

# Immune Matters

WINTER 2015-16



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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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## Letter from the President

I recently looked at the number of La Jolla Institute faculty involved in cancer research and saw that at least a dozen scientists—or half of our principal investigators—are partially or fully engaged in studying cancer as it relates to the immune system.



I'm actually not surprised by that figure. In recent years, cancer immunotherapy has become one of the hottest trends in biomedical research, thanks to many years of intensive basic research conducted in labs like ours, along with equally important advances in genetic engineering.

That the field of immunology would step to the forefront of cancer research just makes sense. What better way to battle this disease than to use the immune system as the engine to attack cancer at the molecular level?

What's really exciting is that compared with the traditional techniques of surgery, radiation, and chemotherapy, which for many cancers have failed to keep the disease at bay, cancer immunotherapy offers us a chance to create treatments and potential cures that will soon begin to extend and save millions of lives around the world. In this issue of *Immune Matters*, you'll meet a number of our scientists engaged in this battle and learn how their remarkable research is on the leading edge of this revolution.

Future scientific careers and the important educational and training mission of the Institute are the subject of another article and we are proud of the role our robust internship program plays in providing young people an entrée into the world of science. I remember a local high school student named Rachel Cotton who was excited to intern in my lab a few years ago. I'm thrilled to report Rachel went on to Notre Dame for her undergraduate degree in biology, and is now at Harvard pursuing a Ph.D. in immunology in an area related to the research she was exposed to in my lab that summer.

In our Q&A section, we explore the work of Chris Benedict, Ph.D., Associate Professor in the Division of Molecular Immunology. Chris' fascinating research focuses on the role that signaling by TNF-related cytokines plays in antiviral defense, and what viruses do in turn to counteract these cytokines.

Finally, I think you'll enjoy the profile of our newest board member, Richard S. Bodman. Dick, who is one of the smartest and most capable individuals I've ever met, is a true triple treat, having high-level experience in industry, government, and science. We are looking forward to drawing heavily on Dick's background and skills to help lead the Institute.

Reading about all of the subjects in this issue of *Immune Matters* will give you a strong sense of the caliber and capabilities of those who are associated with the Institute. They, along with our valued group of partners—including individual donors, foundations, and federal funding sources—are all working toward a common goal: supporting and furthering the critical research we believe one day will lead to *life without disease*.

Sincerely,

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

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



# The Promise of Immunotherapy

*LJI researchers call on the body's own defenses to attack cancer*

Dr. Ezra Cohen and  
Dr. Stephen Schoenberger

Cancer has been inextricably linked with people's lives since the dawn of humanity resulting in pain, suffering, and ultimately cutting short the lives of many. And despite billions spent to combat it, the "Emperor of All Maladies," as one author recently called it, still looms large.

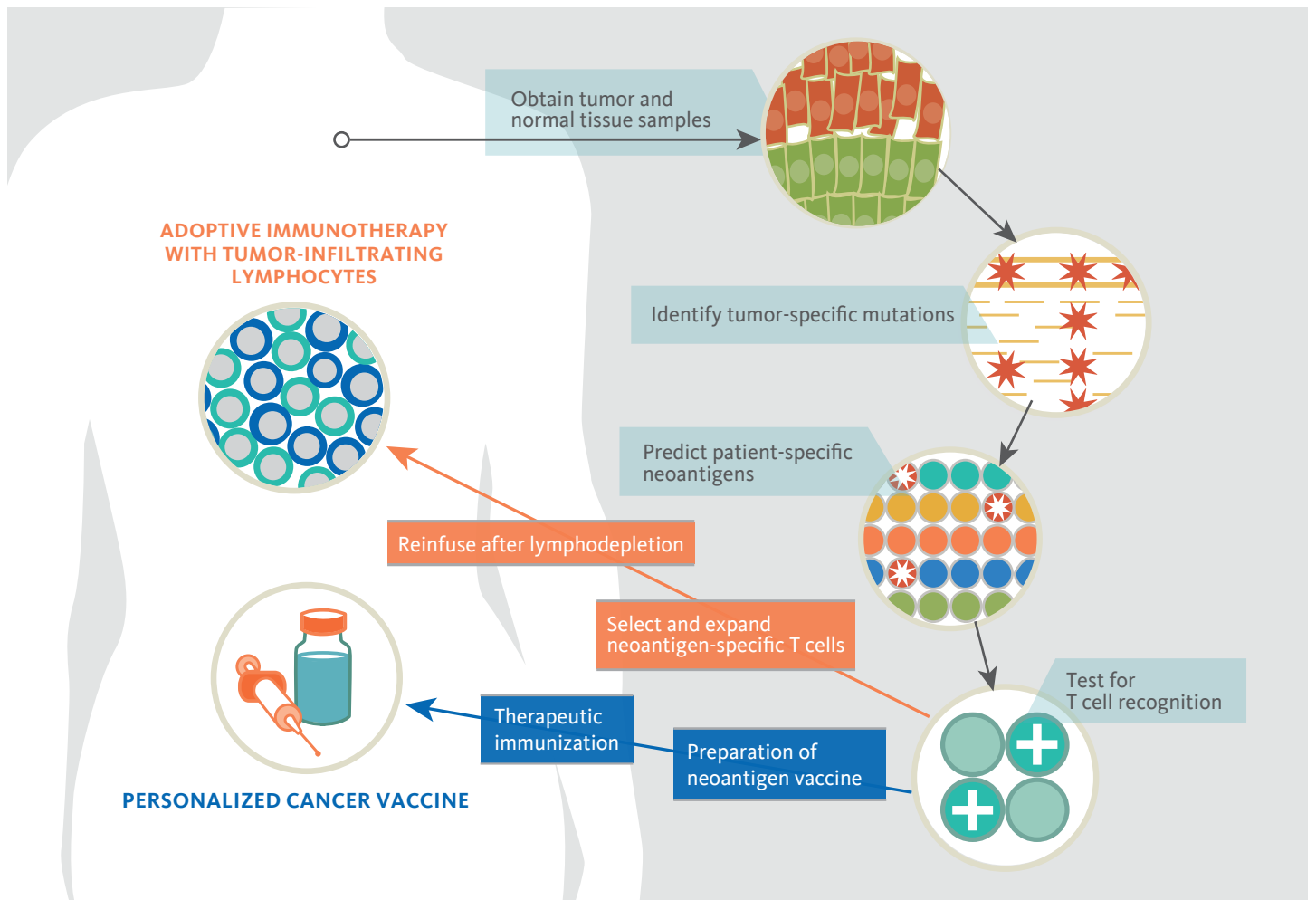
But, as amazing as it may seem, an effective new strategy is pushing back against cancer's reign of terror. The potent weapon that has begun to fight the disease is cancer immunotherapy. A sizable army of scientists around the world, including a number of groundbreaking researchers at the La Jolla Institute (LJI), are mobilizing the power of the body's own immune system to attack the disease.

"Thanks to recent and rapid advances in cancer immunotherapy, we've just entered one of the most exciting periods in the 26-year history of our Institute," says Mitchell Kronenberg, Ph.D., LJI President and Chief Scientific Officer.

"The painstaking basic research we've done to learn how the immune system works is about to pay some major dividends in the form of therapies that will complement surgery, radiation, and chemotherapy to produce more effective methods to extend and save the lives of cancer patients, and with far fewer debilitating side effects."

Actually, cancer immunotherapy doesn't rely on just one method, but a number of different approaches to attack the disease on several molecular fronts. Whether they employ "designer" T lymphocytes engineered to specifically kill tumor cells, genetically engineered therapeutic vaccines, or monoclonal antibodies to prevent the action of the immune system's "brakes" (so-called checkpoint blockers) or to attack cancer cells directly, these techniques are designed to boost the immune system's ability to recognize and kill cancer cells. This multi-pronged approach is critical because

*continued on page 4*



cancer is probably the most challenging and subversive disease biomedical researchers will ever face, according to Amnon Altman, Ph.D., Director of Scientific Affairs.

“Unlike infectious bacteria, viruses, or other pathogens that invade the body from the outside and are usually easily recognized as being foreign by the immune system, cancer cells arise from your body’s own cells, which makes it harder for the immune system to distinguish them and mount an effective response,” Dr. Altman says. “Combine that with the fact that tumor cells are constantly mutating, are prone to spread throughout the body, and often demonstrate a remarkable ability to actually switch off the body’s immune response, and it’s easy to see why cancer has been such an intractable disease.”

One of the most fascinating and innovative immunotherapy approaches at the Institute—and one LJI Professor Stephen Schoenberger, Ph.D., believes could soon begin saving the lives of head and neck cancer patients—uses a new type of personalized approach, based on targeting an individual patient’s tumor-specific mutations, to seek out and kill cancer cells through a process known as neoantigen-specific immunotherapy. This precision-medicine strategy can attack

existing tumors as well as provide future protection against their recurrence and is specific for a given patient’s tumor and immune system.

Dr. Schoenberger’s approach hopefully will soon yield important results, though it has been far from an overnight success. It came only after this internationally recognized immunologist invested nearly two decades of intensive research into the mechanisms that govern the immune system’s T cells, a type of white blood cell that circulates throughout our body searching for and eliminating cellular abnormalities and infections.

“My feeling over all these years has been that if we could learn the basic rules that control the behavior of T cells, especially how CD4+ helper T cells assist the function of CD8+ cytotoxic killer T cells, we could take that knowledge, combine it with the huge advances in genomic science, and actually train the immune system to attack and destroy cancer cells,” Dr. Schoenberger says.

That’s exactly what Schoenberger and his team are doing, and here’s how he has taken his unique insight into T cell behavior and translated it into a powerful weapon: First, a tissue sample is taken from the patient’s tumor and its DNA

sequenced to identify tumor-specific mutations or changes in the DNA. Some of these may be fueling the cancer cells' unbridled growth, but other so-called passenger mutations may simply be the result of errors in replication of the genes due to rapid cell growth. Both types of mutations are then tested against a patient's own T cells to identify which ones are recognized. These "neoantigens" then form the basis of either a personalized cancer vaccine, or can be used to expand a patient's tumor-specific T cells into a highly focused army of killer cells that can be returned to the patient in large numbers.

If the process successfully duplicates what has already been shown in mice, these tumor-infiltrating lymphocytes will multiply, recognize, and destroy cancer cells throughout the patient's body for many years. [See infographic on opposite page]

Dr. Schoenberger, who is collaborating closely with noted cancer researcher Ezra Cohen, M.D., at UC San Diego's Moores Cancer Center, to bring the novel therapy to the clinic, says the approach will be attempted in humans for the first time next summer. Because these patients have recurring metastatic head and neck cancers with few treatment options and therefore face a grim prognosis, Dr. Schoenberger says he has never been more excited, hopeful—and anxious—about how his approach will perform.

"One is always cautious, but because our research is scientifically sound, I'm hopeful that within a relatively short time, maybe one to three months, we should see these patients' tumors begin to recede and actually disappear in some cases," Dr. Schoenberger says. "If that



Dr. Michael Croft

happens, we will have provided patients who were almost certainly facing death the opportunity to live longer and quite possibly survive their disease completely. I can't think of anything more satisfying to work towards."

If Dr. Schoenberger's work is an example of a scientist starting with basic research and then following that path through to translation to actual patients, there are other scientists at the Institute whose groundbreaking investigation serves as the foundation for others around the scientific world to build upon.

Michael Croft, Ph.D., who heads the Institute's Division of Immune Regulation, is just such a scientist. He and his research team study protein molecules that are members of the tumor necrosis factor (TNF) and tumor necrosis factor receptor (TNFR) family. In particular, Dr. Croft is one of the leading experts on the molecules 4-1BB and OX40, key players in how the body's immune system responds to disease. Stimulatory antibodies to 4-1BB and OX40, which promote the activities of T cells and other tumor fighting cells known as NK cells, are currently in clinical trials for several types of cancer. Parts of these

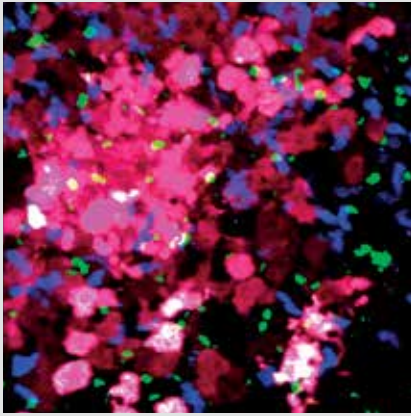
molecules are also being used in other clinical trials to help enhance the ability of adoptive T cell transfer immunotherapy to work and eliminate cancer cells.

Interestingly, Dr. Croft himself is not a cancer researcher—he's a top immunologist studying inflammatory diseases like asthma, multiple sclerosis, and diabetes—but his work applies to cancer as well.

"My approach to the immune system is that if you can understand what controls T cells, you've got an excellent chance to understand how it can be modulated to attack a number of different diseases, including cancer," Dr. Croft says. "Fortunately, we've succeeded in revealing some of the basic mechanisms that regulate how T cells respond and they're proving useful to cancer researchers in other labs."

Dr. Croft is being somewhat modest. He and his team actually discovered how membrane-bound co-stimulatory protein molecules signal T cells to proliferate in numbers, which in turn dramatically increases the T cells' killing power when they launch an assault on infected or abnormal cells. For his own research, Dr. Croft is interested in how to actually

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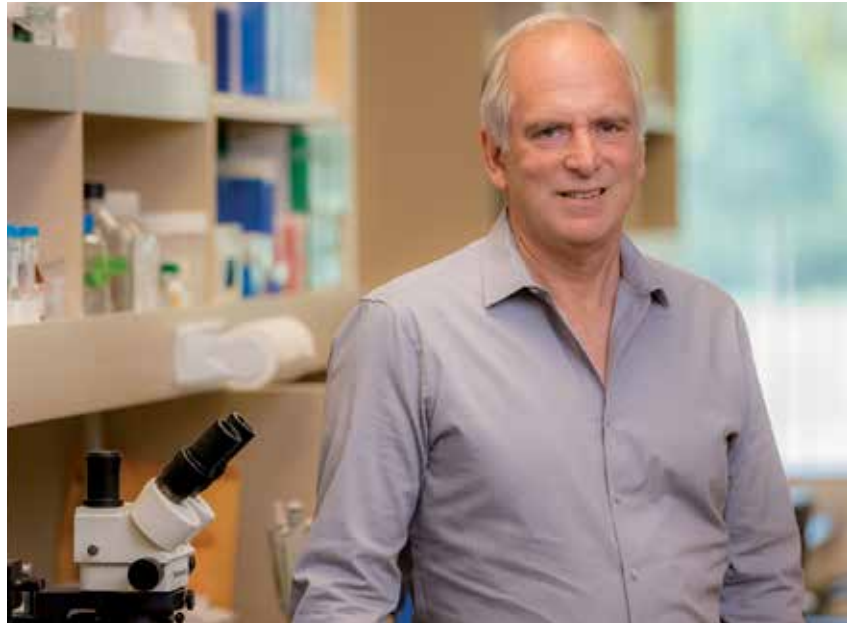
## Unexpected Finding Leads Institute Scientist to Discover Potential Therapy for Metastatic Lung Cancer

Two years ago, Richard Hanna, Ph.D., experienced a moment in the lab most scientists can only dream of. After injecting a mouse with a new form of monocyte (white blood cell) therapy, he made an unexpected observation:

“At first, it was a little hard to believe what I was seeing, but you could quite clearly see the monocytes attacking and destroying cancer cells in the blood vessels”, says Dr. Hanna, a researcher in the lab of Principal Investigator Catherine “Lynn” Hedrick, Ph.D. “I knew if this could be proven, it had tremendous implications for treating metastatic cancers.”

Flash forward to the present: Dr. Hanna not only was able to prove that monocyte therapy is a bona fide cancer killer, he and Dr. Hedrick just published a major paper summarizing their findings in the journal *Science*. Most importantly, the therapy has the potential to enter human clinical trials in the next few years, and if everything goes as the two scientists hope, a powerful new treatment to extend and possibly save the lives of patients with metastatic lung cancer may emerge.

“Since I’ve always tried to work on research projects I believe have the potential to be translated into the clinic, seeing this new therapy actually benefit real patients would be one of the highlights of my career,” Dr. Hanna says.



Dr. Joel Linden

dampen that strong immune response rather than encourage it, since uncontrolled T cell responses can trigger autoimmune and allergic disease. But he understands why cancer researchers are excited to go the other direction and use the research to mold T cells into tumor-fighting machines.

“I have to say I’ve been pleased and fascinated to see how cancer scientists have taken our research and run with it,” Dr. Croft says. “A number of pharmaceutical companies are testing approaches that can not only build armies of T cells, but train them to specifically target a patient’s tumor. From a scientific standpoint, that’s fantastic, and we’re really proud to have played a role in a new and important era in cancer immunotherapy that fairly soon should lead to much more effective treatments for patients.”

Another groundbreaking approach, led by Joel Linden, Ph.D., in the Institute’s Division of Developmental Immunology, strikes at cancer’s ability to suppress the immune system.

“Tumors often don’t trigger much of an immune response because they’re made up of your own cells,” Dr. Linden says. “But another problem is that tumors produce immunosuppressive molecules. One important such molecule is called adenosine. It accumulates at high concentrations in tumors and can actually shut off the immune system, leaving tumors to grow unchallenged.”

A pharmacologist by training, Dr. Linden’s goal was to unravel how adenosine inhibits immune cells and then test a number of experimental blocking compounds as well as strategies for locally delivering high concentrations of blockers into solid tumors. Neutralizing adenosine should free up the immune system to more effectively kill cancer cells in the tumor environment. Within the past few years, Dr. Linden’s team has begun to record what can only be called astounding results.

“Once we found a way to effectively block adenosine’s immunosuppressive effect within tumors, it unleashed such a powerful immune response in mice that we began to see melanomas shrink and in some cases disappear entirely,” Dr. Linden says. “But that wasn’t the only effect. The T cells were also able to track down and destroy cancer cells anywhere in the mouse, which means the therapy could be invaluable in treating metastatic cancer. Importantly, T cells

## Institute Scientists Attacking Cancer on Multiple Fronts

*More than a dozen principal investigators at the La Jolla Institute focus some or all of their research on understanding the role the immune system plays in cancer. Here's a look at several of their projects.*

developed long-term anti-tumor memory. When we re-introduced the same tumors into surviving mice months later, the immune system remembered and went to work and wiped out the tumors in exactly the same way. It is immune memory that distinguishes immunotherapy from other types of treatments focused on direct killing of tumor cells.”

In early 2016, several companies will begin clinical trials based on blocking adenosine signaling in tumors, and while he knows that outstanding results in mice don't always translate to success in humans, he's confident his research will not only be confirmed in the clinic, but eventually will be expanded to treat a number of different cancers.

“Until recently, progress against cancer has been very slow, but the remarkable advances in immunotherapy may be a real game changer,” Dr. Linden says. “The truth is that I wouldn't be surprised if cancer immunotherapy in combination with other approaches like Dr. Schoenberger's substantially increased cancer cure rates over the next several years.”

As Dr. Schoenberger waits for the results of his own human studies, he couldn't agree more with his colleague's assessment.

“All of us here at the Institute want our research to come to fruition as soon as possible because we hate seeing this terrible disease destroy productive lives far too soon and far too often,” he says. “If our therapies work as we believe they will, the opportunity to expand the power of the immune system to treat and cure many types of cancer makes our work even more thrilling. We're at a unique moment in time where immunology, with its sophisticated arsenal of new weapons, has emerged as the leader in offering biomedical science's greatest hope for waging a truly effective and lasting assault on cancer.” ●

### TET TUMOR SUPPRESSORS PLAY KEY ROLE IN CANCER

**Dr. Anjana Rao's** lab studies how proteins in the cell nucleus respond to signals from outside the cell and control gene expression. Through the use of high-throughput sequencing and other technologies, Dr. Rao is revealing how specific genes are regulated and how the TET family of tumor suppressors, which were discovered in her lab, prevent cancer and autoimmune disease.

### X-RAY CRYSTALLOGRAPHY AND EARLY CANCER DETECTION

**Dirk Zajonc, Ph.D.**, Associate Professor in the Division of Cell Biology, is a pioneer in using x-ray crystallography and protein engineering to probe the 3D shape and function of complex proteins. He uses this information to generate tools so sensitive his team can compare molecular changes on the surfaces of malignant cells to their healthy counterparts. If successfully applied to tissue samples or in patients, Dr. Zajonc believes these tools will be able to detect ovarian cancer and possibly other types of cancer at a much earlier stage.

### TAKING THE BRAKES OFF T CELLS TO BOOST IMMUNE RESPONSE TO CANCER

**Amnon Altman, Ph.D.**, Director, Scientific Affairs, Head of the Division of Cellular Biology, studies the biochemical changes that occur in T cells when they encounter cancer cells. He has identified an enzyme called protein kinase C-eta (PKC $\eta$ ), which is essential for the suppressive function of regulatory T (Treg) cells, a subset of T lymphocytes that inhibit immune responses. More specifically, Dr. Altman is searching for ways to block this enzyme to enhance the body's immune response against cancer and other diseases.

### REPROGRAMMING T LYMPHOCYTES

**Hilde Cheroutre, Ph.D.**, Division Head and Professor, Division of Developmental Immunology, is a leading researcher into the function of T cells, and in particular, cytotoxic T cells that have the ability to attack and eliminate cancer cells. The latter could lead to the development of therapeutic anti-cancer therapies. One of Dr. Cheroutre's major discoveries is a network of transcription factors (Runx family) that govern the reprogramming of CD4 T helper cells to cytotoxic T cells, which can function as potent cancer-fighting immune cells.

### BOOSTING THE INNATE IMMUNE SYSTEM'S ABILITY TO TARGET TUMORS

**Sonia Sharma, Ph.D.**, was recently awarded a five-year \$1.1 million grant from the National Cancer Institute to study how the body's innate immune system recognizes and is stimulated by genomic DNA released by damaged or dying tumor cells. She is specifically looking at how the vascular endothelial cells that line blood vessels may be capable of promoting active and long-lasting innate immunity against highly vascularized tumors, including those found in lung cancer and melanoma.



Sujan Shresta, Ph.D., Rajvir Grewal, Edward Vizcarra

## Institute Interns Gain Skills and Motivation to Join Next Generation of Research Scientists

**T**hey come to La Jolla Institute young, wide-eyed and eager to explore one of the most outstanding research environments in the world. A few months later, they return to high school or college, equipped with invaluable lab skills, insight into how the scientific process works and, quite often, the confidence and desire to become groundbreaking biomedical researchers themselves.

These are the interns who each summer are invited into the labs at La Jolla Institute to assist with leading-edge research on the immune system, and autoimmune and inflammatory diseases such as diabetes, arthritis, cancer, and asthma.

“I feel so lucky to have been an intern because it was definitely one of the most fascinating and valuable experiences of my life,” says Veronica Romines, who interned in Dr. Lynn Hedrick’s lab after her junior year in high school. “I learned things I could never get in a classroom. I came in with a basic knowledge of biology, but the Institute gave me a true understanding of how everything in our bodies functions as a whole system rather than different parts. I’m now 100 percent sure I want to have a career in science or medicine.”

Romines’ experience is exactly what the Institute seeks with its internship program, according to Sujan Shresta, Ph.D., one of the world’s leading researchers of infectious diseases, including dengue fever.

“We love having interns in the lab,” Dr. Shresta says. “Their young energy and curiosity uplifts the entire lab atmosphere. It’s really fun to see their excitement as they learn what it is to be a scientist and hopefully use that knowledge to someday become researchers themselves.”

From a practical standpoint, Shresta says, the internship program is also invaluable to the Institute.

“Most of our experiments are highly labor intensive, so we couldn’t function without interns,” she says. “There’s an added benefit that our postdocs gain important mentoring experience. In training the interns my postdocs are challenged to think critically about the fundamental questions underlying their work, and that benefits everyone.”

One former intern who can attest to the benefits of the program is Victor Pontis, who credits his internship five years ago in Dr. Patrick Hogan’s lab for influencing both his educational and career paths.

“I just graduated from MIT with a degree in computer science and physics, and I studied computational biology in part because of my experience at the Institute,” Pontis says. “What I observed in the lab has also been helpful in my first job out of college. I work for Benchling and we make an electronic lab notebook that enables life scientists to keep track of their research and more easily collaborate with their colleagues.”





Veronica Romines

“I learned things I could never get in a classroom. I came in with a basic knowledge of biology, but the Institute gave me a true understanding of how everything in our bodies functions as a whole system rather than different parts. I’m now 100 percent sure I want to have a career in science or medicine.” – Veronica Romines

Among Pontis’ most positive memories of his time at the Institute were the high level of work he was allowed to do, and how his colleagues treated him.

“I was trained how to do actual technician’s work, like gel electrophoresis, which is a method for separating and analyzing DNA,” Pontis says. “And, even though I was really young and inexperienced, it was awesome how willing they were to accept me as a co-worker and not dumb things down just because I was a high school student.”

Edward Vizcarra had a similar experience when he interned with Dr. Shresta in 2014 just before graduating from UC San Diego.

“I had worked in other labs, but I found the Institute one of the most welcoming places to be an intern,” Vizcarra says. “They encouraged me to ask questions, and I asked a lot of them. The Institute also got me really interested in infectious disease research. It’s such a problem, especially in underdeveloped countries, and seeing how hard the Institute is working to solve it has inspired me to go down a similar career path as a research scientist.”

Rajvir Grewal felt similarly inspired when she interned in the same lab a year ago as she worked on her masters in bioinformatics at San Diego State University. One of the sources of that inspiration was the dedication she observed in the researchers.

“I was so impressed with the scientists I got to work with,” Grewal says. “They’re not only brilliant and innovative, I could see that they had a real passion for their

work and accomplished something important with their discoveries.”

Grewal says she achieved two key personal goals with her internship: She wanted to study with Dr. Shresta because of the researcher’s groundbreaking work in studying dengue fever, and she wanted to gain practical biomedical research skills to go with what she’s learned in the more data-driven computational biology.

“I’m from India and my dad got dengue fever a few years ago,” Grewal says. “He came through it okay, but I saw some really bad scenes at the hospital with so many people suffering from the disease. What I learned at the Institute by working on actual experiments has rounded out my knowledge and skills. I now feel confident I have all the tools I need to assist in developing the kind of next generation technologies I hope will significantly increase the speed and effectiveness of research into dengue and other infectious diseases.”

Both Grewal and Vizcarra ended up being hired at the Institute as full-time lab technicians in Dr. Shresta’s lab following their internships. In the year since, they’ve drawn attention for their skills and creativity, most notably after they joined forces to enter and win an internal Institute research competition last March.

Their proposal, chosen the best among 14 submissions, earned them a special lunch with Mitchell Kronenberg, Ph.D., Institute President and Chief Scientific

Officer, and the green light to actually conduct the research with the help of the Institute’s Center for Functional Genomics. The project utilizes genome-wide screening to study the molecular mechanisms that regulate how the dengue virus infects human cells.

Vizcarra says the seeds for the winning proposal were planted during his internship.

“I owe a tremendous amount to those two months I interned at the Institute,” he says. “I was able to observe some of the best scientists in the world engaged in using revolutionary experiments to attack one of the world’s worst infectious diseases. I really believe it’s helped shape me into a better scientist and motivated me to work harder so I can fulfill my dream of someday having the same kind of impact on research in this important field.” ●



Victor Pontis



Dr. Chris Benedict and his wife Grace

# Q&A

The origin of the arms race between viruses and the immune system reaches back eons. Chris Benedict investigates how the warring factions try to gain the upper hand.

*As a scientist Chris Benedict, Ph.D., came of age during the heyday of gene therapy. But when the first clinical trials failed, the initial excitement quickly faded and gene therapy fell off the cliff. “I did my Ph.D. during that window,” remembers Benedict, Associate Professor in the Division of Immune Regulation, who was working on retroviral vector gene therapy at the time. “I started when gene therapy was red hot and I finished when gene therapy was almost dead, although it may be resurrected with newer technologies.”*

*After completing his Ph.D., Benedict was still very much interested in viruses but decided to take two steps back and change perspective. Instead of trying to engineer viruses to stay under the radar of the immune system while slipping their therapeutic payload into cells, he became interested in the continually evolving power balance between the immune system and viruses trying to gain a foothold in our body. He uncovered several important mechanisms that allow viruses to evade the immune system and identified a subset of immune cells that keep cytomegalovirus, a rarely mentioned member of the herpes virus family, at bay.*

**Q:** What sparked your interest in science?

**A:** The Science Olympiad was paradigm-shifting for me. I got involved when I was in high school and our team made it to a couple of the Nationals. One year we built a catapult that we launched to hit a pin over 30 feet away and we hit the pin. That was the moment when I got excited about the idea of maybe majoring in science. I always had a bit of a competitive edge in me—I was a tennis player and on a tennis scholarship—and when we put the Science Olympiad competition together it struck a chord with me and for the first time I could see myself as a scientist.

**Q:** What is the overarching interest that drives your research?

**A:** My research program has two distinct aspects: What can we learn from how cytomegalovirus (CMV) thwarts our immune system? Can we use the information to develop drugs? CMV is very efficient in inhibiting our immune system. What if we could employ the same principles in treating arthritis or lupus? The second aspect is: How can we help people who are really affected by CMV?

**Q:** Why CMV? It seems to be a rather obscure virus.

**A:** CMV is actually the No. 1 infectious cause of congenital birth defects in the world. Half of the population in the U.S. has been infected with CMV and infected individuals will carry the virus for the rest of their lives. In most people it doesn't cause any symptoms and you wouldn't even know that you've been infected. But when babies are infected in the womb it can cause severe birth defects such as hearing loss, brain damage, and even death. The virus can also be reactivated in immune-suppressed people and it is a big concern in transplant recipients. Fifty percent of late stage AIDS patients go blind from CMV-induced retinitis.



Left: Dr. Chris Benedict and his son Cole. Right: Members of the Benedict lab.



“Every discovery shows you what more you don't know. That aspect of the job is really exciting to me.”

— CHRIS BENEDICT

**Q:** Why can't our immune system fight off the virus?

**A:** CMV and other members of the herpes virus family have a lot of tricks up their sleeve. CMV dedicates more than half of its large genome to throw up a smokescreen for the immune system. Its genome or genetic material is nearly 20 times bigger than influenza virus, and therefore, it has enough room to incorporate genes it has stolen from its hosts over time. We found that one of them is a TNF-receptor-like molecule, a molecule important for immune cell communication. This was really an important moment for me. Here's a virus that has been evolving with us and took some of our immune system genes, molding and shaping them to establish a détente with the immune system. As a result it can hang around and never gets cleared. There is a lot of information we can glean from studying CMV.

**Q:** Which aspect of being a scientist to you enjoy the most?

**A:** The best part is the puzzle. The puzzle is never solved. I am a person who is easily distracted or gets bored if I don't have a new challenge to work on. Every discovery shows you what more you don't know. That aspect of the job is really exciting for me. There's also an altruistic aspect to it in that I really would like to help develop a CMV vaccine,

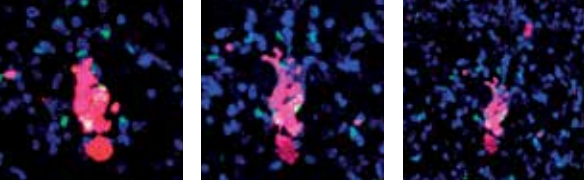
especially in the context of congenital CMV infection.

**Q:** What's your advice to the next generation of scientists?

**A:** Embrace the frustration. Any scientist who is successful will tell you that things go in ebbs and flows. Scientific progress is the sum total of a lot of slow processes, which, over time, leads to an Aha! moment—if you are lucky. To get there, you have to push through many failures and you have to be able to embrace that. You have to tell yourself that you are working on the cutting edge of knowledge and it is not going to be easy.

**Q:** How do you get out of a rut?

**A:** When I hit a roadblock, I push really hard and then I push some more. If I still don't get anywhere, I back off, try to clear my mind and come back with a fresh point of view. These are hard questions and sometimes you can't just power through it. To give myself a break I play soccer or tennis with my son or go surfing. I just bought a bike to get my stress out. I've always been a firm believer that it is very important to have interests outside the lab, to read widely, and to spend time with the family. Having that kind of balance has always allowed me to refresh my mind and come back and solve problems. ●



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Pillsbury Winthrop Shaw Pittman LLP

Mr. and Mrs. Larry Spitcaufsky

Fred and Pamela Wasserman

**\$10,000 - \$24,999**

Claire and Amnon Altman

The Bell Charitable Foundation

BioMed Realty Trust, Inc.

John and Pamela Blakely

Richard S. and Karna S. Bodman

Skip and Terri Carpowich

Celgene Corporation

Michael and Linda Croft

Barbara Donnell & Scott Markus

Patricia A. Elam

Mr. and Mrs. Mark A. Fischer

Willis & Jane Fletcher Family Fund II  
at The San Diego Foundation by  
Mary E. Harker

Dr. and Mrs. Nabil Hanna

Mr. and Mrs. Patrick H. Ho

International Oncology Network

Kurz Family Foundation, Ltd.

Marshall D. Lees

Dr. Klaus Ley and Dr. Catherine Hedrick

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Family Fund of The Seattle Foundation

The Senyei Family Foundation

Jocelyn and Dick Vortmann

David and Lila Webb

Herbert Wertheim, OD, D.Sc.

Stephen Wilson, Ph.D.

Timothy J. & Cynthia K. Wollaeger

Walter J. and Betty C. Zable Foundation

“Over the years many of my friends, including a number with challenging health issues, have counted on me to keep up with advances in medical science. That’s why I’m so excited about the research at the La Jolla Institute on the immune system. It’s the one system that has the critically important role of keeping us healthy and disease free, and the Institute is learning what happens when that system is overactive or not active enough. It’s fascinating when Dr. Steve Wilson says in his talks at the Institute that there’s no reason that people with a healthy immune system shouldn’t live in good health to the age of 125. Now that’s something to get excited about!”



**Linda Masters**

*President’s Council member,  
Institute Ambassador, and donor*

**\$5,000 - \$9,999**

Mr. and Mrs. Steven R. Altman  
 BIOCUM  
 CONNECT  
 Dendreon Corporation  
 Bob and Ann Dynes Charitable Fund  
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 Arthur J. Gallagher & Co.  
 Stephen J. Galli, M.D.  
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 LaVerne and Blaine Briggs  
 Mr. and Mrs. Harold G. Buchanan II  
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 Drs. Shu and K.C. Chien

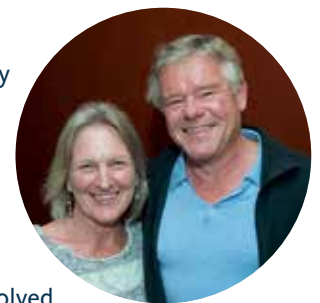
Kenneth and Adriane Coveney  
 Shane and Anna Crotty  
 Derry and Lois Eynon  
 In Honor of Dori Fettu  
 iGive.com Holdings LLC  
 James Isaacs  
 Justin and Rachel Jonte  
 Katina Tsakopoulos Investment  
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 Elliott Lasser  
 Dr. and Mrs. Richard S. Levy  
 Morag Mackay  
 Toshihiko Maruoka  
 Meyer Pharmaceuticals, LLC  
 Mr. and Mrs. Paul Mirabella  
 Dave Mitchell and Judy Bradley  
 Moss Adams LLP  
 Mr. and Mrs. Frederick T. Muto

“There are several reasons we’ve been eager to donate to the La Jolla Institute, but the most personal is that we have a son who came down with type 1 diabetes four years ago at age 20. We’ve watched with growing concern as this horrible disease has become a national epidemic, so we were thrilled when we learned that the Institute is not only deeply engaged in studying diabetes, but is a world leader in this critical area of biomedical research. We love what the Institute stands for and we couldn’t be more pleased to support such a brilliant and hardworking group of scientists who are so clearly dedicated to helping people through their groundbreaking research.”

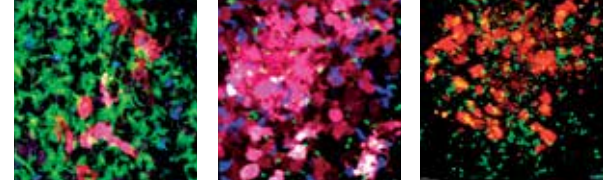
**Rachel Perlmutter**

*who along with husband Robert, is a La Jolla Institute donor*

“After attending a couple of fascinating lectures given by some very enthusiastic and knowledgeable Institute scientists, my husband and I quickly realized this was an organization we wanted to become more deeply involved with. Personally, I love science and I was trained as a nurse, so I’ve always enjoyed observing breakthroughs in medical research. What’s so exciting about the Institute is that they’re on a really promising path that combines immunology and genetics to get at the root causes of so many diseases. The Institute represents the future of medicine and we’re proud to support it in any way we can.”

**Raydene St. Clair**

*who along with husband Peter, is a La Jolla Institute donor*



**\$2,500 - \$4,999 continued...**

Dr. Walter K. Nishioka  
 Rachel and Robert Perlmutter  
 The William R. and Mary Jane Rohn  
 Family Foundation  
 La Jolla Golden Triangle Rotary  
 Club Foundation  
 Dr. Sujan Shresta and  
 Dr. Olivier Laurent  
 SIGA Technologies, Inc.  
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 Barbara Woodbury  
 Junji Yodoi, M.D., Ph.D.  
 Mr. Lawrence Zynda

“My involvement with the Institute over the past seven years has been one of the most rewarding experiences of my life. My daughter has type 1 diabetes, so I first became involved with the Juvenile Diabetes Research Foundation, which led me to meet a number of the Institute’s researchers, including Dr. Matthias von Herrath. I’ve been in a lot of labs, but I’ve never seen a more remarkable combination of incredible scientific skills and passion for discovery than I see at the Institute. Matthias is a great example. He was recently named the world’s number one expert on diabetes, but he also happens to be a great human being driven to make sure his research helps actual patients take care of or cure their diabetes. I know there are important breakthroughs coming in diabetes research and I truly believe many of them are going to come out of the La Jolla Institute.”



**Barbara Donnell**

*President’s Council member, Institute Ambassador, and donor*

*The information listed above represents contributions as of Oct. 30, 2015.*

## Former AT&T Executive Believes Institute is Poised for Historic Strides in Immunology

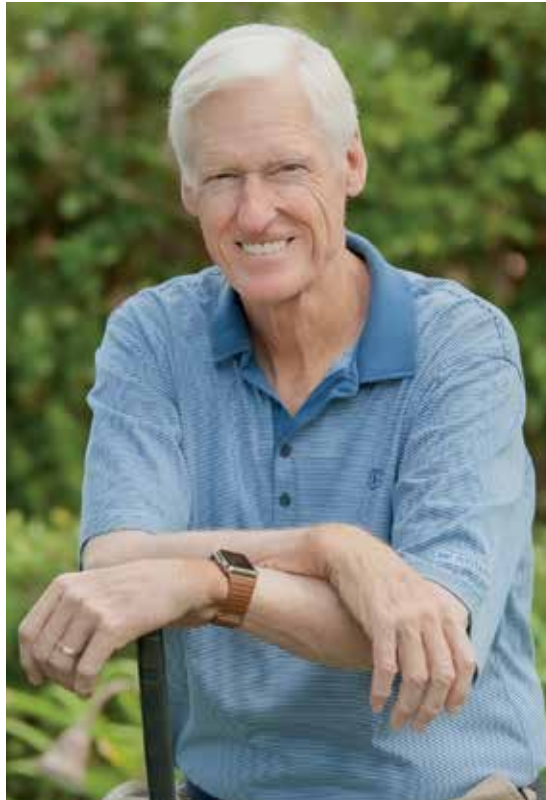
The newest member of the La Jolla Institute Board of Directors predicts the Institute's field of study, fueled by the groundbreaking research of its scientists, is poised for an "explosive" period of growth and significance.

Although Richard S. Bodman has only been on the board since last summer, his background in several important areas of American industry, including cell phone technology, satellite communications, and venture capital, allowed him to quickly size up the Institute's capabilities. He also has scientific credentials as a board member of The Buck Institute for Research on Aging in Novato, California, along with government experience.

"I was immediately impressed with the Institute's very ambitious goal of 'Life Without Disease.' What I quickly learned is that it is not just a brilliant concept, but a highly organized, potentially life-changing process that is well under way at the Institute. It is fascinating to see that their scientists have already achieved some critical breakthroughs in understanding the immune system," he says.

Bodman is confident in his prediction about the Institute's future. "Drawing on my own experience, especially in technology, I think that health science and delivery are at the same point that high tech was 10 years ago before it took off," and adds: "I believe the Institute and the field of immunology are just about ready to explode with truly groundbreaking advancements that will have amazing implications for humanity in terms of preventing and curing some of the most challenging diseases we face."

Bodman, who holds a B.S. in Engineering from Princeton University and an M.S. in Industrial Management from the Massachusetts Institute of Technology, currently is Managing



Richard S. Bodman

General Partner of VMS Group, which provides administrative and advisory services to more than 185 venture capital funds. He is also Chairman of TDF Ventures, which manages several telecommunications venture capital funds, and Co-Founder and Chairman of PurThread Technologies, Inc., a maker of antimicrobial textile products for the healthcare community and consumer use. Bodman is also General Manager of Bodman Oil & Gas, LLC.

Earlier Bodman served as Senior Vice President of AT&T's Management Executive Committee and Lead Director of Sandia National Laboratories. He then acquired AT&T Ventures, which he had founded at AT&T, and became its Co-Managing Partner. The firm was renamed Venture

Management Services (VMS Group).

Prior to AT&T, Bodman was CFO of Communications Satellite Corporation (COMSAT) and, subsequently, President and CEO of Comsat General Corporation and President of Satellite Television Corporation. Early in his career Bodman served as Assistant Secretary of the U.S. Department of the Interior and Assistant Director of the Office of Management and Budget in the White House.

Bodman and his wife, Karna, who served President Ronald Reagan as Senior Director of the National Security Council and is now an author, maintain residences in Rancho Santa Fe, Calif., Naples, Fla., and Washington, D.C.

In closing, Bodman comments, "I hope I have something to contribute to the future direction of the Institute. I am energized and challenged by the opportunity to work with such an interesting and important organization." ●

# La Jolla Institute

FOR ALLERGY AND IMMUNOLOGY

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La Jolla, CA 92037

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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](http://www.facebook.com/LifeWithoutDisease)

