INSIDE » Marc Montminy Elected to NAS » Salk Receives $6.6 Million CIRM Grant » Joanne Chory Appointed to Newman Chair

InsideSalk

Where cures begin.

THE SALK INSTITUTE FOR BIOLOGICAL STUDIES

07|09

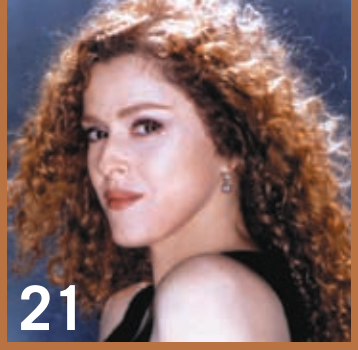
Meet the President

Salk's Discovery-Driven Science, California's 'Wild Ideas' are Music to His Ears

ALSO IN THIS ISSUE

July 2009
Inside Salk

Joanne Chory (center) named to Newman Chair



Bernadette Peters Headlines Symphony at Salk

William R. Brody, M.D., Ph.D.
President

Marsha A. Chandler, Ph.D.
Executive Vice President

Rebecca Newman
Vice President,
Development and Communications

Susan Trebach
Senior Director,
Communications

Mauricio Minotta
Director, Communications
Editor, Inside Salk

Gina Kirchweger
Director,
Scientific Communications

Sarah Loffler
Production Coordinator

Joe Belcovson and Kent Schnoeker
Photographers

♻ *Inside Salk* is printed on recycled paper

Inside Salk is published by the Salk Institute for Biological Studies. We welcome your input. Please send comments to communications@salk.edu or contact the Communications department at 858.453.4100 x1226.

ON THE COVER

Salk Institute President William R. Brody, M.D., PhD., in the Theodore Gildred courtyard.

Marc Montminy Elected to National Academy of Sciences

Marc Montminy (center) and members of his lab celebrate his election to the National Academy of Sciences in April.

Salk researcher Marc R. Montminy, a professor in the Clayton Foundation Laboratories for Peptide Biology, has been elected to the National Academy of Sciences, the nation's most prestigious honorary society for scientists. The Academy made the announcement in April during its 146th annual meeting in Washington, DC.

Throughout his career, Montminy has been interested in the complex network of brain signals, hormones, and physiological mechanisms that modulate the body's energy balance and set the stage for metabolic disease. While investigating the genetic basis of diabetes, Montminy uncovered a family of genes that act as metabolic switches, turning other genes on or off.

One of them, called CRTC2, acts as a "fasting switch" and plays a crucial role in the development of Type II diabetes. It flips on glucose production in the liver when blood glucose levels run low during the night. Montminy's research revealed that CRTC2 is on in many patients with Type II diabetes. As a result, the liver acts like a sugar factory on overtime, churning out glucose throughout the day.

Initial experiments suggest drugs that prevent CRTC2 from getting stuck might be useful in lowering glucose levels in diabetics and reducing long-term complications associated with the disease. Montminy's honor brings the number of Salk faculty elected to the NAS to 15.

Reuben Shaw

Reuben Shaw Selected as HHMI Early Career Scientist

Salk Institute scientist Reuben J. Shaw, a Hearst Endowment assistant professor in the Molecular and Cell Biology Laboratory, has been selected a Howard Hughes Medical Institute Early Career Scientist. He is one of 50 researchers chosen out of more than 2,000 applicants for the prestigious six-year appointment.

Shaw is particularly interested in understanding the molecular link between cancer and metabolism. While studying one of the most commonly mutated genes in lung cancer, he discovered an ancient energy-sensing pathway that shuts down cell growth and reprograms metabolism when nutrients are scarce.

Epidemiological studies have shown that individuals with Type II diabetes have an elevated risk for certain forms of cancer. Shaw thinks that deregulation of the energy-sensing mechanism may explain why some cell types are more likely to give rise to cancer when metabolism is altered.

On the upside, existing diabetes therapeutics may prove useful as chemotherapeutics for forms of cancer with mutations in this pathway, which he plans to further explore with his new appointment.

Shaw's lab is also searching for additional components of the pathway to fill in the understanding of how the molecular intersection between nutrition, diabetes and cancer truly functions. He plans to use mouse studies to further explore this critical connection and tease out the precise role of each component of the signaling pathway.

These studies will lead to future therapeutic targets and new intervention points in both cancer and Type II diabetes. Shaw's appointment brings the total number of HHMI investigators at the Salk Institute to eight.

Salk Ranks Top for "Highest Impact" Research in Neuroscience and Behavior

The Salk Institute garnered the top discovery spot in the latest international ranking in the category "Neuroscience and Behavior" by *Science Watch*, a scientific organization that measures the citation impact of research published worldwide. Citations are an important measure of the value and influence of scientists' work and reflect the impact made by that work on scientific understanding.

"The importance of this ranking is conferred by the judgment of peers in the same field who mark the research of Salk scientists as points of departure for their own work," says Salk President **William R. Brody**. "Paper for paper they wield tremendous influence and set the direction for the future."

Naturally, big institutions publishing large numbers of papers have a greater likelihood of collecting more citations than smaller institutions publishing fewer papers. In order to reveal the "heavy hitters" based on per paper influence, not mere overall output, all rankings are based on citation per paper.

Science Watch, produced by Thomson Reuters in Philadelphia, openly publishes institutional impact scores for different areas of science only intermittently, but in the company's online evaluation system Essential Science Indicators and related databases, the Salk Institute consistently emerges in top spots. Last year, for example, it ranked second worldwide in the "Molecular Biology and Genetics" category.

"The consistency of our high rankings at the Salk Institute reaffirms our belief in the power of curiosity, creativity and problem-driven science," says Brody. "The international impact of our faculty's work reveals the extraordinary quality of Salk science."

Inder Verma Receives ASGT's Outstanding Achievement Award, Named First Incumbent of Jacobs Chair

Investigator Inder Verma was named the 2009 recipient of the American Society of Gene Therapy's Outstanding Achievement Award in May. The award recognizes an ASGT member who has conducted groundbreaking research or achieved a lifetime of significant scientific contributions to the field of gene therapy.

An American Cancer Society Professor of Molecular Biology in the Salk Institute's Laboratory of Genetics, Verma pioneered the use of stripped-down versions of viruses, HIV in particular, to ferry intact versions of genes that are defective or missing to cells throughout the body. His innovations revolutionized gene therapy, stem cell and cancer research, and other areas of molecular biology.

He is a member of the National Academy of Sciences, Institute of Medicine, American Academy of Arts & Sciences, American Philosophical Society, Third World Academy of Sciences and the recipient of the 2007 Cozzarelli Prize and 2008 Vilcek Prize. Earlier this year, Verma was also named the first incumbent of the **Irwin Mark Jacobs** Chair in Exemplary Life Sciences. Established to honor its namesake's exceptional leadership in business and philanthropy, the honor is given to an internationally renowned senior Salk scientist who has made extraordinary discoveries in basic biomedical research and has contributed to the direction and vitality of the Institute.

Irwin Jacobs with Inder Verma

Tatyana Sharpee Receives McKnight Scholar Award

Tatyana Sharpee

Tatyana Sharpee, an assistant professor in the Salk Institute's Laboratory for Computational Biology, has received the McKnight Scholar Award, which recognizes young neuroscientists in the early stages of establishing their independent laboratories.

She was among six scientists from across the country selected for this prestigious recognition in May. McKnight's Endowment Fund for Neuroscience sponsors the annual competition. As a recipient, Sharpee will be awarded $225,000 over three years to further her research program.

Sharpee, who is interested in how the brain processes information, is an authority on applying information theory to parse the code neurobiological systems use to handle widely varying inputs. Neurobiologists' perennial quest centers on deciphering how the brain codes and processes information.

Sharpee developed a statistical method that allows her to analyze the response of brain cells to natural stimuli. Using this approach, she discovered that brain cells adjust their filtering properties to make the most sense of the incoming information. Currently, she is expanding her method to include higher-level brain cells, which are very specific to particular combinations of inputs.

Martin Hetzer Receives Promotion

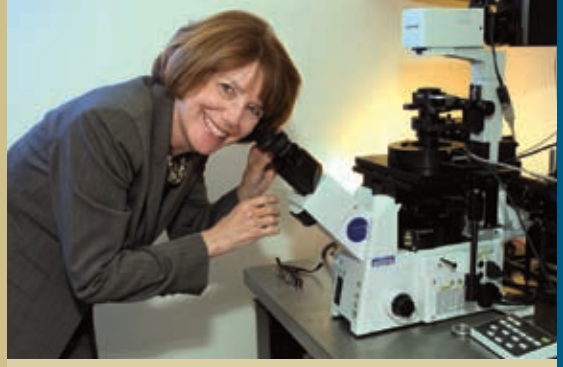
Martin Hetzer

Researcher Martin Hetzer has been promoted to associate professor in Salk's Molecular and Cell Biology Laboratory. Hetzer, who joined the Institute in 2004, uses live cell imaging and biochemistry as well as genetic and computational approaches, to understand the molecular basis of nuclear assembly and its regulation during cell division.

Most recently, Hetzer received the 2009 Scholar Award from the American Cancer Society and the 2009 Early Career in Life Science Award from the American Society of Cell Biology.

Research from his laboratory is shedding new light on the nucleus and how the breakdown of its structure is implicated in disease. In a study earlier this year, his team found a strong connection between the long filaments found in the brains of Parkinson's disease patients and the deterioration of a class of proteins that makeup nuclear pores' structure.

They discovered that as cells age, the structure fails, allowing unwanted proteins to leak into the nucleus and causing havoc. By finding ways to prevent or reverse the leakage, Hetzer's lab may be on course to identify novel approaches to treating neurodegenerative conditions.



Congresswoman Susan Davis

A Congressional Visit

Congresswoman Susan Davis, who represents California's 53rd District in the heart of San Diego, visited the Institute in May when she met with several members of the faculty to learn about Salk's research. A strong supporter of increased NIH funding for the advancement of scientific innovation, Davis is pictured in **Sam Pfaff**'s laboratory where she looked at spinal cord neurons derived from mouse embryonic stem cells.

Joanne Chory Appointed to the Newman Chair

Joanne Chory (center) was honored with an endowed chair in April during a luncheon attended by Howard and Maryam Newman (left) and Irwin and Joan Jacobs.

Salk scientist Joanne Chory has been appointed as the inaugural holder of the Howard H. and Maryam R. Newman Chair, which was created through a $2 million gift to the Institute earlier this year (see related story page 20).

It is the first endowed chair established as part of the Joan Klein Jacobs and Irwin Mark Jacobs Senior Scientist Endowed Chair Challenge. By terms of the Challenge, the Jacobs will augment Newman's gift with an additional $1 million.

A Howard Hughes Medical Institute investigator, Chory studies the mystery behind how plants compete for and respond to sunlight in their effort to grow and survive. Plant biologists' understanding of these basic mechanics is crucial to ultimately learning how to increase yield in crops such as wheat, corn and rice.

Work in Chory's lab has also led to the discovery of a steroid hormone, brassinolide, that controls plant development in response to light, and has identified the plant steroid receptor and signaling pathway.

Launched in 2008 with a $10 million matching fund, the Jacobs Chair Challenge enables donors to create a prestigious and permanent chair in support of senior faculty members at Salk.

Meet the President

Wearing Khakis, comfortable shoes and toting a modest back-pack, William R. Brody walks up N. Torrey Pines Road at a determined pace, channeling a professor on his way to class.

But Brody is not your garden-variety academic. He is the MD-PhD successful inventor-entrepreneur and former Johns Hopkins University president who now leads the Salk Institute.

After more than a dozen years in Maryland, the new Salk president appreciates every chance he gets to soak up San Diego's sunny warmth. Brody either walks or bicycles the three miles from his residence to his office, unless he needs his car for business during the day.

Wendy, his wife of 41 years, shares her husband's active lifestyle. The couple spent a month trekking across New Zealand just prior to arriving in La Jolla. And they set a brisk pace with their dog, a Welsh Corgi named Molly, this spring when they participated with Salk staff members in the March of Dimes' March for Babies in Balboa Park.

> **"Where the real exciting things happen are at a lunch table or in the hallway. The chance to encounter one another is a very powerful stimulus to creativity..."**

The Brodys made an early, lasting impression as Johns Hopkins' "first couple" by donning roller blades and gliding across campus greeting freshmen and parents on their first fall move-in day. "It was a big hit," Brody recalled. "And it sort of set the tone for the presidency." Subsequently, they welcomed students to campus riding bicycles, Razor-scooters and assorted wheeled conveyances. Once, Brody sought to perform their annual welcoming ritual on horseback, but the Baltimore mounted police declined to cooperate.

At Hopkins, Brody devoted some of his considerable energy to making the campus more pedestrian and jogger-friendly, greening the campus, banishing cars and overall making it less stodgy. "Geography and architecture play an enormous role" for an institution, Brody observed. "Things that allow people to bump into one another and interact on a casual basis are as important as the offices in which they work."

The physical beauty and the opportunities for scientists to interact informally are part of what Brody already deeply admires about the Salk Institute. "Where the real exciting things happen are at a lunch table or in a hallway," he says fervently. "The chance to encounter one another is a very powerful stimulus to creativity."

Even more than the aesthetic appeal of the place, Brody says he is astonished by the exceptional level of collaboration among Salk scientists. When he sits down in the cafeteria or on the patio with a group of graduate students and post-docs, he feels a sense of wonder at the breadth of research interests – even within a single group. "One day I joined six or seven people from Inder Verma's lab," he said. "Most of the researchers talked about their projects on cancer, but a few were probing the causes of depression. Their work across disciplines is surprisingly exhilarating."

Bill Brody pictured with Salk senior scientists Inder Verma (from left), Fred "Rusty" Gage and Walter Eckhart.

So where does the highly accomplished multi-talented executive fit into the powerful Salk leadership picture? "I can help increase the resources we need to be successful, and develop the strategy we need through a planning process that involves eliciting both faculty and external points of view," he suggests.

"There's no place to hide at Salk. You are either at the top of your game or you're not going to make it."

Brody believes the Salk's toughest challenge is "to combine big science with small science." By that he means making the major investments – in people, space and equipment – to conduct research that keeps the Salk at the top of the world's scientific institutions, while maintaining its collegial intimacy.

On the "big" science side of the equation, Brody explains: "We can buy a microscope. But to do truly innovative, cutting-edge things with imaging and be leaders in the field (like establishing the new Biophotonics Center) we need to recruit a group of people with the backgrounds and skills to really develop the capabilities of the instruments, and to invent new ones. So we need to build a core of imaging technology support, a big investment, without doubling the size of the institute.

"Small science is keeping the Salk at a scale in which you run into people," he continued. "Those chance encounters can be critical to your work."

Addressing the big-small problem requires setting an extremely high bar in hiring, promoting and tenuring only outstanding scientists, Brody said. "There are lots of good violinists, but only a few like Heifetz and Zuckerman. And there are lots of good scientists, but the number of great ones is small. We don't want to get too big and dilute our talent pool. For discovery it is the creative mind you really want. The best institutions have to have a ruthless commitment to excellence."

Brody says part of his responsibility is to support a positive research culture and to make the Salk a lively place to do science. And he must help attract the resources to accomplish all of the institute's goals through both public grants and private philanthropy, including assembling the money for hefty research start-up packages for new faculty, and building a fund supporting the pursuit of high-risk ideas.

While this may seem like a daunting to-do list, Brody says that after his tenure at the sprawling Hopkins, leading the Salk is a real treat. He can concentrate more on science, he is surrounded by an amazing group of vastly creative and innovative people, and he admires California as a uniquely brash and stimulating environment for research (despite its current economic woes). Back East, there is a certain constrained atmosphere to science, he says. "You can have more wild ideas out here, and discovery is about wild ideas, about challenging the status quo, and that's the excitement of California and of the Salk."

While he was clearly comfortable and enormously successful in university settings, Brody admits he feels somewhat liberated by the Salk's discovery-driven focus and structure. In a university, faculty work in individual departments, conducting research in particular disciplines and academic silos, engaging in classroom teaching and/or clinical responsibilities, recruiting graduate students and seeking grants. "In the traditional academic setting, there are built-in constraints that make science harder."

At the Salk, faculty can focus on their science, he says. "You meet people like **Greg Lemke**, who started out in neuroscience, then shifted into immunology because of discoveries he made. Here you live or die based on your ability to do your research and obtain grants. There's no place to hide at Salk. You are either at the top of your game or you're not going to make it."

Brody elected to move west while at the top of his game. Part of the process of the Brodys' transition from Baltimore to La Jolla involved downsizing. One rather large item reluctantly left behind was a nine-foot concert grand piano, donated to the Peabody Conservatory.

Bill Brody with Salk President's Club members Lew Klein and Carol Lieberman

"I can help increase the resources we need to be successful..."

There is a wistful quality to his voice as Brody describes playing the instrument. He is a classically trained pianist who now plays only recreationally: "Mostly jazz, show tunes, some Chopin – it is my form of psychotherapy."

Brody also picks up a guitar on occasion, typically strumming 1960s folk tunes. "Music is good for the soul. It is a form of expression, it is relaxation, and it is a technical challenge. I would love to be able to paint. But I can be creative with music."

The Brodys are Stockton, Calif., natives, so relocating to San Diego is a homecoming of sorts. But Bill Brody says California has changed dramatically and he hardly recognizes the State of his youth. "Stockton was kind of like growing up in Kansas – mostly flat farmland, midway between San Francisco and the mountains," he says.

Wendy and her family moved into Bill's neighborhood, across the street, when she was five years old, and the two families became friends. But Bill and his future spouse were years apart in age and never attended the same schools at the same time. Definitely not childhood sweethearts.

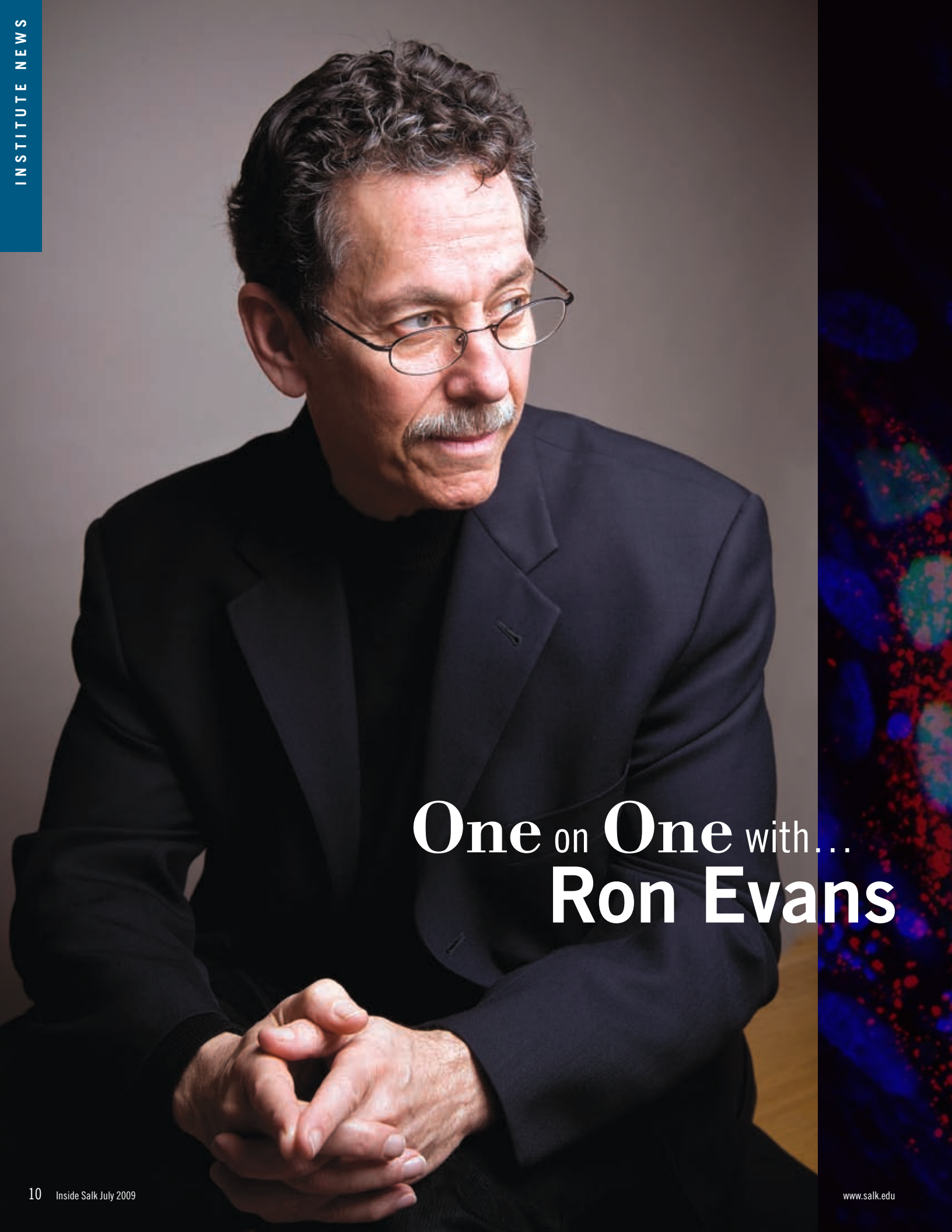
"When I was a senior at MIT, Wendy was a freshman at Mills College. I came home for the Christmas holidays and we went to a movie as friends. Then we decided we'd had a date," he says, smiling. Brody chose Stanford for medical school but then Wendy went off to study in France "so it took a while."

Today they have two grown children, one on each coast. Their son is a Silicon Valley software engineer, and their daughter is in New York, mothering the couple's baby grandchild.

Meanwhile the Brodys are enthusiastically pursuing their latest adventure, adapting to life in Southern California and at the Salk. One more priority item on Bill Brody's list? To raise the institute's profile in San Diego. He wishes the Salk were better appreciated in its home community – that it could be acknowledged as more than just one of several fine institutions on the mesa. (And as though it were timed to support his message, *Science Watch* recently published a 2009 ranking of American institutions with the highest scientific impact in Neuroscience and Behavior. The Salk ranked Number One. Full Inside Salk story on page 4)

Brody vows he will do what he can to increase both local and national respect for a superb organization that does not directly serve patients but has huge impact on human health. "You're a prophet without honor in your hometown," he says. "The farther away you get, the more you realize there's this pillar of excellence, this shining star. It is an extraordinary place."

Bill Brody with his wife of 41 years, Wendy, and the family dog, Molly.



One on One with...
Ron Evans

RON EVANS, A HOWARD HUGHES MEDICAL INSTITUTE INVESTIGATOR AND A SALK PROFESSOR in the Gene Expression Laboratory, is credited with the discovery of nuclear hormone receptors, which have since led to more than a half-dozen drugs for cancer, diabetes and heart disease. Earlier this year, he reached two major milestones: his 60th birthday and the 30th anniversary of his laboratory at the Institute – both were celebrated with a one-day symposium and a party that drew 145 of his former students. Throughout his career, Evans has received some of medical science's most coveted awards and has published more than 250 papers, many among the most cited in the world.

It must have been an overwhelming feeling of nostalgia to see so many of your former students gathered at the same time.

Having them all come back together was like being whole again. Seeing everyone and reliving the work and the camaraderie … it's not just about the science. The science is born out of the intensity and the hard work. While the paper represents hard and cold facts, it's the product of people who are putting in 100 percent effort for weeks, months and years at a time. So getting back together after all this time was just so enriching and moving for me – really one of the best days of my life.

It must have been a joy to see how the progression of your lab's discoveries was represented in each of the people who were there to celebrate with you since each of them contributed their part to the research.

In a way, they each had a small part and a big part in the evolution and progression of the lab. People joined my lab to work with me and advance their own aspirations. While they changed and evolved, I changed and evolved both as a lab head and as an individual. The lab environment was and continues to be an ever-dynamic process. We are solving problems that by finishing one, illuminates the next. That dynamic of change and challenge and having people at your side to pick up that gauntlet and run with it is such a wonderful part of science.

In your career so far, what has been the discovery that fascinated you most?

The growing realization that so much of body physiology, endocrinology and behavior is really about the control of gene networks. My initial interests in the early '80s were to study the mechanics and logic of how the genome is controlled. Our interests in cloning hormone receptors ultimately provided us with a key to unlock the secrets of the genome. In the beginning, science is about overcoming technical challenges, which in the end open new avenues of approaching complex problems.

The thing for me is that Salk is an amazing environment where people ask bold questions and able to bask in the glow of people like Francis Crick, Roger Guillemin, Renato and Sydney Brenner. I think all of us here aspire to not only carry on that legacy but to take Salk to the next level. It takes that kind of imagination that they have—to learn from it and pass it along to the next generation.

Is that what keeps you passionate about science?

Science to me is like the ultimate chess game where the opponent is Mother Nature. You're trying to win secrets in a never-ending duel. There's nothing more thrilling than pitting yourself against problems that are not yet solved. It's fun, it's challenging, it's often competitive and it's one of the ultimate things that I think you can do as an individual because it's curiosity driven. The process of science tells us about the process of life and that was really brought home by seeing the cadre of people who have been with me over the years and who have gone on to become leaders in their own right. We are one golden age that dissolves into the next. The people who have come through the lab really reflect what can be done by individuals. Science is driven forward by the imagination, and the people who come through the lab bring in the spirit and energy to power discovery.

I know you play guitar. What do you get out of playing that science doesn't provide?

Research is intense and it's frustrating because it's hard to solve the unknown problems for which you're seeking answers. So you have to have a way to pull away from it and often times the only thing that dissolves one intensity is something that you're passionate about in another part of your life. So for me it's the guitar. I love the guitar and I can lose myself in it. It refreshes the spirit.

(continued on next page)

(continued from page 11)

Any particular genre you enjoy playing?

Guitar for me is a little bit like science. It's ever evolving. In my early days, it was finger picking and folk music. That progressed to blues, then to jazz then that progressed to classical. I like guitars themselves. I like the artistry of the craftsmanship in the wood.

You're a sports fan, right? And you recently received an honorary degree from Mt. Sinai School of Medicine along with Earvin "Magic" Johnson. What was that like?

He is just as he is on television, which is that he seemed like a big 6-foot 10-inch, 300-pound Teddy bear. You know what I mean? He's a very engaging, interactive and interesting guy.

In what way?

Magic is very friendly. He extended his hand to me and congratulated me for receiving my honorary degree. I congratulated him and told him now he can be the real "Dr. J," which he liked (laughs). He was completely accessible which is nice because he's a celebrity and celebrities are often not that way. He's done a lot in his career, he's overcome a lot and he's a leader. He's done just as much off the court as he's done on the court. In addition to the honor of meeting him, I love the Lakers so it was a double bonus.

Your lab drew worldwide media coverage last summer with the "Exercise in a Pill" study. While the research was conducted on mice, how plausible is the idea that one day those who cannot physically exercise because of disease, frailty or obesity will be able to get the benefits of physical activity by taking a pill?

I think the work clearly demonstrates, that in mice, it is possible to develop drugs that have the capacity to enhance muscle performance without actually exercising. That is a major advance. It also identifies two key drug targets for which the next generation of more effective muscle-enhancing drugs can be produced for people. In fact, the drugs that we used have already been used in people. So now I would say it's going to take a large pharmaceutical company to develop the right type of program in muscle biology.

You never really know, but my guess is that probably within four to five years we'll see the next generation of drugs, while the current generation of compounds is being explored for this purpose. The challenge in bringing this forward is getting the FDA to agree that frailty and obesity can be treated with muscle-enhancing drugs. You have to cure disease to get a drug approved. We think we can make people a lot more healthy. But making people healthy is not an FDA approval end point. We need to educate the public and the medical community to move the FDA toward accepting the benefits that can be achieved by this kind of program.

What's the one scientific question in your field you'd like answered in your lifetime?

Since we are in the bicentennial of Charles Darwin's birth, I would like to know the origin and evolution of physiology. Understanding the origin would give us a much deeper insight into how general physiology goes bad. When physiology itself is not controlled, it's highly destructive to the body. When it is controlled, it's everything that we call life. We want to get a handle on that. We would like to exploit all of that for the purpose of developing a new generation of drugs that control metabolic disease. That includes diabetes, heart disease and using our understanding of genomics and genomic control to develop muscle-enhancing drugs.

Ron Evans celebrated his 60th birthday and the 30th anniversary of his lab with 145 of his former students who attended a one-day symposium at Salk and a party that followed in April.

Salk Signs Strategic Alliance with Sanofi-Aventis

The Salk Institute signed a strategic alliance agreement with Sanofi-Aventis, establishing a joint program that supports cutting-edge research and promotes an exchange of discoveries focused on scientific advances and therapeutic applications.

For a period of up to five years, the Sanofi-Aventis Regenerative Medicine Program (SARP) will sponsor institute-wide discovery grants in promising research areas that address the organizations' mutual interests. SARP provides for long-term, multiple-participant collaborations between Salk and Sanofi-Aventis scientists – allowing both groups to benefit from each other's specific areas of expertise and potentially develop further partnerships. SARP will also provide unrestricted support for the Institute's stem cell core facility.

"This is a collaborative relationship without restrictive preconditions between two leading organizations," said **William R. Brody**, president of the Salk Institute for Biological Studies. "Our scientists will continue to freely explore cutting-edge research and publish their work, with the added benefit of advancing the science through this unique association that provides access to extensive resources at Sanofi-Aventis."

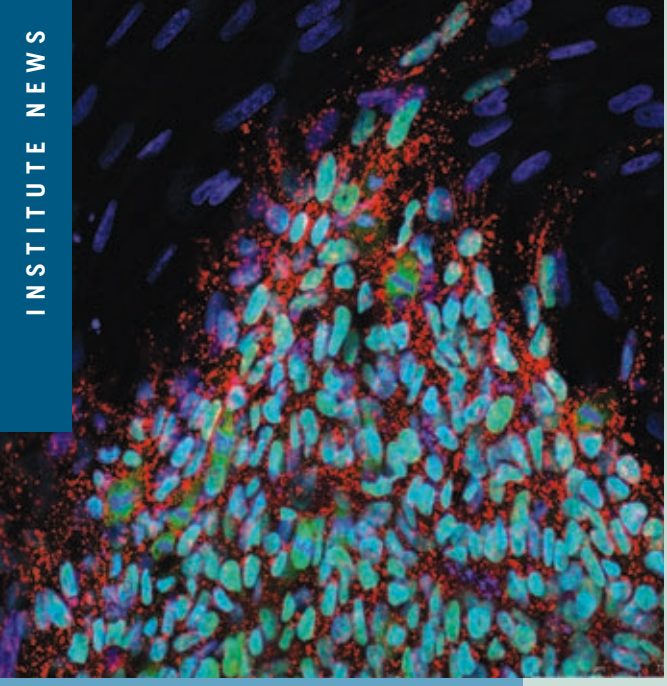
Further collaboration and scientific exchange will be reinforced through annual Salk/Sanofi-Aventis research retreats and extended working lab visits between scientists from both organizations.

"Our goal is to advance scientific knowledge, mostly in stem cell research, and apply major discoveries made under this strategic alliance toward diagnostics or therapies for human disease," said Dr. Marc Cluzel, senior vice president, Research & Development, Sanofi-Aventis. "We believe one way this can be expedited is through a collaborative research agreement in which the talents and expertise from Salk and Sanofi-Aventis are joined in an environment that favors creativity and early access to sciences."

Although Sanofi-Aventis and Salk had previously crossed paths at scientific and business meetings, the introductions between representatives from both organizations was facilitated in part by Stéphane Richard, a former postdoctoral Salk researcher who founded French BIO Beach, a San Diego-based networking group created to bridge the French government with local biotech companies and their counterparts in France.

"Salk's culture of openness and collaborative research is an ideal fit with Sanofi-Aventis' philosophy," said Remi Brouard, M.D., vice president, External Innovation, Sanofi-Aventis. "I'm confident this new relationship will bring forth discoveries that will positively serve our mission."

SARP is an innovative win-win model for U.S. researchers and the pharmaceutical industry, according to **Marsha Chandler**, executive vice president at the Salk Institute. "The arrangement benefits Salk scientists through direct financial support of their research and access to an array of resources that facilitate commercialization of discoveries," she said. "It benefits Sanofi-Aventis through access to top-quality basic science and cross fertilization in complementary areas like stem cell research."



Pictured are colonies of Fanconi anemia-specific iPS cells (stained in green) derived from human skin cells.

Photo courtesy of the Belmonte lab.

> "The opportunity to work with human cells from patients with these diseases will further demonstrate why we believe these cells are perfect candidates for transplantation therapy."
>
> **Juan Carlos Izpisúa Belmonte**

Salk Receives $6.6 Million Grant to Develop Stem Cell-Based Treatments for Incurable Diseases

The Institute has been awarded a $6.6 million grant – the largest single award in the latest competition – by the California Institute Regenerative Medicine (CIRM) for research aimed at translating basic science into clinical cures. The funds are part of $67.7 million Early Translational Grants CIRM provided to 15 research organizations in April.

Led by senior scientists **Inder Verma** and **Juan Carlos Izpisúa Belmonte**, the research will focus on developing treatments for Fanconi anemia and X-Linked Severe Combined Immunodeficiency (X-SCID), more commonly known as the "bubble boy" disease. Both are diseases of the blood and each is caused by the mutation in a single gene.

Using pioneering gene therapy and stem cell reprogramming techniques developed by Verma and Belmonte, they will work with mouse models that mimic each of the diseases. The human hematopoietic (blood precursor) stem cells used in their work are derived from patient hair follicle cells that have been induced into a pluripontent stem cell state (iPS) and corrected of its defective gene. The genetically corrected cells will then be coaxed back into the cells that form the blood and immune systems and used for transplant therapy. (See related story on page 16.)

"Working with human patient and disease-specific cells will help us demonstrate the feasibility and evaluate the safety in a pre-clinical setting to advance these techniques, which combine the latest developments in regenerative medicine and gene therapy," said Verma, a professor in the Laboratory of Genetics. "This work will also benefit the successful stem cell-based therapies for many other diseases like Parkinson's and diabetes."

"The opportunity to work with human cells from patients with these diseases will further demonstrate why we believe these cells are perfect candidates for transplantation therapy," said Belmonte, a professor in the Gene Expression Laboratory. "The chances of rejection are drastically reduced when the cells are derived from the patients themselves."

The 15 Early Translational grants approved by the CIRM's board were awarded to 13 not-for-profit and two for-profit organizations. They are intended to either lead to a drug candidate for an unmet medical need or address a bottleneck in the development of new therapies.

"With these Early Translational grants CIRM has taken the first step in funding translational research that will be critical for the development of future therapies," said Alan Trounson, CIRM president. "These grants are an important part of CIRM's strategy to fund the best basic research and then bring the results of that work to patients."

Investigators Share Passion for Research During Month–Long Science Festival

Members of Salk's faculty, including Nobel laureate **Roger Guillemin**, participated in the inaugural San Diego Science Festival – a multidisciplinary event that highlighted a wide range of research topics through interactive activities, lay presentations and stage shows in March.

Guillemin participated in the *Lunch with a Laureate* program in which he shared the story of his 1950s groundbreaking research of brain hormones to a large group of high school students.

Guillemin's discovery of somatostatin, a neurohormone, laid the foundation for further development of a new class of substances that regulate growth, development, reproduction and responses to stress. His finding also advanced the study and treatment of a variety of disorders, including thyroid diseases, infertility, diabetes and several types of tumors.

Five principal investigators from Salk also spoke to San Diego-area students as part of the festival's *Nifty Fifty* program, which featured the region's top researchers who shared their experience and passion for science in an effort to inspire tomorrow's scientists.

Among them was **Geoff Wahl**, a professor in the Gene Expression Laboratory, who studies the genetic basis and progression of cancer. He is also working toward the development of new therapeutic strategies. His presentation was timely as public health officials reported that cancer had eclipsed heart disease as the No. 1 killer in San Diego County.

Salk professors **Inder Verma**, **Joanne Chory**, **Terry Sejnowski** and **Fred. H. Gage**, also gave presentations at various middle and high schools. The month-long festival ended with the *Science of You Expo Day* in Balboa Park, where representatives from Salk's Mobile Science Lab hosted an activity booth to give visitors the opportunity to perform DNA extractions from wheat germ.

"It was wonderful that the San Diego Science Festival provided so many varied ways for the Salk Institute to interact with students of all ages," said Salk Education Specialist Dona Mapston. "I am certain that the excitement for science we saw among all the students will have a lasting impact on their education."

Visitors extract DNA from wheat germ at Salk's Mobile Science Lab booth during *Science of You Expo Day.*

Ellen Potter and Dona Mapston

Ellen Potter Receives Partnership Award for Mobile Science Lab

Ellen Potter, founder of Salk's Mobile Science Lab, received the 2009 Partnership Award by the San Diego Science Alliance in May in recognition of her "exceptional efforts to enhance K-12 science education in San Diego County."

A neurobiologist and coordinator of the Institute's education outreach program, Potter launched the Mobile Science Lab in 1996 in conjunction with the San Diego County Office of Education. Since then, the Mobile Lab has developed to fill the need for state-of-the-art laboratory activities at the middle school level.

Each year, Potter and Education Specialist Dona Mapston load up a van and visit 18 schools in the San Diego region along with volunteer graduate and postdoctoral students who teach DNA structure and techniques used for DNA fingerprinting. They also assist the younger students in performing various experiments such as extracting DNA from wheat germ.

In the last decade, the privately funded program has reached more than 20,000 students. Potter and Mapston have also forged partnerships between the Mobile Science Lab and the Reuben H. Fleet Science Center, the Birch Aquarium in La Jolla and the San Diego Science Festival to take the program beyond the classrooms and into the community.

"The strength of this program lies in the opportunity for young students to interact with researchers on a one-on-one basis," Potter says. "Without support from the Salk faculty, administration and wonderful volunteers, the Salk Mobile Lab would never have been able to last this long or continue to excite students in the joys of science. We are truly grateful to everyone for their support."

Discovery Roundup

Combined Stem Cell-Gene Therapy Approach Cures Human Genetic Disease in Vitro

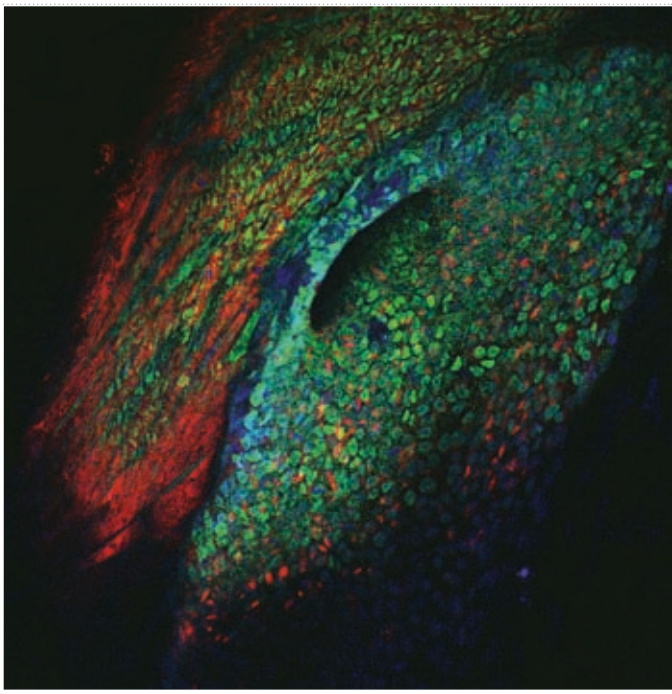
A team of researchers led by **Juan Carlos Izpisúa Belmonte**, a professor in the Gene Expression Laboratory, has proved in principle that a human genetic disease can be cured using a combination of gene therapy and induced pluripotent stem (iPS) cell technology.

Belmonte's team, working with Salk colleague **Inder Verma**, a professor in the Laboratory of Genetics, and colleagues in Madrid, focused on Fanconi anemia (FA), a genetic disorder responsible for a series of hematological abnormalities that impair the body's ability to fight infection, deliver oxygen, and clot blood.

After taking hair or skin cells from patients with Fanconi anemia, the investigators corrected the defective gene in the patients' cells using gene therapy techniques pioneered in Verma's laboratory. They then successfully reprogrammed the repaired cells into induced pluripotent stem (iPS) cells using a combination of transcription factors. The resulting FA-iPS cells were indistinguishable from human embryonic stem cells and iPS cells generated from healthy donors.

Since bone marrow failure as a result of the progressive decline in the numbers of functional hematopoietic stem cells is the most prominent feature of Fanconi anemia, the researchers then tested whether patient-specific iPS cells could be used as a source for transplantable hematopoietic stem cells. They found that FA-iPS cells readily differentiated into hematopoietic progenitor cells primed to differentiate into healthy blood cells.

"We haven't cured a human being, but we have cured a cell," Belmonte explains. "In theory we could transplant it into a human and cure the disease."



Colonies of Fanconi anemia-specific iPS cells stained in green.

A Biochemical Pathway for Blocking Your Worst Fears?

Scientists have found that glutamate, the most prominent neurotransmitter in the brain, plays a key role in the process of "unlearning." The team's study, led by **Stephen F. Heinemann,** a professor in the Molecular Neurobiology Laboratory, could eventually help scientists develop new drug therapies to treat a variety of disorders, including phobias and anxiety disorders, particularly post-traumatic stress disorder.

"Most studies focus on 'learning,' but the 'unlearning' process is probably just as important and much less understood," says Heinemann. "Most people agree that failure to unlearn is a hallmark of post-traumatic stress disorders and if we had a drug that affects this gene it could help soldiers coming back from the war to unlearn their fear memories."

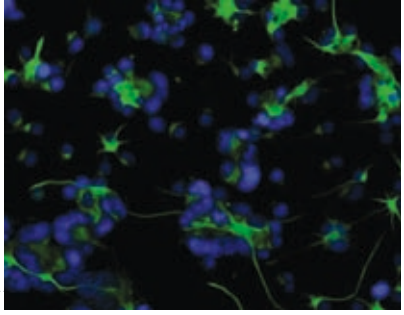
Post-traumatic stress disorder or PTSD is an anxiety disorder that can develop after exposure to a terrifying event or ordeal in which grave physical harm occurred or was threatened. PTSD affects about 5.2 million Americans, according to the National Institute of Health. As many as one in eight returning soldiers suffer from PTSD.

Scientists Discover How Obesity Increases Risk for Diabetes

Obesity is probably the most important factor in the development of insulin resistance, but science's understanding of the chain of events is still spotty. Now, researchers at the Salk Institute have filled in the gap and identified the missing link between the two. Their findings explain how obesity sets the stage for diabetes and why thin people can become insulin-resistant.

The Salk team, led by **Marc Montminy**, a professor in the Clayton Foundation Laboratories for Peptide Biology, discovered how a condition known as ER (endoplasmic reticulum) stress, which is induced by a high-fat diet and is overly activated in obese people, triggers aberrant glucose production in the liver, an important step on the path to insulin resistance.

In healthy people, a "fasting switch" only flips on glucose production when blood glucose levels run low during fasting. "The existence of a second cellular signaling cascade—like an alternate route from A to B—that can modulate glucose production, presents the potential to identify new classes of drugs that might help to lower blood sugar by disrupting this alternative pathway," says Montminy.



An abundance of glial cells (shown in green) is caused by the synaptojanin-1 protein

Stem Cells Provide Clues to Glial Cells Glut

A newly identified molecular pathway that direct stem cells to produce glial cells is yielding insights into the neurobiology of Down's syndrome and several other disorders of the central nervous system that are characterized by an overabundance of glia.

The findings, made by a team of scientists led by **David Schubert**, a professor and head of the Cellular Neurobiology Laboratory, indicate that synaptojanin-1, a central component of the pathway, is essential to production of glia, brain cells that act as neurons' personal assistants. Down's syndrome, spinal cord injury, Alzheimer's disease, and stroke all are linked by an overproduction of glia. Understanding this molecular pathway may also have implications for the onset of glioblastoma, the most common and malignant type of brain tumor.

"The discovery of this molecular signaling pathway promises to completely change the way we think about central nervous system maladies, allowing the development of drugs that inhibit glial proliferation and improve the prognosis of patients with a host of devastating conditions," Schubert says.

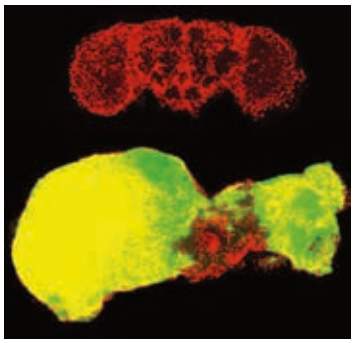
Fruit Flies Soar as Lab Model

Researchers led by Salk's John B. Thomas, a professor in the Molecular Neurobiology Laboratory, have transformed the fruit fly into a laboratory model for an innovative study of gliomas, the most common malignant brain tumors. The investigators looked to the fruit fly as a useful model since most of its genes are conserved in humans, including 70 percent of all known human disease genes.

"Gliomas are a devastating disease but we still know very little about the underlying disease process," said Thomas. "We can now use the power of Drosophila genetics to uncover genes that drive these tumors and identify novel therapeutic targets, which will speed up the development of effective drugs."

Better models for research into human gliomas are urgently needed. Last year alone, about 21,000 people in the U.S. were diagnosed with brain and nervous system cancers, Senator Edward M. Kennedy the most famous among them.

About 77 percent of malignant brain tumors are gliomas and their prognosis is usually bleak. While they rarely spread to elsewhere in the body, cancerous glial cells quickly infiltrate the brain and grow rapidly, which renders them largely incurable even with current therapies.



Top: Normal fly brain for comparison. Glial cells are shown in red.

Bottom: Tumor cells (shown in green) have overtaken almost the entire brain of an adult fly.

Photo courtesy of Dr. Renee Read, Salk Institute

Missing Genomic "Fence Posts" Explain Inactivated Tumor Suppressor Genes in Breast Cancer

Scientists led by Beverly Emerson, a professor in the Regulatory Biology Laboratory, have found that a breakdown in molecular fences blurs the lines between genomic neighborhoods and leads to the inactivation of at least two tumor suppressor genes. Their findings explain how a single event can put a cell on the road to becoming a tumor cell.

Tumors result when changes in the genome activate cancer-causing genes or inactivate tumor suppressor genes that tip this delicate balance in favor of uncontrolled cell growth. In many different types of cancers, the tumor suppressor gene p16 gets buried deep inside heterochromatin, a tightly condensed structure that protects DNA. As a result, it cannot be read by the transcription machinery and is unable keep watch over cell growth.

Most people looked for clues within the immediate vicinity of the gene but came up empty-handed. When postdoctoral researcher Michael Witcher extended his search further upstream, however, he discovered a binding site for CTCF, short for CCCTC-binding factor, which forms the centerpiece of the molecular fence posts that separate heterochromatin from the rest of the genome.

"We found that the binding of this protein is lost from several binding sites in numerous types of cancer cells, leading to the collapse of the molecular boundary," he says. "Once the boundary was gone, the adjacent heterochromatin encroached and silenced the nearest gene."

Further experiments revealed that CTCF was missing because it lacked a chemical modification known as "PARlation," lab lingo for poly(ADP-ribosyl)ation, which allows the protein to bind to select sites in the genome.

"Without PARlation, CTCF fails to form the complex necessary to regulate p16 and the tumor suppressor RASSF1A and possibly others, explaining why breast cancer cells always contain both silenced p16 and silenced RASSF1A," says Witcher.

Institute Receives Discovery-Driven Media Coverage

Photo by Sam Hodgson

The *Voice of San Diego* featured Travis Berggren, director, Stem Cell Core Facility, in an article on the state of stem cell research in March.

Salk investigators and their research have been the subject of significant media coverage this year with profiles and feature stories on television, radio and print outlets.

The United Kingdom's *Times Online*, *New Scientist* and *The San Diego Union-Tribune* each highlighted a study by **Juan Carlos Izpisúa Belmonte** and **Inder Verma** that showed how a combined stem cell and gene therapy approach was used to cure the human genetic disease Fanconi anemia in vitro.

United Press International distributed articles on two important Salk studies: one led by **E. J. Chichilnisky,** associate professor in the Systems Neurobiology Laboratories, that provided new insight into the retina's precision and mechanics to enable vision; and another by **Inder Verma**, professor in the Laboratory of Genetics, whose team developed a mouse model for glioblastoma, the most common and most aggressive type of primary brain tumor.

Fred H. Gage, professor in the Laboratory of Genetics, also generated strong coverage from several outlets, including *CNN.com*, with a study that used a computational model to demonstrate how newborn brain cells put a time stamp on memories.

Marc Montminy, professor in the Clayton Foundation Laboratories for Peptide Biology, received national attention when *U.S. News & World Report* published a story on a study that showed how a molecular switch in fat tissue of obese mice plays a critical role in the development of insulin resistance.

The finding suggests that activity of the switch could provide an early warning for obese people who are predisposed to develop insulin resistance and may lead to new diabetes treatments that would not require weight loss.

Andy Dillin, associate professor in Molecular and Cell Biology Laboratory and Director of Salk's Glenn Center for Aging Research, was prominently featured on KPBS's *Envision San Diego*, a monthly television show that highlighted research on aging at the Institute and other local institutions. KPBS radio also featured a study by **Richard Krauzlis**, associate professor in the Systems Neurobiology Laboratory, whose research on rapid eye movement provided new insights into our normal vision process.

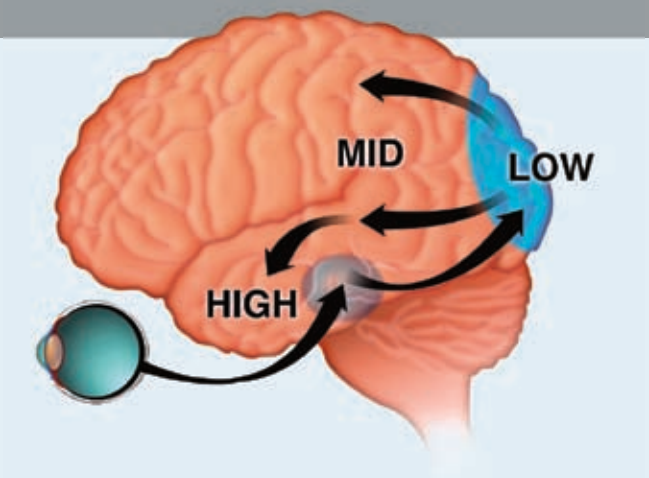
News of President Barak Obama's decision to abolish federal restrictions on human embryonic stem cell research in March also drew strong interest from reporters who sought expert opinion and reaction from the Salk Institute. Channel 10 News, an ABC affiliate in San Diego, interviewed **Travis Berggren**, director of the Stem Cell Core facility, for its evening broadcast on the subject.

He was also highlighted in a Q&A piece published by *Voice of San Diego*, which covered the state of stem cell research and put in perspective the potential advancements as a result of the president's decision.

To see the latest media coverage of the Salk Institute, visit www.salk.edu and click on "News & Press."

Workshop on Vision/Brain Research Draws Journalists to Institute

The Salk Institute's Communications department hosted a science writers' workshop that drew a dozen San Diego-area staff and freelance journalists to hear the latest research on vision and the brain in April.



The vision process takes place in three general stages within the brain. Information is first collected in the retina before it is sent to the back, middle and frontal areas of the brain for low, mid and high levels of processing.

Illustration courtesy of the Albright Lab.

The event, designed as a networking opportunity with journalists, featured a lively roundtable session and talks by three of Salk's leading investigators (and one from UCSD) who discussed their respective areas of science, which represent some of the work that has led San Diego to emerge as a major hotbed for vision research in the last decade.

Providing a broad overview of studies and discoveries over the last 50 years, **Thomas Albright**, professor and director of Salk's Vision Center Laboratory, described the various stages of visual processes and the biology behind the visual system, which neuroscientists are using as a tool to ultimately understand the brain.

"The treatment of vision-related diseases depends on understanding brain structure and function," he said. "It's like fixing your car. If you don't understand how the car is put together, there's no chance you're going to be able to fix it. The same is true with the brain. If we want to be able to fix the brain when it breaks, we have to understand how it's put together."

One way to understand the brain is to tease apart its circuitry, which was the focus of **Edward Callaway**'s presentation. A professor in the Systems Neurobiology Laboratory, he explained the novel technique he developed using a modified rabies virus to identify the connections to single neurons. This discovery is the first step toward developing a wiring diagram of the brain to eventually treat disorders such as schizophrenia, depression and Parkinson's disease.

UCSD Professor of Psychology **Karen Dobkins** focused her presentation on her studies of autism, and offered several hypotheses in her field, including one suggesting that the developmental disorder, which affects one in 150 children, could be associated with problems in the visual system.

She explained that autistic children have deficiencies in their ability to remember faces and detect motion, sensory functions that are processed in the primary visual cortex. This area of the brain is also responsible for sending signals to the frontal lobes that are involved in cognitive and behavioral functions. Social behavior and communication deficits, it turns out, are among the hallmarks of autism.

"This might sound like a stretch, but we are playing with the idea that autism might possibly originate with a problem in sensory processing," Dobkins says. "In other words, before I can act appropriately to my world, I have to perceive my world appropriately."

The workshop culminated with an overview of the building blocks of the visual system by **E. J. Chichilnisky**, whose goal is to learn the mechanics behind the retina in sufficient detail to replicate its activity so that his lab can one day contribute to a visual prosthetic that could help the blind to see.

Comparing the retina's computational capacity to a 1-megapixel digital camera, Chichilnisky described how the various cells in the retinal tissue gather incoming information through the eye before sending it via nerve fibers to the brain where the signals are developed into a visual representation of what is being perceived.

His lab is able to record this activity, he said, using specially designed electrode electronics that can take several hundreds of readings from retinal cells simultaneously. By learning to interpret and replicate these signals, Chichilnisky said a prosthetic device is possible in the future.

"I thought there was a good mix of basic information and specific research applications," said Lynne Friedman, editor of *ScienceWriters*, a publication of the National Association of Science Writers. "Equally important was how the speakers described the unanswered questions in the field, which will help writers evaluate future journal articles on the topic."

Gift by Trustee Howard and Maryam Newman Establishes Endowed Chair

Howard Newman places his well-worn canvas bag on the floor and settles comfortably into a chair after what has been a long but productive week of board meetings at the Salk Institute.

Maryam Razavi Newman, his wife of 21 years, has accompanied him on the trip from New York to participate at a luncheon honoring Salk scientist **Joanne Chory** with an endowed chair.

The Howard H. and Maryam R. Newman Chair is the first to grow out of the Jacobs Chair Challenge. Salk Board Chairman **Irwin Jacobs** and his wife, Joan, pledged up to $10 million in a fundraising campaign intended to create 10 new permanent chairs in support of senior faculty members. For every $2 million contribution, the Jacobs will augment each gift with an additional $1 million.

Newman, a trustee since 2002, was the first to take up the challenge. "One of the things we wanted to do with this chair is to let the world know just how special Joanne and plant biology are at Salk," he says.

"Plus, when you have a laboratory that's pre-eminent in its field, a recognized world leader, you want to lead with it and focus on it. So we hope that, in this small way, we can bring some well-deserved attention to a part of Salk that really appeals to us."

Newman is president and CEO of Pine Brook Road Partners, LLC, a private equity firm, and has no formal background in science. But he quickly became fascinated by and comfortable with Salk's scientific research. The gregarious trustee was also quick to make Institute acquaintances.

"I remember Maryam and I were walking around Salk and we bumped into (scientist) **Tony Hunter**," Newman says. "We were talking and quickly realized that he and I were graduate students together at Christ's College at the University of Cambridge. It turns out we used to drink coffee and play chess together.

"As we went around meeting all the senior scientists, I was captivated by their curiosity-driven research. One of my mottos in my firm is that there's no such thing as an uninteresting fact. Salk buys into that. And once you understand what the scientists do, you just fall in love with it."

The Newmans were equally impressed by the investigators' passion for their work and their ability to explain it at just the right level – a level at which they could appreciate it, yet also learn enough to be further intrigued.

"They have that ability to carry a conversation that's a little bit beyond where you are comfortable walking so that you have to jog a little to keep up," Newman says. "It's wonderfully refreshing. You come away with your mind having been stretched, but in a very gentle way, which is really nice."

Trustee Howard Newman with his wife, Maryam, and daughter, Elizabeth.

A psychotherapist by profession, Maryam Newman says she has a personal interest in the neurobiology laboratories, which are working toward understanding brain function as well as looking at the molecular basis of mental disorder.

"I'm waiting for researchers to come up with a molecular explanation for serious mental illness," she says. "Perhaps their work will provide answers to free people from these life-destroying conditions.

"I believe research at Salk is pure science and the findings have applications to many other areas of research," she says. "If you don't have basic science, you don't have translational research."

The Newman Chair is hardly the first time the couple has contributed to the Institute. Members of the President's Club since 2002, they also made a generous contribution the following year to establish the Razavi Newman Center for Bioinformatics. The center provides a valuable service by collaborating with and assisting many Salk laboratories to create databases using advanced computational and statistical techniques.

As he grabs his bag to leave for his next business trip to Portland before heading home to Manhattan, Newman offers one last reason for his belief in research at the Salk Institute:

"Salk is simply a unique place. It attracts world-class scientists who work in a collaborative environment. That's what attracts us to it," he says. "It's a treasure that needs to be supported."

A Taste of Discovery

John Codey, vice president and secretary of the Leona M. and Harry B. Helmsley Charitable Trust (center), was in New York City with Salk President **Bill Brody** (left) and Chairman of the Board **Irwin Jacobs** to attend the Institute's A Taste of Discovery luncheon where Salk Professor **Ed Callaway** gave a presentation on his latest research.

Salk Launches Nutritional Genomics Center with $5.5 Million Grant from Helmsley Trust

A $5.5 million grant from the Leona M. and Harry B. Helmsley Charitable Trust has established the Salk Center for Nutritional Genomics, a multi-lab endeavor that takes a molecular approach to understanding how nutrients affect health.

Capitalizing on the Salk's strength in collaborative research, the new center draws expertise from leading laboratories at the Institute to deepen its diabetes research with the intent to unravel the mechanisms that modulate the body's energy balance and the factors that set the stage for metabolic disease.

"Given the fact that metabolism has clearly established itself as a common denominator in many research fields, I am very pleased that our scientists will have the opportunity to collaborate further and delve even deeper into this vitally important area of biological science," said Salk President **William R. Brody**.

"The Salk Center for Nutritional Genomics will enable our investigators to develop new approaches to understand the metabolic changes associated with Type I and Type II diabetes, cancer and aging," he said. "It will also help accelerate the development of new therapies and disease-prevention strategies."

Received in April, the grant will also fund a Metabolic Core Facility, an interdisciplinary Fellows Program and breakthrough technologies, including the study of gene networks based on massive parallel sequencing of millions of genomic DNA fragments, which allow scientists to investigate a huge number of variables simultaneously and dramatically increase the speed and effectiveness of their work.

Adult obesity, which has increased 75 percent since 1980 in the U.S., is associated with a slew of metabolic disorders, including glucose intolerance, insulin resistance, high cholesterol and high blood pressure – all of which are well-established risk factors for cardiovascular disease and Type II diabetes.

A major strength of the Salk Institute is its approach to fundamental aspects of medical physiology and endocrinology from the perspective of the genome. Its scientists look at metabolic control as a product of the regulated activity of metabolic genes, which undergo dramatic shifts, not only in response to fasting or feeding, but also in aging and disease.

"The study of metabolic control will provide fundamental answers that have profound implications for human disease and its treatment," said **Marc Montminy**, professor in the Clayton Foundation Laboratories for Peptide Biology at Salk. "Our scientists look at the genomics of metabolic control as the hub of a wheel whose individual spokes lead out to new insights into other disorders such as diabetes, cancer, neurodegenerative diseases, and aging."

Broadway Star Bernadette Peters to Headline Symphony at Salk

This year's Symphony at Salk – A Concert Under the Stars will feature two-time Tony Award-winner Bernadette Peters, who will perform with the San Diego Symphony and returning guest conductor Thomas Wilkins on Aug. 22. The al fresco fundraiser supports basic biological research and the Institute's community education programs.

A performer of amazing versatility with a career that spans five decades, Peters has starred in musical theatre, films and television as well as headlining solo concerts and recordings. Most recently, she guest-starred on the hit TV show, *Ugly Betty*, as Editor Jodie Papadakis.

One of the most critically acclaimed Broadway actresses and the youngest person ever inducted into the Theatre Hall of Fame, Peters has won virtually every major theatrical award, including two Tonys (*Song and Dance*, 1986; *Annie Get Your Gun*, 1999) three Drama Desk Awards and a Golden Globe. She recorded four Grammy Award-winning Broadway cast albums, along with six solo albums that have produced several popular singles.

The *New York Times* wrote: "She is the voice of Sondheim, the face of Broadway, an actress as beloved for her concerts and recordings as for her iconic stage roles. As an actress, singer, comedienne, and all-around warming presence, Bernadette Peters has no peer in musical theatre right now and her vivid theatricality registers with rare impact."

Maestro Wilkins returns to lead the San Diego Symphony for the fifth consecutive year – bringing the dynamic energy, warmth and charm that have made him a highly sought after guest conductor across the United States. This year, Wilkins began his first season as Principal Guest Conductor of the Hollywood Bowl Orchestra.

Honorary chair of Symphony at Salk is internationally renowned artist **Françoise Gilot**, widow of **Jonas Salk**. Gilot's artwork, *Sun Emblem* (1980), provides this year's visual theme. It is part of the artist's Floating Paintings series, a selection of which was recently on display at the Salk Institute.

Tickets to Symphony at Salk will be available beginning July 12 for $250 each. Event festivities include a champagne reception at 5 p.m.; Institute tours at 5:15 p.m. and 5:45 p.m.; supper at 6 p.m.; and musical program at 7:30 p.m. To purchase tickets, call 858-453-4100, ext. 1882, or e-mail: hodges@salk.edu.

salkexcellerators

Celebrating the Nexus of Science and Philanthropy

Inder Verma (from left), Salk Trustee Ted Waitt and Martin Hetzer.

Ted Waitt was interested in funding a scientific program at the Salk when he asked **Inder Verma** to invite **Ron Evans** and other senior investigators to dinner so they could discuss research areas where the Institute could expand over the next five years.

A Salk Trustee since 2004, Waitt turned to Evans and asked: "What's the one thing that's going to be a catalyst … the thing that will make a difference and have a lasting impact?"

His bottom-line question over dinner in 2006 received a unanimous response: Biophotonics – the science that blends biology, nanotechnology, and computer science and gives researchers the ability to probe and record the inner workings of living cells in real time at unprecedented visual resolutions.

The synergistic partnership that evolved between the scientists and the philanthropist, who, through his family foundation, contributed $20 million to establish the Waitt Advanced Biophotonics Center, was the focus of the season-ending event of the salkexcellerators, a group of philanthropically minded, young business leaders.

"I realized that night if we had the ability to see how a specific protein behaves inside a cell in real time, then we could transform how scientific research is done," Waitt said. "As a technology guy, this made sense to me."

The May 6 event also featured talks by **Martin Hetzer**, associate professor in the Molecular and Cell Biology Laboratory, and Verma, who put what biophotonics technology can offer into perspective.

"We are all biologists, but we are more or less like archeologists. We look at cells, we break them up and then we put the pieces back together," he said. "But wouldn't it be nice to look at a cell as it is functioning, to actually see when a cancer starts. That would revolutionize the way we think and the way we do science."

Hetzer's lab has already shown proof of concept with a modified microscope his lab developed through a grant provided by Salk Chairman **Irwin Jacobs**. Unlike off-the-shelf microscopes, Hetzer's machine uses sound waves to delve into the nanoworld, allowing his team to follow individual protein complexes within living cells twice as fast and in three dimensions, Hetzer said.

His researchers found a connection between the breakdown of the protein complexes in neurons and the development of filaments, the accumulation of which have long been associated with neurodegenerative conditions such as Parkinson's disease.

"There's no other way we could have seen this before," Hetzer said. "We believe that the breakdown of these complexes are the very early events that lead to the filaments."

Waitt's multi-million-dollar contribution last year wasn't the first time he had invested in technology believing that it would lead to revolutionary innovation. He found much success after co-founding the personal computer company Gateway, Inc. in the late 1980s.

"When I look for things to invest in, I want to feel that I'm making a difference," Waitt said. "I want to know that what I'm contributing to will really be leveraged. That's why I'm putting my philanthropic money in the sciences.

"I know biophotonics has the potential to truly transform and lead to multiple breakthroughs in science. I believe in science and I believe in innovation because it's going to take innovation to lead to discoveries and job creation," he said. "That is what our future depends on."

salkexcellerators Ashley and Ryan Stone (left) and Brian and Laura Tauber

More than 50 Institute employees came together in April to participate in the March of Dimes' March for Babies, the nationwide event designed to raise funds for research in premature births and infant health. Team Salk, which also included Institute President **Bill Brody** and his wife, Wendy, helped raised $9,380 by walking at the event held in San Diego's Balboa Park.

Dear Friends,

In the first few months since arriving at the Salk Institute, I've had the opportunity to take a good look at all the working parts of this amazing place and to see how they all come together to make Salk one of the most productive and innovative research institutes in the world.

What make Salk's environment so rich are the dedicated scientists who tirelessly work in the laboratories and the administrative staff that support them. Meeting with faculty members has also given me a greater appreciation of the Institute's place in history and, just as importantly, the solid position it holds for making important discoveries as we enter a new era of basic scientific research.

We are in the renaissance of biomedical science, and being at the Salk must be similar to having been in Florence during the Italian Renaissance. The impact of our discoveries on human health is critical to the aging of the world's population. Without ways to cure chronic illnesses, governments will have to spend their entire GDP on health care.

The good news is that the major discoveries being made in laboratories like the Salk will have a profound impact on finding new ways to cure disease and alleviate suffering. And medicine in the future will be personalized, as we better understand how a person's genetic makeup allows a particular form of therapy to be applied successfully.

At the heart of Salk's leading research is the collaborative spirit under which it's conducted. It's not uncommon, for example, for a plant biologist to have discussions with a human stem cell scientist in an effort to find solutions to common scientific problems in their respective labs. It's this interdisciplinary camaraderie between investigators that keeps science moving forward at Salk and it is what steadily nurtures the creative nature of biomedical research.

This commitment and belief in collaboration to expedite discovery was strengthened further in March when the Institute forged a very important strategic alliance with Sanofi-Aventis. The non-restrictive relationship is a win-win model for both organizations. Salk scientists benefit from financial support of their research while the French pharmaceutical company has access to top-quality basic science.

The Institute also has an ongoing strategic relationship with Ipsen, another French pharmaceutical company that sponsors targeted research programs focusing on proliferative diseases with particular emphasis on novel therapeutics. Established last year, the Ipsen Life Sciences Program at Salk also funds core grants for basic research on chronic inflammation and its contribution to malignant diseases, and innovation grants, which provide funding for the exploration of advanced scientific concepts.

The engine of discovery requires philanthropic support as well as government research grants and partnerships with industry. I am pleased to report that despite the difficult financial environment, our donors have stepped up to the plate and we are on track to have one of the Salk's best fundraising years ever. We need your support more than ever and I have been gratified to see the large number of people who are committed to the Salk's mission.

I feel privileged to be at the Salk Institute. Looking at the extraordinary talent of its researchers and their history of seminal scientific contributions, most recently in metabolism and stem cell research, there's no doubt that our position as a world leader in basic science is secure. And as we enter an era of a resurgence and interest in science, I'm excited by what we can accomplish and the possibilities that lie ahead.

William R. Brody

"We are in the Renaissance of biomedical science, and being at the Salk must be similar to having been in Florence during the Italian Renaissance. The impact of our discoveries on human health is critical to the aging of the world's population."

William R. Brody
President

SALK INSTITUTE
FOR BIOLOGICAL STUDIES

STREET ADDRESS
10010 North Torrey Pines Road
La Jolla, California 92037-1099

Telephone: 858.453.4100
Fax: 858.552.8285
www.salk.edu

There are many ways to support the Salk. For information on how you can help, please email giving@salk.edu or call 858.550.0472

Salk **Calendar**

AUGUST 2009

12–16 **Mechanisms & Models of Cancer Meeting**

22 **Symphony at Salk – featuring Tony Award-winner Bernadette Peters**

SEPTEMBER 2009

11 **Usha Mahajani Symposium**

OCTOBER 2009

29 **Marguerite Vogt Lecture**

JANUARY 2010

13–15 **Salk and Fondation Ipsen Symposium on Biological Complexity: Sensory Systems: Smell, Taste, Touch, Hearing, and Vision**

FEBRUARY 2010

4 **Renato Dulbecco Nobel Lecture**

11 **Stem Cells and Cancer Symposium**

18 **Leslie Orgel Memorial Lecture**

For additional information on these and other Salk events, contact the Development Department at 858.453.4100 x1658

High School Science Day 2009

Nearly 200 students attended Salk's High School Science Day in February when they went on lab tours, heard presentations from scientists and participated in hands-on experiments.