

# Immune Matters

FALL 2014

La Jolla  
Institute  
FOR ALLERGY AND  
IMMUNOLOGY

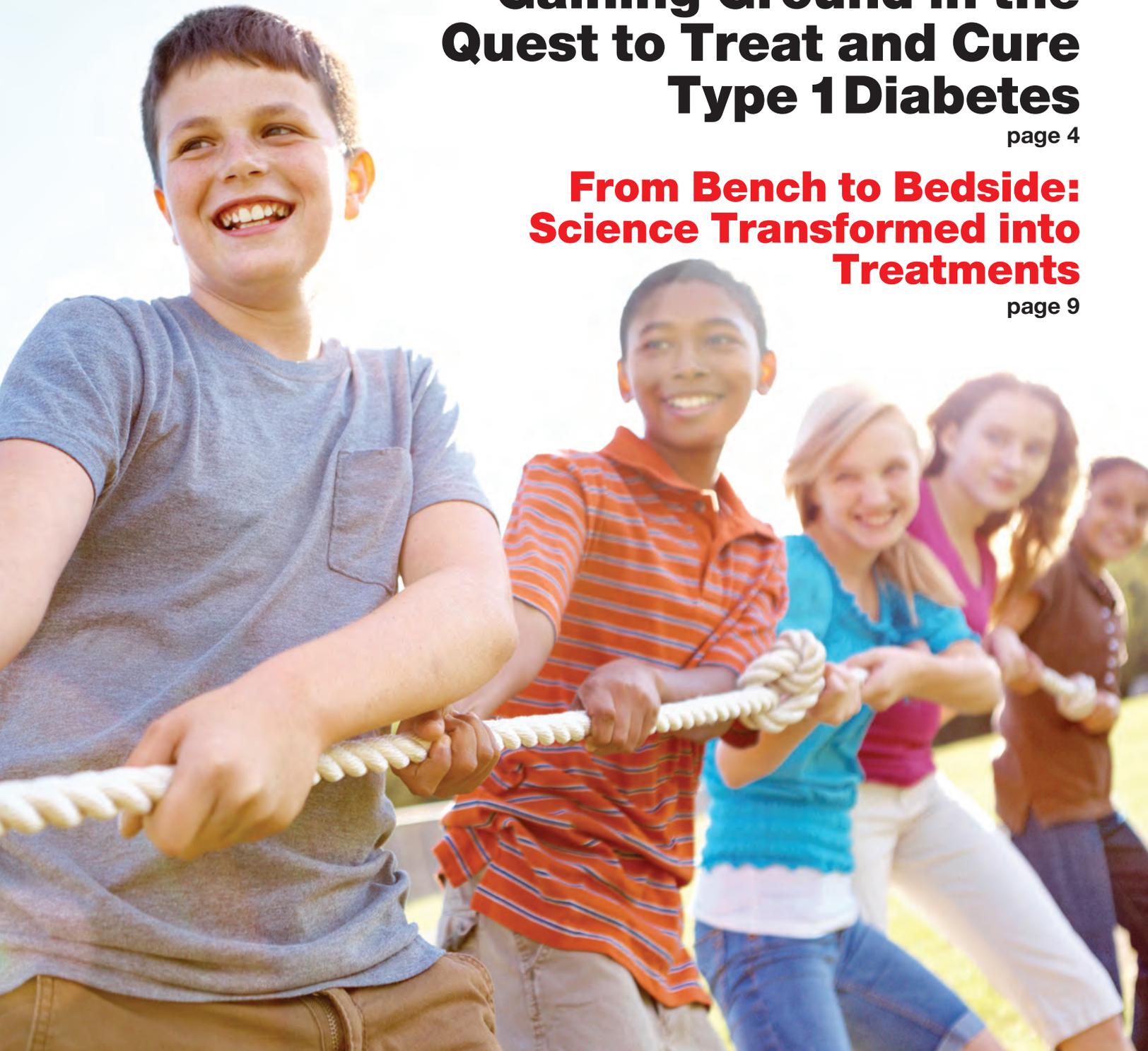
Life  
Without  
Disease.

## Gaining Ground in the Quest to Treat and Cure Type 1 Diabetes

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## From Bench to Bedside: Science Transformed into Treatments

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La Jolla Institute for Allergy and Immunology is dedicated to understanding how the immune system works and to applying that knowledge to promote human health and prevent a wide range of serious diseases. Since its founding in 1988 as an independent, nonprofit research organization, La Jolla Institute has made numerous major advances leading toward its goal: life without disease.

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# Letter from the President



Diabetes is so prevalent today it touches the lives of just about everyone, whether you have the disease yourself or are connected to someone who does. The impact of diabetes, both medically and economically, is staggering, afflicting over 29 million Americans. More importantly, as anyone whose loved one has struggled with the daily management of the disease can tell you, the emotional toll is also quite high.

This is why for the past decade the La Jolla Institute has made diabetes research one of its key scientific objectives. As a leader in the field of immunology, investigating diabetes is a perfect fit for the Institute: type 1 diabetes—often called “juvenile diabetes” (although 50 percent of new cases are now diagnosed in adults)—is an autoimmune disease, and type 2—known as “adult onset”, but tragically afflicting more and more children—is the result of chronic inflammation. Since autoimmunity and inflammation are two of the pillars of our research, our scientists are uniquely positioned to investigate these diseases in a collaborative environment.

We didn’t have to look far in our own La Jolla Institute community for examples of people who share a passion for finding a cure for diabetes. I hope you will enjoy reading about a few of these people, from LJI researcher Matthias von Herrath, M.D., recently ranked the world’s number one expert in type 1 diabetes, and Lynn Hedrick, Ph.D., whose own life and career path were influenced by witnessing her mother’s struggle with diabetes, to Eric Zwisler, our newest board member, who was motivated to get involved by his son’s diabetes.

Whether it’s diabetes or another disease we investigate here at the Institute, we’re driven not just by our mission to expand knowledge and understanding of immune-based illness, but by a desire to make sure our discoveries are ultimately turned into treatments that can change people’s lives.

The Institute’s bench-to-bedside process—that important time when our various discoveries move from the laboratory to proof-of-concept research and patenting—was transformed in 2007 when we created our Technology Development Department. In this issue of *Immune Matters* you’ll learn about the process of turning discoveries into treatments. You will note the critical phase, sometimes called the “Valley of Death,” where we must find investors and private sector companies to partner with to ensure the discoveries continue on their journey to become treatments for patients. While the process can be full of frustration and setbacks, it also has the potential for major success.

At the La Jolla Institute, we believe that the power of the immune system has the potential to preserve and restore human health, and that our understanding of this power can help us conquer diseases such as diabetes, heart disease, and cancer. We are proud to be a world leader in the study of immunology and we are deeply thankful for the support we receive from individual donors, foundations, and federal sources that enables our critical work to flourish. I hope you enjoy this issue of *Immune Matters*, as we are delighted to share with you the news of our continuing efforts toward life without disease.

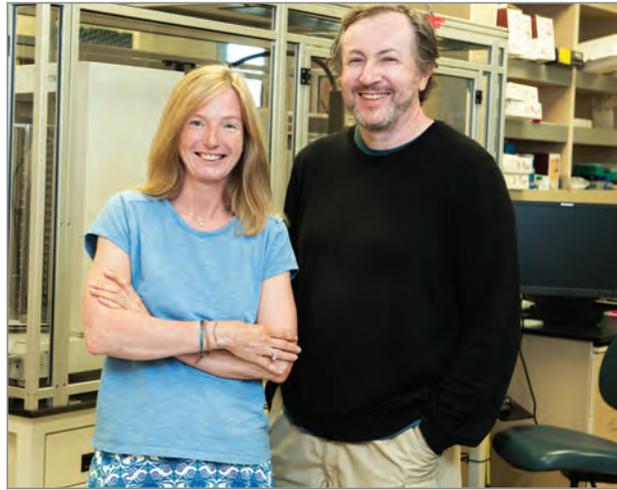
Sincerely,

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

## LJI RNAi Center “Sparks” Research Projects with New Grants

La Jolla Institute is home to The RNAi Center, a state-of-the-art facility that allows scientists to explore new ways of disrupting disease processes based on altering gene function. RNAi, short for RNA interference, is a technology that allows scientists to silence genes to determine what proteins they produce.

By rapidly sifting through thousands of genes, scientists are able to pinpoint the exact gene that codes for specific malfunctions of the immune system. The RNAi Center at LJI is the first of its kind in San Diego and one of only a handful of dedicated RNAi centers in the nation, making it



*Faculty members Lynn Hedrick, Ph.D., and Don Newmeyer, Ph.D., in The RNAi Center*

a significant addition to the Institute. In an effort to encourage and enable (“spark”) more labs to incorporate this technology into their research, LJI recently announced the SPARK Grant funding program. Grants will support RNAi screening projects to be performed at The RNAi Center in 2014. Several factors were considered in choosing the grant recipients, including whether the proposal tackles an important problem in the field and if it is likely to promote new collaborative interactions in the Institute.

Read about the winning projects below:

### **Understanding How Cells Die** *Yulia Kushnareva, Ph.D. and Don Newmeyer, Ph.D.*

Inside cells in the body there are structures called mitochondria, commonly known as the cell’s energy factories, which are necessary for cells to function properly. Surprisingly, mitochondria also promote cell death in some situations. As a normal part of physiology, some cells die in order to maintain the proper proportions of different cell types. When cells fail to die at the right time they can accumulate inappropriately, leading to diseases such as cancer. Indeed, cancer therapy involves the selective killing of malignant cells, making it very important to understand the processes through which cells die. The Newmeyer laboratory has been studying the critical events that occur in mitochondria that convert them from powerhouses into cell-killing structures. This RNAi SPARK grant will fund efforts to identify proteins needed for mitochondria-induced cell death. Such discoveries will set the stage for future research to discover precisely how mitochondria regulate cell death and will hopefully pave the way for future therapies for cancer and other diseases where cell death is dysregulated.

### **Different Proteins for Different Cell Types** *Lynn Hedrick, Ph.D.*

Our immune system protects us via a network of more than a trillion cells, working together in tissues and organs to keep foreign invaders out, or failing that, to destroy them once they enter our bodies. One type of these cells, called monocytes, originates from stem cells in bone marrow. Once they mature they circulate throughout the body where they maintain a healthy vascular system and quickly respond to vascular and tissue injury. There are at least two subsets of monocytes: “inflammatory” monocytes and “patrolling” monocytes. Dr. Hedrick’s lab has recently identified a protein that is required for the development of “patrolling” monocytes and, using the RNAi SPARK grant, will seek to uncover proteins that are unique to these different monocyte types with the goal of identifying new regulatory factors required for their development.” ●

## Gaining Ground in the Quest to Treat and Cure Type 1 Diabetes

**Matthias von Herrath, M.D., Combines Passion for Basic Research with New Bench-to-Bedside Focus to Develop Better Patient Treatments**

There are two ferocious and fascinating wars raging in the realm of type 1 diabetes.

The first has been waged for millennia within the human pancreas: the body's own immune system attacks and destroys the beta cells that produce insulin, the hormone that moves glucose from the blood into

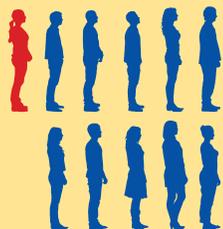
cells to produce energy. Over eons, the casualties have been immense, as the resulting condition known as type 1 diabetes, has meant severe illness and ultimately death for those afflicted.

The second war is the hard-fought ongoing battle by medical science to determine the cause of diabetes, treat, and cure the disease. The first triumph didn't come until just over 90 years ago, but it was monumental: In the 1920s, Canadian physician Fredrick Banting and his colleagues not only discovered insulin, but figured out

### DIABETES IN THE UNITED STATES

#### DIABETES

**29.1 million Americans have diabetes**



That's about **1 out of 11**



**1 out of 4** do not know they have diabetes

#### THE COST

**245 billion**

Total medical cost and lost work and wages for people with diagnosed diabetes



Risk of death for adults with diabetes is **50% higher** than for adults without diabetes

Medical costs for people with diabetes are **twice as high** as for people without

**2x\$**



People with diabetes are at higher risk of serious health complications:

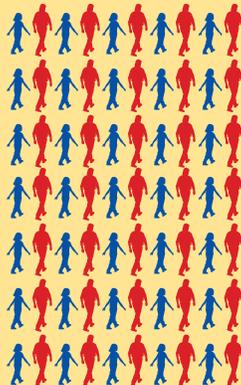
**blindness, kidney failure, heart disease, stroke, loss of toes, feet, or legs**

#### DIABETES-TYPES

#### TYPE 1

Body does not make enough insulin

- Can develop at any age
- No known way to prevent it



More than **18,000 youth** diagnosed each year in 2008 and 2009

**50%** of all new cases of type 1 diabetes are in adults

#### DIABETES-TYPES

#### TYPE 2

Body cannot use insulin properly

- Can develop at any age
- Most cases can be prevented



Currently, at least **1 out of 3 people** will develop the disease in their lifetime

More than **5,000 youth** diagnosed each year in 2008 and 2009.

#### Risk Factors for Type 2 Diabetes:

- Being overweight
- Having a family history
- Having diabetes while pregnant (*gestational diabetes*)

Take a diabetes risk test [www.cdc.gov/diabetes](http://www.cdc.gov/diabetes)

#### INSULIN

Insulin is made in the pancreas ▶ allows body to use glucose from food for energy 24 hours a day ▶ maintains delicate balance of blood sugar level.

This is your pancreas



More than **370 million** people with diabetes worldwide, **90%** with type 2



*Matthias von Herrath, M.D.*

how to extract it from the pancreata of animals for injection into humans. Not only did this keep people from dying from diabetes, it enabled them to lead relatively long and healthy lives.

Today, a sizable global army of researchers is attacking type 1 diabetes on multiple fronts. The La Jolla Institute is in the center of the battle and has on its faculty one of the world's most effective leaders in this fight against diabetes, Matthias von Herrath, M.D. Given his singular focus and dedication to diabetes, Dr. von Herrath is utilizing every tool and angle he can think of to approach this monumental task.

So much so that he made a career shift a few years ago to expand his access to the resources necessary to get closer to a cure. With his reputation secure as one of the foremost diabetes researchers, Dr. von Herrath felt the urge to broaden his horizon into the area of translational medicine even if it meant essentially adding another full-time job to his life.

"I was proud of what I had achieved as a diabetes

researcher using animal models, but at the same time was frustrated by the slow pace. During my years of working as a clinical physician at the beginning of my career, I had witnessed first hand how devastating the disease can be on the lives of patients and their

families—problems ranging from organ damage and blindness to other terrible side effects," Dr. von Herrath says. "So I had a really strong desire to see research move as quickly as possible into clinical human trials and ultimately into more effective patient treatments and hopefully someday soon a cure for this disease."

Keeping his position as Professor and Director of the Institute's Center for Type 1 Diabetes Research, Dr. von Herrath

accepted a position at the pharmaceutical giant Novo Nordisk in 2012 as Director of the company's Seattle-based Type 1 Diabetes Research and Development Center. Novo Nordisk, a Danish healthcare company with 40,000 employees in 75 countries, is a leading producer of insulin and has been at the forefront of diabetes research and treatment for 90 years.

**"I had a really strong desire to see research move as quickly as possible into clinical human trials"**

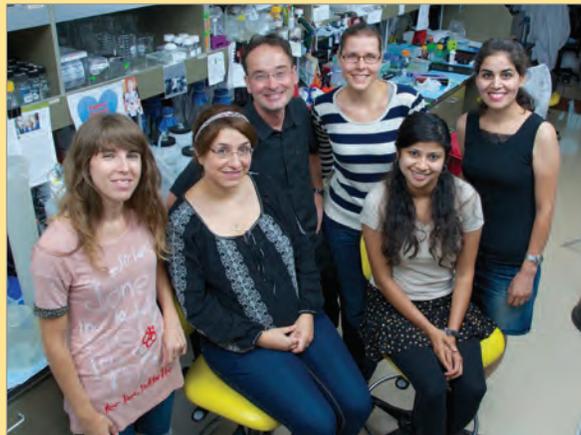
## Get to Know the World's Top Diabetes Researcher

Just a week after Matthias von Herrath's father retired in West Berlin, he suffered a stroke and died within 24 hours. That tragedy ultimately compelled the younger von Herrath to pursue a career in medical science.

"It was a terrible time for our family," Dr. von Herrath recalls. "The shock instilled in me a basic insecurity about health and later motivated me to study medicine to understand human disease in hopes that I might be able to ease people's suffering and prevent illnesses from happening in the first place."

Today, 40 years after that life-altering occurrence, Dr. von Herrath is a world leader in type 1 diabetes research. His groundbreaking work has resulted in numerous honors, including the Juvenile Diabetes Research Foundation's Scholar Award, the American Diabetes Association's Outstanding Scientific Achievement Award, and the 2014 Paul-Langerhans Medal awarded by the German Diabetes Society. This past summer, the healthcare information website Expertscape named Dr. von Herrath the world's number one expert in type 1 diabetes.

Dr. von Herrath, one of the more humble top scientists you will meet, says, "What awards of this kind really mean to me and our team is that we're on the right track in our research, and that the credibility and



*Dr. von Herrath and his research team*

hopefully additional resources we receive as a result will enable us to help more people with type 1 diabetes."

Although research was always one of his interests, diabetes was not on Dr. von Herrath's radar when he received his M.D. from the Freiburg Medical School in Germany in 1988.

Dr. von Herrath enjoyed treating patients as a physician, but he felt constrained when he was only allowed to pursue his research interests at night, leading to 20-hour days and less-effective results in the lab. Learning there was much more freedom for researchers in the United States, he joined The Scripps Research Institute in La Jolla, where he worked in the Neuropharmacology and Immunology departments and first began to study diabetes.

Feeling the need for even more freedom and a chance to pursue his own research ideas, Dr. von Herrath

joined the La Jolla Institute in 2001.

"Coming to the Institute has been by far the best move I've ever made," Dr. von Herrath says. "There's a wonderful collegial spirit among the many talented scientists here that motivates us to collaborate with each other rather than compete, and that leads to better science and more breakthroughs."

Dr. von Herrath says the steep challenges facing scientific institutions today—not the least of which are severe cutbacks in federal funding for science—threaten even the most stable and high-achieving organizations. That's why he hopes individuals and private organizations that believe in the Institute's research will consider supporting that work financially.

"The Institute has already produced some of the most important breakthroughs in immunology over the past 25 years," Dr. von Herrath says. "If we're able to maintain and even expand the financial resources that are the lifeblood of this organization, I really believe we'll not only continue making discoveries but actually begin to develop cures for a number of diseases, including diabetes. That's been my dream for most of my life and I'm really excited that it's now within my grasp." ●

# “Working as a clinical physician I witnessed first hand how devastating the disease can be on the lives of patients and their families”

Dr. von Herrath, who oversees translation of all research at the company, not just his own, was attracted to both the extensive resources of the company and its commitment to solving the many complicated challenges diabetes presents.

“We’ve created an incredible model at Novo Nordisk which I believe has a chance to accomplish some major breakthroughs and in a relatively short time frame,” Dr. von Herrath says. “It starts with the company’s mandate to find a cure for type 1 diabetes, which is unusual in the pharmaceutical industry today. Then we’ve combined basic research and early proof-of-concept human trials under one roof, which gives us the best of both worlds. This will really speed up the process of finding new and innovative ways to treat the disease.”

The process is already moving fast enough that several lines of research are close to being ready for trials. Dr. von Herrath’s excitement is palpable when he describes one such effort that could be tested in human patients as early as 2015.

“It’s a unique combination immunotherapy that uses beta-cell protein immunization to re-tune the body’s immune system to better regulate itself and not attack and destroy the beta cells. We’re going to target the immunization so that it only reduces the inflammation around the beta cells in the pancreas and avoids suppressing all immune responses throughout the body, which could make it vulnerable to severe infections and other diseases. It’s a fine line we’ll be walking, but if we succeed, it has the amazing potential to lead us to development of a universal childhood vaccine against diabetes.”

As thrilled as Dr. von Herrath is about his translational path, he hasn’t lost his desire to continue investigating the pathology of diabetes through the basic research he conducts at the Institute. In fact, his distinguished research achievements led Expertscape, a healthcare information website, earlier this year to name him the world’s number one expert in type 1 diabetes.

In his 13 years at the Institute, Dr. von Herrath and his team have made some remarkable discoveries, most of them centering on why the body’s own immune system attacks insulin-producing beta cells and what immune-based therapies can be used to interrupt or prevent that process.

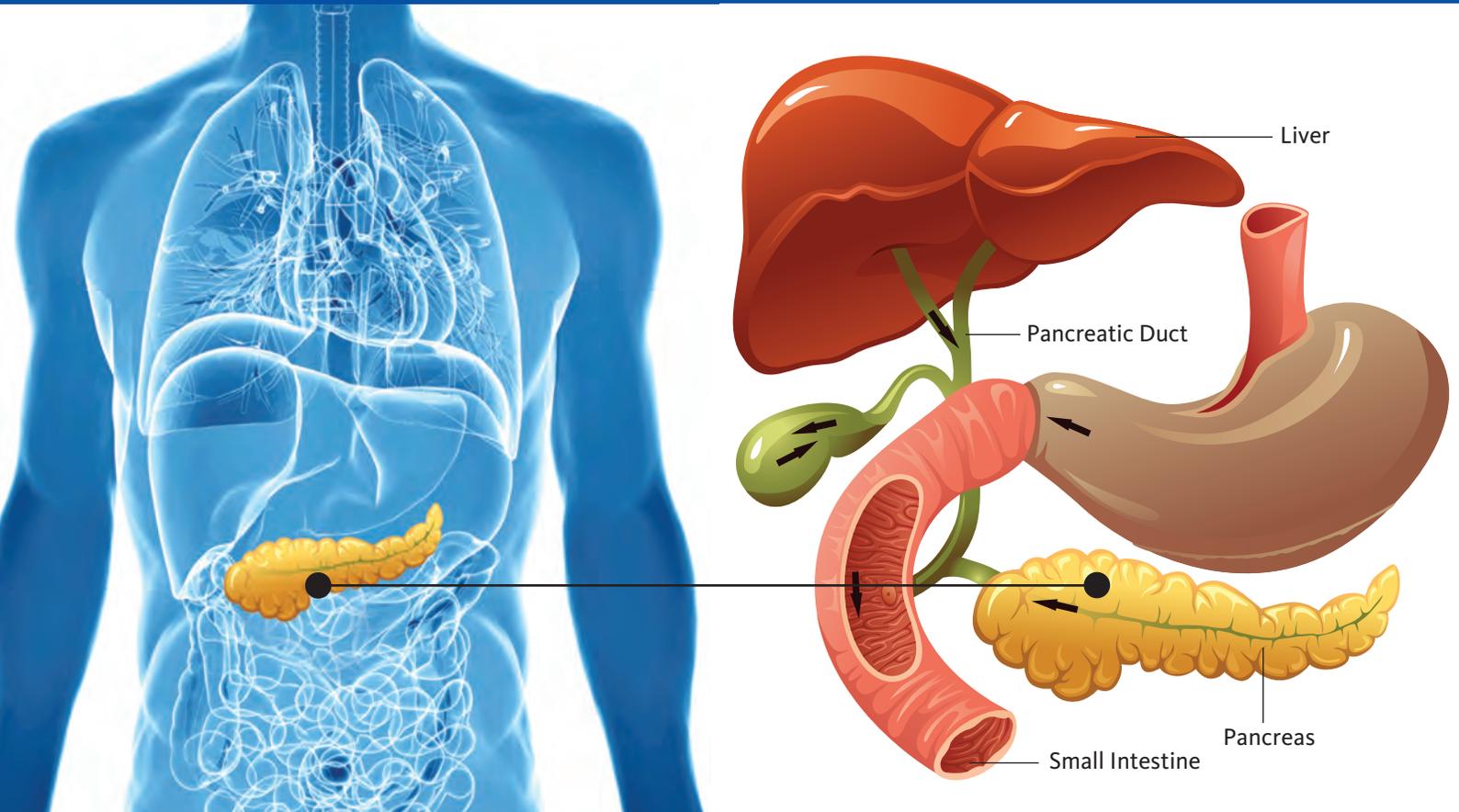
Here are just a few of Dr. von Herrath’s most significant discoveries:

- Created a computer model that uses a virtual simulation of nasal insulin therapy to optimize dose timing and frequency to enhance the treatment’s effectiveness. It allows scientists to explore different treatment options that are difficult or impractical to measure in the lab or clinic.
- Created the first real-time movies showing the destruction of beta cells in the pancreata of mice. These movies have provided new insight into the pathology of the disease. Prior to this, researchers had an incomplete picture of the process because they had to rely on still photos, computer models, or lab experiments to study cell destruction.
- Discovered that stimulating the immune system with beta cell proteins in animals via DNA vaccines resulted in a beneficial immune response that he believes may eventually prevent type 1 diabetes in humans.
- Discovered that introducing immune response modifiers, such as small molecules called “cytokines,” or certain antibodies, can put the immune system back on track and prevent it from attacking the body’s own cells.

Dr. von Herrath believes the basic research he conducts at the Institute, combined with the translational efforts he oversees at Novo Nordisk, offer the most powerful one-two punch in the fight against diabetes.

“We still don’t even know the cause of diabetes, so it’s a battle that is far from over,” Dr. von Herrath says. “Yet the incredible progress we’ve made over the past 10 to 15 years in understanding the disease shows me it is a battle that we can ultimately win, and by win, I mean a cure. And while that will take a number of years to realize, it’s extremely gratifying to me that on the way, we’re going to be developing an amazing number of new therapies and treatments that will vastly improve the health and quality of life for millions of people with diabetes. When I get tired and low on energy as I do sometimes with my schedule, it’s always that knowledge that inspires and revitalizes me to keep driving forward.” ●

# Pancreas Donation Program is Unveiling the Mysteries of How Diabetes develops



While thousands of scientists around the world study diabetes from a variety of angles, the actual mechanism of how the disease develops in the pancreas has remained shrouded in mystery.

That's changing dramatically thanks to an ambitious pancreas organ donation program sponsored by the Juvenile Diabetes Research Foundation.

The Network for Pancreatic Organ Donors with Diabetes, or nPOD, is finally lifting the veil to reveal previously unknown processes that accurately depict the pathology of diabetes.

La Jolla Institute is one of about 50 nPOD member research facilities around the country that receives frozen tissue samples from donated pancreata that are invaluable in the type 1 diabetes research conducted by

Matthias von Herrath, M.D. and others.

"It's hard to believe, but until this program came along a few years ago, we knew close to nothing about the histology of diabetes as it relates to the pancreas," Dr. von Herrath says. "We simply didn't have access to the living organ. We obviously couldn't study the pancreas of living humans, and following death, the pancreas deteriorates after five hours because it has digestive enzymes, so donated organs were worthless for research purposes."

The key, says Dr. von Herrath, is that nPOD harvests a donor's pancreas as if it is going to be transplanted. Organs taken both from diabetes sufferers and from healthy donors for control purposes are pristinely frozen and tissue sections are shipped to participating research facilities where they are analyzed to answer a host of

questions about the disease.

"nPOD has provided all of the researchers with a leap forward in knowledge," Dr. von Herrath says. "Fundamentally, it's beginning to confirm what we suspected, that there is not just one cause of diabetes, but several, including genetic and immunological. One of the critical benefits of the program is that all data collected is shared in real time among the research institutions. It's team science at its best. Over time, this huge expansion of our understanding of the pancreas and diabetes will lead to vastly better treatments for patients."

**nPOD**  
Network for Pancreatic Organ  
Donors with Diabetes



## Overseeing the Pipeline that Turns Research Breakthroughs into Medical Treatments

**T**hey may be the two most exciting moments in medical research: first, a scientist makes a groundbreaking discovery, and then years later, patients take a medication derived from that research saving their lives or significantly improving their health. So what happens between those moments to enable the research to make it out of the laboratory and into the medicine cabinet? The answer is biomedical translation, a “bench-to-bedside” process that is one of the most complicated, lengthy, expensive, and sometimes frustrating systems ever invented.

That’s why La Jolla Institute is fortunate to have a Technology Development Office staffed by a talented and

committed team to oversee this complex process. It is a critically important job, according to Mitchell Kronenberg, Ph.D., the Institute’s President and Chief Scientific Officer.

“We have some of the world’s best scientists conducting leading-edge research, but their work is only the first stage of what we hope will lead to the prevention, treatment, and cure for human immune disorders,” Kronenberg says. “We need to get those discoveries out of the lab, and that’s why we’ve made it a major priority to develop a technology transfer team with the expertise to harness the Institute’s intellectual property and strategically position these technologies for commercial development.”

*From left to right: Daniel Lam, Jenifer Jacobsen, Patrick Ho, Jennifer Floyd, Margaret Ng Thow Hing*



It also helps if your Technology Development Office is led by a dynamic and energetic Chief Business Officer like Patrick Ho. Like Ho, most members of his team have both scientific and legal experience and training. “Most people have some insight about biomedical research and they understand that it leads to the development of drugs, but very few are familiar with the process that links the two,” Ho says.

For Ho’s department, that process begins when a scientist’s research leads to a novel discovery and the resulting intellectual property needs to be protected in order to attract commercial interests. Ho’s team works closely with the researcher on a patent application, a process itself that can take several years. While the patent application process is underway, Ho’s staff works hand in hand with the researchers to search for potential collaborative partners that have the resources, including funding, to help further the discovery to the “proof-of -concept” stage (i.e., where the discovery can be shown to hold value as a potential human therapeutic).

This critical stage in the drug development process is often referred to by those in the industry as the “Valley of Death” largely due to the lack of consistent funding from the NIH or pharmaceutical industry.

“At this point we really have to utilize all of our skill sets (i.e., scientific, business, and legal) to attract

industry partners and investors who might be willing to take a chance on our discoveries,” Ho says. “As terrific as it would be to turn our discoveries into drugs ourselves, the fact is, we don’t have all the necessary resources to do it. Each drug can take hundreds of millions up to a billion dollars to go from bench to bedside. This makes it increasingly important to form partnerships with pharmaceutical companies that have the means to pay for this expensive process. Thanks to the incredible

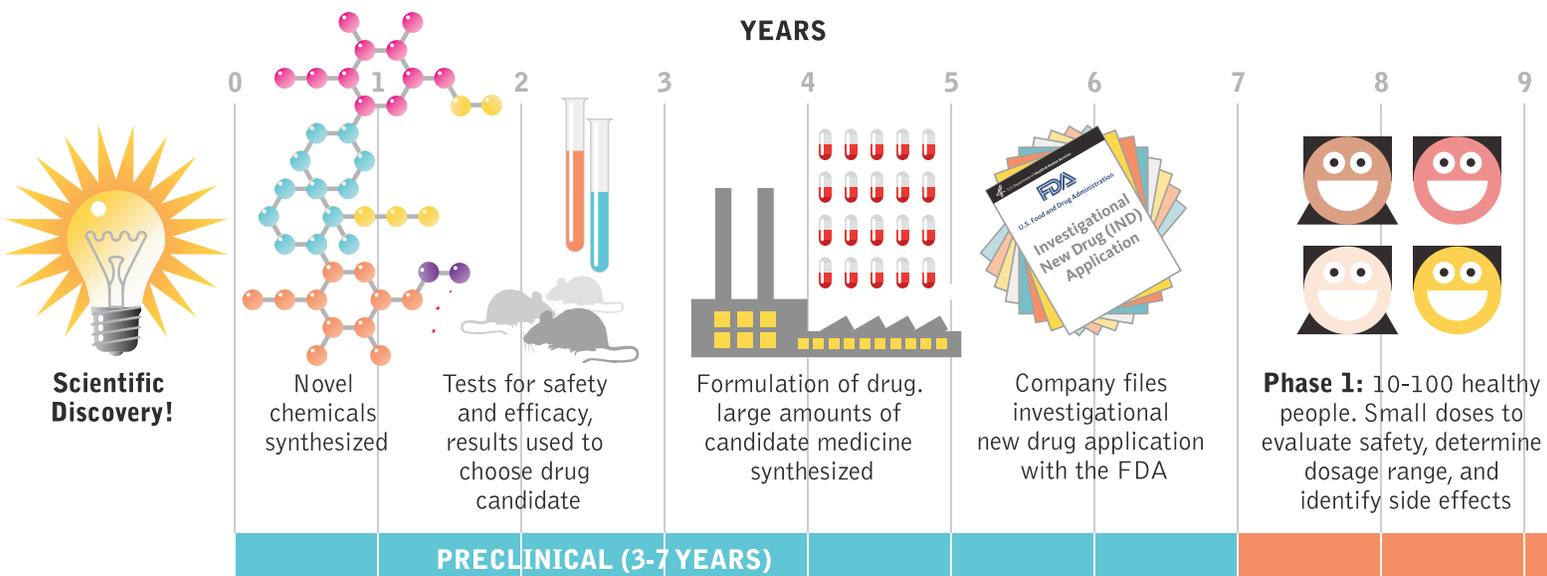
science coming out of our labs, we’ve been able to establish partnerships over the years with high quality companies that have the resources to translate our discoveries for clinical development.”

The Institute partnership with Kyowa Hakko Kirin Co. Ltd., a global specialty pharmaceutical company based in Japan, is the perfect illustration of a successful academia-industry relationship. Established 25 years ago, the partnership is unique because KHK provides discretionary funding for a significant portion of the Institute’s research. The freedom that

arrangement has given the Institute’s scientists has been mutually beneficial for both partners with a number of research efforts being developed into drugs and moving on to clinical trials.

One of the best examples is a discovery by Institute scientists of a potential new antibody therapy for ulcerative colitis and Crohn’s disease. Due to the partnership, researchers were able to discover a molecule

“Each drug can take hundreds of millions up to a billion dollars to go from bench to bedside”



known as LIGHT, a key signaling molecule that triggers a cascade of interactions leading to inflammation in the body. Inflammation is the underlying cause of many autoimmune diseases, including ulcerative colitis and Crohn's.

"What's exciting for the scientists and our team is that the partnership with KHK has allowed us to take the research to a higher level where KHK can make reagents to establish that the Institute's discoveries can be translated into potential therapeutics," Ho says. "In this particular research, we've actually been able to test the anti-inflammatory response to an antibody that blocks the action of the LIGHT molecule, thus lessening inflammation caused by these diseases."

For all research projects that move to the pre-clinical, "proof of concept" stage, validation of the scientist's original findings means the drug emanating from the original discovery is ready to be submitted for human clinical trials. This arduous, multiple-stage process, governed by the U.S. Food and Drug Administration, can take anywhere from five to eight years.

Throughout pre-clinical development and human clinical trials, Ho's team monitors the progress of the technology. La Jolla Institute currently has three discoveries in phase 1 and phase 2 clinical trials, with several in the pre-clinical phase. For every success story, however, there are far more examples of where technology development efforts are constantly forced to overcome frustrating scientific and financial hurdles, any one of which can permanently derail the process.

"Scientific discovery by its very nature is extremely uncertain," Ho says. "Sometimes you get to a certain point and discover that the data no longer supports the

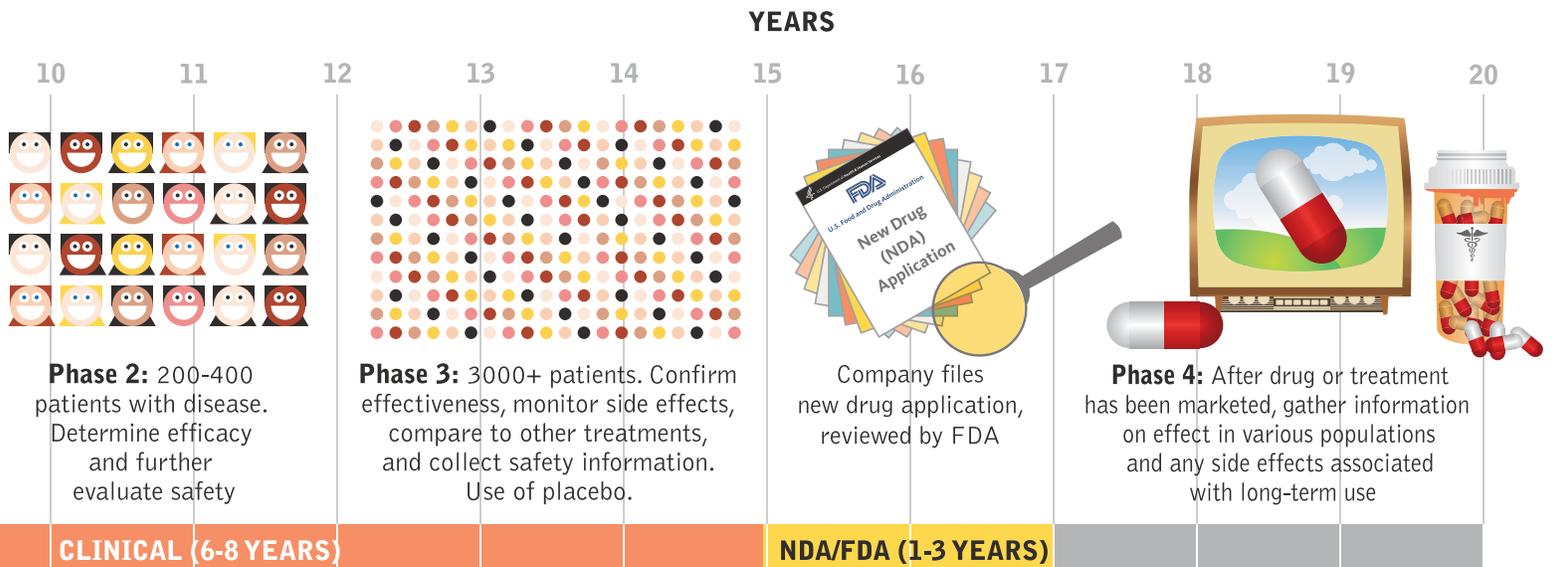
scientific hypothesis and you have to start over, or the treatment falls out of trials because it causes more harm than good."

Even if you overcome all of the obstacles and emerge with an effective treatment that's ready for the market, the entire process can take up to 15 years to complete.

"Considering the patent life of a drug is 20 years from the date the patent is first filed, there are only a few years left to break even before competitors are allowed to create a generic. "If you think about it," Ho says, "it's really not a sustainable business model. If I went to a bank and asked for a loan to fund this type of endeavor, they would think I was crazy. It's why drug development today is such a risky venture and why increasingly only the largest pharmaceutical companies have the resources for it."

Fortunately, if the science is innovative and has a positive impact on human health, then business partners can be found to support its development into therapies. There are still opportunities to transform research into life-changing treatments and its that potential that drives Ho and his team.

"Everyone in our department lives and breathes technology transfer," he says. "We're thrilled we have a chance to be involved in groundbreaking research. We take our role as champions of technology seriously and see our work as an important bridge between academia and industry. The hard work becomes worthwhile when we see how our technologies can benefit human health and relieve pain and suffering." ●

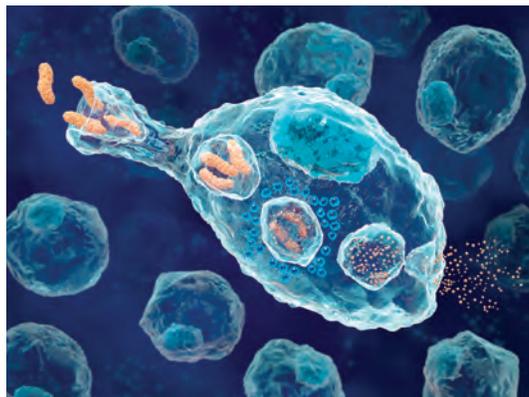




# Q+A

## Discovering Cause of Heart Disease May Create Potent Tools to Battle Other Diseases

*When La Jolla Institute faculty member Lynn Hedrick, Ph.D., was a young girl, she knew two things for certain: she wanted to be a scientist, and she wanted to find a cure for her mother's diabetes. Hedrick fulfilled the first dream by becoming one of world's foremost researchers in cholesterol metabolism and its role in atherosclerosis. And, as a Professor in the Institute's Division of Inflammation Biology, Dr. Hedrick hasn't yet found a cure, but she is conducting groundbreaking research in why cardiovascular disease is accelerated in patients with type 2 diabetes. Dr. Hedrick received a B.S. in Biology from Salem College in Winston-Salem, North Carolina and a Ph.D. in Biochemistry from Wake Forest University. After serving from 1995 to 1999 as a junior faculty member in the Division of Cardiology at UCLA, Dr. Hedrick moved to the University of Virginia in Charlottesville, where she eventually became an endowed professor. She joined the Institute in 2009.*



*A macrophage engulfing and destroying invading cells*

like a sentry that identifies viruses, bacteria, or other invaders and protects the body by eliminating them. In our tissues, mature monocytes called macrophages are involved in tissue repair, removing dead cells, and keeping everything healthy, including cholesterol modulation. The problem is that when these cells are overwhelmed by LDL—the bad cholesterol—they become

impaired and die, forming the beginning of a plaque, which over time builds up, narrowing the arterial walls and potentially causing a heart attack. This is a real problem for diabetics because they're four times more likely to die of a heart attack than the general population.

**Q:** Your research focuses on the function—and potential malfunction—of a specific type of white blood cell known as a monocyte. What role do monocytes play in cholesterol metabolism and atherosclerosis?

**A:** Monocytes are among the most powerful “good guys” in the human immune system. They're like that old video game Pac Man where the little yellow character goes around and eats the dots. Monocytes act

**Q:** What have you learned about monocyte function?

**A:** We've discovered there are actually multiple types of monocytes with different kinds of immune functions. We've also learned some of them can go haywire and actually turn against the body. Most importantly, we've discovered a gene that controls the development of a particular monocyte that is an especially “good guy” that does not malfunction and maintains its invaluable protective anti-inflammatory role in the body. We've already had success with manipulating this gene in animal models, causing these monocytes to function even better or to replicate, creating a potential army of them to wield against disease.



Lynn Hedrick, Ph.D.

**Q: What is the potential importance of this discovery?**

**A:** By first understanding how monocytes work, we believe we'll eventually understand at least one of the underlying causes of atherosclerosis and heart disease, the latter of which we know, unfortunately, has multiple causes, both genetic and environmental. It's going to be several years before we can test our thesis in human clinical trials, but we're excited that we may be able to marshal these monocytes to shore up a person's failing cardiovascular system. If we can do that, we should be able to slow the progression of heart disease and save lives.

**Q: Does your work have implications for other diseases?**

**A:** It has tremendous implications, actually, and this is what probably excites us the most in our lab. Because most diseases have an inflammatory basis or at least a component, we believe monocyte therapy has the potential to lead to groundbreaking treatments for a number of illnesses. One example is the remarkable work Richard Hanna, Ph.D., one of our Instructors, is doing with cancer and monocytes. He's injected one type of monocyte into mice that not only prevents a tumor from metastasizing, he actually has microscopic imaging of the monocytes attacking and destroying the cancer cells in

the blood vessels. This is a very exciting discovery, and we will publish this work in a major medical journal soon.

**Q: You've invested more than a quarter of a century of your life in research. What still motivates you to continue your scientific journey?**

**A:** There are so many things that still drive me today, not all science related. The most important is that I want to be the best mother possible to my 10-year-old son. Another is spreading the word to the public about what a special place the La Jolla Institute is and why it's worthy of their support. We're not a large institution, but we have some of the world's brightest and most creative scientists conducting immunological research that will eventually lead to cures and treatments for a number of diseases.

I also love the mentoring part of my job because it's incredibly rewarding to take young researchers with little experience and help them mature into the next generation of leading scientists. And I still really love the process of scientific discovery itself. I think about it all the time, even when I'm jogging. I can't turn it off. I think it goes back to the emotion I felt when I saw my mother struggling with her diabetes and my desire to help her. I'm truly motivated by the hope that something our team discovers in the lab may really help people down the road. ●

# INSTITUTE RELATIONS

## Our Most Important Partner: YOU!



Every gift to the La Jolla Institute advances our quest to solve the mysteries of the immune system. We are especially grateful for our annual donors and Members who share our commitment to focused research on the immune system and support our efforts to strive towards Life Without Disease.

While government and corporate sources fund the largest percentage of the Institute's research budget, philanthropic donations allow our researchers to pursue their most exciting, innovative, passion-projects that don't always qualify for funding from these sources.

The Institute offers special benefits and opportunities for involvement to those who donate \$250 or more annually. These membership levels and benefits include:

### **Friends: \$250 - \$999**

- Invitations to a stimulating series of community lectures describing the latest scientific discoveries at the Institute and their potential impact on human health
- Advance invitations to Life Without Disease Seminar Series and reception
- Subscription to the Institute's magazine *Immune Matters*
- Listing on the annual donor roster in *Immune Matters* magazine

### **President's Council: \$1,000 - \$9,999**

- All "Friends" level benefits, plus:
- Private tour of the Institute
- Annual President's Council Luncheon with LJI President Mitchell Kronenberg, Ph.D.
- President's Council lapel pin
- Advance notice of important LJI scientific discoveries and other news
- Listing on the Institute's permanent Donor Wall

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- All President's Council level benefits, plus:
- Private roundtable lunch with a scientist for up to four of your friends and family members to ask all of your immune health-related questions.

For more information about giving opportunities, please contact Rachel Jonte at [rjonte@lji.org](mailto:rjonte@lji.org) or (858) 752-6542.





## SON'S DIABETES MOTIVATES ERIC ZWISLER TO JOIN LA JOLLA INSTITUTE BOARD OF DIRECTORS

In the five years since Eric Zwisler's son Taylor was diagnosed with type 1 diabetes, the health technology executive has provided a father's support but otherwise felt helpless in addressing the disease.

That all changed this past spring when Zwisler, the Chairman and former President of Cardinal Health China, accepted an invitation to join the La Jolla Institute's Board of Directors.

"I had several desires in looking for a health-based non-profit to become involved with, but the most important was that the organization had to be conducting groundbreaking research in diabetes," Zwisler says. "After meeting with La Jolla Institute's impressive leadership, touring the lab of Matthias von Herrath, M.D. (see cover story), and hearing this world-class scientist talk about his exciting discoveries in type 1 diabetes, I knew I had found a great place to contribute to a really important effort."

With nearly four decades as a top executive and entrepreneur in the medical technology field, Zwisler has a lot to offer the Institute. After moving to Asia over 27 years ago, he's worked for several healthcare companies. Twenty years ago he established a groundbreaking healthcare distribution company in China and rose to CEO of Zuellig Pharma Asia Pacific, leading a multi-billion dollar company with 8,000 employees in 15 Asian countries.

In 2010, Zwisler sold Zuellig Pharma China to Cardinal Health, a U.S. Fortune 22 company, and agreed to serve first as President and now Chairman of the combined company that enjoys more than \$3 billion in annual sales in China. The Shanghai-based Zwisler, who speaks Mandarin fluently, has been honored by the Chinese government with a number of awards, including the Friendship Medal and Shanghai Honorary Citizen.

"We're thrilled and honored to have Eric join the Board," says Mitchell Kronenberg, Ph.D., President and Chief Scientific Officer. "His extensive private

sector experience in medical technology, along with his vast expertise in China and Asia, will be invaluable to the La Jolla Institute as we move more of our discoveries into the commercial arena and seek expanded international business opportunities and investors."

Zwisler's chairman role at Cardinal Health allows him more time for a portfolio of activities, including volunteering with worthy organizations such as LJI and the advisory board of UC San Diego's School of International Relations and Pacific Studies, as well as several corporate boards. He and his wife, Tori, also plan to continue their long relationship with and support of the Jane Goodall Institute in Shanghai, an NGO promoting sustainable ecological concepts to the youth of China, founded by Tori 15 years ago.

In his free time, Zwisler has no shortage of personal activities to pursue. "I'm a country boy from Wisconsin so I love to get outside, whether it's digging in the dirt in my garden or going on a long hike," he says. "My wife and I also enjoy travel, we love fine food and wine, and I'm a huge jazz fan. Our sons, Taylor, who is now 22 and his older brother Evan have their own busy lives, but we always like spending as much time as we can with them."

Zwisler says Taylor is doing an excellent job of managing his diabetes, but his dad looks forward to a day when the daily management of diabetes will be a lot easier medically—or not necessary at all.

"I know enough about medicine that envisioning a cure for diabetes is probably not realistic in the immediate future," Zwisler says. "At the same time, the work at La Jolla Institute has already led to a number of important new therapies, which in turn are laying the groundwork for people with diabetes to live in better control and with hope of a possible cure. I can't wait to roll up my sleeves and help this effort in any way I can." ●



# La Jolla Institute

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## About La Jolla Institute for Allergy and Immunology

- **MOTTO:** Life Without Disease.
- **MISSION:** To understand how the immune system works, and to apply that knowledge to promote human health and prevent disease.
- **VISION:** To become the world's preeminent scientific organization engaged in research on the immune system.
- **FOUNDED:** November 14, 1988 in San Diego as a nonprofit 501(c)(3) public benefit corporation.
- **RESEARCH STAFF:** 23 faculty investigators, 145 postdoctoral fellows and other trainees, and 180 technicians and support staff.
- **SCIENTIFIC PRODUCTIVITY:** Published nearly 2,000 scholarly papers in prestigious scientific journals since 1988. Numerous patents (and patents pending) for discoveries designed to yield revolutionary clinical applications.
- **ACCOLADES:** Ranked #5 in the world in scientific impact in immunology. In 2013, ranked #1 in the "Best Places to Work in Academia" and #2 in the "Best Places to Work for Postdoctoral Researchers" in the annual survey of research institutions throughout the world, conducted by *The Scientist* magazine.

 For regular updates, "like" us on Facebook at [www.facebook.com/LifeWithoutDisease](http://www.facebook.com/LifeWithoutDisease)

