



My best friend | Your dad | My daughter's teacher |  
Your former coach | **Or worse yet, my child**



LA JOLLA INSTITUTE  
*for*  
ALLERGY & IMMUNOLOGY



We all know so  
affected by an  
that is tied to  
the immune sys



*meone*

ilness

tem

## Inside this Report

Institute welcomes five new faculty	3
Letter from the President	4
Immune system reflects yin and yang	5

### Autoimmune Diseases

Scientist's visionary proposal earns prestigious Pioneer Award	6
Potential Crohn's treatment advances in pharmaceutical research	8
<b>Profile:</b> Crohn's disease	9
Researcher's discovery points to causes of Inflammatory Bowel Disease	9
New Center advances novel approaches against type 1 diabetes	10
<b>Profile:</b> Type 1 (juvenile) diabetes	11

### Infectious Diseases

Institute study reveals key H1N1 data	12
Researcher's landmark finding uncovers trigger for better vaccines	14
Tuberculosis threat grows	15
Institute takes aim at dangerous infectious diseases	15

### Cancer

Allergy researcher finds unexpected tumor blocker	16
---	----

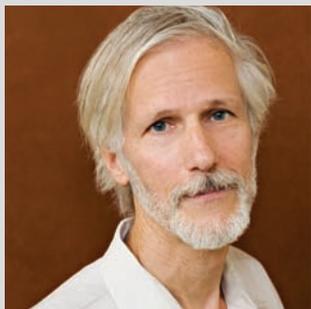
### Inflammation Biology

Institute explores new approaches to heart disease	18
Researchers publish notable findings	17
Financial update	20
Celebrations	22
The opportunity to make a difference	24
Leadership	25

# The scientists at La Jolla Institute work passionately for their families and yours

Disease, like death, is no respecter of persons. It strikes the playful child, the busy father and the wise, elderly grandparent with equal disregard. Each of us knows someone—a neighbor, a friend, a member of our family—who is touched by disease. Researchers at the La Jolla Institute for Allergy & Immunology have devoted themselves to finding answers that will relieve the suffering wrought by a multitude of diseases. Their focus is the human immune system because of the vast number of diseases that it impacts and the incredible potential that it holds for improving human health. The Institute's work has led to its recognition as one of the world's leading research institutions and it is San Diego's only research institute focused on solving immune-mediated diseases. So, whether you know someone with type 1 diabetes, heart disease, cancer, rheumatoid arthritis, multiple sclerosis, or who has suffered from the H1N1 flu or some other infectious disease, then you know someone who could benefit from our discoveries.

# Institute enhances disease focus with five new faculty



**Patrick Hogan, Ph.D.**, began his career in the Department of Neurobiology at Harvard Medical School, where he headed a research laboratory and taught neurobiology. He continued to teach at Harvard College and Harvard Medical School, before joining the La

Jolla Institute. Together with Dr. Rao, his laboratory has been involved in the characterization of a molecule that is required for immune cell function by allowing calcium ions to enter the cell. Patients with a defect in this molecule suffer from severe immune deficiencies. Dr. Hogan will run the Institute's new Division of Signaling and Gene Expression along with Dr. Rao. His studies focus on how genes are switched on. "My laboratory is interested in the processes by which proteins interact with each other and with DNA to turn on genes in the nucleus. That's the whole secret of how T cells work," he said, referring to the body's infection-fighting white blood cells. "The interactions we study are subtle but they may hold the key to human health and disease."



**Joel Linden, Ph.D.**, came to the Institute from the University of Virginia, where he was a professor in the Robert M. Berne Cardiovascular Research Center for 10 years.

Dr. Linden specializes in understanding the role of inflammation in heart disease and is a world-renowned expert on adenosine, a signaling molecule that binds to receptors known to be important in preventing inflammation in the cardiovascular system and elsewhere. Over the years, he has made a number of important discoveries, including a novel molecule binding to adenosine receptors that is currently in Phase III clinical trials as a potential therapy to improve cardiac stress testing. While at the University of Virginia, he co-founded a successful pharmaceutical company based on his novel adenosine receptor findings. Dr. Linden received the University's Edlich-Henderson Inventor of the Year Award in 2002.



A member of the National Academy of Sciences, **Anjana Rao, Ph.D.**, joined the Institute after many years as a faculty member at the Harvard Medical School. A prominent genetics and cell biology researcher, Dr. Rao studies one of the major molecular mysteries of our time: How do the more than 20,000 genes that make up every human being actually function? "Genes encode proteins, and what most proteins do is still unknown," said Dr. Rao, who heads the Institute's new Division of Signaling and Gene Expression. "The Human Genome Project gave the world the entire nucleotide sequence of every human gene. While this was monumental, we still know little about how genes work individually and collectively to affect disease processes." Dr. Rao is using RNA interference screens and other state-of-the-art technologies to better understand how genes affect the function of cells and sometimes trigger disease. The results from her ongoing studies already are providing powerful information that could lead to new therapies for cancers of blood cells and autoimmune diseases.

**Lynn Hedrick, Ph.D.**, a former faculty member at the University of Virginia, brings a focus on heart disease and type 2 diabetes, and seeks to understand the relationship between the two diseases. "Type 2 diabetics are four to five times more likely to suffer a heart attack than non-diabetics," said Dr. Hedrick, who notes that cardiovascular



disease is also emerging as a complication of type 1 diabetes. "We're exploring how white blood cells, which are cells of the immune system, contribute to increased cardiovascular disease in diabetes patients. We're finding some intriguing answers that we hope will one day make a real difference." Prior to joining the Institute from the University of Virginia, Dr. Hedrick was a faculty member at UCLA.

**Nunzio Bottini, M.D., Ph.D.**, researches genetics-based approaches to type 1 diabetes. He came to the Institute from USC's Institute for Genetic Medicine, where he was an assistant professor. Prior to that, he served as an Assistant Professor of Medicine at the University of Rome in Italy. Dr. Bottini started his career as a physician, but switched to research to find new and better ways to help patients fight disease. His decision to focus on the role of genetics in auto-



immune diseases, particularly type 1 diabetes, was partly family tradition and partly fascination. "One of my earliest memories is of my father, a professor of genetics, discussing the importance of a molecular family known as phosphatases," he said, referring to the same group of genes he now studies. Dr. Bottini said he's found that phosphatases are involved in triggering the beta cell destruction, which causes type 1 diabetes. "We're working to block their action to switch off the attack," he said.

# We believe immunology, at the core of so many diseases, is the right science for today's world

Someone, perhaps a close relative or friend whose health has suffered because of a disease related to the immune system, is at the core of what motivates every one of us at the La Jolla Institute for Allergy & Immunology.

In this Annual Report for 2009, you will find the personal stories of two young people, Kyle Montgomery, and Katrina Donnell. As children, each was struck with diseases of the immune system for which there are no cures. Because of progress in understanding immune system function, each one, along with their families, is hopeful that a cure for their disease will be found *during* their lifetimes. But there is still a long way to go until we reach that goal.

Reflecting on the past year at the La Jolla Institute, we remain fully committed to making groundbreaking discoveries through basic biomedical research that could one day lead to better preventions, therapies, and ultimately cures. To achieve this, we have broadened our research in inflammation and diabetes by welcoming scientists Joel Linden, Lynn Hedrick, and Nunzio Bottini. To capitalize on the revolution in genomics research, we established the Division of Signaling and Gene Expression with the recruitment of Anjana Rao and Patrick Hogan from Harvard's School of Medicine.

Our model is to have independent laboratories working on different aspects of the immune system collaborating with each other, as well as with other scientists in San Diego, nationally, and internationally. One successful example is the recent award by the National Institutes of Health of \$18.8M to four of our scientists, led by Alex Sette, director of the Institute's Center for Infectious Disease, to work on improving vaccines. (See page 15.)

And yet, so often the promise of basic biomedical research is the surprise discovery it yields. For example, scientist Toshiaki Kawakami's allergy research resulted in a finding that could lead to the suppression of certain blood cancers. (See page 16.) While the government funds the majority of biomedical research, philanthropy is critical to enabling high-risk studies that provide unexpected insights, such as the one described here, to proceed.

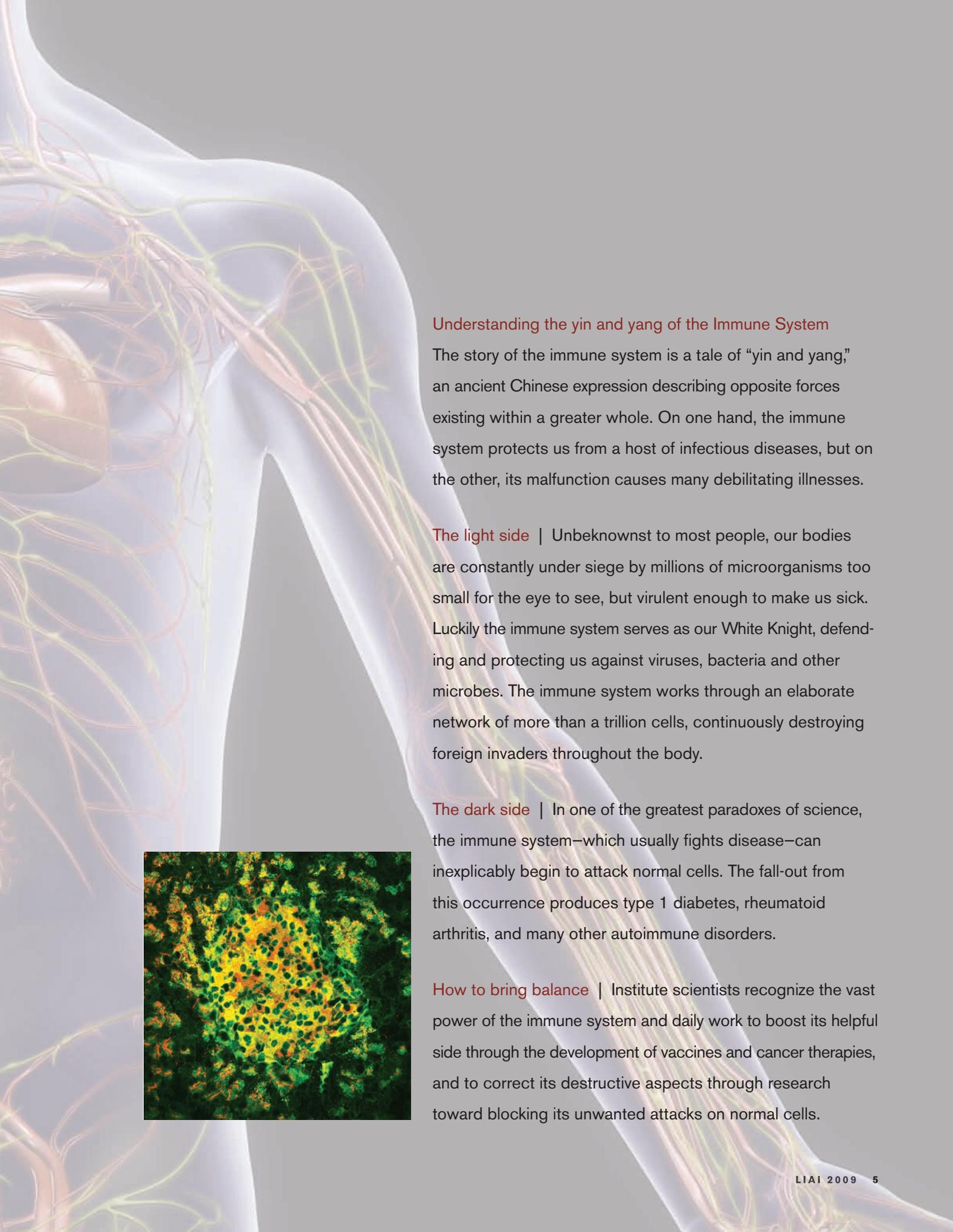
I encourage you to read through this Annual Report, and to get to know our scientists and the commitment of everyone at the La Jolla Institute for Allergy & Immunology to "Finding Cures Faster."

Sincerely,



Mitchell Kronenberg, Ph.D.  
President & Chief Scientific Officer





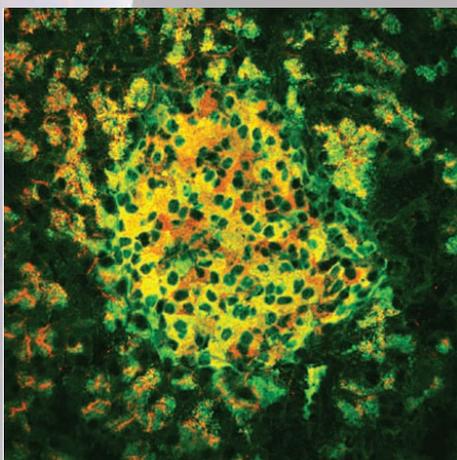
### Understanding the yin and yang of the Immune System

The story of the immune system is a tale of “yin and yang,” an ancient Chinese expression describing opposite forces existing within a greater whole. On one hand, the immune system protects us from a host of infectious diseases, but on the other, its malfunction causes many debilitating illnesses.

**The light side** | Unbeknownst to most people, our bodies are constantly under siege by millions of microorganisms too small for the eye to see, but virulent enough to make us sick. Luckily the immune system serves as our White Knight, defending and protecting us against viruses, bacteria and other microbes. The immune system works through an elaborate network of more than a trillion cells, continuously destroying foreign invaders throughout the body.

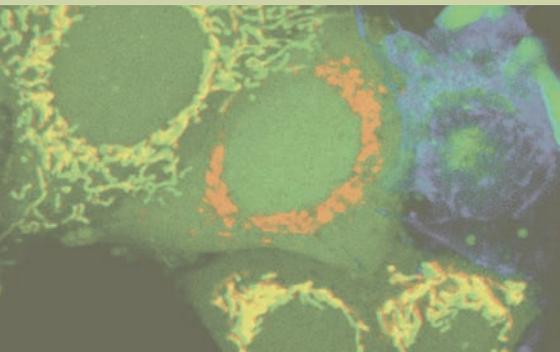
**The dark side** | In one of the greatest paradoxes of science, the immune system—which usually fights disease—can inexplicably begin to attack normal cells. The fall-out from this occurrence produces type 1 diabetes, rheumatoid arthritis, and many other autoimmune disorders.

**How to bring balance** | Institute scientists recognize the vast power of the immune system and daily work to boost its helpful side through the development of vaccines and cancer therapies, and to correct its destructive aspects through research toward blocking its unwanted attacks on normal cells.



# NIH selects Hilde Cheroutre as one of 18 Pioneer Award winners nationally to pursue visionary research

*“The NIH is giving recipients the chance to explore our most imaginative concepts... It’s a once in a lifetime opportunity.”*  
 —Hilde Cheroutre, Ph.D.



What if you took some of the most brilliant researchers in the country and enabled them to pursue out-of-the-box ideas that could profoundly alter the face of human health? That’s exactly what the National Institutes of Health (NIH) is doing with the Pioneer Award, which annually funds a select group of researchers who propose novel, visionary approaches to major challenges in biomedical research.

Hilde Cheroutre, Ph.D., was among 18 scientists selected for the 2009 award from among 2,300 applicants nationwide. The prestigious prize—one of the NIH’s top awards—provides Dr. Cheroutre with \$4.7 million over five years to enable her innovative and daring project to proceed.

Dr. Cheroutre received the award from NIH Director Francis Collins during a ceremony at the Pioneer Symposium in Bethesda, Maryland last fall. In presenting the awards, Dr. Collins called the event “a celebration of innovation” which recognizes “high-risk, high-reward investigator-initiated research.”

He said the highly competitive awards focus on the principal investi-

gator and are designed to give those individuals the “freedom to pursue creative thought.”

Dr. Cheroutre’s proposal, if successful, would create a new way of detecting, treating and possibly preventing autoimmune diseases, with the potential for identifying high risk for autoimmunity in newborns. In essence, Dr. Cheroutre’s work could make terrible diseases like type 1 diabetes, multiple sclerosis and rheumatoid arthritis a thing of the past.

“The NIH is giving recipients the chance to explore our most imaginative concepts,” said Dr. Cheroutre, noting she was exhilarated to receive the award. “It’s a once in a lifetime opportunity.”

Ben Barres, M.D., Ph.D., a Stanford University neurobiology professor and member of several Pioneer selection panels, praised the philosophy underlying the award.

“NIH says, ‘Tell us in five pages what you would do if you could do anything you wanted—no holds barred, no strings attached. Tell us the most high-risk, high-impact project you can think of, and we’re going to enable you to do it,’” he said. What



**Pioneer Award recipient Hilde Cheroutre, Ph.D., hopes to create a new way of detecting, treating and possibly preventing autoimmune diseases. (Inset) NIH Director Francis Collins presented Dr. Cheroutre with the Pioneer Award, one of the NIH's top awards.**



results is “some of the most creative science imaginable.”

Indeed, the NIH developed the Pioneer Awards in 2004 to encourage novel proposals that might not fit into the traditional grant application process. The NIH describes the awards as part of its ongoing efforts to en-

courage highly creative scientists to explore bold ideas that have the potential to catapult fields forward and speed the translation of research into improved health.

Putting forth highly imaginative concepts is not unusual for Dr. Cheroutre. In fact, she is a world renowned expert on mucosal immunity, whose findings have frequently bucked conventional wisdom or broken new ground. Such was her 2007 discovery that retinoic acid, a vitamin A derivative, can play a critical role in controlling inflammation in the body, which is the chief cause of several autoimmune diseases. *Nature Medicine* named it one of the key biomedical research advances of the year.

# Institute discovery moves into pharmaceutical research for potential treatment of Crohn's disease and colitis

A discovery by Institute scientists has entered pharmaceutical research for use in the creation of a potential new antibody therapy for ulcerative colitis and Crohn's disease, intestinal disorders collectively known as inflammatory bowel disease (IBD). The discovery—of a molecule known as LIGHT—was made in the laboratory of Carl Ware, Ph.D.

"We are elated to see this finding move toward use as a new treatment to improve human health and relieve suffering," said Mitchell Kronenberg, Ph.D., Institute president & chief scientific officer. "As a nonprofit biomedical research institute, our mission is to find the molecular causes of diseases, with the hope that our discoveries will one day be translated into new and better therapies. This is an important step toward that goal."

Dr. Ware's research found that LIGHT is a key signaling molecule which triggers a cascade of interactions, leading to inflammation in the body. Inflammation is the underlying cause of many autoimmune diseases, including Crohn's disease and ulcerative colitis. The potential therapy would work by using an antibody to block the action of LIGHT in order to lessen the inflammatory effects of these diseases.

La Jolla Institute partnered with Kyowa Hakko Kirin Co., Ltd. (Kyowa

Hakko Kirin), a global specialty pharmaceutical company, to develop Dr. Ware's discovery of the LIGHT molecule, and the antibody that blocks it. Earlier this year, Kyowa Hakko Kirin signed a collaboration and licensing agreement with Sanofi-

aventis (EURONEXT: SAN and NYSE: SNY), a global healthcare company, to advance the development of the new anti-LIGHT antibody therapy.

**Scientist Carl Ware, Ph.D., discovered the LIGHT molecule.**



## Crohn's may affect career direction



In the summer before his sophomore year, Kyle Montgomery (above) had the exciting opportunity to go to Germany with his soccer team. But when he returned home to find he'd lost 20 pounds in a week and a half, Kyle's family knew something was wrong.

Trips to the doctor confirmed that 15-year-old Kyle had Crohn's disease, a chronic disorder of immune cell function in the intestine that affects up to two million Americans.

Kyle admits his diagnosis was initially frightening. Not surprising since Crohn's produces symptoms such as abdominal pain, weight loss and diarrhea and its complications can be life-threatening.

But today the active 21-year-old college student is definitely in the driver's seat on his illness, which is leading him toward a career in medicine.

"I've always been interested in science and biology," he said. "But I feel like because I have Crohn's, it gives an extra sense of meaning to being a doctor. It has made me more aware of other people's struggles with disease and made medicine something I can be passionate about."

Kyle, who will be a pre-med student at Cal Poly San Luis Obispo, said Crohn's has also taught him about taking charge of one's disease through proper treatment and diet.

"It's made me be more responsible," he said. "But I don't let Crohn's stop me. I just move on with my life."

## Researcher sheds new light on causes of inflammatory bowel disease

Crohn's disease and ulcerative colitis, collectively referred to as inflammatory bowel disease (IBD), are chronic diseases that disrupt the lives of sufferers, often causing serious intestinal problems and sometimes life-threatening complications.

Thankfully, researchers like Mitchell Kronenberg, Ph.D., La Jolla Institute president & chief scientific officer, and Carl Ware, Ph.D., are working on novel ways to combat excessive inflammation in the body, which leads to IBD. Dr. Ware's discovery (see story, opposite page) uses an antibody approach, while Dr. Kronenberg focuses on IBD from the standpoint of the regulatory T cells (TREGs). His findings were recently published in the prestigious journal *Nature Immunology*.

"The job of TREGs is to quiet down the immune system and stop it from causing inflammation," said Dr. Kronenberg, noting excess inflammation causes diseases ranging from IBD to rheumatoid arthritis. "In our colitis model, we found two specific triggers which can cause the TREGs to lose their ability to dampen inflammation."

One of these involved Interleukin-10 (IL-10), an anti-inflammatory molecule key to enabling TREGs to calm the immune response. "It was thought that TREGs produced enough



**Mitchell Kronenberg, Ph.D., found two molecular triggers that are important in IBD.**

IL-10 on their own to sustain their inflammation-fighting abilities. Instead we found that TREGs must 'drink in' a substantial amount of IL-10 from other cells."

The finding is important because it could explain why TREGs sometimes fail and inflammation overruns the body. "If TREGs can lose their ability to regulate inflammation, can they regain it?" said Dr. Kronenberg, who is now exploring this question. "If this proves true, it may give us a new way to reduce or stop IBD by reactivating TREGs."

# Institute dedicates Type 1 Diabetes Research Center to accelerate progress toward a cure

People with type 1 (juvenile) diabetes work hard to go about the business of a normal life. But for sufferers of this life-long disorder, “normal” takes on a whole new meaning.

“Their lives are filled with rigorous day-to-day demands,” said Matthias von Herrath, M.D., director of the Institute’s Type 1 Diabetes Research Center dedicated in 2009. “People with type 1 diabetes must take insulin in order to stay alive. This means undergoing multiple injections daily or wearing an insulin pump, testing their blood sugar many times a day and dealing with diet and other issues.” And even with all these measures, type 1 diabetes can, over time, produce organ damage,

blindness and more because controlling blood sugar with artificially-produced insulin is a difficult process.

Fortunately, the La Jolla Institute has made fighting this disease a major priority and created a Center led by Dr. Von Herrath, one of the top type 1 diabetes researchers in the world and recipient of the 2008 Outstanding Scientific Achievement award from the American Diabetes Association. Eight Institute faculty members contribute to the Center’s research, which focuses on new immune-based approaches against type 1 diabetes.

The Center’s faculty, which includes Nunzio Bottini, M.D., Ph.D., who studies genetics-based approaches to type

1 diabetes, also collaborate with local and national scientists to speed up efforts toward new treatments or a cure.

“The mission of our Center is based on two important realizations,” said Dr. von Herrath. “The first is that it will be impossible to cure this disease without correcting the misdirected immune system that attacks the insulin-producing beta cells. The second realization is that tackling this disease will necessitate the cooperation of many, not

**Center Director Matthias von Herrath, M.D., (right) and Nunzio Bottini, M.D., Ph.D., are among eight faculty members that research novel immune-based approaches against type 1 diabetes.**



## Strength drawn from type 1 lessons



Most people recall their parents admonishing them to “look for the silver lining in a dark cloud.” But Katrina Donnell, diagnosed with type 1 diabetes at age 11, took that adage to heart. “Type 1 diabetes has opened my mind to all the issues people have to deal with due to illness,” said Katrina, now 20 (above, with her mom, Barbara). “Some people can take diabetes and feel bad about it. For me, I think, ‘look what I can teach people. I’m proof that you can have diabetes and still live a healthy life.’”

A San Diego resident attending the University of Oregon, Katrina concedes that growing up with diabetes hasn’t been easy. “My life became complicated with all the shots, the diet, the monitoring.” But Katrina was determined to deal with those challenges.

As time went on, she and her mother volunteered with diabetes organizations. Katrina visited newly diagnosed kids. “I told them, ‘your life is not over. Type 1 diabetes is a struggle. But you will learn to work with it just as I have.’” She also volunteered at a diabetes camp for children. “I met a lot of wonderful people I wouldn’t have met otherwise,” she said, noting her efforts have steered her toward a career with children.

Since going off to college, Katrina admits that controlling her diabetes has become more daunting, and she must be even more vigilant. However, despite its many demands, diabetes has taught her a lot. “I know it’s made me a stronger person.”



**The La Jolla Institute dedicated its Type 1 Diabetes Research Center and Elam Discovery Wall, a high-tech scientific education and research tool, in October. The Elam Discovery Wall was dedicated in memory of William N. Elam, Jr., M.D. (From left) Kevin and Debbie Keller; Patricia Ann Elam, Kevin’s mother and wife of the late Dr. Elam; Matthias von Herrath, M.D., director, Type 1 Diabetes Center; Mitchell Kronenberg, Ph.D., president, La Jolla Institute; Falko Kuester, Ph.D., Calit2 Professor, UC San Diego. See additional pictures on page 22.**

only scientists from the La Jolla Institute, but in particular, the cooperation between basic researchers and clinicians.”

In this vein, the Center has developed close ties with the Pediatric Diabetes Research Center of UC San Diego, the Sanford Children’s Health Research Center at the Sanford-Burnham Institute, and Rady Children’s Hospital, along with several private San Diego biotechnology companies, and the Brehm Coalition, a national consortium of eight leading scientists battling type 1 diabetes. In addition, the Center supports a clinical fellow

and a research fellow, both M.D.s, using funds donated through the federal workplace fundraising campaign.

One of the Center’s primary areas of study is on a combination therapy developed by Dr. von Herrath, which has shown significant promise in mouse models at stopping type 1 diabetes when caught in the early stages. The therapy has drawn international interest and led to Dr. von Herrath’s receipt of the American Diabetes Association award. Dr. von Herrath is hopeful that clinical trials will start on the combination therapy in the near future.

# Researchers provide critical H1N1 data at height of influenza pandemic

In the early days of the H1N1 pandemic, when fear gripped the world and public health experts braced for a potential influenza crisis, Institute researchers provided critical data when the world needed it most. “What we have found,” said Alessandro Sette, Ph.D., director of the Institute’s Center for Infectious Disease, “is that the swine flu has similarities to the seasonal flu, which appear to provide some level of pre-existing

immunity. This suggests that it could make the disease less severe in the general population than originally feared.”

Released at the height of public concern, the findings were greeted by intense scientific interest and a flurry of worldwide media coverage. The

**Alessandro Sette, Ph.D., director of the Institute’s Center for Infectious Disease, said the H1N1 virus has similarities to the seasonal flu which blunted its impact.**

*“We’re glad that we could use these resources to provide important (H1N1) information and perspective as the world faced a potential public health emergency.”*

*—Alessandro Sette, Ph.D.*

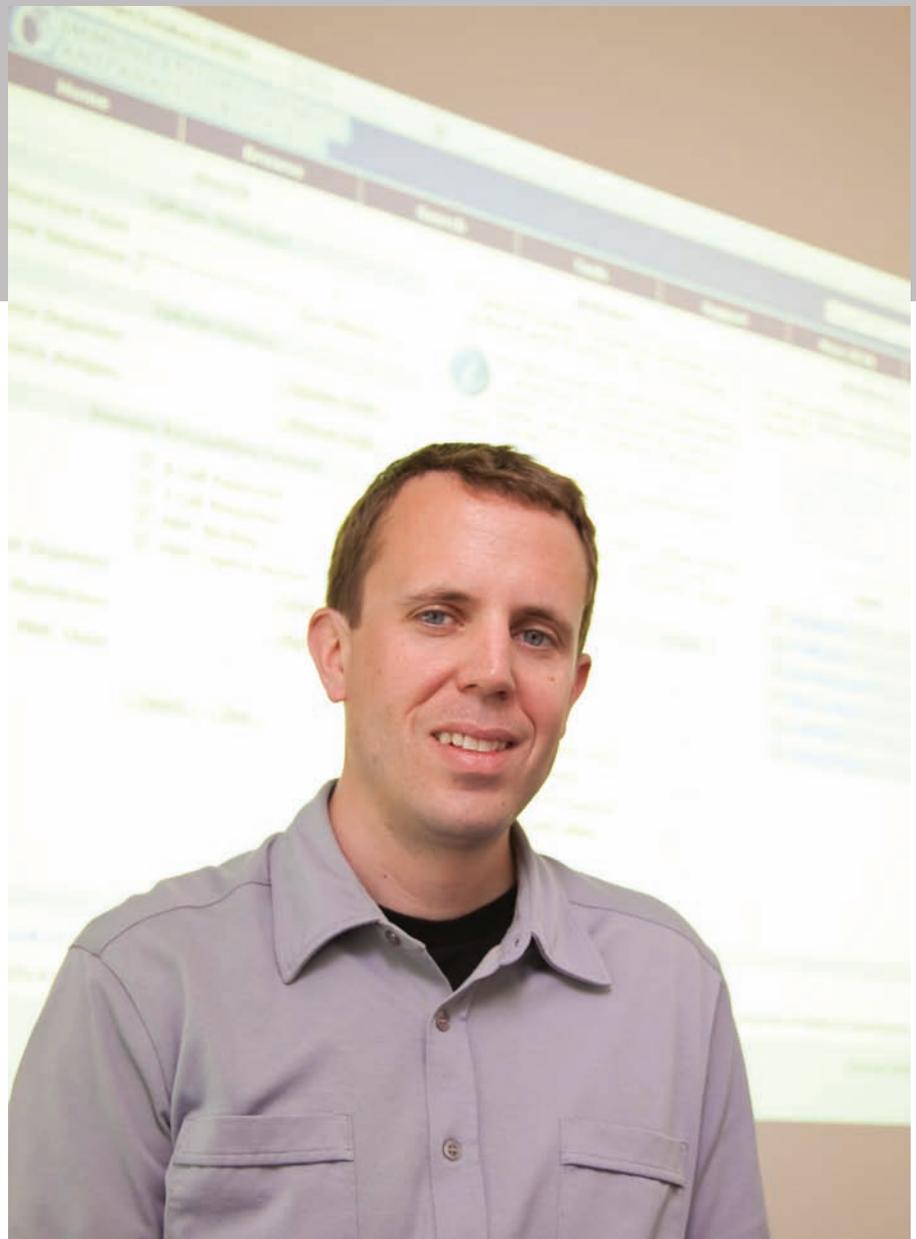


**Bjoern Peters, Ph.D., was lead author on the H1N1 study that showed the general population would likely have some level of pre-existing immunity.**

study, led by Institute scientist Bjoern Peters, Ph.D., points to a possible reason that the H1N1 pandemic has not produced widespread death as originally feared. It also may help to explain why the H1N1 virus has affected children and young adults more severely than healthy older adults, since the older population would have experienced more previous influenza exposures.

“Our Institute has an internationally recognized program in vaccine biology and we host the world’s largest database of epitopes, which are molecular structures key to vaccine development,” said Dr. Sette. “We’re glad that we could use these resources to provide important information and perspective as the world faced a potential public health emergency.”

In his study, Dr. Peters compared molecular markers for seasonal influenza viruses dating back 20 years against those of the H1N1 virus. “We found that the immune system’s T cells



can recognize a significant percent of the markers in swine flu,” said Dr. Peters, adding that T cells are infection-fighting cells of the immune system. “If infected, our data suggests that T cells in those who have previously been exposed to influenza may make the infection less severe.”

Dr. Peters said his research also bore out the wisdom of being vaccinated against the H1N1, since T cells help to reduce an infection’s severity, but do not keep people from being infected in the first place. Vaccines are designed to protect against initial infection.

# Researcher's landmark antibody discovery could lead to new and better vaccines

**B**iomedical scientists, by nature, are puzzle solvers. Each day, they study molecular mysteries in hopes of one day constructing a clear picture that will reveal disease processes. Sometimes the puzzles they decipher answer small, incremental questions. But occasionally, they offer huge leaps in knowledge that transform scientific understanding and provide hope for major improvements in human health.

Such was the groundbreaking discovery by Shane Crotty, Ph.D., published in the prestigious journal *Science*, which pinpointed BCL6 as the gene that switches on the production of antibodies—the body's disease-fighting warriors and the basis for most vaccines.

"The finding is enormous in terms of its long-term benefit to science and society as a whole because it illuminates a pivotal piece of the vaccine development puzzle," said Mitchell Kronenberg, Ph.D., La Jolla Institute president and chief scientific officer. "This knowledge opens the door to developing ways to boost antibody production, thereby creating stronger and more effective vaccines."

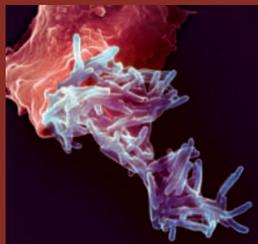
**Shane Crotty, Ph.D.'s groundbreaking discovery of the molecular switch for antibodies answered a critical question long sought by the scientific community.**

The finding was front page news in San Diego and also drew national interest, landing Dr. Crotty as a guest on National Public Radio. It wasn't the first time Dr. Crotty's achievements have earned national notice. Most

notable, in 2005 he was named one of America's "Most Promising Biomedical Researchers" by the Pew Charitable Trusts, which describes recipients as those expected to advance the scientific frontier.



## Tuberculosis takes on new urgency



Until 50 years ago, there were no medicines to cure tuberculosis—an infectious

disease that kills about 1.6 million people worldwide each year. Today, the good news is that several successful treatment regimens exist. However, a new phenomenon is emerging which heightens worldwide concern. Beginning in the mid-1980s, multi-drug-resistant tuberculosis strains began to appear, which do not respond to previously successful standardized antibiotic treatments.

The World Health Organization estimates that 511,000 new multi-drug-resistant tuberculosis cases occurred in 2007, with more than half of these in China, India and the Russian Federation. Meanwhile, the U.S. has not escaped this emerging threat, with more than 2,500 such cases occurring within the last 15 years.

“The emergence of these drug-resistant TB strains demonstrates why researchers must continually work to stay one step ahead of these dangerous agents,” said Alessandro Sette, Ph.D., director of the Institute’s Center for Infectious Disease, who along with Shane Crotty, Ph.D., is leading an effort to find new molecular targets for developing a more effective tuberculosis vaccine.

In addition to the multi-drug resistant strains, an even more treacherous form, known as extensively drug-resistant tuberculosis, is emerging worldwide. This strain resists both the standard antibiotic treatments and a second, stronger round of drugs. Cases have been confirmed in more than 50 countries, including 83 cases in the U.S. between 1993 and 2007.

## NIH awards Institute \$18.8m to combat dangerous infectious diseases—malaria, tuberculosis and dengue virus targeted

Consider these sobering statistics: Every year there are 250 million malaria cases and nearly one million deaths. In Africa, one of the hardest hit areas, every 30 seconds a child dies from this dreaded disease.

While global initiatives seek to reduce malaria, which occurs primarily in the poorest countries, one of the biggest obstacles remains the lack of an effective vaccine.

But Institute researchers, led by internationally recognized scientist Alessandro Sette, Ph.D., have joined forces with the National Institutes of Health (NIH) and international research teams, to create new inroads toward the development of a first-ever malaria vaccine. The five-year study is part of a group of Institute projects launched in 2009 with \$18.8 million in NIH funding. The studies will also focus on aiding the development of a more effective vaccine for tuberculosis—an annual killer of 1.6 million people worldwide. In addition, the design of a first-ever vaccine for dengue virus is being pursued by Sujan Shrestha, Ph.D., a dengue expert and co-investigator on this project. Dengue virus infection produces 500,000 severe cases each year and is nearing U.S. borders.

Specifically, Institute researchers will focus on identifying epitopes for each of the infections. Epitopes are



(From left) Shane Crotty, Sujan Shrestha, Alessandro Sette and Bjoern Peters, Ph.D.s, will work on the NIH-funded projects.

pieces of a virus or microbe that cause the body’s immune system to launch an attack, and which are key to developing new and more effective vaccines, explained Shane Crotty, Ph.D., tuberculosis co-investigator. The set of projects also includes a study led by Bjoern Peters, Ph.D., on the smallpox vaccine, the most effective vaccine ever developed. “By analyzing in detail which mechanisms make the smallpox vaccine work, we can develop better vaccines for other diseases in the future,” explained Dr. Peters.

Dr. Sette said significant advances in bioinformatics and genomic sequencing over the last 10 years will enable researchers to identify epitopes more effectively than ever before.

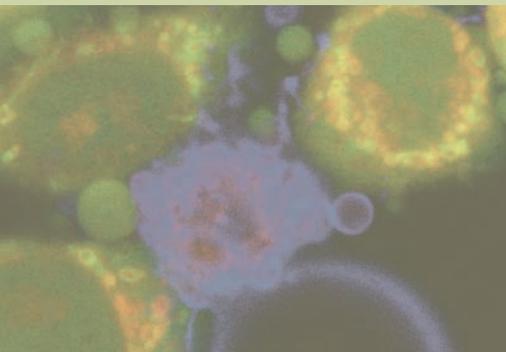
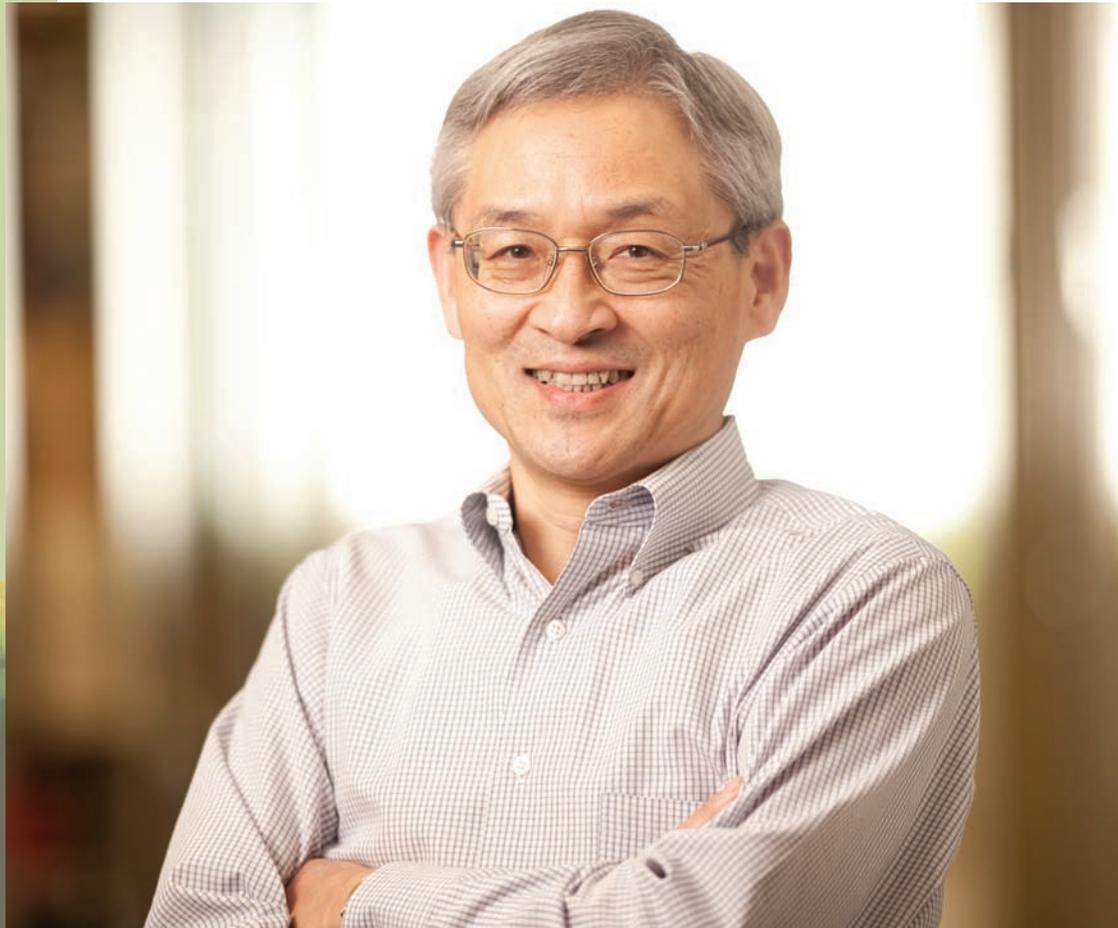
# Allergy researcher's surprising finding offers new hope against blood cancers

American author and naturalist Henry David Thoreau once said that “it’s not what you look at that matters, it’s what you see.” Nothing could be more apt to describe the recent finding by Toshiaki Kawakami,

M.D., Ph.D., who set out to explore an enzyme’s possible role in allergies, and instead discovered a tumor suppressor mechanism that no one knew existed. An internationally known allergy researcher, Dr. Kawakami’s finding has significant implications for under-

*“PLC-beta 3 is an enzyme believed to be key in allergy onset, but the function we found shows it also plays a role in blocking the production of certain cancerous cells.”*

*—Toshiaki Kawakami,  
M.D., Ph.D.*



standing the formation and growth of certain blood cancers.

“PLC-beta 3 is an enzyme believed to be key in allergy onset, but the function we found shows it also plays a role in blocking the production of certain cancerous cells,” said Dr. Kawakami.

His finding could one day lead to new therapies for sufferers of myeloproliferative diseases, disorders characterized by an overproduction of blood cells, and some types of lymphoma and leukemia.

Tony Hunter, Ph.D., director of the Salk Institute Cancer Center and a professor in Salk’s Molecular and Cell Biology Laboratory, called the finding an “important” step in advancing understanding of blood cancers. “It’s very interesting that this molecule acts in this way independently of its enzyme activity,” he said. “It’s quite an unexpected finding and it definitely has the potential for helping the scientific community understand the mechanisms leading to some types of leukemia.”

**Toshiaki Kawakami, M.D., Ph.D.,  
an internationally known allergy  
researcher, made an important finding  
on certain blood cancers.**

Dr. Kawakami said he and his research team got their first inkling of something unusual fairly early on in their experiments. “We wanted to better understand the PLC-beta 3 enzyme’s possible role as a signaling pathway in asthma and other allergic diseases, so we began working with mice genetically engineered not to have that enzyme,” he said. “We noticed that these mice developed a strange phenotype—myeloproliferation and a variety of tumors including lymphomas and some carcinomas.”

Dr. Kawakami said this surprising occurrence suggested that PLC-beta 3 acted as a safeguard that inhibited the development of a variety of tumors. Further testing confirmed his observation.

Dr. Kawakami is excited by the finding and is delving deeper into its inner workings. “I hope my work may one day lead to drugs to fight certain cancers by boosting this tumor-blocking mechanism.”

## Numerous impressive discoveries published in 2009

The Institute’s discoveries—like those at academic institutions around the world—are continually being shared with great scientific minds here and abroad through the publication of papers in scientific journals. In 2009, Institute scientists published more than 125 papers. These contain impressive research advancements, with several appearing in the most prestigious journals in the world. Scientific papers—in which investigators explain their latest findings—must go through a rigorous peer-review process prior to publication. Publication is a milestone for researchers and validates that their work is of such importance that it should be shared with the international scientific community. The Institute’s major published findings in 2009 illustrate the range and power of immunology research. Some examples include Dr. Shane Crotty’s seminal finding on the genetic trigger for antibody production, published in the journal *Science*, Dr. Matthias von Herrath’s surprising results on the effects of viral infection on the generation of type 1 diabetes, published in the *Journal of Clinical Investigation*, and Dr. Bjoern Peters’ study on the H1N1 virus, published in the *Proceedings of the National Academy of Sciences*.

# Institute pioneers immune-based approaches to heart disease

**W**hen it comes to heart disease—the nation’s No. 1 killer—cholesterol is only part of the story.

“Heart disease is now recognized to have a major inflammatory component,” said Joel Linden, Ph.D., one of two new faculty members in the Institute’s Division of Inflammation Biology. The division explores new ways to fight heart disease and other chronic inflammatory diseases using the immense power of the immune system. It is one of the few such groups in the world.

“The statins (cholesterol-lowering drugs) have taken a big chunk out of the numbers of people who suffer from heart disease and heart attacks,” said Klaus Ley, M.D., a pioneer in vascular (blood vessel) immunology and division director. “We hope we can bite off another chunk by controlling the impact of inflammation-causing immune cells on heart disease.”

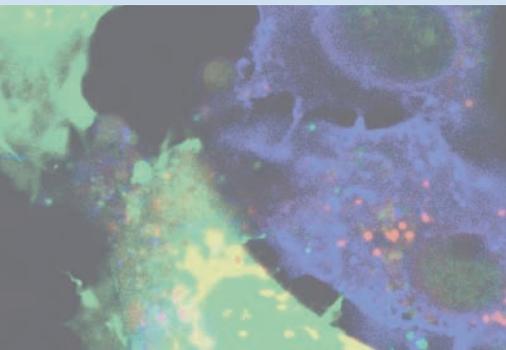
Launched in 2007, the division has already made important findings on the immune system’s role in atherosclerosis, which leads to blockages in

*“Scientists used to believe that atherosclerosis was due to plaque formation caused solely by cholesterol buildup, but that is not the whole story.”*

— Klaus Ley, M.D.



**Klaus Ley, M.D.,** is director of the **Inflammation Biology Division** and a pioneer in vascular immunology.





**Joel Linden, Ph.D., studies ways to reduce heart problems and currently has a compound in clinical trials for cardiac stress testing.**

arteries and is the underlying cause of most heart problems. In 2009, the addition of two faculty members further boosted its research power. Dr. Linden is a renowned expert on a molecule called adenosine's role in heart function and preventing inflammation, and Lynn Hedrick, Ph.D., is a prominent scientist exploring the link between diabetes and heart disease.

Dr. Ley said the immune system's role in heart disease is a relatively recent finding. "Scientists used to believe that atherosclerosis was due to plaque formation caused solely by cholesterol buildup, but that is not the whole story."

Dr. Ley said inflammation is key to plaque formation, eventually leading to weakening and rupture of the artery wall, which produces a heart attack. He is studying ways to stop inflammatory white blood cells, known as macrophages, from contributing to artery wall destruction.

Dr. Linden's research, meanwhile, looks at harnessing adenosine's inflammation-blocking abilities to counter certain heart problems. Among those are ischemia reperfusion injury, caused by over-exuberant immune cells that rush to reopened

arteries following a heart attack. Dr. Linden hopes to use adenosine to stop this onslaught, and already has an adenosine compound in Phase III clinical trials for cardiac stress testing.

Dr. Hedrick is shedding new light on the association between type 2 diabetes and heart disease. "Type 2 diabetics are four to five times more likely to suffer a heart attack than non-diabetics," she said. "We're exploring this correlation and are finding some intriguing answers."

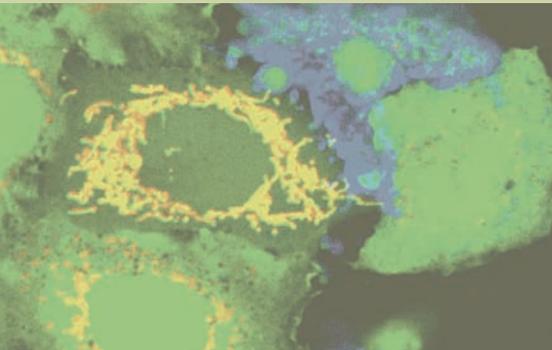


**Lynn Hedrick, Ph.D., looks at the correlation between diabetes and heart disease.**

# 2009 financial picture reflects Institute growth



*“This investment in an expanded research program has further strengthened La Jolla Institute as one of the world’s preeminent institutions focused on solving immune system diseases.”*



Fiscal year 2009 was a year of significant growth for La Jolla Institute. Shortly after moving into our new re- search facility in July 2006, we embarked on a plan to recruit five prominent scientists, and

build out shell space to accommodate and equip their new labs. The plan was successfully completed in 2009, and the associated costs of \$6.7 million have been fully funded. This invest- ment in an expanded research program has further strengthened La Jolla Institute as one of the world’s preeminent institutions focused on solving immune system diseases.

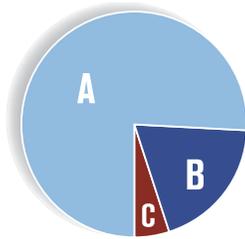
The Institute continues to operate in a strong and stable financial position, with total revenues reaching an all- time high of \$40.16 million in 2009. In addition, as shown on the accom- panying bar graphs, total revenues and net assets have increased steadily

during the past five years, evidencing a period of sustained growth. This growth is largely due to a track record of excellence by our scientists in obtaining competitive, peer reviewed research funding from the National Institutes of Health (NIH).

Of note, stimulus funding from the 2009 American Recovery and Reinvestment Act provided a signifi- cant short-term boost to the NIH budget, and the Institute was success- ful in securing some of this funding. However, competition for NIH dollars is fierce, and future NIH funding levels after the two-year stimulus period are uncertain.

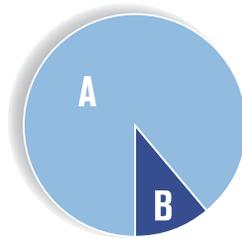
Recognizing this, an ongoing strategic goal for the Institute is to diversify and enhance revenues from technology licensing and philan- thropy. We are placing increased efforts on achieving this goal, and our efforts are showing signs of success. For example, in 2009 the Institute earned license revenue of seven figures for the second consecutive year.

In addition, Kyowa Hakko Kirin California, Inc., our longtime industry partner, continues to provide strong support. Since our inception in 1988,



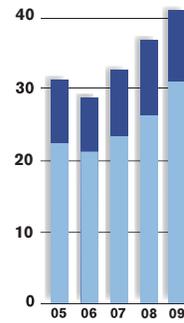
**Revenues**

- A) NIH grants and contracts 76%
- B) Private grants and contracts 19%
- C) License and other revenue 5%



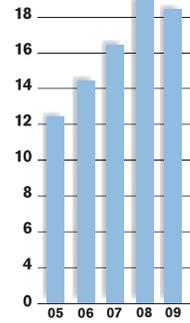
**Expenses**

- A) Research 89%
- B) G&A and Fundraising 11%



**Revenue Growth**  
in millions of dollars

■ NIH GRANTS AND CONTRACTS  
■ TOTAL REVENUES



**Net Asset Growth**  
in millions of dollars

■ NET ASSETS

Kyowa Kirin has provided a stable source of unrestricted research funding while facilitating the translation of our discoveries into potential treatments for human disease. This sponsored research funding aides our scientists in pursuing promising, innovative research, and is committed through the year 2015. We would like to recognize and thank our colleagues at Kyowa Kirin for their enduring partnership and vision.

In summary, La Jolla Institute’s financial position and outlook remain positive. We are proud of the fact that a high percentage of every Institute dollar spent goes directly to research (89 percent in 2009), and we are committed to ensuring the Institute’s long-term financial health. This, coupled with our extraordinary scientists, dedicated staff, and world-class research facilities, will continue to provide the foundation for breakthrough discoveries that lead to improved human health.

**Charles A. Carpowich, Jr.**  
Executive Vice President & COO/CFO

**STATEMENT OF FINANCIAL POSITION**

Cash and investments	\$ 8,847,000
Grants receivable and other	8,918,000
Property, net	8,008,000
<b>Total assets</b>	<b>\$ 25,773,000</b>
<hr/>	
Accounts payable and accrued expenses	\$ 7,023,000
Deferred revenue	490,000
<b>Total liabilities</b>	<b>\$ 7,513,000</b>
<b>Total net assets</b>	<b>\$ 18,260,000</b>
<b>Total liabilities and net assets</b>	<b>\$ 25,773,000</b>

**STATEMENT OF ACTIVITIES**

<b>Revenues:</b>	
NIH grants and contracts	\$ 30,344,000
Private grants and contracts	7,771,000
License revenue	1,423,000
Contributions	277,000
Investment return and other	347,000
<b>Total revenue</b>	<b>\$ 40,162,000</b>
<hr/>	
<b>Expenses:</b>	
Research	\$ 36,044,000
General and administrative	4,443,000
Fundraising	167,000
<b>Total expenses</b>	<b>\$ 40,654,000</b>
<b>Change in net assets</b>	<b>\$ (492,000)</b>

The above 2009 financial data was summarized from the Institute’s December 31, 2009 audited financial statements. To receive a copy of the La Jolla Institute’s audited financial statements, contact Charles Carpowich at 858-752-6510 or e-mail skip@lai.org.

# Celebrations!

## Dedication of Elam Discovery Wall & Type 1 Diabetes Research Center

On October 29th, friends of the La Jolla Institute and the William N. Elam, Jr. M.D. family, along with many who have a passion for finding a cure for type 1 diabetes, gathered together in a shared Dedications ceremony and reception. This heartwarming event eloquently stated the case for critical immunological research to end suffering from type 1 (juvenile) diabetes and also honored the life of a physician who cared for others, with the dedication of a “beyond the state of the art” research tool for discovery. See additional picture on page 11.



- 1.) Mitch Kronenberg, MaryAnn Stewart, Bob Dynes
- 2.) Brian Jiang, Kevin Keller, Katina Tsakopoulos, Lucy Jiang
- 3.) Rob and Deanne Seiler
- 4.) Mitch Kronenberg, Keith and Lori Edwards
- 5.) Mitch Kronenberg
- 6.) George Eisenbarth
- 7.) Larry Smarr, Ann and Bob Dynes
- 8.) Jerry Mohr, David Bergman
- 9.) Cindy Mort, Erwin Omens, Esther Perkins



# Welcoming new faculty



In December, the La Jolla Institute hosted a reception to welcome five new outstanding scientists who joined the Institute's faculty during 2009. More than 100 members of the San Diego community attended the event, generously sponsored by the companies listed below. We wish to especially acknowledge InvivoScribe Technologies as our Platinum Sponsor and Celgene as our Gold Sponsor for their enduring support. Pictured above: Patrick Hogan, Ph.D.; Anjana Rao, Ph.D.; Mitchell Kronenberg, Ph.D., president, La Jolla Institute; Lynn Hedrick, Ph.D.; Nunzio Bottini, M.D., Ph.D.; Joel Linden, Ph.D. See page 3 for additional information.



## Platinum Sponsor

InvivoScribe Technologies

## Gold Sponsor

Celgene Corporation

## Sponsors

Biomed Realty Trust, Inc.

Kyowa Hakko Kirin California, Inc.

Moss Adams LLP

Pillsbury Winthrop Shaw Pittman LLP

DavenportMajor Executive Search

CalciMedica, Inc.

Cytori Therapeutics, Inc.

Merrill Lynch

Biogen Idec

Millipore Corporation

# Giving—the opportunity to make a difference

*“It is the hope and promise of biomedical research, over the long-term, that outstanding science will improve human health and make life better for people.”*



Our 2009 Annual Report is our chance to share with you the dedication of our scientists towards making discoveries that will make a difference in the lives of someone you know—your younger brother, your friend from college, your new grandchild. It is what we are all about: making a difference in someone’s life. It is the hope and promise of biomedical research, over the long-term, that outstanding science will improve human health and make life better for people.

We want to thank Kyle, and Katrina, and their families, for allowing us to share their personal stories with you. Theirs are among the faces we recall when working in the labs, maintaining the research environment, or educating future scientists, all for the purpose of “Finding Cures Faster.”

We are also grateful to those who have supported us throughout 2009 with their charitable giving, which enables us to delve deeper into existing projects and open up new avenues of research. Every gift makes a difference, *especially yours*.

It is in this spirit that we invite you to join us as we work to help all those special someones, who suffer from debilitating diseases. Because of people like you, who understand the hope, the promise and the opportunity of basic biomedical research, many great things are possible. Together, we can make a difference.

With kind regards,

A handwritten signature in black ink that reads "MaryAnn F. Stewart". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

**MaryAnn F. Stewart**  
Vice President, External Relations  
& Chief Development Officer

# LA JOLLA INSTITUTE FOR ALLERGY & IMMUNOLOGY

## Board of Directors

SAMUEL STROBER, M.D., CHAIRMAN  
*Professor of Medicine, Division of Immunology  
and Rheumatology  
Stanford University School of Medicine*

HAROLD G. BUCHANAN, II  
*Managing Partner  
CE2 Capital Partners*

DAVID DOMINGUEZ  
*Chief Executive Officer  
The Andrew Lauren Company*

ROBERT C. DYNES, Ph.D.  
*President Emeritus  
University of California*

LEROY HOOD, M.D., Ph.D.  
*President  
Institute for Systems Biology*

RICHARD K. KORNFELD  
*Board Member  
CommNexus San Diego*

MITCHELL KRONENBERG, Ph.D.  
*President & Chief Scientific Officer  
La Jolla Institute for Allergy & Immunology*

JOHN E. MAJOR  
*Chairman of the Board  
Broadcom, Inc.*

MICHAEL J. MARTIN  
*President  
Waveland Capital Group LLC*

TOSHIFUMI MIKAYAMA, Ph.D.  
*Managing Officer, Vice President,  
Head, Research Division  
Kyowa Hakko Kirin Co., Ltd., Japan*

STEVEN M. ODRE  
*Adjunct Professor, Intellectual Property  
IIT-Chicago Kent School of Law*

SUSAN L. SWAIN, Ph.D.  
*President Emeritus  
Trudeau Institute*

## Faculty

MITCHELL KRONENBERG, Ph.D.  
AMNON ALTMAN, Ph.D.  
NUNZIO BOTTINI, M.D., Ph.D.  
CHRISTOPHER BENEDICT, Ph.D.  
HILDE CHEROUTRE, Ph.D.  
MICHAEL CROFT, Ph.D.  
SHANE CROTTY, Ph.D.  
HOWARD M. GREY, M.D.  
LYNN HEDRICK, Ph.D.  
PATRICK HOGAN, Ph.D.  
TOSHIKI KAWAKAMI, M.D., Ph.D.  
KLAUS F. LEY, M.D.  
JOEL LINDEN, Ph.D.  
YUN-CAI LIU, Ph.D.  
DONALD D. NEWMAYER, Ph.D.  
BJOERN PETERS, Ph.D.  
STEPHEN SCHOENBERGER, Ph.D.  
ALESSANDRO SETTE, Ph.D.  
SUJAN SHRESTA, Ph.D.  
ANJANA RAO, Ph.D.  
MATTHIAS VON HERRATH, M.D.  
CARL F. WARE, Ph.D.  
DIRK M. ZAJONC, Ph.D.

## Scientific Advisory Board

MARK M. DAVIS, Ph.D., CHAIRMAN  
*Director, Institute for Immunity,  
Transplantation and Infection  
The Burt and Marion Avery Family Professor  
of Immunology  
Professor, Department of Microbiology  
& Immunology  
Stanford University School of Medicine  
Investigator, Howard Hughes Medical Institute*

DANIEL LITTMAN, M.D., Ph.D.  
*Helen L. and Martin S. Kimmel Professor of  
Molecular Immunology  
Professor of Pathology and Microbiology  
NYU School of Medicine  
Investigator, Howard Hughes Medical Institute*

ELLEN ROTHENBERG, Ph.D.  
*Professor, Division of Biology  
California Institute of Technology*

SAMUEL STROBER, M.D.  
*Professor of Medicine, Division of Immunology  
and Rheumatology  
Stanford University School of Medicine*

SUSAN L. SWAIN, Ph.D.  
*President Emeritus  
Trudeau Institute*

## Leadership Team

MITCHELL KRONENBERG, Ph.D.  
*President & Chief Scientific Officer*

AMNON ALTMAN, Ph.D.  
*Director, Scientific Affairs*

CHARLES A. CARPOWICH, JR.  
*Executive Vice President & COO/CFO*

MARYANN F. STEWART  
*Vice President, External Relations &  
Chief Development Officer*

STEPHEN S. WILSON, Ph.D.  
*Vice President & Chief Technology Officer*

MATTHEW R. DEVOL  
*Senior Director, Finance & Accounting*

MELINDA DIAMOND  
*Senior Director, Human Resources*

LEO V. FERNANDEZ  
*Director, Imaging Facility*

PATRICK H. HO  
*Director, Business & Technology Development*

JOHN E. KEEGAN  
*Director, Facilities & Operations*

MORAG MACKAY  
*Director, Department of Laboratory Animal Care*

ERIN K. RIGHETTI  
*Director, Development*



LA JOLLA INSTITUTE  
*for*  
ALLERGY & IMMUNOLOGY

9420 Athena Circle • La Jolla CA 92037 • [www.liai.org](http://www.liai.org)

[www.liai.org](http://www.liai.org)



Photo courtesy of BIOCOM

**2009 High School Summer Internship Program**  
**Klaus Ley, M.D., Division Head, Inflammation Biology;**  
**Megan Bradley, Intern, San Dieguito Academy**