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InsideSalk

Where cures begin.

THE SALK INSTITUTE FOR BIOLOGICAL STUDIES

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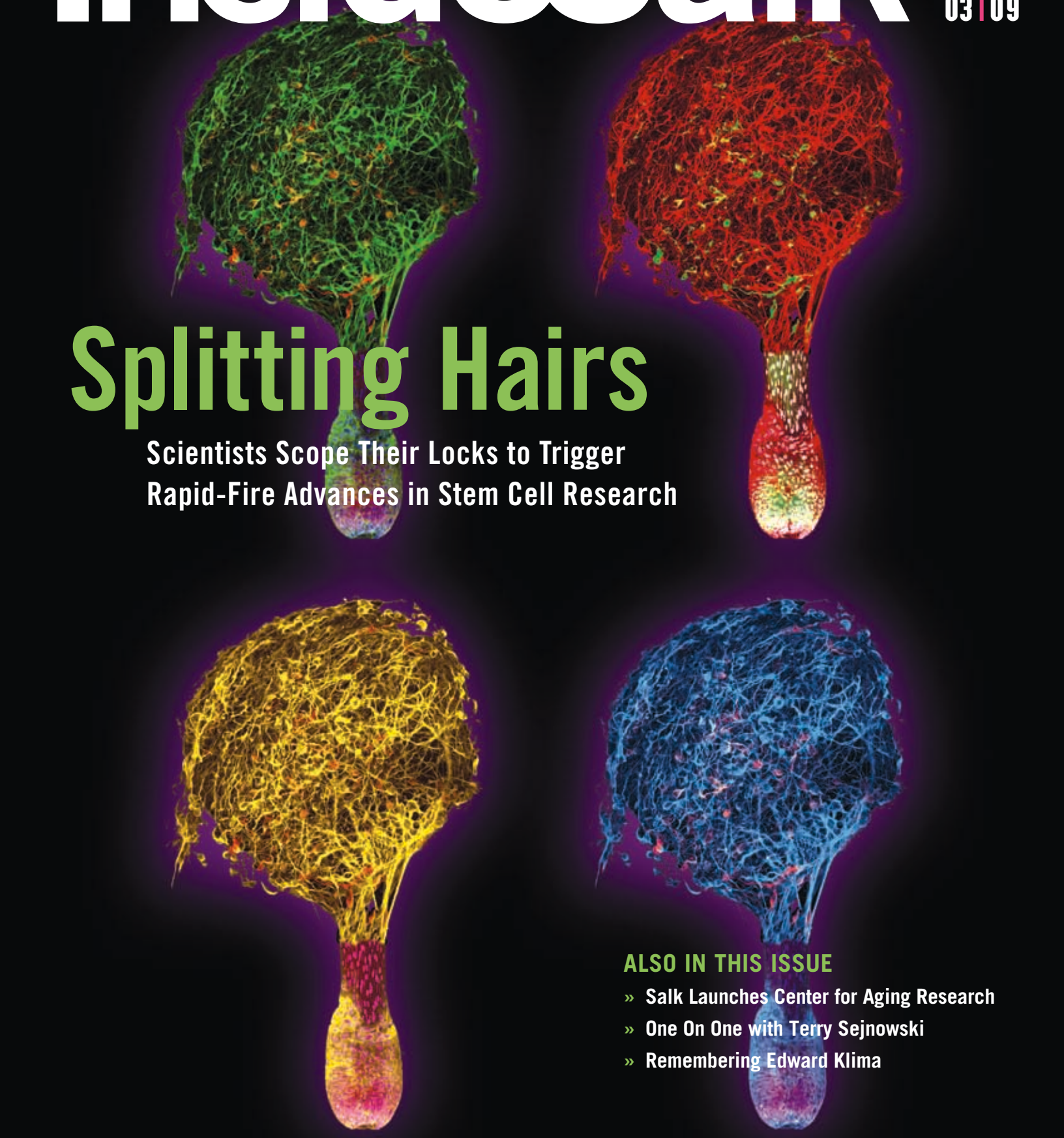

Splitting Hairs

Scientists Scope Their Locks to Trigger Rapid-Fire Advances in Stem Cell Research

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March 2009
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One on One with Terry Sejnowski

Remembering Dr. Edward S. Klima

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

The images on the cover of this issue are meant to represent life-giving "trees" that produce a host of differentiated cell types that medical science believes may one day be used therapeutically to treat and cure disease. The illustrations have been digitally created by superimposing clusters of dopaminergic neurons (upper portion) that derived from reprogrammed keratinocytes – cells taken from the root section (bottom portion) of hair plucked from a human scalp.

Joanne Chory

> "If we want to feed over 9 billion people by the year 2050, then understanding the basic mechanics of plant growth is required. This knowledge will ultimately lead to our ability to increase the amount of crops that are produced."
>
> – Joanne Chory

Salk Offers Free Community Events During Science Festival

THE SALK INSTITUTE WILL HOST SEVERAL free public events in collaboration with the inaugural San Diego Science Festival (SDSF), which takes place at various locations throughout the county during the month of March.

Planned as a multicultural and multidisciplinary celebration of science, SDSF highlights a wide range of scientific topics through interactive activities, lay presentations and stage shows coordinated by more than 125 business and research organizations.

Five principal investigators from the Salk Institute will participate in the festival's Nifty Fifty Program, which features San Diego's top researchers who will share their experience and passion for science at area middle and high schools in an effort to inspire the scientists of tomorrow.

Joanne Chory, professor and director of Salk's Plant Molecular and Cellular Biology Laboratory, is among the event's Nifty Fifty speakers representing Salk who will present at the Options School in Chula Vista on March 13. 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 this process has great importance on a global level, she says.

"If we want to feed over 9 billion people by the year 2050, then understanding the basic mechanics of plant growth is required," Chory says. "This knowledge will ultimately lead to our ability to increase the amount of crops that are produced, such as wheat, corn and rice, while decreasing the need for pesticides."

Fred H. Gage (San Elijo Middle School, March 10; and Poway High School, March 24), **Terry Sejnowski** (El Capitan High School, March 24) **Geoff Wahl** (Lincoln High School, March 27), and **Inder Verma** (La Jolla Country Day, March 10) will also participate in the Nifty Fifty Program.

Students who want to learn first-hand about science's most exciting discoveries will have the opportunity to sit with Salk's Interim President **Roger Guillemin** on March 30 at Escondido High School during the Lunch with a Laureate Program. The meetings offer individuals the opportunity to have an informal discussion with Nobel Prize-winning scientists.

The Salk Mobile Science Lab will also have an activity booth in Balboa Park where the public will be invited to perform DNA extractions from wheat germ at the Science of You Expo Day, the festival's culminating event on April 4.

Nifty Fifty Participants

Fred H. Gage		
	San Elijo Middle School	March 10
	Poway High School	March 24
Inder Verma		
	La Jolla Country Day	March 10
Terry Sejnowski		
	El Capitan High School	March 24
Geoff Wahl		
	Lincoln High School	March 27
Roger Guillemin ***Interim President***		
	Escondido High School	March 30

For more information about Salk's activities during the San Diego Science Festival, contact Dona Mapston at mapston@salk.edu or visit www.sdsciencefestival.com.

Geoffrey M. Wahl Named 2008 AAAS Fellow

SALK RESEARCHER GEOFFREY M. WAHL, a professor in the Gene Expression Laboratory, has been awarded the distinction of AAAS Fellow, an honor bestowed upon members of the American Association for the Advancement of Science by their peers.

Wahl was among 486 individuals awarded membership by the AAAS for their scientifically or socially distinguished efforts to advance science. The new Fellows were presented with an official certificate and a gold and blue rosette pin during the 2009 AAAS annual meeting in Chicago on Feb. 14.

Wahl and his team of investigators study the genetic basis of the origin and progression of cancer, while also working toward the development of new targeted therapeutic strategies. Their work has demonstrated that integrity of the p53 tumor suppressor pathway is essential for maintaining genome stability.

Their current research uses the p53 pathway as a model to understand the mechanisms by which normal and cancer cells sense and respond to the diverse stresses that contribute to cancer development. Wahl and his team are identifying, isolating and characterizing stem cells in different tissues, and developing safer and more effective strategies to convert differentiated cells into stem cells for use in therapies.

A past President of the American Association for Cancer Research (2006-2007), which is the largest and oldest organization devoted to cancer research in the world, Wahl remains a strong supporter of cancer research outside of the laboratory by lobbying Congress for increased funding, and has written about the societal and economic benefits of cancer research for the lay press.

Geoffrey M. Wahl

CIRM Awards Institute $1.5 Million Training Grant

THE SALK INSTITUTE HAS BEEN TENTATIVELY awarded a training grant that represents a portion of the $58 million approved January 29 by the governing board of the California Institute for Regenerative Medicine (CIRM).

Under the direction of Salk professor **Juan Carlos Izpisúa Belmonte**, the Institute will receive $1.5 million to fund postdoctoral fellows who are conducting stem cell research. The 29-member Independent Citizen's Oversight Committee voted to support 26 grants pending future financial availability. The ICOC said CIRM can fund all existing commitments through September of 2009.

"This CIRM grant is important for the training and further development of the next generation of postdoctoral fellows who will carry the stem cell research field forward," Belmonte says. "The grant also benefits the Salk as a whole since it provides opportunities for further collaborations on new projects between different scientists throughout the Institute."

Dr. William R. Brody

FACULTY, BOARD MEMBERS AND THE media gathered for a press conference and welcoming reception at the Salk Institute in October when Board Chairman Irwin Jacobs introduced **Dr. William R. Brody** as Salk's new president. Inside Salk will feature Dr. Brody in an upcoming issue.

Sedra Shapiro (center), director of the Science & Technology Group Program and the Blasker-Rose-Miah Fund at the San Diego Foundation, visited Salk to meet with postdoctoral fellows **Naden Krogan** and **Vivian Ciaramitaro** who were awarded $37,000 and $73,000, respectively, from the Blasker Science and Technology Grants Research Award Program.

Sunna Bohlen's *Among the Stones* Now on Display

THE SALK INSTITUTE HOSTED AN OPENING reception on Feb. 17 for it's latest exhibit, *Among the Stones*, *Works by Sunna Bohlen*, which will remain on display through June 2009.

"Sunna Bohlen's luminous canvases evoke a sensation of misty atmospheres of light and color that beckon viewers to linger in a space between emotion and serenity," said Mel Yoakum, curator and director of the F. Gilot Archives, who gave an engaging presentation, titled *Sunna Bohlen: Art and the Creative Mind*, prior to the reception.

Born and raised in Korea, Bohlen began painting and writing poetry at a very young age before she moved to San Diego when she was 22. She married former Salk researcher Peter Bohlen and continued painting as his cancer research took them to Switzerland and New York.

An active San Diego philanthropist and former Board member of the San Diego Opera Association, Bohlen's pieces currently on display at Salk represent some of her latest abstract work. For more on the artist and her work, visit www.salk.edu.

Sunna Bohlen

Salk Interim President Roger Guillemin (center) hosted Pierre Vimont, French Ambassador to the U.S. (left), and David Martinon, French consul general in Los Angeles, during their visit to the Institute in December.

Postdocs Receive $335K in Fellowship Awards

TEN POSTDOCTORAL FELLOWS AT THE SALK Institute have been awarded a total of $335,000 in support of their research in fields ranging from neurobiology, and molecular and cell biology.

The Pioneer Postdoctoral Endowment Fund provided eight researchers from as many laboratories with $32,500 each in January. Longtime Salk supporter Helen McLoraine established the fund in the early 1990s to support the Pioneer Scholar Awards. It was the first postdoctoral fellowship endowment at the Institute.

The Catharina Foundation Postdoctoral Fellowship Program provided two awards of $37,500 each. Established in 1997, the program supports European postdoctoral scientists at Salk.

Members of the Verma Lab.

Verma Lab Develops Novel Glioblastoma Mouse Model

RESEARCHERS LED BY INDER VERMA, professor in the Laboratory of Gentics, have developed a versatile mouse model of glioblastoma—the most common and deadly brain cancer in humans—that closely resembles the development and progression of human brain tumors that arise naturally.

"Mouse models of human cancer have taught us a great deal about the basic principles of cancer biology," says Verma. "By definition, however, they are just that: approximations that simulate a disease but never fully capture the molecular complexity underlying disease in humans."

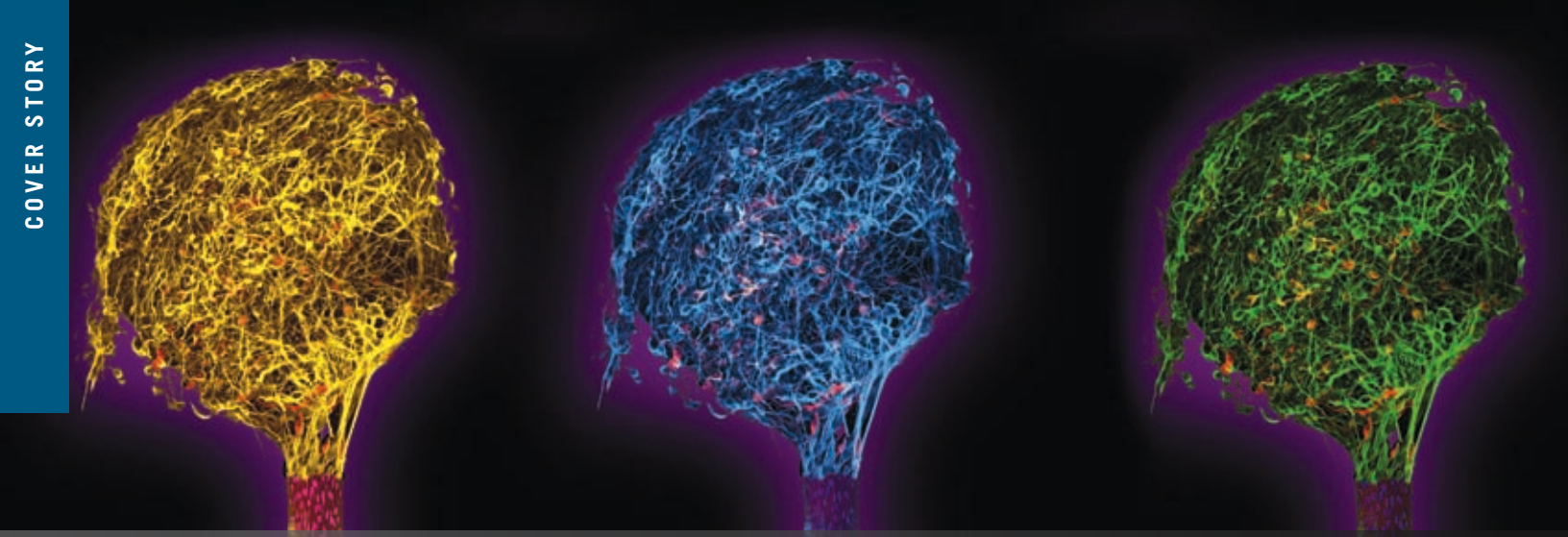
Trying to mimic randomly occurring mutations that lie at the heart of all tumors, the Salk researchers used modified viruses to shuttle cancer-causing oncogenes into a handful of cells in adult mice. Their strategy, described in the Jan. 4, 2009 issue of the journal *Nature Medicine*, may not only prove a very useful method to faithfully reproduce different types of tumors, but also to elucidate the nature of elusive cancer stem cells.

Splitting Hairs

Scientists Scope Their Locks to Trigger Rapid-Fire Advances in Stem Cell Research

Finding the safest route to make stem cell therapy possible to treat or even cure certain human diseases is what the Belmonte lab and others at Salk are working toward.

Juan Carlos Izpisúa Belmonte



Japanese and U.S. scientists made major headlines two years ago when they successfully reprogrammed adult skins cells into stem cells. It was the first study showing that researchers could turn back the clock to develop human embryonic-like stem cells, while circumventing the ethical debate sparked by the traditional method to harvest them.

THE NEW CELLS, CALLED INDUCED PLURIPOTENT STEM (IPS) cells because of their ability to become any other cell type in the body, opened the floodgates to new research and led teams of scientists at the Salk Institute and elsewhere to develop methods to coax iPS cells into several types of tissues, the kind that medical researchers believe may one day be used to replace cells that have been damaged due to trauma or disease.

As magnificent as the iPS cell breakthrough was, the method to achieve it is woefully inefficient. Only one out of 10,000 cells could be reprogrammed in a process that takes four months to achieve. But a team of researchers at the Salk Institute and the Center of Regenerative Medicine in Barcelona, Spain, led by **Juan Carlos Izpisúa Belmonte** has taken the science of cell reprogramming one step further, drastically improving the technique.

In their paper, which *Nature Biotechnology* featured on the cover of its November 2008 issue, the team boosted the reprogramming efficiency by 100 fold. They managed to turn back the clock in one out of 100 cells in just 10 days. But rather than using skin cells, they chose to work with keratinocytes — cells that are found in the root section of human hair.

Plucking strands of hair from the human scalp is much less invasive than a skin biopsy, says Belmonte, who believes his team's study is yet another tool that can very likely be applied toward individualized medicine to treat disease.

"Having a very efficient and practical way to generate patient-specific stem cells, which unlike human embryonic stem cells wouldn't be rejected by the patient's immune system after transplantation, brings us a step closer to the clinical application of stem cell therapy," says Belmonte, professor in Salk's Gene Expression Laboratory and director of the Center of Regenerative Medicine in Barcelona.

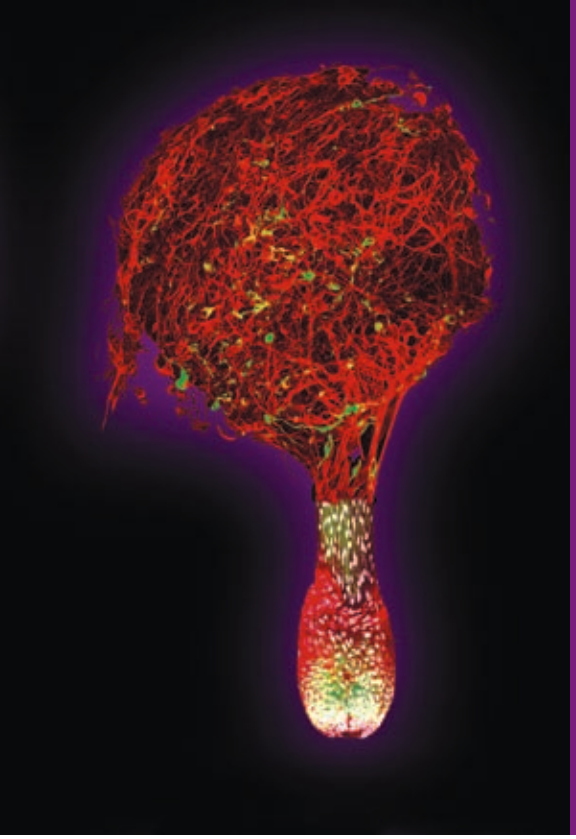
The editors at *Science* were equally optimistic about the Belmonte study, including it in the journal's annual December feature, which highlighted the rapid development of cell reprogramming as the Breakthrough of the Year for 2008.

"It's an important study and it gives an alternative method for potentially making progress of iPS cells," says Larry Goldstein, professor of Cellular and Molecular Medicine and director of the UCSD Stem Cell Program. "The fact that it's more efficient is certainly an improvement. At the end of the day, it's important to have as many variants as we can to find things that are safe and effective for patients."

Finding the safest route to make stem cell therapy possible to treat or even cure certain human diseases is what the Belmonte lab and others at Salk are working toward. Much has been learned from the keratinocytes reprogramming study, but the universal method used by researchers to develop iPS cells has one flaw: it uses a virus to shuttle the four reprogramming genes into the genome. In some cases, the virus has been known to activate the expression of other genes that cause cancer in lab models.

Some scientists are attempting to circumvent this bottleneck by working with compounds to chemically introduce the proteins that are needed to start up the reprogramming process. However, the Belmonte lab is taking a different approach. They are trying to create iPS cells from adult mouse cells using non-viral vectors, hoping they will be able to achieve the same results without disturbing the host cells' genome.

"I think these advances will definitely change the speed in which this technology can eventually be applied," says Belmonte. "If you have a safe reprogramming method that does not use a virus, it's



> "Having a very efficient and practical way to generate patient-specific stem cells, which unlike human embryonic stem cells wouldn't be rejected by the patient's immune system after transplantation, brings us a step closer to the clinical application of stem cell therapy."
>
> – Juan Carlos Izpisúa Belmonte

much more acceptable to take hair samples from a patient, reprogram the cells and then differentiate them into heart, pancreas or any cell type that's diseased, and implant them into that patient because the risk involved with using a virus is no longer an issue.

"We have to be cautious not to generate false expectations since there is still much to be studied, but what was science fiction up until a year ago is real science today," he says. "Developments in this field are moving along at such a rapid pace that I think now it would be fruitful to start a dialogue with clinicians."

The speed of progress is just as surprising to veteran scientists like Goldstein. Only 10 years go researchers in Wisconsin announced that they had cultured human embryonic stem (hES) cells.

"I'm shocked. I mean it can never be fast enough, but it's really quite remarkable how quickly some of these problems are being addressed," Goldstein says. "But I never underestimate the creativity of my colleagues."

There are serious hurdles that need to be overcome, one of which the Belmonte lab, in collaboration with other investigators at Salk, is already addressing to potentially make stem cell therapy a reality. Although scientists worldwide have learned to differentiate iPS cells, there's no standard protocol for developing a single cell type.

With current methods, researchers angling for neurons, for example, may also end up with pancreas cells that contaminate the colony. But progress is steadily being made in this area at Salk, too, using Belmonte's non-viral, episomal vector approach, he says.

Despite the rapid-fire breakthroughs in the cell-reprogramming field, medical science is still several years away from using the process to cure a disease, at least in humans. But Belmonte and his collaborator, Inder Verma, professor in Salk's Laboratory of Genetics, are hard at work to move one step closer to the ultimate goal—correcting genetic defects in patient-specific iPS cells and use those to replace the defective ones in the patient's body.

The Salk researchers are still experimenting with mice, but if successful, their study will represent a solid leap forward in stem cell research that Belmonte believes will trigger further collaborations and new scientific approaches to gain insights into some of today's incurable diseases.

Belmonte's team boosted the reprogramming efficiency by 100 fold. They managed to turn back the clock in one out of 100 cells in just 10 days. The study made the November 2008 cover of *Nature Biotechnology.*

One on One with... Terry Sejnowski

RECENTLY ELECTED TO THE INSTITUTE OF MEDICINE OF THE National Academies, **Terry Sejnowski** is credited with pioneering the field of computational neuroscience in the 1980s by drawing on his training in both physics and neurobiology. His laboratory, staffed by an eclectic team with backgrounds in mathematics, electrical engineering, physics, and even philosophy, uses computer models based on physiological experiments to make predictions that call for additional experiments to test the model. Along the way, his lab has contributed major breakthroughs in understanding how the brain works, developed powerful technology that is used in industry, and helped launched many successful scientific careers.

How did you become interested in the brain and eventually decide to apply your training in physics to Neuroscience?

After I finished my Ph.D. doing a computer-modeling thesis about neurons, I took a course at Woods Hole in Neurobiology where I learned a lot of really exciting techniques that taught me how neuroscientists collect and analyze data. I realized as a consequence of that course that what I really would like to do for my career was to integrate the two. There were other people who had been doing theoretical work before me, like John Hopfield, who was my mentor at Princeton. And there were many people doing physical experiments, but there were very few who were capable of being able to both think of a good theoretical modeling study and then design a good experiment to carry it out and do that in the same lab. So that is really what makes my lab almost unique.

You pioneered the field of Computational Neuroscience. Can you put in perspective how this approach has changed scientific research?

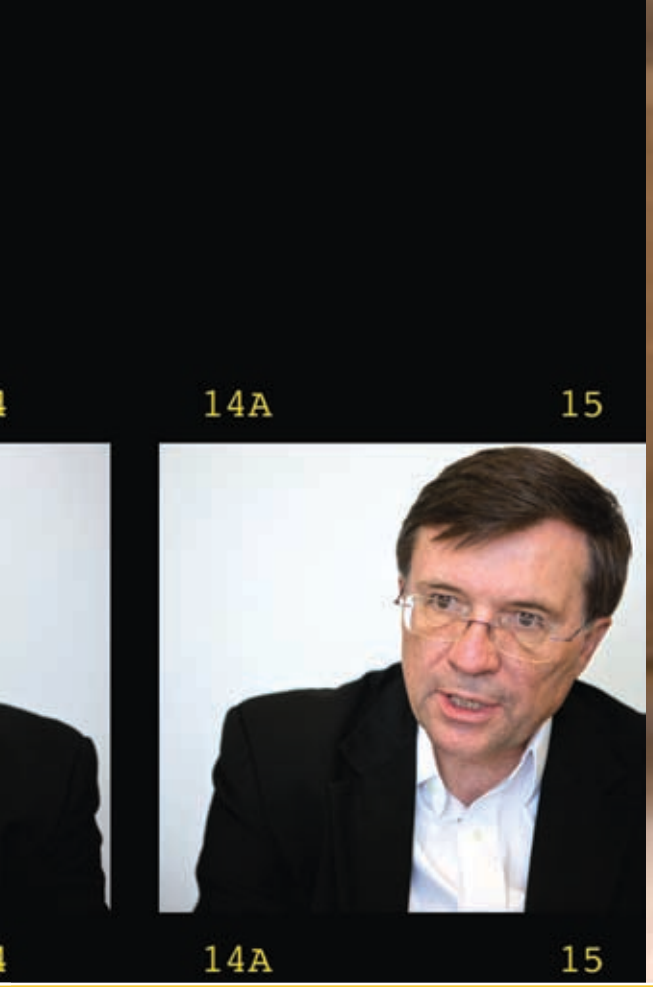
There's an enormous shift that's occurred in the last 10 years in neuroscience as new techniques have made it possible to collect larger and more complex data sets, and the work we've done in computational neuroscience has helped to analyze and interpret these data. The new optical recording techniques that we're now developing require even higher throughput computer systems that wouldn't have been possible 10 years ago because computers weren't fast enough. This new technology allows us to make progress much faster, and to test the theoretical modeling studies and make more powerful predictions.

One of the areas of interest in your lab is how the brain creates and stores memory. How much do we know at this point about that process in the brain?

I don't think we've gotten to the bottom of it yet. We know where to look and we have some tantalizing hints from the biochemical and the physiological studies that have been done, primarily in the hippocampus and the cerebral cortex. However, the link between these changes that occur at synapses and changes in behavior is very weak. There are hundreds of microscopic changes that occur in neurons, so how do you know which one of those is going to be relevant for explaining the changes in behavior?

One of the advantages now is a highly detailed synaptic modeling program we've developed called MCell, which is giving us a very powerful way to put together all the information that neuroscientists have found at

> "...something as obscure as honeybee learning could



the molecular and cellular levels. One of the recent modeling studies we've done is on priming – subconscious learning that affects your behavior. We want to know how the information that is constantly flowing into our brain is integrated into our current knowledge base, and how is that done in such a way that allows us to recall relevant details and make timely decisions. It's a complicated problem, but we are making progress by reconstructing the biophysical and biochemical changes that occur within neurons in the first seconds of a new memory.

There have been some fascinating technological breakthroughs that have come out of your lab. Can you share some recent examples?

SoftMax, a company that grew out of an independent component analysis (ICA) algorithm that we developed 10 years ago, worked on noise cancellation in cell phone headsets. It involved two microphones, using the two signals to cancel out the background noise that makes it difficult for the person who is trying to listen to you. It was so successful that Qualcomm bought the whole company for the technology and the engineering talent, which included one of my former postdocs. My lab went on to apply ICA to electroencephalogram (EEG) recordings from the scalp and functional Magnetic Resonance Imaging (fMRI), which is now used routinely in hundreds of labs around the world.

Now a new company, NeuroVigil, is analyzing EEG to score automatically the various stages of sleep. One of the bottlenecks in the sleep labs around the country is that it takes a human expert about four hours to analyze eight hours of sleep EEG. But with the technology we've developed we can now do that in about 10 seconds with higher accuracy. It's like a microscope for looking into sleep. Ultimately, we think it will have a major impact on the way sleep is understood, both scientifically and from a medical perspective, to help patients who have sleep disorders and to diagnose other diseases.

In your career, what has been the discovery that has fascinated you most about the brain?

About 10 years ago, two very talented postdocs in my lab made a spectacular breakthrough that started with a simple model for honeybee foraging. Bees are risk aversive and they're very good at learning. That initial paper came out in *Nature* and led to a breakthrough in understanding human reward learning. We went on to model the dopamine neurons in the mammalian brain and showed that the very same algorithm that we used for the bee also works for the human, which is the basis for a whole new field called Neuroeconomics. What was fascinating was how a relatively small insight into something as obscure as honeybee learning could lead to a new understanding of the brain and behavior. And it applies not just to reward learning, but also to addiction because every addictive drug works through the dopamine pathway that we identified as being important for predicting future reward. Now that we know how this works, it may lead to much better insight into what motivates us and the limits of free will.

lead to a new understanding of the brain and behavior."

continued on page 12

You and Francis Crick were friends. Please share some of your memories of him?

My wife and I were close to the Cricks and often did things socially. I remember when Francis was sick with cancer, we took him and Odile out to see the movie "Crouching Tiger, Hidden Dragon." It was a fun movie. I don't think it was Francis' cup of tea, but I'm sure he appreciated the opportunity to take some time off from worrying about his health.

He would also come to my lab's tea every day. He loved discussing science. It was great because we benefited from his insights and wisdom. I missed him when his health declined and he was only able to come to the Salk for an hour or two in the morning.

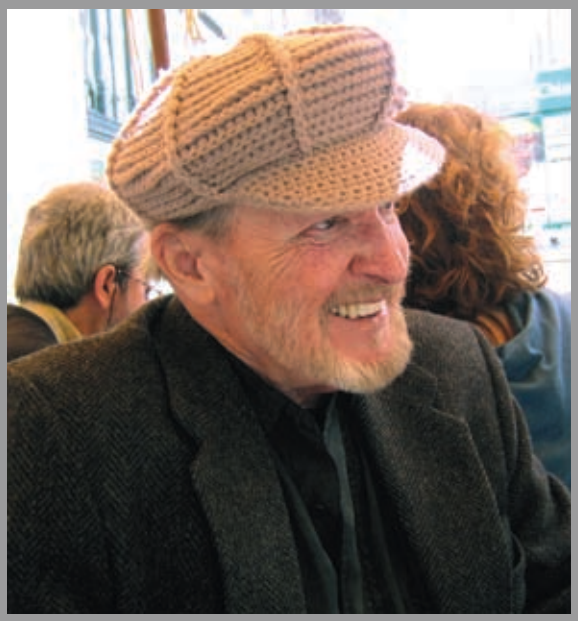
He was very generous. I think what was remarkable about him was that if you had something interesting to say it didn't matter who you were. What mattered was the science.

What's the best piece of advice he ever gave you?

He once told me that I had become too fond of my computer models, and that I had lost track of the fact that the purpose of a model is to make predictions and to set up a killer experiment that no one else would ever have thought of doing. I think he was right in that creating a model often does become an end in and of itself. He had a healthy attitude. He saw the value of many different approaches. One of the main reasons why I came to Salk was that he appreciated what I was doing long before a lot of others did.

You organize several workshops each year, including the annual Neural Information Processing Systems Conference. You've authored several books in your field and you're the founding editor of the journal *Neural Computation*. What drives you to stay so busy?

It's not so much what drives me – it is what comes naturally. What drives you to eat and sleep? It is part of my natural rhythm. I enjoy getting people together, so I organize workshops and meetings. I have a great lab and it's a great source of pleasure and pride that so many of my former students are doing well. I was a postdoc with Steve Kuffler at Harvard, who was famous for developing new preparations and encouraging students to carry on with them and build their own careers. If a single lab produces a single offspring, that's replacement. My lab probably has produced about 25 first-rate researchers who now have their own labs, which is way outside the normal curve. So my impact is probably going to be far greater through the students I've trained than by the papers I've published.



Edward S. Klima

Ursula Bellugi

Remembering Dr. Edward S. Klima

LANGUAGE IS EASY TO TAKE FOR GRANTED. BUT THE FACT IS, OUR VOCABULARY and the rules for its use, the syntax, are a reflection of the human mind, revealing the way we assimilate, process, and express ideas—the way we think.

Edward S. Klima, associate director of the Cognitive Neurosciences Laboratory at the Salk Institute and professor emeritus at UC San Diego until his death last September at age 77, dedicated his life to understanding language, from the way words and sentences are created to their neurobiology. Together with his wife, Salk Professor **Ursula Bellugi**, the two changed the linguistics landscape with their research on American Sign Language (ASL), for which they received the American Psychological Association's Distinguished Scientific Contribution Award in 1992.

Klima and Bellugi met in Cambridge, MA., where Klima had been invited by Noam Chomsky to teach graduate courses at the Massachusetts Institute of Technology.

"I remember someone invited me to go listen to the best syntactician there was," says Bellugi. "The class only had about 20 students enrolled in it, but more than 75 people came to the course to listen to his lectures." Soon after meeting, the two began collaborating on studies of development of language in children.

In 1968 they married and moved to La Jolla when Klima accepted a professorship at the new UC San Diego Linguistics Department. A year later Bellugi was invited by Jonas Salk to establish a small laboratory at the Salk Institute. The couple wondered how to integrate their research at Salk, where molecular biology is dominant, and decided to investigate the biological foundations of language by studying how deaf children of deaf parents learn a visual rather than an auditory language.

At the time "deaf communication was disparaged as either a loose collection of gestures or universal pantomime," recalls Bellugi, who is excited by the incredible path of their research, which today is widely recognized as a fundamental contribution to the neurobiology of language. "Essentially nothing was known about whether there was any structure to signs or sentences. We had to ask new questions and invent new ways of answering them."

Deaf children, even those born to deaf parents, were not permitted to use signs in school, instead urged to learn to speak and lip read, rather like forcing a left-handed child to write with the right hand.

What Klima and Bellugi's research revealed about ASL was groundbreaking. In their award-winning book, *The Signs of Language*, they revealed how ASL displayed the properties of a distinct, independent language with its own form of grammar based on a visual-spatial modality. They discovered that over time, sign languages lose their iconicity as structure emerges within signs and in sentences. For example, sentences clearly have their own syntax based on patterning in space so that there is a grammatical and ungrammatical way to sign sentences. Interestingly, they found that sign languages differ systematically from one another – American and British Sign Languages arose independent of one another.

ASL signs also display duality of patterning, which means that they are built from sign elements such as the position of fingers and hand relative to the body, elements that mean nothing on their own.

"There was skepticism and debate among members of the deaf community when this research was first published," recalls UCSD Professor of Communications Carol Padden, who worked as a graduate student with Bellugi and Klima in the 1970s. "But because they collaborated directly with many deaf signers and the Salk Institute is so highly regarded, this helped bring a lot of legitimacy to the findings."

Padden, the daughter of deaf parents who were professors at the world's only deaf college, Gallaudet University in Washington, D.C., invited her parents to meet Klima and Bellugi while she was working at Salk.

"My parents were surprised," she says. "Ursula and Ed weren't asking questions to learn about deaf people for the sake of rehabilitation or education, as was usually the case. They were firm about shifting the discussion of sign language to the science of cognition.

"They invited deaf people—children and adults, artists and poets and actors—into their lab and asked questions that even deaf people hadn't ever thought about before: 'What does the speed of signing mean?' 'How are our sentences structured?' 'What is the morphology of our words?' It wasn't about helping deaf people, it was about understanding the human capacity for language. Their research legitimized deaf culture and gave us a vocabulary to discuss it, transforming the way that even deaf people talk about themselves."

It also opened a new channel for research in cognitive psychology and neuroscience, explains Greg Hickok, a professor at UC Irvine who joined the Klima-Bellugi team in the 1990s as a post-doctoral researcher. "If their research on sign language had shown it to be just a collection of gestures, then we wouldn't be able to use it now to understand how language is organized in the brain," Hickok says.

Klima and Bellugi, together with Hickok and others, have shown that despite the difference in the perception of language (vision versus hearing) and production (movement of hands in space versus voice), the organization of spoken language and sign language in the brain are remarkably similar, leading to a new understanding of neural circuitry of language.

As a result, researchers like Padden are now able to work with communities of deaf and hearing people around the world who have developed new sign languages that are three or four generations old compared to the 200-year-old ASL. This allows them to observe what cannot be seen in any other way: the spontaneous generation and evolution of human language.

"Edward and Ursula were there at the very beginning of this research, at a time when almost nothing was known about the structure of sign language, other than impressionistic descriptions," says Padden. "Now, there is so much research underway. We couldn't do the work that we're doing without the tools that Ursula and Ed developed."

Upon hearing the news of his death, friends and colleagues sent letters of condolence, recalling his enthusiasm for art, dance, music, and experimenting with recipes in the kitchen, as well as the family-like dynamic that Klima and Bellugi fostered among members of their laboratories.

"He was probably the most open-minded person I've ever met in research," says Hickok. "Scientists often become very attached to their theories and have trouble looking outside of their own ideas to consider other possibilities. But Ed was always willing to entertain the ideas of others. And the farther an idea was from the standard theories, the more excited he would get about it, as long as it made sense."

"He was probably the most open-minded person I've ever met in research...Ed was always willing to entertain the ideas of others. And the farther an idea was from the standard theories, the more excited he would get about it, as long as it made sense."

–Greg Hickok

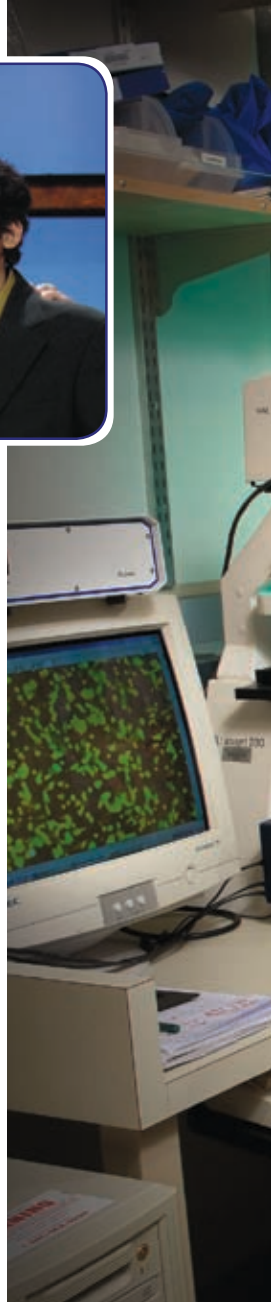
His friends and colleagues also remark on Klima's careful contemplation of not only research questions and study designs, but on nuances of word meanings and usage, and how they are interpreted in poetry, literature, and other writing.

"He made us really think about what we were saying on a much deeper level than people normally do," says Yvonne Searcy, a research assistant in Bellugi's lab who remembered once spending an hour with Klima discussing the use and meaning of the word "intelligence" in a paper she had written.

Klima was known for his precision with words and ideas and his quick wit. He spoke gently, discreetly, and was admired for his rapid play on words and his puns (humor is, after all, a heightened use of language), always uttered with modesty and, as his friend Adele Abrahmson recalled in a letter, "flashing that amazing twinkle in his eye as he [dropped] one of his trademark bon mots."

Dr. Klima's family has established a Web site in memory of Dr. Klima at www.edwardsklima.com, *where you can read more about his research and view letters and photos from family and friends.*

‘Jeopardy!’ and Spelling Bee Champ Discovers the Life of a Scientist at Salk



APPARENTLY IT TAKES MORE THAN WINNING A NATIONALLY televised spelling contest to be recognized with a personalized Wikipedia page. At least that’s what Anurag Kashyap discovered in October when he went to the Web site and launched a search for his name. His inquiry resulted in a cold response: “Person not notable.” (And not to be confused with an Indian film director of the same name!)

Of course this was a few weeks before the 17-year-old San Diego high school senior won the “Jeopardy! Teen Tournament.” Despite his second appearance on national television, Kashyap recently seemed most proud of the fact that his name and his accomplishments could now be found online for the world to see.

“Now when you go to Wikipedia, it says that I won on ‘Jeopardy!’ and the 2005 Scripps National Spelling Bee,” he says with a toothy smile. He is only the second person to garner both honors, according to Wiki.

Both wins resulted in handsome cash prizes, which Kashyap says will go toward funding his science studies when he goes to MIT next fall. Although he is interested in many subjects, Kashyap says he will pursue a career in research, despite his mom’s concerns.

“She wants me to go into medicine because she thinks research might be more risky,” Kashyap explains, “but I think it’s really about whatever makes you feel more fulfilled. So I probably will go into academia.”

With the basics under his belt, Kashyap spent time working in Salk’s Stem Cell Core facility culturing human embryonic stem cells and learning how to differentiate them into bone marrow.

“It was inspiring, actually, to see someone so young and engaged in all the things we were doing and who is capable of understanding it all,” Woods says. Parker agreed: “By the time he came to Bjarne and I, we could actually focus on the science. We never had to tell him anything more than once. We’d tell him a scientific fact and he’d remember it two weeks later.”

Verma agreed to let the young scientist work in his lab over the summer at the request of Kashyap’s father, who introduced his son to Verma at a local event.

“I met Anurag soon after he won the Spelling Bee and remember being very impressed with his maturity and genuine drive to learn,” Verma says.

Although he considers his high school relatively well equipped for science and regularly reads books on microbiology (though he’ll read anything with literary merit), Kashyap says none of that could have prepared him for working in a world-renowned lab.

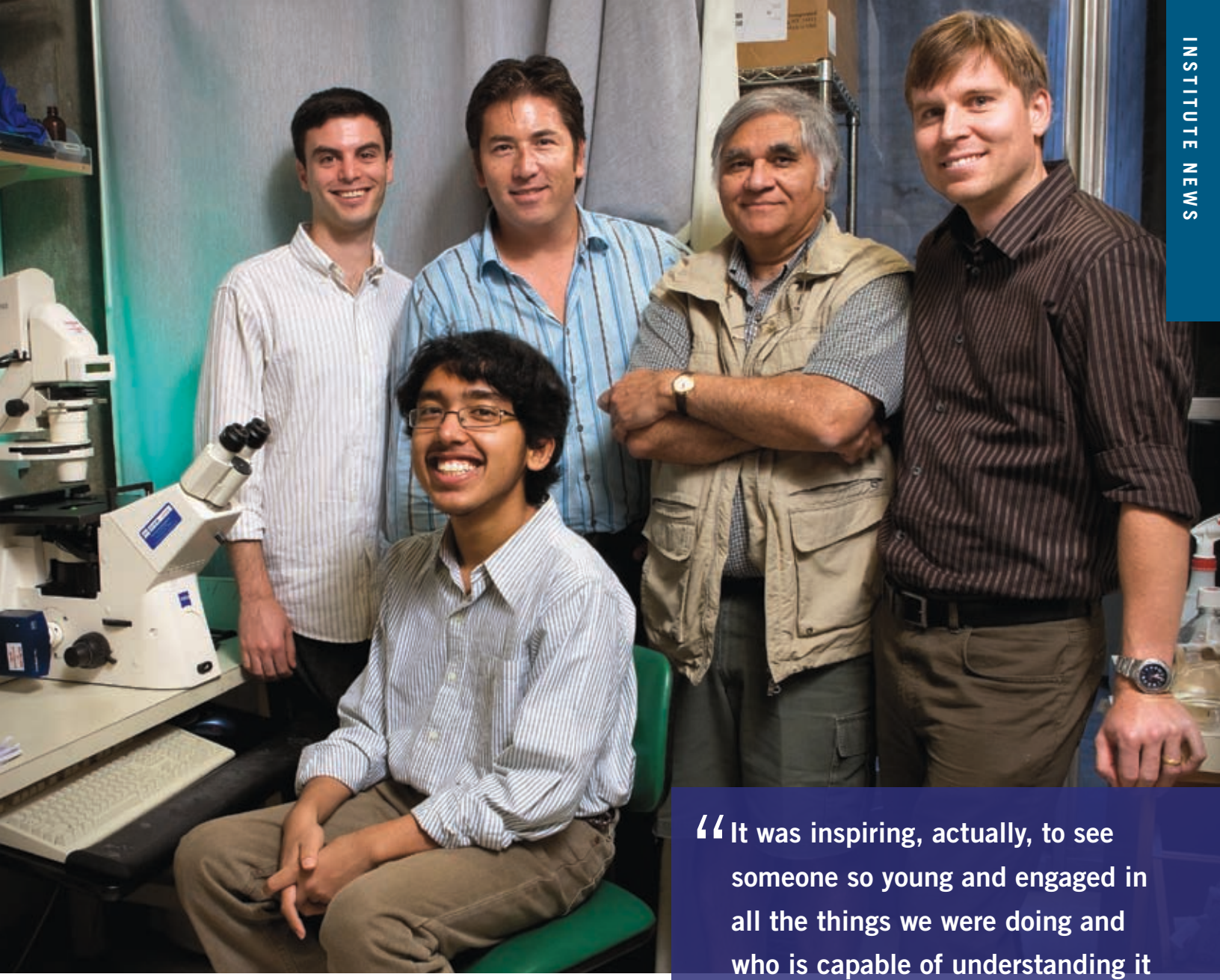
> “Once you’ve been in this lab, there’s just no comparison, so this experience is a lot more meaningful. It has taught me a lot about what real laboratory science is like.” – Anurag Kashyap

Kashyap had a taste of the research life when he spent seven weeks in **Inder Verma**’s laboratory last summer. Under the tutelage of Lab Manager Mark Schmitt, postdoctoral researcher Niels-Bjarne Woods, and graduate student Aaron Parker, Kashyap learned several basic lab procedures well enough to eventually work independently and conduct a final experiment.

“It was pretty intimidating when I first got here because the first thing Mark did was slap down a bunch of reading materials so I could understand what they were doing,” Kashyap says. “Then Mark took me through some of the basic procedures like setting up a [cell] colony and maintaining cultures. These procedures would enable me to do more complex work in a lab.”

“Once you’ve been in this lab, there’s just no comparison, so this experience is a lot more meaningful. It has taught me a lot about what real laboratory science is like,” he says.

About 10 high school students are given a similar opportunity each year through Salk’s Summer Enrichment Program. Supported with philanthropic dollars and founded more than 30 years ago by Jonas Salk, the program exposes students to life in the lab through hands-on experiments under the mentorship of Salk scientists.



Anurag Kashyap (seated) got a taste of the scientist's life last summer when he spent six weeks working in the lab with his mentors Aaron Parker (back row, from left), Mark Schmitt, Inder Verma and Niels-Bjarne Woods. Inset: Kashyap with "Jeopardy! host Alex Trebek.

"It was inspiring, actually, to see someone so young and engaged in all the things we were doing and who is capable of understanding it all...We'd tell him a scientific fact and he'd remember it two weeks later." – **Aaron Parker**

Throughout the eight-week program designed to encourage careers in science, students are involved with a full-time research project as well as enrichment activities. They learn how to formulate and test hypotheses, prepare experiments and draw conclusions. At the end of the program, students present their research projects to their mentors, lab members and families.

Just like any other researcher, Kashyap also attended weekly lab meetings where scientists present results from their experiments and participate in scientific discussions – a key component to advancing scientific research.

"It was impressive because we would have discussions about things that I didn't learn about until my first year of graduate school, yet Anurag would be participating and adding to them," Parker says.

Kashyap didn't waste time either. When he wasn't in meetings and had spare minutes between experiments, Kashyap would find a quiet corner in the lab and study for Quiz Bowl, yet another national competition he's set to participate in later this year.

For now, he's back at school where he now realizes how his 12th grade science class could be so much more meaningful to his classmates if the program were better funded.

"If people got the chance to do the labs the way they are meant to be done, and actually experience science as opposed to having to use results the teacher has taken off the Internet because they can't afford to actually do the experiment for themselves, a lot more people would definitely be interested in science."

In an Unstable Market, Gift Annuities Make Financial Sense for Some

LIKE MANY INVESTORS DURING THESE TOUGH ECONOMIC TIMES, HELEN HAUER is weighing her options for getting the best return on her money. She was in a similar position 10 years ago when she decided to make a contribution to the Salk Institute through a charitable gift annuity. She's never regretted it.

"I was going to have to pay a sizeable chunk of capital gains tax if I didn't roll over an investment I had at the time," she explains. "I had heard about annuities so I figured I'd put the entire amount in one with Salk and have a monthly income for the rest of my life. I avoided having to pay capital gains, plus, I was able to claim a deduction over six years on my tax returns."

Charitable gift annuities allow participants to donate a gift of cash or securities in return for a guaranteed fixed income for life, typically at a much better rate than a Certificate of Deposit (CD), for example. The Institute eventually receives the remaining principal for support of research.

"It's worked out great for me because I like to know exactly what my income will be each month," Hauer says, "and it also provided a better return that allowed me to increase my income."

Besides the financial benefit, Hauer made her contribution to Salk for another more personal reason. Her late husband, Arthur, suffered a sever stroke in 1994, and she hopes that her gift will help scientists advance their research of the brain, particularly how stem cells can be applied toward treating or curing neurodegenerative diseases.

"It was the first time I had known anyone to have a stroke," says Hauer of her husband. "But it affected his brain in such a way that he eventually no longer knew me or anything else. Doctors told me at the time that when certain cells die, that's it, you can never recover them. But they were wrong as I have learned from going to lectures at Salk. So I'm very curious about the brain."

An avid golfer who lives in La Jolla, Hauer likes to point out the certificate she received from the Lomas Santa Fe Executive Golf Course for shooting a hole-in-one. Although she hasn't golfed recently due to a minor shoulder injury, she's looking forward to get back out on the course while she plans her next financial move.

She's considering other charitable gift annuities, but says this time she may choose to structure them to benefit her children as well.

Helen Hauer

> "I had heard about annuities so I figured I'd put the entire amount in one with Salk and have a monthly income for the rest of my life."
>
> – Helen Hauer

GIFT ANNUITIES AT SALK

When you make a gift of $20,000 or more, the Salk Institute can offer you (and/or your loved one) a fixed income for life. A charitable gift annuity will also generate a tax deduction and can reduce capital gains. Your age, financial needs and current interest rates determine the annuity rate. For example, a 75 year old who sets up a gift annuity with $25,000 would receive a payout rate of 6.3% or $132 per month for life.

RATES AT A GLANCE

Age	Annuity
60	5.0%
70	5.7%
80	7.1%
90	9.5%

* Annuity rates are subject to change. However, once you make your gift, the rate remains fixed.

For more information on Salk's Charitable Gift Annuities program, please contact Cheryl H. Dean, Esq., Senior Director, Planned Giving at (858) 453-4100 x1228 or cdean@salk.edu

Salk Launches Center for Aging Research with a $5 Million Donation from Glenn Foundation

Andrew Dillin (right) with Glenn Foundation President Mark R. Collins, who announced a $5 million gift to Salk during the Institute's annual Symposium on Biological Complexity in January.

THE SALK INSTITUTE RECEIVED A $5 MILLION GIFT FROM THE Glenn Foundation for Medical Research, becoming the third institution (with Harvard University and MIT) to receive major Glenn funding for studying the molecular basis of aging.

The Glenn Center for Aging Research will draw from nine of Salk's leading laboratories specializing in genetic analysis, stem cell biology and metabolism research to address the overarching goal of defining a healthy lifespan, or healthspan, and answer one of the most elusive questions in biology: Is there a defined biological process of aging that is universal to all organisms?

"The exponential growth of aging research in the last decade has clearly shown us that aging is a multi-faceted process in which several biological events interact to influence aging of an entire organism," said **Andrew Dillin**, Glenn Center director and associate professor of the Molecular and Cell Biology Laboratory. "Salk's well-established culture of collaboration puts us in an exceptional position to move aging research forward and lay the foundation that may stave off a multitude of age-related diseases."

Glenn Foundation President Mark R. Collins announced the grant during the opening reception for the annual Symposium on Biological Complexity at Salk on Jan. 8. Collins said he was "pleased and honored" to be supporting the work of Dillin and others at Salk.

"Why research on aging?" said Collins. "The biology of aging underlies all the major human diseases. To understand the fundamental aging process and to intervene is to delay the onset of disease, to extend the healthful years of life and reduce costs to society."

Dillin said the Salk's Genetic Analysis Group capitalizes on its expertise in a variety of cell types to explore new questions about key genetic pathways involved in cell maintenance and aging, and fully investigates how newly defined genes alter the aging process.

While scientists have learned that stem cells' capacity to self-renew and differentiate into functioning cells dramatically decrease during the aging process, they still do not know how or why. The Glenn Center's Stem Cell Group, led by **Fred H. Gage**, professor in the Laboratory of Genetics, studies the specific molecular components associated with aging in stem cells. These studies can help elucidate the procedure stem cells establish to stay healthy - which could explain why and how humans age.

Likewise, the Metabolism Group, led by **Ron Evans**, professor in the Gene Expression Laboratory, seeks to understand the molecular underpinnings associated with decreased metabolism and the aging process. Specifically, the group looks at how aging affects metabolism across key organ systems and attempts to explain how restrictive diets can alter the expression of different genetic programs.

In support of Salk's commitment to collaboration and training of young scientists, the Glenn Center also includes a Fellows program for graduate and postdoctoral students whose research is focused on the mechanisms of aging, as well as a Scholars program designed to provide resources for scientists to visit Salk where they can work with senior faculty members for up to six months.

Mary Jane Salk (left), who underwrote A Taste of Discovery in New York, with artist Francoise Gilot-Salk at the Nov. 13 event.

A Taste of Discovery: Demonstrating the Impact of Philanthropy

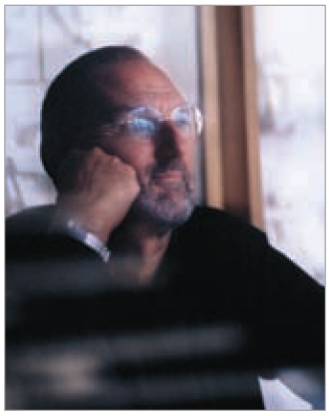
THE SALK INSTITUTE HOSTED TWO successful A Taste of Discovery events in November. Members of the President's Club learned how their philanthropic investments are having an impact on innovative and ambitious research.

Fred H. "Rusty" Gage's presentation on Nov. 5 in San Diego focused on his lab's studies of neural stem cells, and how his team has learned to induce such stem cells to become mature, functioning nerve cells in the adult brain and spinal cord. Better basic understanding of these and other methods of regeneration is vital to replacing tissues that have been lost or damaged due to trauma or neurodegenerative diseases.

Marc Montminy and **Reuben Shaw** each presented on Nov. 13 in New York, discussing their groundbreaking research with strong applications toward obesity, diabetes and cancer. In a collaborative study, for example, the two scientists found that Metformin, a drug known to lower blood glucose levels, specifically targets a genetic switch that Montminy previously discovered remains permanently "on" in many Type II diabetes patients. By identifying Metformin's molecular target, they have opened the door for new, more effective drugs to be developed.

"Major philanthropic support is absolutely vital to accelerating the pace of scientific discovery and we are grateful to our donors for their generosity," says Salk Executive Vice President **Marsha A. Chandler**. "Gifts to the Salk Institute help us retain and attract world-renowned scientists such as Marc, Reuben, and Rusty, and assure them the funding needed to carry out innovative—and often unconventional—research projects that have the potential to improve human health."




Left to right: Frank Gehry, Tod Williams with Billie Tsien, David Adjaye, Thom Mayne and Enrique Norten.

Lecture Series Gathers Acclaimed Architects

RENOWNED ARCHITECT FRANK GEHRY doesn't mince words when it comes to setting standards for buildings around the world.

"Public buildings deserve to be iconic," he told a packed audience at the Salk Institute on Feb. 8, opening an architectural speaker series on the legacy of Louis Kahn.

Gehry who, like Kahn, is internationally known for some highly innovative public spaces, said that public buildings like the Sydney opera house, Gehry's own Guggenheim Museum in Bilbao, Spain, and Millennium Park in Chicago are examples of high-impact projects that "upgrade" their surrounding cities.

Generously sponsored by Salk Board of Trustee member Linda Chester and Dr. Kenneth Rind, *Master Architects Lecture Series: In Celebration of Louis Kahn and the Salk Institute,* is jointly organized by Salk and the Museum of Contemporary Art San Diego (MCASD) and features presentations from six of the world's most notable architects.

The series continues this spring with presentations by Tod Williams and Billie Tsien (Feb. 27) and David Adjaye (March 11) at Salk; Thom Mayne (May 8) and Enrique Norten (April 3) at MCASD.

Single tickets are $25 for President's Club members, seniors and students; and $30 for the general public.

To purchase tickets, contact Diana Mason at dmason@mcasd.org or 858-454-3541.To learn how to become a President's Club member of the Salk Institute, contact Judy Hodges, director, Annual Fund, at hodges@salk.edu or call 858-453-4100 x1882.

In Tough Economic Times, Salk Keeps Eye on Its Science and the Bottom Line

Marsha A. Chandler

IN THIS TIME OF ECONOMIC INSTABILITY MOST ORGANIZATIONS ARE experiencing financial strain. The Salk Institute is no exception.

Our major revenue streams are government research funding, private philanthropy from individuals and foundations, and our endowment. We have a solid track record for attracting research funding, and with the reputations and discoveries of our internationally renowned faculty members, we anticipate a continued base of research support.

As you know, the federal government is expanding its investment in basic research as part of the economic stimulus package. We expect to benefit from this temporary increase in the budgets of federal research agencies like the NIH and NSF.

However, we are concerned about our revenues from both philanthropy and our endowment. Many individuals and foundations, faced with their own dwindling resources, may be less able to continue their current levels of philanthropy. Regrettably, our own endowment has already declined by close to 30%.

And so, like many organizations, we are aggressively looking for ways to cut costs and manage our remaining resources more efficiently. Mindful of our uncertain and potentially prolonged economic environment, we are engaging our entire community in a campaign to save energy and identify areas for meaningful cost cutting. We are examining every way in which we work, seeking everyone's best ideas and exploring a range of options.

But being exceptionally cost-conscious can only take us so far. Our private philanthropic support is critically important to help the Salk recruit and retain some of the world's brightest scientists and maintain our research vitality.

> "Despite the economic turmoil our nation is experiencing and the stress it places on us all, we are committed to strengthening the Salk's ability to produce major advances in basic life science."

One recent example of strategic philanthropic support is a $5 million gift from the Glenn Foundation for Medical Research in January – making the Salk the third Glenn-funded institution (joining Harvard and MIT) to study the molecular basis of aging. The new Glenn center draws from nine of Salk's leading laboratories specializing in genetic analysis, stem cell biology and metabolism research to address two overarching goals: defining a healthy lifespan; and determining if there is an underlying biological process of aging that is universal to all organisms.

Despite the economic turmoil our nation is experiencing and the stress it places on us all, we are committed to strengthening the Salk's ability to produce major advances in basic life science. By the time you receive this edition of *Inside Salk* our new president, **William R. Brody**, will be on board. You will learn more about our distinguished scientist-leader and hear from him in our next issue.

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There are many ways to support the Salk. For detailed information on opportunities, please email giving@salk.edu or call 858.550.0472

Salk **Calendar**

MARCH 2009

11 **Master Architects Lecture Series (David Adjaye)**

APRIL 2009

3 **Master Architects Lecture Series (Enrique Norten)**

MAY 2009

8 **Master Architects Lecture Series (Thom Mayne)**

13-15 **37th Annual Tax Seminar**

JUNE 2009

19-23 **Cell Cycle Meeting**

AUGUST 2009

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

22 **Symphony at Salk**

No Sorrow in Pathos No. 38 (2002) is among the pieces on display as part of Salk's latest exhibit, *Among the Stones, Works by Sunna Bohlen.*