



## Finding Cures Faster



LA JOLLA INSTITUTE  
*for*  
ALLERGY & IMMUNOLOGY

# Millions of people,

# a multitude of devastating diseases...



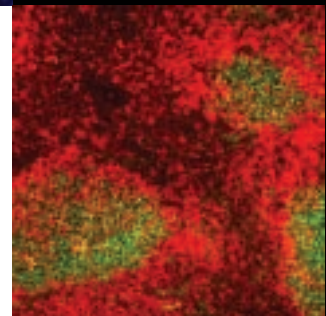
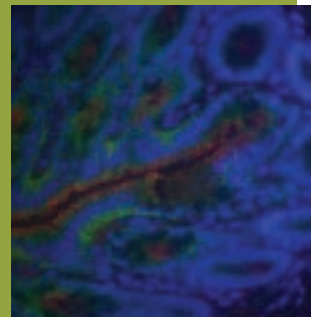
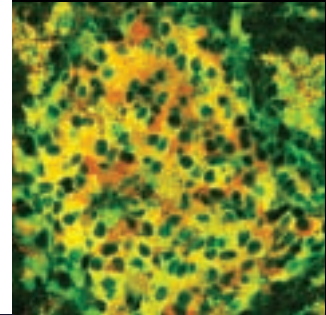
One immune system.

We are making  
discoveries that  
matter for you,  
your family,  
and your friends.



# Inside this Report

Letter from the President	6
Understanding the Two Sides of the Immune System	8
Four Potential Therapies Emerging from Institute Discoveries	10
Major Asthma Finding Licensed	14
Profile: Rheumatoid Arthritis	15
Protecting our Nation's Youth: Smallpox Treatment Discovery May be Stockpiled	16
Scientist Pioneers New Model for Fighting Dangerous Dengue Virus	18
Researcher's Finding Boosts Fight Against Lyme Disease	19
Profile: Lyme Disease	19
Institute's New Type 1 Diabetes Center to Accelerate Research Advances	20
Profile: Type 1 Diabetes	21
Institute Continues Rich History of Allergy Innovation	22
Institute Scientists Receive Major Awards	23
Financial Update	24
20th Anniversary Gala	26
Giving Update	28
Institute Leadership	29



# Research is the light at the end of the tunnel for all who have traveled the dark pathways of disease.

It offers hope for a better tomorrow and the promise of a better life free of the debilitating symptoms and frustration that often accompany illness. At the La Jolla Institute for Allergy & Immunology, our purpose and our passion is making breakthrough discoveries toward new treatments or cures to end the suffering wrought by the host of diseases related to immune system function. As a nonprofit biomedical research institute, it is the reason we exist. Our scientists carry this mission with them every day and their work speaks volumes about their dedication and success. Four new therapies—currently at various stages of clinical development—were born in our laboratories. And many more are waiting in the wings. Please read on to learn more about how we are exploring the immune system and shedding light on many exciting new pathways against disease.

# We draw upon the power of because it holds the key to debilitating diseases.



Did you know that vaccines—which stimulate the immune system—remain the most powerful and cost-effective medicines ever developed? Yet, what happens if one of the most deadly diseases ever known, smallpox, reappears due to an act of bioterrorism? Shane Crotty, Ph.D. and his research team are working on the development of a treatment that could be used one day to protect the unvaccinated—our youth—from smallpox,

should the dreaded bioterrorism event occur. The story of Dr. Crotty's efforts is just one of several highlights that I am pleased to present to you in the 2008 Annual Report for the La Jolla Institute for Allergy & Immunology.

2008 marked the 20th year anniversary for the La Jolla Institute. While we are known internationally in the scientific community for our excellent research, discoveries made here are now moving through the licensing and clinical development process, with the expectation of clinical trials to advance new therapies and improve human health. Asthma sufferers are among those who may be helped by our research, based on a technology from the laboratory of Michael Croft, Ph.D., licensed earlier this year.

In this Annual Report, we've highlighted "Four Potential Therapies..." from research done by several of our faculty on a family of proteins called Tumor Necrosis Factor. Autoimmune diseases and inflammatory diseases are two areas where such research is making a difference. Moreover, this area of research is an excellent example of the success of our collaborative environment, which promotes the sharing of ideas and efforts, thereby quickening the pace of discovery.

# the immune system curing hundreds of

We also feature the stories of three individuals, people we know, for whom a disease of the immune system has had significant impact on their lives and the lives of those who care about them. For two of them, research led to therapies that helped to turn their lives back around, but for the third, hope for a cure remains a daily wish.

Finally, we recognize that 2008 was a year of tremendous change and challenge in the global economy. Yet, we are convinced that the ability to discover and to create new technology, with a focus on the vitally important immune system, is more important than ever before. At the La Jolla Institute for Allergy & Immunology, our scientists are drawn to the study of the immune system because we know that our research focus can have powerful effects improving the lives of millions of people.

We are making, and will continue to make, discoveries that matter for you.

Sincerely,



**Mitchell Kronenberg, Ph.D.**  
President & Scientific Director

The only way of finding  
the limits of the possible  
is by going beyond them  
into the impossible.

—Arthur C. Clarke,  
author, inventor and futurist

# We push the limits of scientific discoveries we make today.

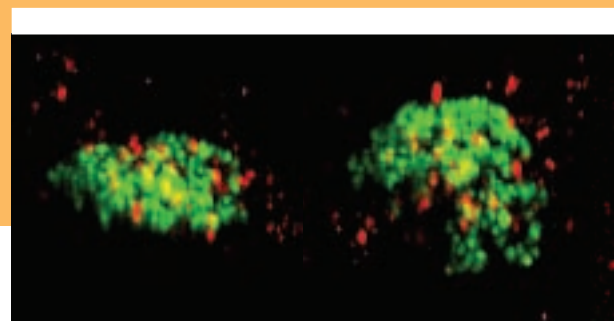
**The Immune System—defender or attacker?** The immune system is a vast network of cells that holds the amazing power to keep us well or make us sick. Composed of more than a trillion cells circulating throughout the body, the immune system offers one of the greatest scientific avenues for improving human health. And yet, most of us only think of it when catching a cold. But to researchers at the La Jolla Institute, who are unmasking its

mysteries to fight diseases ranging from infectious diseases to cancer, its inner workings are a biomedical puzzle of vast importance.

“Most people understand that our immune system protects us from colds, flu and life threatening infections,” said Mitchell Kronenberg, Ph.D., president & scientific director. “But they may not realize the central role it plays in other disorders—known as autoimmune diseases—in which the immune

system mistakenly attacks healthy tissues.” Dr. Kronenberg said this category includes type 1 diabetes, where the immune system destroys insulin-producing cells in the pancreas, and multiple sclerosis, in which it attacks the lining of nerve cells that control muscle movement. Rheumatoid arthritis, inflammatory bowel disease, allergies, asthma and many other disorders also result from inappropriate immune responses.

Institute researchers are getting an as-it-happens view of the cellular interactions that destroy insulin-producing beta cells in the pancreas, the cause of type 1 (juvenile) diabetes, thanks to the Institute’s two-photon microscope (shown here). This highly advanced technology enables researchers to make movies of cellular activity and to see, track and analyze events at a much greater depth than conventional imaging methods. This capability is giving researchers important insights into the pathogenesis of type 1 diabetes and other immune-mediated diseases.



# fic understanding of tomorrow lie in the

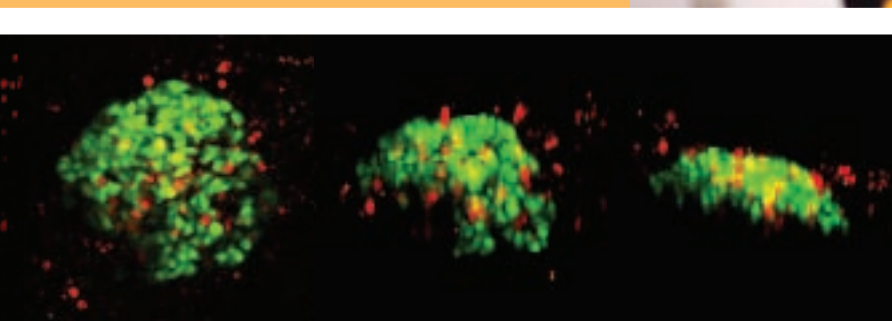
“This is the dark side of the immune system, which actually causes many terrible diseases,” said Dr. Kronenberg. “On the other hand, the immune system is our defender against viruses and other foreign invaders. It’s a yin and yang situation.”

Dr. Kronenberg said Institute scientists work to boost the helpful side of the immune system through the development of vaccines and cancer therapies, and also to cor-

rect its destructive aspects. Both pursuits are critically important.

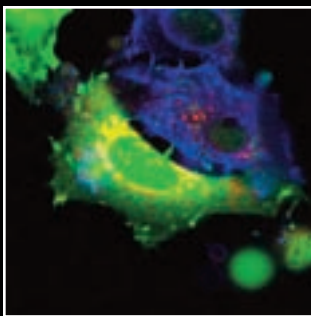
“That’s why our founders formed this research institute

20 years ago,” he said. “They saw the immune system’s extraordinary potential for improving human health.”



# Four Potential Therapies Arising from La Jolla Institute Laboratories

Institute Among Nation's Leaders in Emerging TNF Research Area



For more than a decade, La Jolla Institute researchers have worked diligently to decipher the complex mechanisms of a molecular family that appeared to have strong effects on immune system functioning. Today, that early work has placed the Institute among the world's leading experts on the tumor necrosis factor (TNF) family of proteins and pushed it to the forefront of one of the most exciting new treatment areas in years.

"The TNF family has become a virtual hotbed of research activity because it has been shown to have profound effects on inflammation in the body, which is the underlying cause of many autoimmune diseases," said Mitchell Kronenberg, Ph.D., president & scientific director. "Because of our focus in this area, we now have four potential TNF-based treatments originating from our laboratories. This is quite remarkable for an Institute of our size and we are proud to be a leader in this exciting research area."

Several pharmaceuticals have expressed interest in the Institute's

The important thing is not to stop questioning.  
Curiosity has its own reason for existing.

—Albert Einstein



**Mitchell Kronenberg, Ph.D.**

people with rheumatoid arthritis, Crohn's disease and other disorders. The therapies work by blocking the ability of TNF family molecules to transmit messages that would otherwise cause inflammation.

Institute researchers were key to discovering new TNF molecules in the 1990s, and the family is now believed to have some 30 different members. "We have some of the leading TNF scientists going back to the initial discovery of some of these proteins and in uncovering their roles in inflammatory and disease processes," said Dr. Kronenberg.

He added that certain TNF therapies may work better in some people than others, perhaps due to genetic differences in individuals. For instance, a significant portion of rheumatoid arthritis and Crohn's disease sufferers do not respond well or at all to the existing TNF therapies.

"This opens the possibility of developing other TNF family-blockers to help these sufferers. That's one of the things we are currently working

findings, which are at various stages in the development pipeline.

The TNF family of proteins is a communication system used by inflammation-causing white blood

cells of the immune system. Lymphotoxin and TNE, the family's defining members, are the targets of drugs, called TNF blockers, that were first introduced in the late 1990s to treat



on at the Institute,” he said, adding that Institute researchers are studying the family’s role in diseases ranging from asthma to rheumatoid arthritis to eczema to Crohn’s.

Many believe that existing TNF-blocker therapies, such as REMICADE® and Enbrel®, already used in several diseases by more than 1 million people, are just the first in what may eventually be many TNF-based therapies. This is because, scientists believe, different TNF

family members may play a role in multiple diseases.

Chris Benedict, Ph.D., one of the Institute’s five faculty members studying TNF, explained that the various TNF molecules may act at alternate times during the course of disease or act in concert to regulate varying aspects of inflammation. “So individually, each one can be viewed as strong therapeutic targets for modifying disease pathogenesis,” he said.

The labs of five Institute faculty members working on various TNF members are:

>> Carl Ware, Ph.D., is an internationally recognized expert and trailblazer in TNF research. Dr. Ware’s team of researchers discovered two TNF family members. An inhibitor to one of the TNF family members, Lymphotoxin- $\beta$ , is in clinical trials to treat autoimmune diseases. The other discovery, an inflammatory cytokine known as LIGHT, is a possible target for treatment against various inflammatory diseases.

>> Michael Croft, Ph.D., is world renowned for discovering how

The Institute’s four potential TNF therapies may be used to treat a number of diseases including:

- >> Asthma
- >> Dermatitis
- >> Rheumatoid Arthritis
- >> Inflammatory bowel diseases including Crohn’s disease & ulcerative colitis
- >> Eczema
- >> Psoriasis
- >> Organ Transplant Rejection

members of the TNF family control lymphocytes, and he studies a number of these molecules including OX40, 4-1BB, LIGHT and CD40. His work on OX40 has led to a milestone in asthma research and the potential development of a new treatment for this disease (see story on asthma discovery licensing, page 14).

>> Chris Benedict, Ph.D., was honored in 2007 by the Arthritis National Research Foundation for his work on BTLA, which inhibits the action of some TNF-related molecules, and may be an effective way to help rheumatoid arthritis sufferers who



don't respond well to existing TNF-blocking therapies.

>> Mitchell Kronenberg, Ph.D., also explores BTLA, but his research focuses on Crohn's disease, an inflammatory disorder of the intestines. Dr. Kronenberg has shown in mouse models that using an antibody to block BTLA can stop the uncontrolled response of white blood cells in the intestine that leads to the chronic inflammation of Crohn's.

>> Stephen Schoenberger, Ph.D., has discovered new roles for the TNF molecules, known as TRAIL and CD27, in the regulation of CD8+

**Far left: Chris Benedict, Ph.D.;**  
**left: Carl Ware, Ph.D.; and above:**  
**Stephen Schoenberger, Ph.D.**

“killer” T cells in responding to both self and foreign antigens, thereby opening up new approaches to fighting tumors, controlling autoimmunity and preventing the rejection of transplanted organs. This work builds on his previous studies of the molecule CD40, a TNF molecule that is currently in the development pipeline at a global pharmaceutical company.

### Researcher's Asthma Discovery Licensed by Leading Biotech Finding to be Used in the Development of Potential Asthma Treatment

**A**n innovative and potentially more effective treatment for asthma moved closer to reality in 2008, with the licensing of a major Institute discovery to MedImmune LLC, a leading biotechnology company and subsidiary of AstraZeneca PLC. The discovery, made by the laboratory of Michael Croft, Ph.D., marked a major milestone in asthma research. Asthma affects more than 20 million Americans, including nine million children.

“This agreement with MedImmune is an important first step towards the goal of translating some of Dr. Croft’s groundbreaking work

in the laboratory into an innovative therapy for improving the lives of asthma patients,” said Mitchell Kronenberg, Ph.D., president & scientific director.

Dr. Croft’s finding demonstrated the pivotal role of a TNF family member called the OX40 ligand in asthma. The discovery is particularly

exciting because it offers the potential to control asthma for longer periods of time and with much more specificity than current therapies. MedImmune licensed the discovery to explore its use in the development of a potential drug for treating asthma.

Dr. Kronenberg said such licensing arrangements are a central part of the



**Michael Croft, Ph.D.**

## Woman is Thankful for “Life-Changing” TNF Therapy

mission of research institutes to ensure that discoveries stemming from public and privately funded research are put into direct use for improving human health. “As a nonprofit biomedical research institute, we are dedicated to finding the molecular causes of diseases, with the hope that our discoveries will one day be translated into new and better therapies,” Dr. Kronenberg said. “This agreement with MedImmune is a significant advancement toward that goal.”

Asthma is a chronic disease of the airways that can cause wheezing, coughing and difficulty breathing. It is the most common serious chronic disease of childhood and is the third-ranking cause of hospitalization among U.S. children under age 15. The National Institutes of Health (NIH) estimates asthma-related health care costs in the U.S. at \$14 billion annually.

Dr. Croft’s research has previously shown in experimental animal models that using an antibody to block the interaction of the OX40 ligand with OX40, its receptor, can substantially suppress the lung inflammation and accompanying symptoms of an asthma attack.

“The licensing of this intellectual property by MedImmune further validates the importance of Dr. Croft’s discovery in the field of asthma research,” Dr. Kronenberg said.



In the darkest days of her battle with rheumatoid arthritis, Laura Gallo, now age 35, remembers having so much hip and joint pain that she couldn’t even drive to work. “It hurt to do anything,” she recalled in describing a flare up of the disease that first struck her at age 20. “I couldn’t sleep because there was a stabbing pain in my shoulder. I’d also lost mobility in my left hand. I couldn’t make a fist.”

The terrible symptoms are only a memory for Laura, an engineer, who leads an active, pain-free life. She credits her turnaround to one of the first therapies resulting from research into the tumor necrosis factor (TNF) family of molecules. “It totally changed my life,” said Laura, who began using the drug Enbrel® in the 1990s.

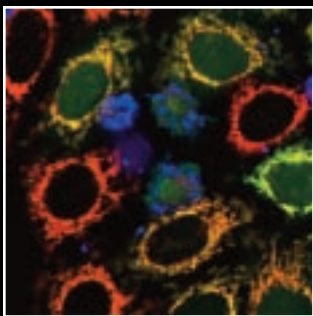
Enbrel® is one of three major anti-TNF therapies released in the 1990s and used for treating rheumatoid arthritis and several other disorders. The therapies, which do not work for all sufferers, block the action of various inflammation-causing TNF molecules in the body. La Jolla Institute researchers were key to discovering more TNF family molecules in the 1990s, and now have four TNF-blocking therapies in development. The Institute hopes the therapies may one day help the significant number of sufferers who do not respond to the existing anti-TNF treatments.

This is good news to Laura. “I want to support research and strides in this area.” She also wants to encourage other autoimmune disease sufferers. “At one time, I wasn’t sure whether I should have children. I didn’t know if I could take care of them because of my illness. But today, my husband and I have a baby boy. I can do all the things I want to do,” she said.

“I am so grateful for drugs like this. And I’m glad there are more therapies in the works. People should never give up hope.”

# Researcher's Discovery May Protect Nation's Youth in Smallpox Outbreak

## U.S. Looking to Stockpile Treatment as Bioterrorism Safeguard



If smallpox ever rears its ugly head again, the work of Shane Crotty, Ph.D., may be the treatment the nation turns to safeguard its children. Regarded as the deadliest disease ever known to man, smallpox was officially eradicated worldwide in 1980 and routine vaccinations against the disease ended in the U.S in 1972. But with the specter of bioterrorism, the smallpox virus has become the subject of intense research interest over the last several years. Concern has led to the creation of government stockpiles of the smallpox vaccine and significant interest in a new, faster-acting treatment.

Dr. Crotty has developed an antibody treatment that appears to quickly fight the smallpox virus and in 2008 received a \$7.1 million grant from the National Institutes of Health (NIH) to fund pre-clinical testing. The NIH is considering stocking mass quantities of the treatment nationwide alongside the smallpox vaccine.

Mitchell Kronenberg, Ph.D., president & scientific director, said Dr. Crotty's work is particularly important because those younger than

## Science does not know its debt to imagination.

—Ralph Waldo Emerson, American essayist, philosopher and poet

37 years old in the U.S. population have not been vaccinated against smallpox. “This makes the need for a strong and fast-acting treatment all the more vital should we ever face a smallpox outbreak,” he said.

Fast-acting is important since, in the event of a terrorist-sponsored outbreak, a critical time lapse would occur before people could receive the

vaccine. “In general, vaccines are preventive,” said Dr. Crotty. “You must receive the vaccine before you are infected or sick. Otherwise, it won’t do you any good.” Unlike the vaccine, the anti-smallpox antibody would provide immediate treatment, even if the person had already been exposed. “While a vaccine might take weeks to be effective, but offers life-long pro-

tection, the antibody would work immediately, but short term,” said Dr. Kronenberg. “This could be very important should people become infected before they have a chance to be vaccinated.”

Dr. Crotty said further testing of the antibody will be conducted using highly sophisticated animal models. No live smallpox virus will be used

in any of the studies. He added that the anti-smallpox human antibody has already proven to be effective in animal testing protocols used by the FDA.

**Shane Crotty, Ph.D.**



## Institute Researcher Pioneers New Model for Battling Dengue Virus Dangerous Pathogen Moves Closer to U.S.

While many had tried before her, it took a fiercely determined researcher originally from Nepal—**Sujan Shresta, Ph.D.**—to give the world its best tool to date for combating the dangerous dengue virus. Dengue virus, while still unknown to most Americans, is a public health threat of pandemic proportions that

is creeping ever closer to U.S. borders. Now categorized by the U.S. Centers for Disease Control as an emerging disease threat, dengue infects an estimated 50 to 100 million people worldwide annually, with 250,000 cases of the severest form reported each year. Primarily found in Southeast Asia and Latin America, dengue cases have now been reported in Mexico and mosquitoes capable of transmitting the virus have arrived on American soil.

**Sujan Shresta, Ph.D.**



Thanks to Dr. Shresta, dengue virus research received a major boost in 2008, with her development of the world's first mouse model showing key aspects of human infection. The model is now in use by two biotech companies seeking to develop first-ever treatments for the disease. "I think the most important reason there is currently no vaccine or treatment for this disease is because, up to now, we didn't have a good animal model," she explained. "With a model, we can watch the progression of disease from its earliest stages."

Other researchers had tried to develop a high-quality mouse model, but only met with limited success, producing models that didn't closely resemble the disease in humans. In 2007, Dr. Shresta set out to create a better model. "I decided to look at nature," she said. "The virus is always being passed back and forth between mosquitoes and humans, which are the only two organisms naturally infected by this disease." So unlike previous efforts that used mouse to mouse transmission to create a model strain, she used mosquitoes to mouse transmission, which more closely resembled the natural cycle.

Dr. Shresta is continuing her studies, now using the model in hopes of one day developing a vaccine.

## Television Reporter Recalls Lyme Disease Struggle

### Lyme Disease Discovery Offers Hope

For sufferers of chronic Lyme disease, life can become an ongoing struggle against a complex and unforgiving foe. Caused by a bacteria transmitted by infected deer ticks, Lyme disease, if left untreated, can spread to the joints, the heart and the nervous system, leading to serious health problems.

In 2008, Lyme disease sufferers received some hopeful news thanks to a major discovery by Mitchell Kronenberg, Ph.D., president & scientific director. Dr. Kronenberg found that natural killer T cells (NK T cells), which are disease-fighting cells of the immune system, are important for clearing the bacteria that causes Lyme disease and for reducing the intensity and duration of its associated arthritis. Lyme disease currently is the most common insect-borne disease in the United States. "Our study offers the possibility of eventually developing immunological agents that can trigger more NK T cells to fight this disease," he said.

A leader in NK T cell research, Dr. Kronenberg has found novel connections between NK T cells and a number of diseases.



The evening that launched Brooke Landau's 14-year struggle with Lyme disease started like any other. "I went to bed perfectly fine," recalled Brooke, now a San Diego Weather-caster and national spokesperson for Lyme disease. "But when I woke up, I was unable to move from the waist down."

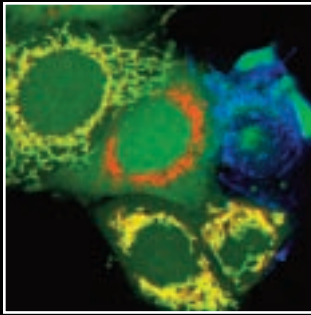
Unbeknownst to her at the time, Brooke had developed a severe case of Lyme disease from a deer tick bite a year earlier in her native Connecticut. Left untreated, the disease had spiraled out-of-control, leaving her bedridden for two months.

After recovering from her initial bout, Brooke, then 23, thought she was fine. "I had just graduated from college and I'd gotten this marketing/sales position at a Fortune 500 company." But soon she was too sick to work as the disease manifested itself in other ways. Its grueling symptoms ranged from severe arthritis and difficulty walking to heart arrhythmias, short-term memory loss, continuous excruciating headaches and the loss of 1/4 of her body weight. "I lost hearing in my left ear, started losing sight in both my eyes and my hair was falling out. Yet no one knew what was wrong with me."

Trips to the doctor left Brooke frustrated. "For 7½ years I had a negative blood test. So even when doctors suspected I had it, they couldn't diagnose and treat it properly." Brooke said it's a common scenario for Lyme disease sufferers. "The test results are inaccurate 60 percent of the time," she said.

Ultimately, Brooke said she found a "Lyme literate" physician and underwent years of treatments that finally put her in remission.

These days Brooke advocates for sufferers through various organizations and occasionally reports on the disease, including a recent segment on the Institute's research (see story, this page). "I really honor people who devote their lives to finding explanations and new treatments for those of us who have been very ill."



# Institute Launches Type 1 Diabetes Center

## Center Will Galvanize Efforts Toward Prevention and Cure

A major center that will advance research toward new therapies to better treat, prevent or cure type 1 diabetes became a reality in 2008 with the launch of the Institute's Type 1 Diabetes Center. Type 1 diabetes, also known as juvenile diabetes, is caused by an attack of the immune system against the insulin producing cells of the pancreas. "Our mission is to be a premier center of

excellence in type 1 diabetes research," said Matthias von Herrath, M.D., the Center's director, who is internationally recognized for his diabetes research. "Our Center will be a place where leading scientists can collaborate in a dynamic environment designed to rapidly advance progress toward the prevention or cure of type 1 diabetes." The Center will focus on novel, immune-based research approaches.



**Matthias von Herrath, M.D., right, with Ken Coppieters, Ph.D.**

## Mother and Daughter Hope for Type 1 Diabetes Cure

Mitchell Kronenberg, president & scientific director, said the Center will work with other leaders in the field, both locally and nationally, to accelerate advances through translational research collaborations, clinical trials, information exchange and professional education. UC San Diego and the Institute are already in discussions regarding joint research and training activities. “Our Center provides the ability to unify like-minded researchers and clinicians from various disciplines,” Dr. Kronenberg said. “It will certainly be a catalyst for new discoveries and for building on those we’ve already achieved.”

One of those discoveries, developed by Dr. von Herrath, is a combination therapy that has shown significant promise in mouse models at stopping type 1 diabetes, when caught in the early stages. The therapy was cited by the American Diabetes Association in awarding Dr. von Herrath its 2008 Outstanding Scientific Achievement award.

The real voyage of discovery consists not in seeking new landscapes, but in having new eyes.

—Marcel Proust,  
early 19th century French novelist



The wish for 11-year-old Melia and her mother, Kathy, is always the same. “Whether we’re blowing on a dandelion, throwing a penny in a wishing well or looking at a falling star, we always

wish for a cure,” said Kathy Haynes, of San Diego, whose daughter was diagnosed with type 1 diabetes, also known as juvenile diabetes, at age 6.

A spunky, determined straight-A student, Melia is matter-of-fact when describing her illness. “I wear my insulin pump all the time,” she said, displaying a little pink waist pouch containing the pump, testing supplies and glucose tablets. Her blood sugar must be tested 8 to 10 times a day, two of those tests during school. “I just test myself quietly in the classroom,” said Melia. “I always use my fingers because it hurts less. Once I even used my toe.”

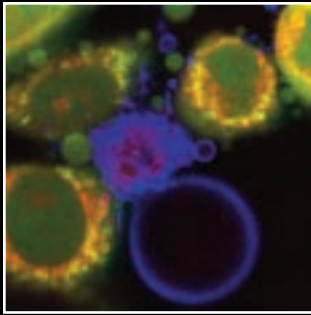
The testing and insulin pump are critical tools for Melia and other type 1 diabetes sufferers. In type 1 diabetes, the immune system inexplicably destroys insulin-producing pancreas cells, needed to convert food into energy. Sufferers must be given insulin or they cannot survive.

“Every time Melia eats she has to receive insulin,” said Kathy. “Otherwise, her body would starve.”

Melia’s parents work hard to monitor her illness, and to give their daughter a normal life. “We don’t let it stop us,” said Kathy. Melia chimed in proudly: “I play soccer, softball, the piano and flute. I do all the things other kids do.”

“It’s still very scary,” Kathy admits softly. “I worry about her, things like blindness and kidney problems. I worry about her going off to college. What if she passed out and people didn’t know what was wrong?” But Kathy counteracts that fear with a medical alert bracelet for her daughter. And she remains optimistic about the future.

“Our biggest hope is to find a cure.”



# Institute Continues Tradition of Pioneering Allergy Research

## Important Strides Mark Second Year of Major Allergy Study

**L**ike the Institute's founding scientists, La Jolla Institute researchers are continuing to break new ground in allergy research.

Led by renowned scientist Alessandro Sette, Ph.D., the Institute is delving deeper than any previous research study to find the root cause of allergy reactions at the molecular level. The five-year project, funded by the National Institute of Allergy & Infectious Diseases, could lead to revolutionary new approaches for treating allergies that are faster and have fewer patient side effects.

Mitchell Kronenberg, Ph.D., president & scientific director, said the study is a continuation of the Institute's rich history in allergy innovation. "A seminal discovery by our two founding scientists changed the face of allergy research more than 40 years ago," he said, referring to the discovery of the immunoglobulin E (IgE) antibody in 1966 by Kimishige and Teruko Ishizaka, M.D.s, Ph.D.s., who later helped launch the Institute.

"It is a continuation of our legacy to lead the way toward a profound change in allergy treatment that could significantly benefit sufferers worldwide."

Dr. Sette, the project's principal investigator, said the study's goal is to drill down to the level of epitopes—which are tiny sites on a protein or other molecule that instigate a T cell response. T cells are white blood cells that are the body's warriors against viruses and other invaders. In the case of allergies, however, the T cells launch an attack against allergens, such as pollen, where no response is needed.

"Our goal is to identify exactly which epitopes are triggering the T cells to attack. This would open the possibility of developing therapies around those epitopes," he said, noting that several clinical trials have already shown promise in treating patients with allergy-related epitopes.

Now entering the study's second year, the research team has successfully synthesized 700 different epitopes from Timothy grass, a common aller-

## Institute Scientists Receive Major Awards



gen and well-known model system. “This represents the universe of possibilities that the human immune system could recognize in this allergen,” said Howard Grey, M.D., project co-investigator. “We will test these epitopes with blood samples from allergic donors to find out exactly which Timothy grass epitopes are triggering their allergic response. This will give us a full profile of each donor at a level of the response never before achieved.”

Knowing this information could allow researchers to create desensitization therapies at the epitope level, whereby patients would receive the

**Alessandro Sette, Ph.D., left, with Howard Grey, M.D.**

allergen epitope which would induce immune tolerance, without instigating an antibody reaction. This would differ from existing desensitization therapies, which often produce adverse reactions because patients already have antibodies to the allergens they are receiving.

“If this proves true, it could produce the same effects as the current desensitization therapies, but in a much shorter period of time and without the allergic side effects,” said Dr. Sette.

The Institute’s impressive research advancements in type 1 diabetes, heart disease and dengue virus resulted in the receipt of several important awards in 2008. In addition, 114 papers, outlining significant Institute discoveries, were published in notable scientific journals throughout the year. Awards in 2008 included:

>> The American Diabetes Association (ADA), the nation’s leading voluntary health organization in the fight against diabetes, gave Matthias von Herrath, M.D., its Outstanding Scientific Achievement Award for 2008. The award, one of the ADA’s most prestigious, recognized Dr. von Herrath’s novel strategies for fighting type 1 diabetes.

>> Klaus Ley, M.D., head of the Institute’s Inflammation Biology division, received the 2008 Marie T. Bonazinga Research Award, the highest honor presented by the Society for Leukocyte Biology. He was recognized for his work illuminating the basic cellular mechanisms underlying inflammation, particularly as it relates to heart disease.

>> The San Diego Foundation’s Science and Technology Working Group chose Sujana Shresta, Ph.D., to receive a \$55,000 Blasker award to support her research on dengue virus, a dangerous disease affecting millions worldwide. The Blasker awards, which are administered by the San Diego Foundation, support local individuals who demonstrate high potential in the scientific, engineering and medical fields.

Discovery consists of seeing what everybody has seen, and thinking what nobody has thought.

—Albert Szent-Gyorgi, Nobel prize-winning scientist

FISCAL YEAR ENDED DECEMBER 31, 2008

## 2008 FINANCIAL PICTURE REMAINS STRONG

The La Jolla Institute for Allergy & Immunology continues to operate in a strong financial position, with total revenues reaching a new high of \$36.9 million for fiscal year 2008. As shown on the accompanying bar graphs, the Institute's federal funding, total revenues and net assets have increased steadily during the past five years. This is largely due

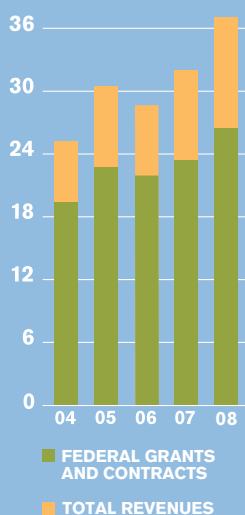
to the continued success of our renowned scientists in obtaining competitive, peer-reviewed research funding from the National Institutes of Health (NIH).

While NIH funding is our mainstay, we are mindful of current economic conditions and government spending patterns that will place increased pressure on NIH funding levels in the future. Accordingly, we have undertaken efforts to diversify and enhance Institute revenue sources from philanthropy and technology development. These efforts are already showing signs of success.

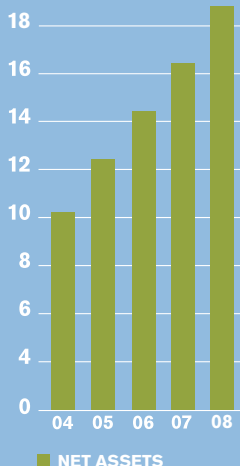
In addition, the Institute's relationship with our longtime industry partner, Kyowa Hakko Kirin California, Inc., remains strong.

Since our inception in 1988, Kyowa Kirin has provided us with a critical and stable source of unrestricted research funding while facilitating the translation of our discoveries into potential treatments for human disease. This sponsored research funding remains an important source of revenue, and provides our scientists with the freedom to pursue the most promising research. As we celebrate 20 successful years of medical research discoveries at the La Jolla Institute, we would like to recognize and thank Kyowa Kirin for their enduring support.

As we move forward into our 21st year, the Institute continues its steadfast commitment to excellent and innovative research activities, while ensuring that general and administrative expenses are kept to a



**Revenue Growth**  
in millions of dollars

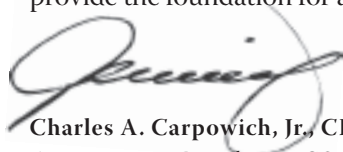


**Net Asset Growth**  
in millions of dollars



minimum. A high percentage of every Institute dollar spent goes directly to research. As shown on the accompanying pie chart, 88 percent of total expenses were used for research in 2008.

In summary, the La Jolla Institute's financial position and outlook remain very positive. This, coupled with our extraordinary scientists, dedicated staff, and excellent research facilities, will continue to provide the foundation for an accelerated pace of discovery.



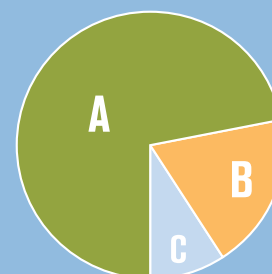
**Charles A. Carpowich, Jr., CPA**  
Executive Vice President & COO/CFO

#### STATEMENT OF FINANCIAL POSITION

Cash and investments	\$ 11,786,000
Grants receivable and other	5,628,000
Property, net	6,128,000
<b>Total assets</b>	<b>\$ 23,542,000</b>
<hr/>	
Accounts payable and accrued expenses	\$ 4,345,000
Deferred revenue	445,000
<b>Total liabilities</b>	<b>4,790,000</b>
<b>Total net assets</b>	<b>\$ 18,752,000</b>
<b>Total liabilities and net assets</b>	<b>\$ 23,542,000</b>

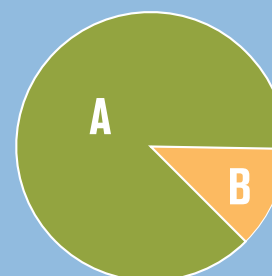
#### STATEMENT OF ACTIVITIES

<b>Revenues:</b>	
Federal grants and contracts	\$ 26,447,000
Private grants and contracts	7,165,000
License revenue	2,219,000
Contributions	542,000
Investment return and other	541,000
<b>Total revenue</b>	<b>\$ 36,914,000</b>
<hr/>	
<b>Expenses:</b>	
Research	\$ 30,214,000
General and administrative	3,853,000
Fundraising	322,000
<b>Total expenses</b>	<b>\$ 34,389,000</b>
<b>Change in net assets</b>	<b>\$ 2,525,000</b>



#### Revenues

- A) Federal grants and contracts 72%
- B) Private grants and contracts 19%
- C) License and other revenue 9%



#### Expenses

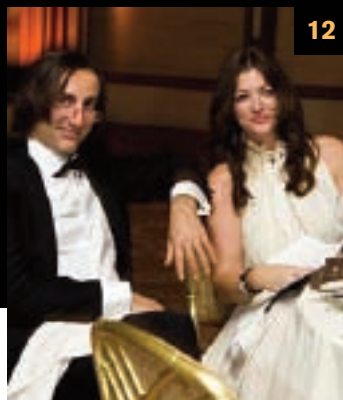
- A) Research 88%
- B) G&A and Fundraising 12%

\* 2008 Financial Data summarized from the Institute's December 31, 2008 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@liai.org.

# La Jolla Institute's 20th Anniversary Gala

On November 1, 2008, the La Jolla Institute marked its 20th Anniversary with a first-ever Gala Celebration at the Del Mar Country Club. Gala Co-Chairs, La Jolla Institute Board Member Mike Martin and his wife, Paula Martin, along with President Mitch Kronenberg, welcomed over 125 guests who enjoyed an elegant evening beginning with a champagne reception, dinner, the debut of a video about the Institute, and a live auction over dessert. Wayne Foster Entertainment provided exceptional musical entertainment and dancing. Anniversary Celebration Sponsors included: International Oncology Network (ION), Dr. and Mrs. Makoto Nonaka, P4 Healthcare, Kirin Pharma, Novartis Oncology, Sanofi Aventis, Pillsbury Law, CONNECT, and BIOCUM.

Most importantly, the proceeds from this very special event, almost \$60,000, will be used to support type 1 (juvenile) diabetes and cancer research.





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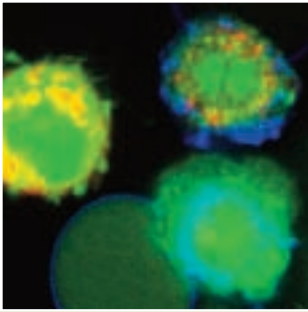


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1. Lila & David Webb, and Alan Lewis; 2. Anjana Rao, Patrick Hogan, and Judith Lewis; 3. Dave and Esther Perkins, Deanne and Rob Seiler, Debbie and Kevin Keller; 4. (back row from left) Annon and Claire Altman, Makoto and Mariko Nonaka, Rose and Fu-Tong Liu, Shelley Hendler; (seated from left) Lucienne and Roger Guillemin, Joyce Hendler; 5. Dinner seating; 6. Klaus Ley bids during the auction; 7. John and Susan Wetherell; 8. Paul and Lauren Mirabella, Doug Storer, Cindy Mullen, Franca Lutufo, Mike Mullen, Paula Martin; 9. Co-Chair Mike Martin and President Mitch Kronenberg; 10. Claire and Annon Altman, Sam Strober; 11. Nathan Fletcher, Terry Carpowich, Jeri and Harold Buchanan; 12. Alex Sette and Suzanne Melvin; 13. David and Martha Dominguez; 14. Kathy and Kip Miller; 15. Dr. and Mrs. Roger Guillemin; 16. Anna and Shane Crotty, June and Ralph Kubo, Mick and Linda Croft, Makoto and Mariko Nonaka, Rose and Fu-Tong Liu



To see things in the  
seed, that is genius.

—Lao Tzu,  
sixth century B.C. philosopher

## GIVING

2008 is a year that will be remembered for many years to come.

For some it will be a pivotal year of connecting world economics with “home” economics. For others the significance will be the changes in the political scene. Yet, for those like Laura Gallo and Brooke Landau, (see Profiles in this Annual Report) every year without the terrible symptoms of arthritis or Lyme disease is another year to be grateful for. And for Kathy Haynes and her daughter, Melia, every year is one of hope that a cure will be found for type 1 diabetes.

While at the La Jolla Institute for Allergy & Immunology, 2008 meant 20 years of scientific excellence, celebrated with an Anniversary Gala as seen on the previous pages, it also presented opportunities to move our discoveries forward. As you’ve read in this Annual Report, it is the scientists who are key to finding the causes of disease and creating pathways to improve human health. And the fact is, it takes multiple sources of funding to keep up the pace and momentum of discovery. We are grateful this year to have received significant support for our scientists from the Legler Benbough Foundation of San Diego.

We appreciate the continuing generosity of all of our donors and friends. Without you, we could not take our research to the highest levels in order to “Find Cures Faster.” Thank you.

With kind regards,

**MaryAnn F. Stewart**

Vice President, External Relations  
& Chief Development Officer



# LA JOLLA INSTITUTE FOR ALLERGY & IMMUNOLOGY

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