the right decision, as he has become one of the world's leading diabetes researchers and last year was named the world's number one expert in type 1 diabetes by the healthcare information website *Expertscape*.

However, those years caring for patients had a profound impact on how von Herrath would conduct his research.

"Once you've been in charge of a medical ward and an intensive care unit where you're responsible for 400 patients during the night shift, it forever influences your outlook on what it's like to be sick and suffer," Dr. von Herrath says. "I've always wanted to alleviate patients' suffering, so that's why in my translational research I never lose sight of their needs. I think about it every day. I personally feel that non-M.D. researchers should undergo some medical training if they choose to work in highly disease-relevant areas. That would give them an entirely new and valuable perspective for their work."



Dr. Jennifer Dan, an Institute Fellow in the lab of Dr. Shane Crotty, treats transplant patients who develop infections at the UC San Diego Perlman Center.

There are still physician-scientists whose love for both patient care and research compels them to build a career in which they can do both. That's the plan of Jennifer Dan, M.D., Ph.D., an Institute fellow in the lab of Dr. Shane Crotty through UC San Diego's Physician Scientist Training Pathway.

Impacting Human Health

"I knew even back in undergraduate school that I not only wanted to be a physician and take care of patients, I also hoped to have an even greater impact by changing medicine in some way to improve it," Dr. Dan says. "That meant I also needed to be a researcher and it's why I did a combined M.D.-Ph.D. program at Boston University. It's given me the best possible preparation for what I want to do in the future, which is an academic medicine position that allows me to do about 80 percent research and 20 percent patient care."

Dr. Dan is already getting a glimpse of her future. In Dr. Crotty's lab in the Division of Vaccine Discovery, she's immersed in research that is attempting to understand why some children develop recurrent strep throat. In the developing world, untreated strep throat can lead to acute rheumatic fever in some children while others go on to suffer life-threatening rheumatic heart disease. At UC San Diego, she treats infections developed by patients in the university's solid organ transplant program and provides primary medical care to HIV patients at the VA.

"It's so rewarding to work with patients to try and figure out what their problem is and then come up with a solution and watch them get better," Dr. Dan says. "At the same time, I'm constantly coming up with questions about other medical problems I don't have answers for. I have this real desire to take those kinds of problems back to the lab and study them in hopes of uncovering the underlying mechanisms. That kind of work is much slower than the immediate gratification you get with patient care, but I'm excited about making a contribution to biomedical research because it has the long-range potential to have an even greater impact on human health."

If Dr. Dan needs a role model for her career, she'll find one close at hand in the person of Dr. Vijayanand. His nearby lab is one of the busiest at the Institute and yet he continues to carve out time to see patients with lung diseases. Strong evidence of his passion for clinical work is that his patients are 5,000 miles from La Jolla at Southampton General Hospital in the U.K., where he did his residency

in the late 1990s after getting his medical degree in his native India.

“I truly love research and it’s the main focus of my career now, but at heart I’m a physician and there’s just something that is immensely fulfilling about caring for patients and saving their lives,” Dr. Vijayanand says. “I’m lucky I’m still able to devote about 20 percent of my time to seeing patients but, because my research lab is so active right now, it’s a logistical challenge and I end up using vacation and personal time in order to see my patients in England. It’s also tough on my family, but I think they understand this is still a very important part of my life.”

Benefitting Patients

And valuable, because that patient contact also informs and guides his research.

“With my grounding as a physician, I just can’t see the value of research if it’s not directly going to someday benefit a patient,” Dr. Vijayanand says. “It keeps me focused on making sure what I do in the lab ultimately is connected to patient health. What I like best is encountering problems with my patients for which there is no apparent solution, and then going back to the lab and coming up with a plan to study and solve those problems.”

An excellent example is asthma. The ailment has both fascinated and frustrated Dr. Vijayanand for nearly two decades, primarily because he was never able to provide his patients with much relief for their suffering. However, thanks to his use of advanced genomic technology, that’s all about to change. In a study last year in the scientific journal *Nature Immunology*, Dr. Vijayanand and his team announced they had identified several of the genes likely to contribute to asthma. It is a key discovery that may well transform

treatment and prevention of a disease that afflicts 200 million people worldwide.

“One of the joys of research and making discoveries is that you feel like you’re doing something, that you’re actually contributing to solutions to medical problems that have plagued humans for a thousand years,” Dr. Vijayanand says. “One of the best things is that it’s changed the atmosphere in the exam room. Now, when I’m asked if there’s anything that can be done, I have a whole list of scientific advances I can share with my patient, and that’s become a really exciting conversation for both of us.” ●

“What I like best is encountering problems with my patients for which there is no apparent solution, and then going back to the lab and coming up with a plan to study and solve those problems.”

– Pandurangan Vijayanand,
M.D., Ph.D.



Dr. Klaus Ley and Jackie Miller, a research technician in his lab. Dr. Ley focuses on research projects he believes will have a direct impact on patients. He is currently working on a vaccine for heart disease.

Clinical Studies Core Serves as Hub for Advanced Study of Immune System



Alyssa Hill explaining the donor consent form to Daniel Moyer.



Shariza Bautista, a trained phlebotomist, draws a blood sample from a donor participating in a clinical research study.

Just walk around the laboratories and talk to the scientists at La Jolla Institute and you'll feel it almost immediately: an exhilarating sense that biomedical research has entered the most exciting period in history with the potential to generate profound benefits for human health.

Amazingly, it's also a phase in which everyday citizens with no scientific background can make a fundamental contribution to the research through the simple act of donating blood.

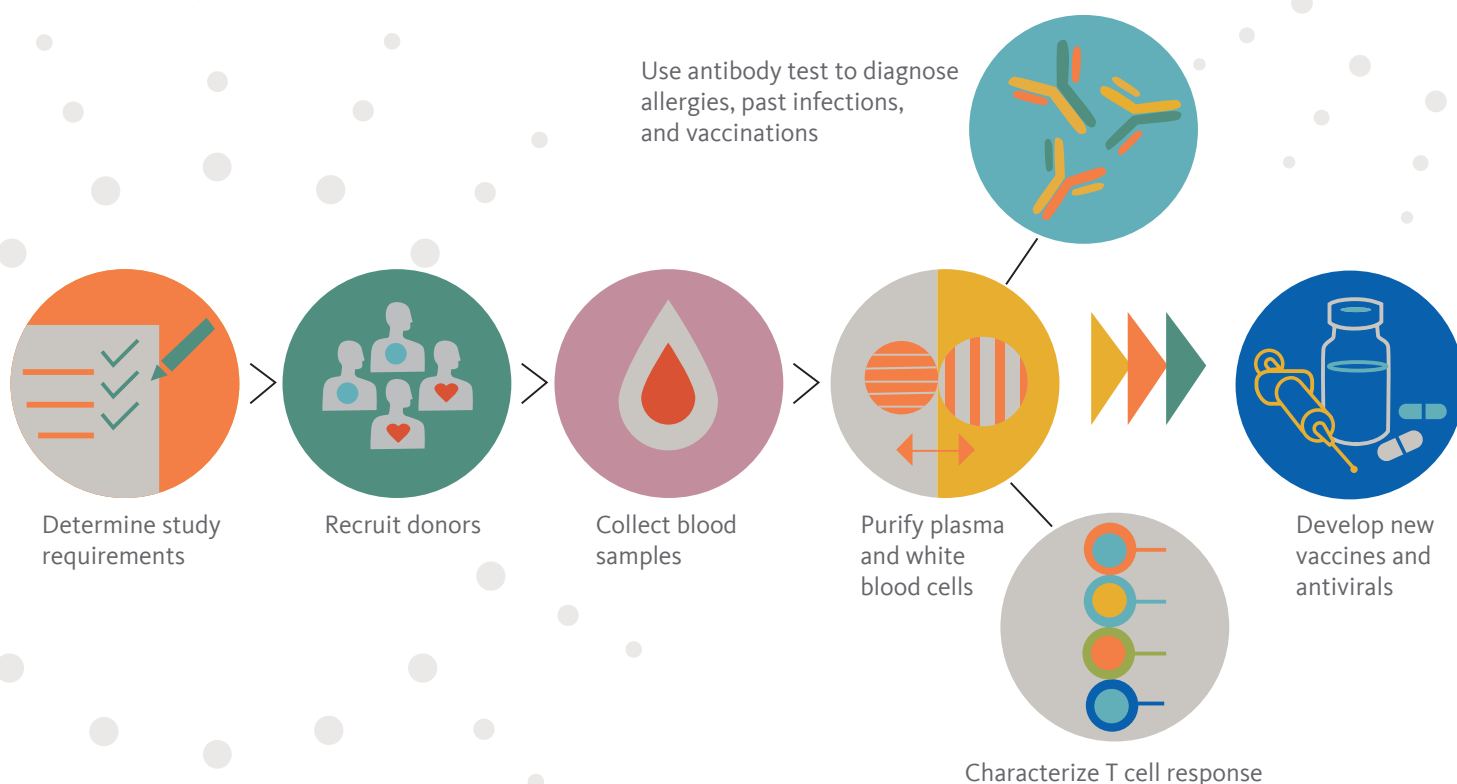
There are some very practical reasons why this new era has dawned and why the scientists are so optimistic. Advances in genomics and next-generation technologies for analyzing genes are rapidly transforming research in the 21st century by providing scientists with a remarkable array of sophisticated and powerful tools to understand the human immune system in ways not even imaginable a few years ago.

To serve as the hub for these research activities as well as foster future efforts, the Institute this past spring created a new Clinical Studies Core that principal investigators can use as a resource to enhance their research.

There is no one more excited about the developments than Stephen Wilson, Ph.D., the Institute's Executive Vice President and Chief Administrative Officer, who was instrumental in putting the infrastructure in place that allows Institute scientists to capitalize on the latest technological developments. He says that while studies of mouse models will continue to play a role in



Dr. Stephen Wilson



“We now have access to incredible new technologies that enable our researchers to take a very deep dive into understanding exactly how the immune system works.” – Dr. Stephen Wilson

research at the Institute, an entirely different mode of investigation has arisen that provides an unprecedented view of the immune system.

“We now have access to incredible new technologies that enable our researchers to take a very deep dive into understanding exactly how the immune system works, down to the molecular level,” Dr. Wilson says. “It’s really a combination of computational biology, rapid and accurate genomic sequencing, high throughput immunologic assays, and advanced forms of bioinformatics.

“These technologies are converging to solve problems that previously kept researchers from discovering the underlying mechanisms of how the immune system protects—and sometimes attacks—our health,” Dr. Wilson adds. “The tools

are so powerful and efficient that we’re now able to observe these mechanisms on a large human scale, looking at genetically complex cohorts of individuals, across varying ages, different lifestyles, and immunologic history.”

The impact on human health of this rapidly expanding picture of the immune system will be immense, Dr. Wilson says, citing several examples:

- Researchers are gaining a unique understanding not only of how the body recognizes and battles infectious diseases, but why pathogens sometimes are able to circumvent the immune system and cause the individual to succumb to disease. Institute researchers will be using this knowledge to develop new ways of creating vaccines, and to fight existing and rapidly emerging threats.

continued on page 10

“One reason the Clinical Studies Core was created was to centralize the critically important sample collection program and make it easy and efficient for scientists to order what they need.”

– Annie Lei

- Allergies have been one of the scourges of the human race, but Institute scientists are using clever profiling techniques and advanced molecular tools to learn why healthy individuals seem to be spared while those who are afflicted have immune system programming that causes them to suffer for life. Understanding, in fine detail, the cause of allergies in a wide variety of people will contribute to developing treatments and perhaps pre-emptive steps—such as vaccines—that could potentially prevent or reverse the allergic response.

The Clinical Studies Core resource that makes all of this possible for the scientists is the blood donation program. Coordinator Annie Lei says her department works closely with the principal investigators to develop a research protocol that determines the types of individuals who are required for their studies, including subjects who are healthy as well as those suffering from a particular allergy or disease the scientist is probing.

Donors, who are compensated for their time and effort, are recruited through advertising in local newspapers, Craig's List ads, social media, cultural groups, and word-of-mouth from previous donors. The coordinators perform the detailed due diligence required to ensure donor consent and safety, and to make sure the subjects' privacy is protected and they are known only as an anonymous number to the researchers. A staff phlebotomist draws the blood from the subjects and it is delivered within a few hours to the scientist's lab.

“One reason the Clinical Studies Core was created was to centralize this critically important sample collection program and make it easy and efficient for scientists to order what they need,” says Lei, who adds that she is a willing and eager donor herself. “This function previously was conducted by several of



Annie Lei spends most of her time on the phone recruiting and scheduling donors.

the labs themselves, so by taking it off their hands we're freeing up valuable time they can invest in their research and analysis.”

Lei's coordinator colleague, Alyssa Hill, says Clinical Studies Core serves another key role as an important link connecting the Institute and the community by providing individuals a unique opportunity to contribute to some of the most advanced immunological research in the world.

“We're grateful so many people are willing to become blood donors because they're crucial partners in our quest for knowledge about the immune system,” Hill says. “Many of them really enjoy knowing they're making a contribution to a scientific process that may not only help them or their family but so many others who suffer from disease.”

Their contributions—along with those of the scientists who study their blood—will soon begin to pay off.

“With the immune system at the core of so many diseases, and because we're finally beginning discover how it functions on multiple complex levels, we're confident that in the coming years the Institute's research efforts will lead to treatments that will stop many of these diseases in their tracks, and in some cases cure them,” Dr. Wilson says. “This vast potential for protecting and enhancing human health is why everyone at the Institute is so focused and energized by an objective that has the potential to help millions of people.” ●

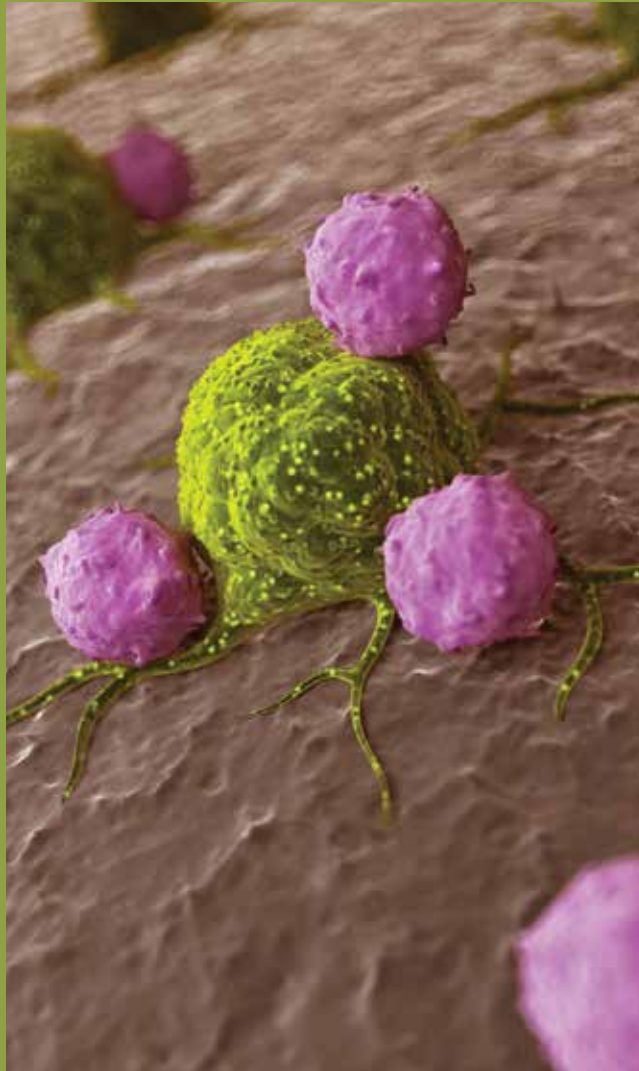
Grant Funds Personalized Cancer Immunotherapy Study

Stephen Schoenberger, Ph.D., a Professor at La Jolla Institute, and Ezra Cohen, M.D., a Professor at the UC San Diego School of Medicine, have been awarded a Clinic and Laboratory Integration Program (CLIP) Grant by the Cancer Research Institute (CRI), a non-profit organization dedicated to furthering the development of effective immune system-based cancer therapies.

The researchers will use the two-year, \$200,000 grant to study whether the immune system of patients suffering from head and neck squamous cell carcinoma (HNSCC) contains immune cells capable of launching an immune system attack directed at tumor cells and how to best increase their numbers and efficiency.

“The results of these studies will provide new insights and opportunities for the treatment of head and neck cancer and bring the possibility of adaptive cancer immunotherapy and personalized cancer vaccines a step closer to clinical reality,” says Dr. Cohen, Associate Director for Translational Science at the Moores Cancer Center at UC San Diego Health and an internationally recognized expert for novel cancer therapies.

Cancer immunotherapy stimulates the body’s immune system to help fight the cancer instead of directly targeting the tumors. CLIP grants, which are specifically designed to bridge the gap between the laboratory and clinical



T cells attacking a cancer cell.

efforts, support clinically relevant research projects aimed at bringing immune-based therapies to patients sooner.

As tumors travel down the path of malignant transformation, they accumulate collections of random mutations that result in tumor-specific proteins, also known as tumor-specific antigens, that the immune system can use to distinguish tumor cells from their normal counterparts. Many tumors, however, evade immune

surveillance by shutting down the very cells that try to fight them. They produce molecules that activate immune check-points—inhibitory switchboards that are hardwired into the immune system and are crucial to preventing autoimmunity.

The CRI-supported study will specifically explore the interplay between tumor-specific T cell responses and checkpoint blockade therapy in patients with head and neck squamous cell carcinoma enrolled in two ongoing clinical trials at Moores Cancer Center.

“Largely due to technological advances in next generation sequencing, a patient’s personal set of tumor-specific mutations can now be affordably and quickly characterized,” says Dr. Schoenberger. “We can then determine whether the patient’s immune system contains T cells capable of recognizing specific antigens expressed by their own tumors, and whether these increase in number or vary in specificity as a result of checkpoint blockade therapy.”

The ultimate goal is to be able to understand precisely how immune cells that can recognize and kill tumor cells in an individual arise and can be therapeutically enhanced. With this understanding, future treatments would use highly effective, patient-specific immunotherapy to fight a primary tumor as well as hunt down stray cancer cells before metastases can establish themselves. ●



Dirk Zajonc, Ph.D.

When Dirk Zajonc, Ph.D., an Associate Professor in the Division of Cell Biology, got a first glimpse of the complex enzymatic processes that tirelessly manufacture, modify, and recycle the molecular building blocks that keep our cells running smoothly, he was hooked. “Our bodies are like huge chemistry labs, where a lot of things are going on behind the scenes,” he says.

During his graduate work at the University of Erlangen-Nuremberg, Germany, he studied the biosynthesis of fatty acids, the main component of lipids. The body synthesizes fatty acids, which contain long tails of alternating carbon atoms, by adding tiny two-carbon molecules to the growing chain until it reaches its target length. “It takes a multi-component enzyme system, which is over 300,000 times the size of that building block to extend the carbon chain from two carbons to a maximum of 18,” says Dr. Zajonc. “It illustrates how complex and fascinating enzymatic processes in our body are.”

As his scientific career progressed, he combined his interest in lipid biology with the tools provided by structural biology and turned his focus on deciphering how lipids can activate the immune system in the right context.

Q&A

Structural immunologist Dirk Zajonc turns architecture’s famous credo of “form follows function” on its head: He determines a protein’s shape to help understand its function.

Q: How did you become interested in x-ray crystallography?

A: During my Ph.D., I studied the function of enzymes that are involved in lipid biosynthesis. Over time, I became interested in what those molecules actually look like and what we could potentially learn from knowing the shape of these proteins. That’s what brought me to San Diego. I joined the lab of Dr. Ian Wilson, a very famous structural biologist at The Scripps Research Institute, to learn protein crystallography.

Q: Can you explain how x-ray crystallography works?

A: When x-rays, which are electromagnetic waves, hit an object, they are scattered. More precisely, the electrons around the atoms diffract the x-rays. However, a single atom does not scatter the atoms enough to gain meaningful information from the diffraction pattern. In order to amplify the signal—similar to your stereo amplifier at home—you need to line up all proteins in the same orientation by coaxing highly purified proteins to grow into a crystal.

In a crystal everything is arranged in a symmetrical lattice that scatters x-rays and creates a distinct diffraction pattern. This procedure coined the term X-ray crystallography. From the intensity and position of the individual, diffracted x-rays and some knowledge about the protein that you are studying you can decipher

the 3D-structure using specialized computer software.

Q: X-ray crystallography has been around for more than a century. What has changed since the early days?

A: The technology has matured and you can determine the structure of bigger and more complex proteins. As a result, it has become more accessible to a wider circle of scientists. In most cases, it is now relatively easy to derive the 3D-structure from a diffracting crystal. Nowadays, the biggest challenge is obtaining diffracting crystals.

Q: After all these years, can protein crystallography still teach us anything new?

A: It is a technique like many others. What you learn does not depend on what technique you use but on what questions you ask and what experiments you perform to best answer those questions. Protein crystallography is very powerful when you want to know exactly how proteins bind to each other or how proteins of the immune system bind bits and pieces of an invading microbe. Using that atomic detail, you can work with synthetic chemists to design compounds that prevent a particular interaction to limit or prevent infection. As an example, Tamiflu®, which prevents the release of the flu virus from the host cell, was the direct result of this process, which is called structure-based drug design.



Dr. Dirk Zajonc

Q: What are the big scientific questions you are interested in?

A: In general terms, we want to use the structural information that we have obtained through our studies to custom-tailor the structure of a protein to a specific purpose. One project that we are really interested in is the structure-based engineering of a particular protein for biomarker discovery in different cancers. Cancer cells often display altered molecules on their surface. We know that in ovarian cancer a particular carbohydrate accumulates on the cell surface. We discovered a protein that recognizes and binds that carbohydrate. Using structure-based protein engineering, we can, hopefully, engineer the protein so it can distinguish slight differences between the

carbohydrates on healthy cells *versus* that of cancer cells. Specific binding probes that recognize cancer biomarkers are currently lacking and protein crystallography combined with protein engineering are the most powerful tools to get the job done.

Q: What was your most exciting finding?

A: On a personal level, it was growing my first protein crystal and obtaining my first diffraction pattern. Solving my first crystal structure came right after that—sometimes it is the little things that excite you the most. In the bigger scheme of things, it was the finding that had the most scientific impact. We discovered how a conserved T cell receptor can recognize a wide variety of glycolipids.

When you think about it in terms of a lock-and-key mechanism, the keys (the glycolipids) all look different but they all open the same lock, which is very strange. When the T cell receptor binds, it pushes the lipids and sugars around until they all in the same position—a lock that molds the key. That was quite surprising.

Q: What's the best part of being a scientist?

A: As long as you can convince others that your work is interesting and important—basically, as long as you can obtain funding—you can pursue any question you want. There is still so much to discover. It's really fascinating. ●



Photos courtesy of Lauren Nygard

The annual “Meet the Scientists” Day, co-sponsored by the La Jolla Institute and the Juvenile Diabetes Research Foundation’s San Diego chapter, brought together researchers and people with type 1 diabetes for a lively and educational event. Nearly 300 guests got to meet scientists and learn more about type 1 diabetes throughout the day, which was highlighted by laboratory tours, speakers, games, and other educational and fun activities. ●

Texas Oilman Channels Passion for Science into Advocating for La Jolla Institute



Hunt Pettit

After building a successful Texas oil and gas exploration company into a firm that is helping America become energy independent, Hunt Pettit is now focusing his own energy on an equally ambitious and important discovery process: finding new treatments and cures for humankind’s most serious diseases.

As one of the newest members of the La Jolla Institute Board of Directors, Pettit says he’s thrilled and honored to help what he calls “one of the finest immunological research organizations in the nation.”

“When I toured the Institute’s labs and heard the scientists describe their work, I could feel their tremendous passion and I could see how they’ve channeled that dedication into some of the most innovative and potentially life-altering research in the world,” Pettit says. “It was really exciting to learn that these remarkable researchers not only are discovering exactly how the immune system works, they’re taking that knowledge and creating new ways to treat disease that will someday soon lead to vaccines and other groundbreaking treatments for cancer, diabetes, and a host of infectious diseases.”

The Texas native has been involved with the organization since hearing an Institute presentation by Executive Vice President Stephen Wilson, Ph.D., at a Dallas business meeting.

Pettit’s passion for science was ignited when he was in college at Texas Tech University. “I actually majored in biology and chemistry, and a one point I thought I was going to medical school,” Pettit recalls. “I didn’t have the long-term mindset necessary for that, and I needed to go out and start earning a

living. But I’ve never lost my fascination for science, research, and understanding how things work.”

It turned out Pettit had a gift for discovery of another kind: energy. He got his start nearly 20 years ago as a “landman” responsible for acquiring the rights to subsurface minerals from landowners for the purpose of oil and gas exploration. In 2008, he started his own Fort Worth-based company, Energy & Exploration Partners, and built it into a highly successful operation. The 80-employee company explores and develops conventional and unconventional energy resources, such as oil shale.

His success has enabled Hunt and his wife, Laura, to become involved with a number of medical causes. After both lost parents to pancreatic cancer, they became major supporters of the Pancreatic Cancer Action Network. Laura also chairs the fundraising committee for Jewel Charity that benefits Cook Children’s Hospital in Fort Worth.

Pettit is eager to serve a similar function for the Institute, especially since he says the need for greater philanthropic support of the organization has never been more critical, given the steep decline in recent years of government funding for biomedical research.

“From the oil business I know just how challenging and expensive the process of exploration and discovery is and that’s why I’m a very vocal cheerleader for the La Jolla Institute,” Pettit says. “I really hope to make a difference in this world, and one way I can do that is make everyone aware that the La Jolla Institute is making fundamental strides in the way we think about and apply medical research. Once people realize just how important this work is to the future health of our species, I think the support for this outstanding Institute will really start to take off.” ●

Business Leader Views Involvement with the La Jolla Institute as His Most Important Investment

Larry Spitcaufsky has enjoyed one of the most varied business careers imaginable, having invested successfully in everything from banks, real estate, and convenience stores, to oil drilling, a national restaurant chain, and Kentucky thoroughbreds.

Yet it is the donation of his time and philanthropic resources as a new member of the La Jolla Institute Board of Directors that Spitcaufsky believes will be the most important investment of his life.

"I've had a great career and I'm proud to have had an impact in a number of areas, including on behalf of several non-profit organizations, but my involvement with the La Jolla Institute gives me a special opportunity to support one of the most remarkable scientific organizations in the world," Spitcaufsky says. "The research the Institute is conducting on the immune system is truly groundbreaking."

Ironically, Spitcaufsky initially passed on becoming a board member. He had been encouraged to consider joining by fellow Rancho Santa Fe, Calif., resident and Institute board member Fred Wasserman, Ph.D. Having been in the business world for more than 40 years, Spitcaufsky had served on boards of all kinds and at this stage of his career was not inclined to add one more to his busy schedule.

Spitcaufsky changed his mind almost immediately when he actually toured the Institute on a couple of occasions earlier this year.



Larry Spitcaufsky with his horse Boogey

"I had the privilege of meeting the scientists and I was amazed not only at the cutting-edge nature of their research but the real passion they show for their work," he says. "Having been involved with countless different businesses, I'm pretty good at picking up on the culture of an organization. The dedication, pride, and team approach I saw in the researchers really inspired me to want contribute to their effort."

Given his wealth of business, organizational, and financial expertise, there's no question Spitcaufsky will make a valuable

contribution to the board. Born in Kansas City, Mo., he left college early to join Arrow Truck Sales, a company co-founded by his father and which eventually grew to North America's leading source of pre-owned heavy-duty and medium-duty trucks. The company was sold to the Volvo Truck Corporation in 1998, by which time Spitcaufsky had also become majority owner of a small regional bank.

Over the past two decades, Spitcaufsky has expanded into wide-ranging investments, selling his chain of convenience stores to Circle K, investing in real estate, starting Petroleum Technologies Inc. to drill for oil and gas, and becoming majority owner of a chain of 16 Southern California restaurants. He also found time to breed and race thoroughbred racehorses in Lexington, Ky. and Del Mar, Calif. Spitcaufsky and his wife, Tiki, who moved to Rancho Santa Fe 10 years ago, have two sons and two grandchildren.

"I'm at the point in my career where I want to do something that helps as many people as possible," Spitcaufsky says. "That's why I'm so excited about the Institute. The progress they're making in understanding disease has the potential to help everyone on the planet. For a mostly self-educated boy from Missouri, it doesn't get any bigger than that." ●

Visit our website
at www.lji.org
for the latest news
and updates.

About La Jolla Institute for Allergy and Immunology

■ **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*.

■ **SCIENTIFIC PRODUCTIVITY:** 22 faculty investigators and 145 postdoctoral fellows have published over 2,000 scholarly papers in prestigious scientific journals since 1988. Numerous patents (and patents pending) have been filed for discoveries designed to yield revolutionary clinical applications.

■ **ACCOLADES:** Ranked #5 in the world in scientific impact in immunology. In 2013, ranked #1 in the “Best Places to Work in Academia” and #2 in the “Best Places to Work for Postdoctoral Researchers” in the annual survey of research institutions throughout the world, conducted by *The Scientist* magazine.

 For regular updates, “like” us on Facebook at www.facebook.com/LifeWithoutDisease

