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InsideSalk

THE SALK INSTITUTE FOR BIOLOGICAL STUDIES

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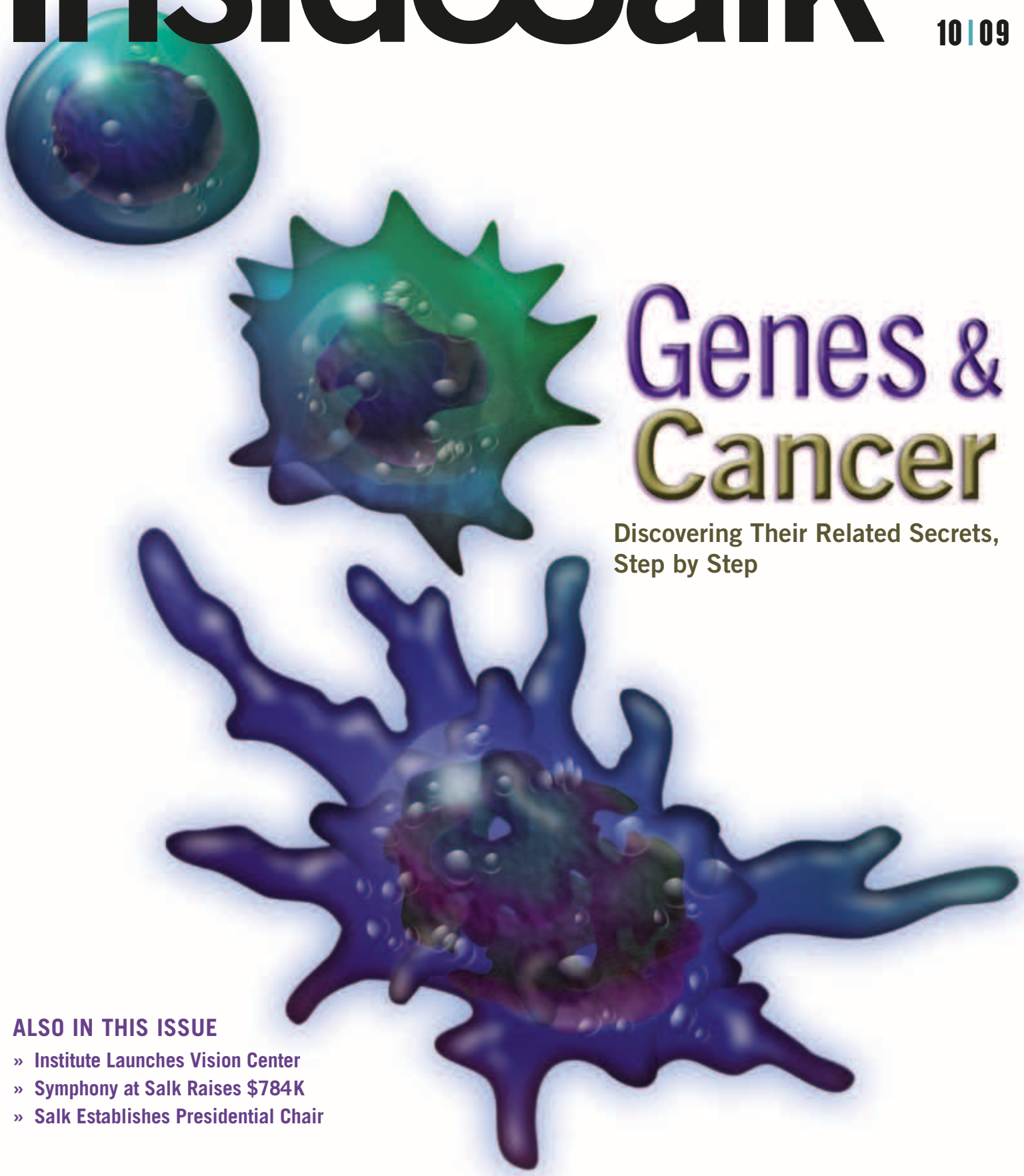

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Discovering Their Related Secrets, Step by Step

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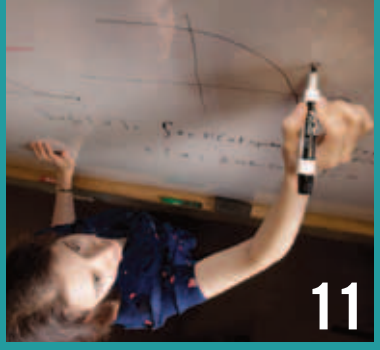

One on One with Tatyana Sharpee

International Council meets in Spain.

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ON THE COVER

Illustration by Jamie Simon demonstrates a healthy cell morphing into a cancer cell.

In Search of Excellence

Dear Friends,

SCIENTIFIC DISCOVERY REQUIRES UNCOMMON MINDS – PEOPLE who understand rational scientific thinking but aren't afraid to take risks and bet on ideas often scorned by others as either unworthy or unknowable. History demonstrates time and again that these rare creative geniuses defy logic to uncover major discoveries that lead to new understanding of how organisms function in health and disease.

To continue the legacy of excellence that has defined the Salk Institute, we are now searching for the next generation of scientific pioneers. I am particularly delighted to give you an early alert regarding our latest faculty recruitment successes.

You will learn more about these exceptional scientists in the months ahead. But as a brief preview, let me tell you about the three extremely promising researchers we have just attracted to the Salk:

Sreekanth Chalasani, assistant professor in the Molecular Neurobiology Lab. Chalasani's research focuses on how the C. elegans worm's nervous system responds to changes in the environment, such as a sudden lack of food. He hopes to learn more about how complex neural circuits process information and guide behavior.

Bjorn Lillemeier, assistant professor in the Immunobiology Microbial Pathogenesis Lab. Lillemeier uses biophotonics technology – high resolution fluorescence microscopy – to study the organization of plasma membranes and their contribution to membrane-associated signal transduction in T-cells. T-cells, the most common type of lymphocytes, attack virus infected cells, foreign cells, and cancer cells, but also play an integral part in the regulation of the immune system's activity. Adding a new perspective on how T-cell responses are controlled during development and disease could identify new targets for the manipulation of T-cell function.

Ye Zheng, assistant professor in the Immunobiology Microbial Pathogenesis Lab. Zheng studies how regulatory T-cells maintain immune system tolerance to prevent autoimmune diseases. He hopes that a better understanding of how these regulatory T-cells are generated and maintained will lead to new therapeutic approaches in a wide range of autoimmune diseases and tumor immunity.

The competition for top flight scientists is definitely global. That's why we are so pleased to welcome each of these gifted junior faculty members over the next few months. Their research will both strengthen and diversify our efforts in Immunology, Neurobiology and Biophotonics – all key directions for us.

The opportunity to recruit new faculty is especially gratifying, given the current economic downturn. It is a tribute to the major gifts we have received in support of scientific discovery, in addition to the creative and collaborative environment for which the Salk Institute is renowned.

The past few months have brought other positive news, including the NIH designation of a National Eye Institute here at the Salk – the only one in the San Diego area, directed by Professor **Tom Albright**. Ours is one of just seven such U.S. centers focused exclusively on basic vision research.

William R. Brody

> **"To continue the legacy of excellence that has defined the Salk Institute, we are now searching for the next generation of scientific pioneers."**

And the California Institute for Regenerative Medicine awarded Salk researchers **Juan Carlos Izpisúa Belmonte** and **Inder Verma** a $6.6 million grant to move ahead on exciting research to develop stem cell-based treatments for some rare, incurable genetic diseases.

We could accomplish none of the above without your generous philanthropic assistance, and I thank you for your steadfast support of the Salk Institute and our mission to advance basic understanding of biology in health and disease.

William R. Brody

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

Irwin M. Jacobs Presidential Chair

NIH Designates Salk One of Seven National Basic Research Centers Focused on Vision

A $3.8 MILLION GRANT FROM THE NATIONAL EYE Institute (NEI) of the National Institutes of Health places the Salk Institute among one of seven NEI-designated centers focused exclusively on the basic research of vision, and is the first basic science facility created by the NEI in nearly a decade.

The only one of its kind in the San Diego region, the new Salk Institute Center for the Neurobiology of Vision is a consortium of 15 investigators led by **Thomas Albright** conducting research on the visual system. The five-year grant funds core facilities that support each of the scientists' research projects.

The new vision center will take a broad approach to understanding the development and plasticity of the visual system, the mechanisms of the neural processing of visual stimuli, and the link between visual perception and behavior.

Understanding the mechanisms that process visual inputs in the retina and the brain and how that affects behavior provides a model system for better understanding the central nervous system. Such basic studies can also one day contribute to the development of prosthetics that restores vision to the blind.

Thomas Albright

President Bill Brody Appointed to CIRM Board

LT. GOV. JOHN GARAMENDI HAS NAMED Salk President **William R. Brody** to serve on the California Institute for Regenerative Medicine's oversight board. Brody replaces Salk Executive Vice President **Marsha A. Chandler**, who served for the last two years.

"Dr. Brody is an accomplished scientist, widely recognized among his peers as one of the nation's forefront thinkers in biomedical engineering and healthcare policy," said Garamendi, who make five appointments to the committee.

Brody, renowned for his achievements in biomedical engineering, spent 12 years as president of Johns Hopkins University before joining Salk.

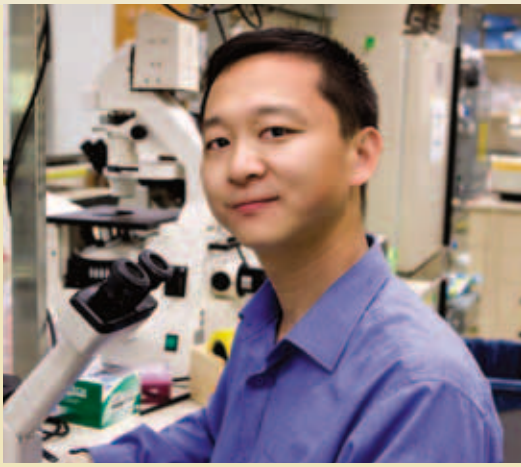
CIRM was created as part of Proposition 71, the California Stem Cell Research and Cures Initiative, which was approved by voters in 2004. Since then, the 29-member oversight committee has approved 295 grants worth $761 million, making CIRM the largest source of stem cell research funding in the world.

Postdocs Honored with Glenn Center Fellowships

SEVEN SALK POSTDOCS HAVE RECEIVED a total of $840,000 in research grants through the Institute's Glenn Center to pursue a research topic central to aging that involves at least two laboratories. They will each receive $60,000 for two years to cover their salaries, benefits and equipment.

The Glenn Center for Aging Research was established in January with a $5 million gift from the Glenn Foundation for Medical Research. Led by **Andy Dillin**, the Glenn Center draws 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 new Glenn Center Fellows are: **Laure Crabbe**, **Toby Franks**, **Star Lee**, **Yair Pilpel**, **Lei Wang**, **Jamie Whyte**, **Katja Lamia**.



Liming Pei

In related news, researcher **Liming Pei**, who works in **Ron Evans**' lab, received a fellowship from the Francis Family Foundation. As a 2009 Parker B. Francis Fellow, Liming will receive $156,000 over three years in support of his research, which focuses on embryonic development of the lung.

Originally from China, Pei graduated from UCLA with a Ph.D. in Molecular and Cellular Pathology in 2006 and joined the Evans lab that same year.

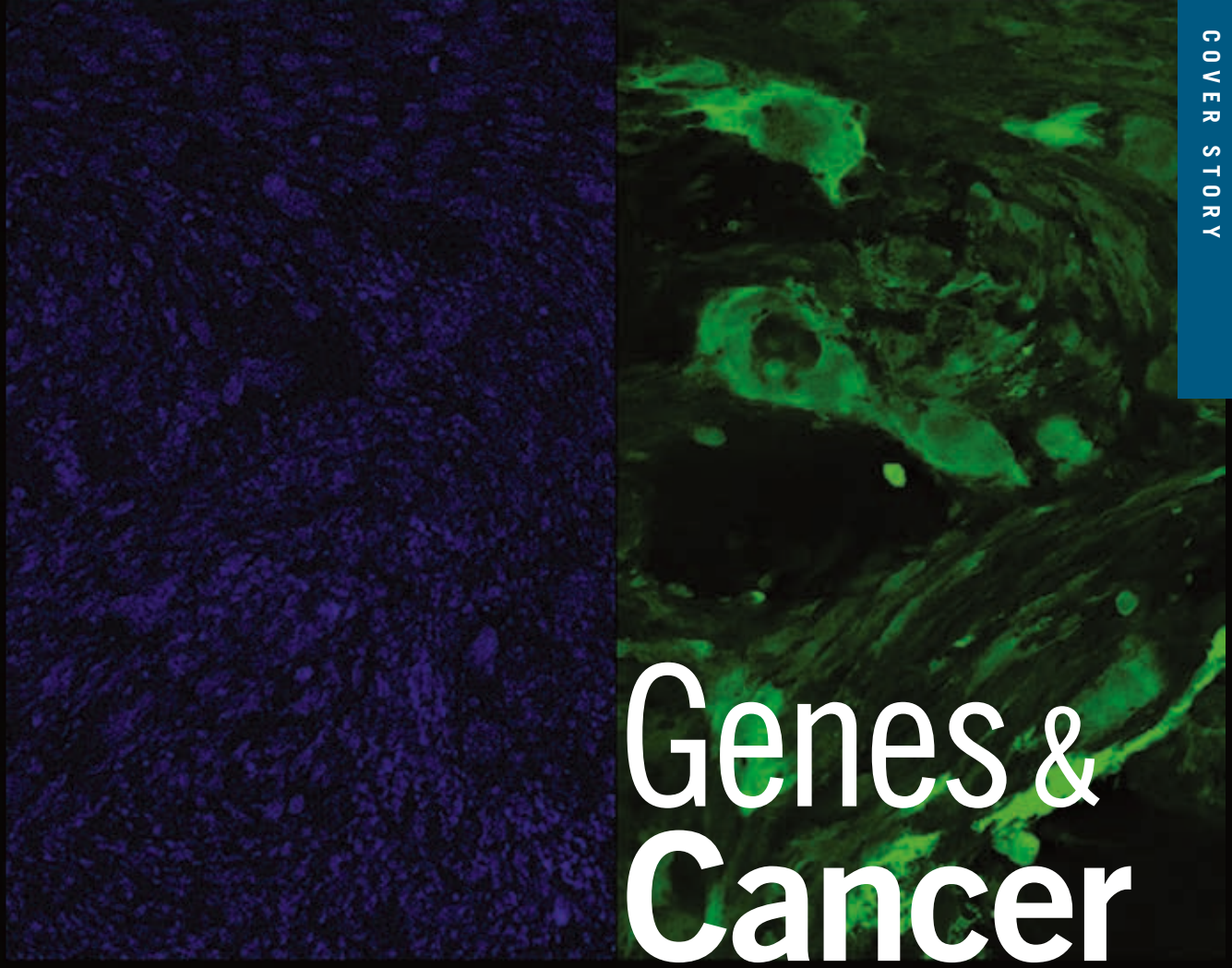
Traffic to Institute's Website Increases Via Twitter and Facebook Pages

THE COMMUNICATIONS DEPARTMENT HAS dived into the social media sphere to increase the number of people it reaches on the Web – leading to a 20 percent increase in traffic originating from referring sites such as Facebook and Twitter.

Since launching the social media pages in the spring, the Salk Institute has gained a combined fan base of more than 645 people and organizations (and growing) that have voluntarily signed up to follow news updates and "tweets."

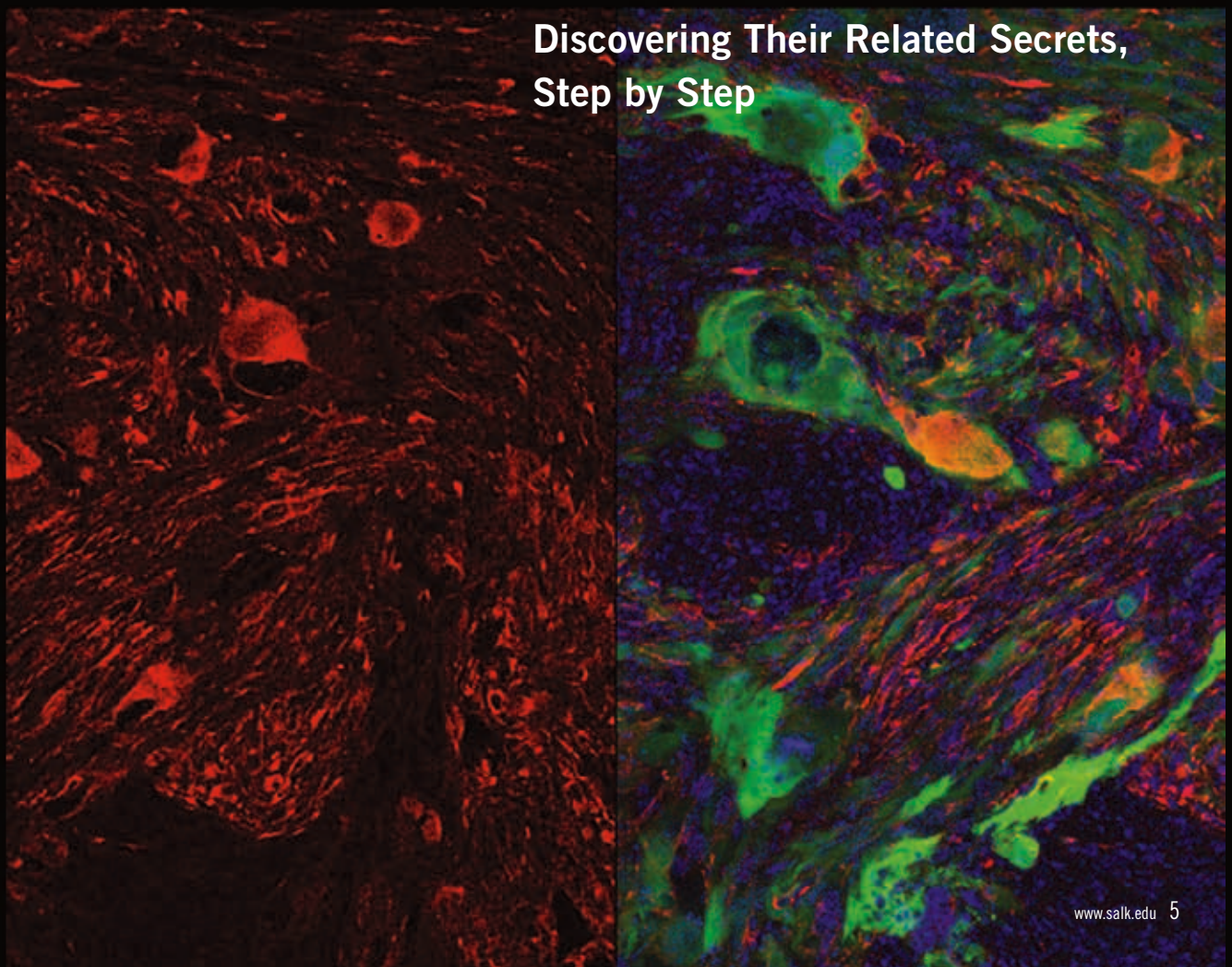
"By adopting social media as another component of our overall communications program, we have been able to reach a whole new audience from around the world and provide them regular news feeds from the Salk," says Communications Director Mauricio Minotta. "This introduces the Institute to potential new supporters and organizations that may be interested in licensing the Salk's technology."

On average, the Institute's website receives about 200,000 unique page views per month. Press releases on the Salk's scientific discoveries and alerts on its symposiums are among the items communicated through the social media platforms. To view the pages, visit www.twitter.com/salkinstitute and www.facebook.com/salkinstitute.



Genes & Cancer

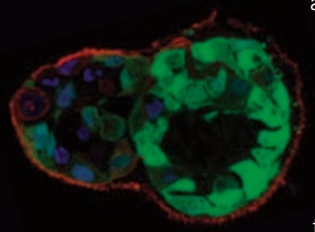
Discovering Their Related Secrets, Step by Step



GEOFF WAHL WILL NEVER FORGET THE DAY IN 1989 when he got a crazy idea for a new experiment. He had already been at home for some time when it hit him just before 9 p.m. He rushed back to his lab at Salk that night hoping somebody would be there. He was in luck. He found his postdoc, **Yuxin Yin**.

"This is what's great about science. I told him, 'I've got this crazy idea, but it's a good crazy idea because it suggests an experiment,' " Wahl says.

For more than a decade, Wahl's lab had been working to understand the mechanisms behind genetic instability and its link to cancer, and by this point they suspected the p53 gene, which is now known to be mutated in half of all human cancers, played a key role.



Wahl's crazy idea came at a time when his lab was studying an anti-proliferating compound. When administered to cancer cells, most would die off, with the exception of a few resistant ones that continued to divide. But what if the drug was applied to noncancerous cells with normal p53 genes?

As Wahl predicted, the cells stopped dividing completely, which led him to test one final idea: replace the mutant p53 gene of a cancerous cell with one from a normal cell. To his team's relief, the cancer cells stopped dividing.

Published in 1992, the series of experiments was among the first to demonstrate p53's role in maintaining genomic stability – leading many in the field to regard p53 as the Guardian of the Genome.

It is in fact at the genetic level where cancer begins. To be precise, it is the mutation of specific types of genes that leads to the development of the disease, which the National Cancer Institute (NCI) estimates will claim more than 562,000 lives this year (1,540 per day) in the United States. It also estimates that nearly 1.5 million more will be diagnosed with cancer in 2009.

Mutations in our genes take place every day of our lives. The simplest examples are DNA damage to skin cells caused by the sun's ultraviolet rays, or in the lining of our gut from toxins in food that we ingest, or in the lung as a consequence of smoking cigarettes. Despite the common frequency of these biological events, many of us may never develop cancer.

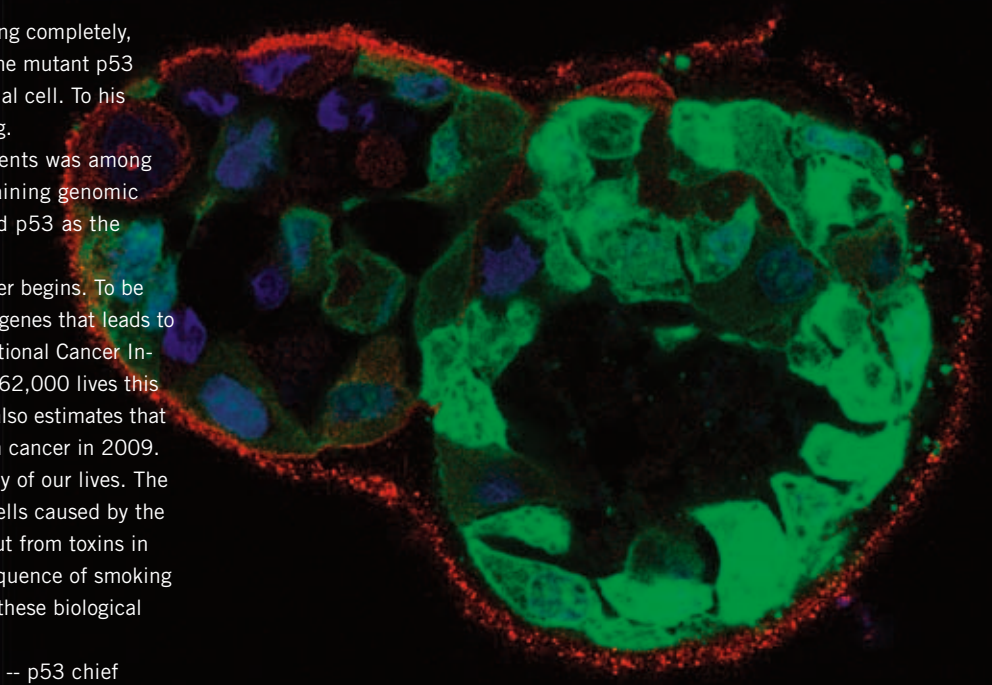
Why? Cells are equipped with mechanisms -- p53 chief among them – that detect and either repair DNA damage or signal the cell to self-destruct if the damage is too great.

"These genes are part of the normal growth process for human beings. This is how we have evolved," says **Reuben Shaw**, Hearst Endowment assistant professor in the Molecular and Cell Biology Laboratory, who, like Wahl, is one of 30 faculty members in the Salk Institute's NCI-designated Cancer Center. "Every species has evolved a mechanism to get rid of the cells that are chronically exposed to something that could be bad for them."

But the machinery isn't fool proof. For reasons not yet completely known, cells with DNA damage sometimes go unrepaired and continue to divide as mutant copies of their original self.

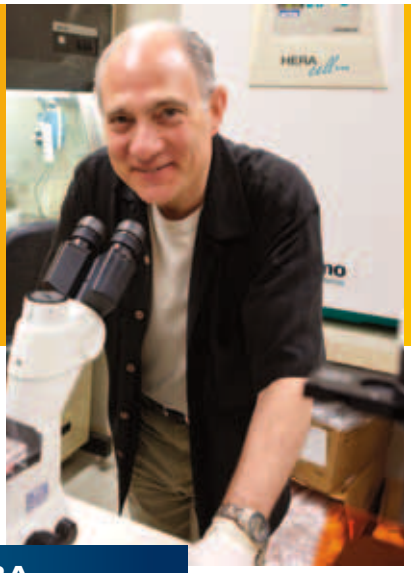
These mutant cells are prime candidates for cancer development in cases where the affected genes are normally designed to regulate cell growth (oncogenes) or cell death (tumor suppressor genes, such as p53). In the unfortunate event a second or third mutation occurs to multiple genes, cancer will always develop. The process is expedited if an oncogene is mutated in combination with damage to p53 in the same cell, Shaw says.

"P53's main function is to serve as a sensor for cells to make sure it is safe for them to reproduce their genetic dowry, or to prevent them from attempting to do so when conditions are suboptimal," says Wahl. "If p53 function is lost because of damage to its gene, then the cell has no ability to sense impending dangers, which enables the cell to divide and leads to production and perpetuation of mutations. This creates opportunities for additional mutation to form, and that's when things really start going haywire. The problem just compounds itself."



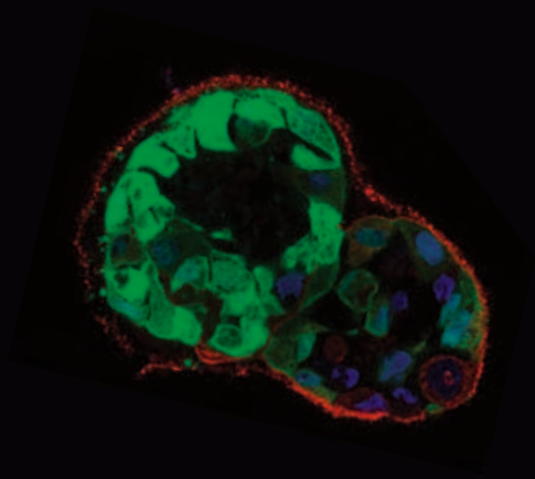
Scientists were first clued into cancer's genetic nature after Salk's Distinguished Professor and Nobel Laureate **Renato Dulbecco** collaborated on a study that explained how oncogene-carrying tumor viruses interact with host cell chromosomes to replicate themselves and induce cancer. The work led to Dulbecco's Nobel Prize in 1975 and revolutionized the way scientists think of the disease.

> "This is what's great about science. 'I've got this crazy idea, but it's a good crazy idea because it suggests an experiment.'"
>
> – GEOFF WAHL



» WEB EXTRA

To hear **Geoff Wahl** discuss p53 further, visit **www.salk.edu/insidesalk/wahl**



The discovery opened the door to new areas of cancer research, which has led to a deeper understanding of the disease over the last three decades. Today, scientists can now identify and quantify the steps that lead to cancer in the body. There is also growing evidence that chronic inflammation can also induce cancer, especially in the liver and pancreas, the latter of which claimed the life of actor Patrick Swayze in September.

Interestingly, some of the rare cases in which patients inherit defective copies of either oncogenes or tumor suppressors have helped scientists zero in on genes that are involved in specific types of cancer in the rest of the population.

"The genes shared by members of a single family are 99 percent identical so you can pinpoint the key genetic difference between the family member who got cancer and the one who didn't," Shaw explains. "Then you study the genes of a completely unrelated cancer patient and trace the mutation back to that same spot in their DNA and bingo, you've found the cancer-causing gene."

There are approximately 22,000 genes in the human genome. To date scientists have identified and decoded more than 300 cancer-causing genes, which has enabled researchers to match them up with the types of cancer they induce. This in turn has led to the development of drugs to counteract the activity of these mutant genes.

Researchers at the Salk's Cancer Center have identified a number of them. Oncogenes FOS and MOS, which are mutated in fibrosarcomas, and REL, which leads to lymphosarcomas, were identified by **Inder Verma**, an American Cancer Society professor in the Laboratory of Genetics.

» WEB EXTRA

To watch video of our interview with Nobel Laureate **Renato Dulbecco**, visit **www.salk.edu/insidesalk/dulbecco**

> "In the long run what we hope is that if enough cancer genomes are sequenced, commonalities will begin to emerge for a particular cancer type so that they can be correlated with more effective treatment." – TONY HUNTER

Work by **Ronald M. Evans**, professor in the Gene Expression Laboratory, led to the discovery of a family of nuclear hormone receptors, a member of which – the estrogen receptor (ER) – is now known to contribute to the development of breast cancers when expressed at high levels. Another nuclear hormone receptor, the retinoic acid receptor (RAR), plays a key role in promyelocytic leukemia when joined to the product of a second gene.

"The fundamental progress in cancer research over the last 30 years has been to identify specific genes that cause cancer," Dulbecco says. "Once the genes responsible for cancer have been identified, you can move forward to therapy."

Founded in 1970 by **Jonas Salk** and designated an NCI Center in 1973, the Salk Institute Cancer Center is led by **Tony Hunter**, an American Cancer Society professor in the Molecular and Cell Biology Laboratory. His discovery of tyrosine phosphorylation, a key event in normal cell growth which can drive tumor cell proliferation when unregulated, eventually led other scientists to develop a new generation of cancer drugs, including Gleevec – a leukemia drug whose developers received the Lasker Prize for their work in October.

The Cancer Center is made up of three distinct research programs: Metabolism and Cancer, Mouse Models and Stem Cells, and Growth Control and Genomic Stability. Thirty of Salk's 57 principal investigators, 161 postdoctoral researchers, and 70 graduate students are part of the Center, which continues to make new breakthroughs with potential for new therapeutic strategies.

Like Wahl's, some discoveries are born from unorthodox ideas.

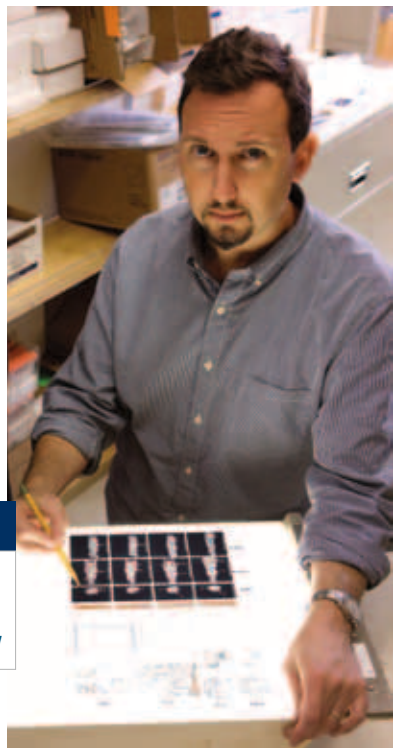
This year, Shaw published a study that demonstrated how he used rapamycin, an immunosuppressant drug normally prescribed to prevent organ transplant rejection, to drastically reduce tumors in lab mouse models developed to mirror Peutz-Jeghers syndrome, a rare cancer of the colon in which patients inherit a mutated copy of the LKB1 gene.

He got the idea after first linking LKB1, a tumor suppressor also commonly mutated in lung cancer, to AMPK, a protein involved with glucose production. Further studies by his team revealed that AMPK regulates TOR, an oncogene that is highly expressed in cancer (its name is short for Target of Rapamycin).

Shaw then asked the question: Will rapamycin work on LKB1-deficient tumors to block TOR activity? He found out that it does. The massive tumors that had developed in the mice's colons drastically shrunk in size and were stabilized in the experiments.

"This is a wonderful example of being able to use basic research and genetic modeling to treat human disease," Shaw says. "We basically put the mice through a clinical trial and test them with different doses of rapamycin."

Current studies in Shaw's lab are examining whether these same therapeutic approaches will work in a mouse model they have developed for lung cancer.



» WEB EXTRA

To hear **Reuben Shaw** discuss his latest experiments using compounds to treat cancer, visit **www.salk.edu/insidesalk/shaw**

Other strategies being tested in the Cancer Center seem born out of science fiction, but show great promise. **Clodagh O'Shea**, assistant professor in the Molecular and Cell Biology Laboratory, and her team have developed a modified adenovirus, normally associated with upper respiratory infections in humans, to undergo selective lytic replication in p53-deficient cancer cells while leaving all other tissues intact.

Once introduced into the tumors, the virus multiplies and causes the cancer cells to implode – releasing thousands of viral offspring in the process to seek out more cancer cells. Initial clinical trials in the United States using an early version of the modified virus showed encouraging results when it was injected directly into the tumor. However, O'Shea believes the latest modified virus will be highly effective.

"In an ideal world, it would be really amazing if we could inject it systemically so it could spread throughout the body and find distant micro metastases in places where we don't even know the cancer has spread," O'Shea says.

"However, the virus we work with is not a naturally blood-bourne virus, so there are factors that can limit its activity. That's why we are also turning to different serotypes/subgroups of virus that naturally infect different tissues, such as the colon and the kidney."

In order to really understand cancer, however, Dulbecco suggested in a 1986 Science article that the human genome would first need to be sequenced so that it could be compared to its cancer counterpart. Four years later the Human Genome Project was initiated by an international group of scientists and completed in 2000.

"Now that it's cheaper to sequence, it's clear that cancer cells have hundreds of mutations, which makes it more difficult to know which genes are important," Hunter says. "But in the long run, what we hope is that if enough cancer genomes are sequenced, commonalities will begin to emerge for particular cancer types so that they can be correlated with more effective treatments."

Most of the cancer-therapy drugs available today work to counteract the uncontrolled activity of oncogenes as a result of p53 mutation. But more is being done to find treatments for the other 50 percent of cancers where p53 is not damaged. In such cases, there are two proteins that are working in conjunction to degrade or completely inactivate the p53 gene: Mdmx2 and Mdmx.

"...we are also turning to different serotypes/subgroups of virus that naturally infect different tissues, such as the colon and the kidney." – CLODAGH O'SHEA

Assistant Professor Clodagh O'Shea (right) with UCSD graduate student Kristen Espantman

> "The fundamental progress in cancer research over the last 30 years has been to identify specific genes that cause cancer. Once the genes responsible for cancer have been identified, you can move forward to therapy." – RENALTO DULBECCO

"These are proteins that are working like anti-tumor suppressors," Wahl explains. "When they bind to p53, the cell can no longer sense DNA damage or initiate the cell death program."

His lab is now working on developing new compounds that impede Mdm2 and Mdmx's ability to bind to p53 and restore the gene's normal protective function.

"It's rare for academia to go into drug discovery experiments, but we felt it was important for us to do so, and we also feel these compounds will be very valuable research tools," Wahl says.

The most recent studies at the Salk involve research of stem cell-like cells and their relationship to cancer. It's a very new field that may provide more answers and possibly new treatments in the future.

Teams of scientists in the Verma and **Fred H. Gage** labs, for example, are using a model for glioblastoma, the deadliest and most common brain cancer in humans, to uncover the nature of specific cancer cells that are capable of spawning new tumors.

"There is increasing evidence that there is a population of cells in most cancers that have stem cell-like properties," Hunter says. "It's a field that's in flux at the moment because how these cells acquire these properties is unclear. There is a school of thought that you have to target these tumor-initiating cells because if you only kill off the rest of the tumor, then it doesn't matter because they simply regrow.

"Chromatin reprogramming is a critical step in the genesis of stem cells and this appears to be true of the stem cell-like cells in tumors," Hunter says.

A recent finding from the Wahl and **Juan Carlos Izpisúa Belmonte** groups has shed light on this idea. They found that p53 itself acts as a block to chromatin reprogramming in somatic cells, suggesting that the lack of p53 in most tumors may predispose cells in these tumors to undergo reprogramming and adopt stem-cell like fates. (See story on page 20.)

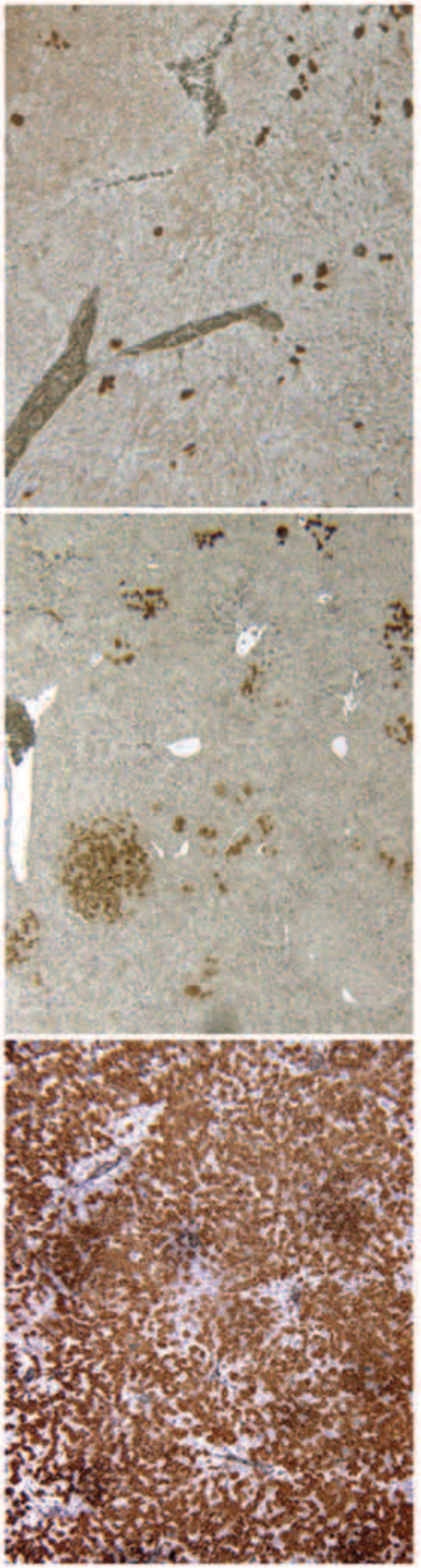
As a result, there is now a heightened interest in using new-generation inhibitors that will block chromatin reprogramming as new types of cancer therapy. The Evans lab is currently testing one novel inhibitor developed by his team on colitis-associated colon cancer in lab mouse models.

"The Salk Cancer Center has a history of significant contributions that have led to a deeper understanding and treatments for cancer," Hunter says. "Over the next few years, new findings hold the promise to lead to new types of cancer drugs, and to alleviate the mortality and suffering from this terrible disease."

Juan Carlos Izpisúa Belmonte

Fred H. Gage

Inder Verma



One on One with… Tatyana Sharpee

ASSISTANT PROFESSOR Tatyana Sharpee is among the newest faculty members at the Institute. Since joining Salk in 2007, she has been recognized with several prestigious research awards, including the Alfred P. Sloan Research Fellowship, the McKnight Scholar Award and named a Searle Scholar – honors that are reserved for scientists who have demonstrated innovative research early in their careers with the potential for making significant contributions to biological research. An authority on information theory, Sharpee's team uses a statistical method she developed to decipher how the brain codes and processes information from natural visual stimuli.

(continued on next page)

I understand you first studied the properties of electrons. What influenced you to turn your attention to neurons?

The theoretical ideas are similar even though the physical systems are very different. And the closest application between statistical physics and information theory is neuroscience. When I was a little girl, I wanted to be a doctor. But I also greatly admired my grandfather, who was a mathematician/physicist. Working in theoretical and computational biology, in particular neuroscience, provides a way to be connected to the two fields. After completing a thesis in theoretical physics, I joined the Sloan-Swartz program during my postdoctoral studies that provides biology training to physicists.

What fascinates you about the brain?

It's remarkably efficient. For example, my desktop computer uses 60 watts of power and some estimate that the brain uses just 12 watts. Yet the brain is very good at doing analog computations that are very hard mathematical problems such as forming a map of surrounding events that come in through our visual system. So for example, your eyes move three times per second and each time you have a pinhole presentation and yet that's not what we perceive. We perceive a whole continuous field. The algorithms for doing this do not exist, except in the brain and we have yet to find out what they are.

You developed a method for analyzing the brain cells' response to natural visual stimuli. What type of stimuli do you use in your experiments and how is it different from standard practice?

We use a collection of scenes that I took while walking through the woods with a video camera. The reason for using such natural stimuli is that they elicit good responses from high-level neurons whose job is to integrate incoming visual information. When such neurons are presented with simplified stimuli devoid of objects, they respond poorly, sometimes not at all. Our hope is that, although we do not know before the experiments which combination of visual features will drive a particular neuron, by taking scenes from the visual world there will be some features of interest to any visual neuron. A collaborative project with Salk professor **John Reynolds**' laboratory was recently funded by NEI to both develop new statistical methods and use them to analyze responses of high-level visual neurons.

So if you only take measurements from just one neuron at a time, how do you know what part of the scene caused it to fire? How do you know it wasn't a shape, or a color that trigged the response?

That's why people were shying away from using natural scenes: they are so complex that when you get a spike, you didn't know what actually triggered it. Although you can't make a determination from just one

"Disorders of the nervous system are devastating. Understanding details of communication with spikes is a pre-requisite for developing better cures."

frame, it actually becomes possible when you analyze responses from 10,000 different images, taking into consideration which combination of features produced spikes and which did not. Together with my postdoctoral advisors, we worked to develop an algorithm that can do this correctly regardless of which frames were presented. It is very important with natural stimuli because they are often poorly controlled. To illustrate the main idea of the methods let's say an image contains three elements, and the next image contains these elements in different positions or perhaps even different elements. Then as you do your analysis, you start to see, a-ha, this one caused a spike, and this one didn't when the elements were moved apart. So you start getting statistics of the most likely feature that is associated with a neuron's response. Using advanced statistical techniques, we can create templates for neuron activity from natural visual stimuli.

Does your work focus solely on visual stimuli?

We also use auditory stimuli to learn more about the auditory cortex, which is not as well known or studied as the primary visual cortex. Auditory studies in some ways are more complicated, and some argue that primary auditory cortex is more equivalent to high-level visual neurons than to the primary visual cortex. We know that a given neuron will prefer a certain frequency in the tone or maybe it'll have a sweep up frequency or a sweep down frequency, but that's about it. But through the auditory experiments, we learn about a different brain area and as theorists we try to make parallels between different senses, such as vision or audition, and search for overarching principles.

What does your lab hope to learn by these types of experiments?

One goal is to learn how signals are integrated in the visual cortex to allow us to perceive objects and shapes. I'm also attracted to theoretical questions of optimization of information transfer in networks. There is an emerging viewpoint that the primary function of many biological networks, either within a cell or between cells, as in neural networks, is the transfer and processing of information. So for example, through phosphorylation a given protein can integrate multiple inputs into a single output that is a graded function of the combination of inputs. At least mathematically, this operation is very much analogous to the integration of signals in the nervous system where a given neuron would sum its synaptic inputs, and produce a spike if the result of integration exceeds a certain threshold. In our recent work (currently in press), we have described how networks of such graded nodes can be set up to convey the maximal amount of information. Assuming the network is optimal, our theoretical analysis also provides a way to infer the strength of interactions with unmeasured parts of the network. This is important because only rarely do we have measurements on a complete circuit in the nervous system. We are looking forward to seeing how these ideas will fare against experimental data.

You grew up in the Soviet Union. Where were you in your academic life during the dissolution period? And was a career in science encouraged for women during that time?

That was around 1992, so I was graduating from high school. The official policy of the Soviet Union was equality for all, to quote a slogan from a classic Soviet film "woman is a human being too." So I think the government tried to promote participation of women. But there's the official language and then there's reality. I wasn't always comfortable based on the peer pressure, but I think at least at the early stages of their careers women participation was encouraged.

Was there anyone in particular who encouraged you to get into science?

Yeah, there were lots of people. I had a very good physics teacher in high school, Anatoliy Israilevich Shapiro, who had interesting techniques for teaching students. For example, he would provide very small blank sheets of paper, just several square inches, and give us problems to solve. He thought that having to express ones thoughts on the small sheets promoted creativity when you really had to think about what to write in such a small space. And a problem could be, for example: "Write 10 ways to speed up the drying process of a wet umbrella." He always emphasized that it was better to solve one problem 10 different ways than to solve 10 problems the same way. My family also influenced me. My grandfather and grandmother are mathematicians and my parents are physicists, so even though I thought I had a choice, in reality I didn't. I was gently steered into this field.

You work in a field that's dominated by men. Do you ever feel the need to encourage other women to consider a career in computational neurobiology?

I recently gave a presentation for Women Scientists in Action at the Rueben H. Fleet Science Center where I spoke to the girls there, but they are so little. I haven't talked to fifth and sixth graders in like 20 years (laughs). So I was trying to tell them about all of the advantages of being a scientist, but I am afraid that my presentation could have been way out of their interests. But it was a learning experience for me as well, so maybe next time I'll be able to connect better with the girls.

You've received several prestigious fellowships in the last year. How will you use the funds to expand your research?

At the genetic level, we know the code in DNA is universal whether it's a fly, a mouse or a human, and that's a great success of molecular biology. In neuroscience, we don't even know exactly what the code is, other than the spikes are important. For example, we don't know to what extent the precise timing of individual spikes matters, and the answer might turn out to be different for neurons in different systems or species. So one of the grants is meant to help my lab search for universal symbols in neurotransmission, comparing the structure of neural code in visual or auditory neurons in mammals, birds, and/or flies.

What would finding these universal codes tell us?

Disorders of the nervous system are devastating. Unfortunately, the cures that are available are rather blunt or nonexistent, and often do not take into account the fine scale organization of the nervous system. Understanding details of communication with spikes is a pre-requisite for developing better cures.

Salk Scientist Vicki Lundblad Shares Her Perspectives on Nobel Prizes, Telomeres, and Risks

WHEN SALK NON-RESIDENT FELLOW ELIZABETH BLACKBURN, Carol Greider and Jack Szostak receive the Nobel Prize in Medicine in early December, Salk Professor **Vicki Lundblad** will have an insider’s view. As Szostak’s invited guest at the Stockholm ceremony, she will celebrate with the winners that the field of telomere biology is receiving this grand international recognition.

Lundblad, a professor in Salk’s Molecular and Cell Biology Laboratory, was a postdoctoral fellow in Szostak’s lab at Harvard, where she made a fundamental discovery about the role of the enzyme telomerase in cell proliferation. Lundblad recalls it was a tremendously heady time, to be present at the start of a new area of study. As a young scientist, “it’s hard to sleep at night, when you have a sense of the magnitude of the discoveries unfolding.”

Lundblad was caught up in a pure basic science problem – how the ends of chromosomes are maintained. It was also an era of strong U.S. commitment to such basic research. “For Jack to get the funding he needed and for me to get a postdoctoral fellowship, it was simple, it just wasn’t an issue.”

When Blackburn (a professor at UC San Francisco), Greider (then a Blackburn grad student) and Szostak pursued their theories about telomerase working with a ciliated pond organism and baker’s yeast – “nobody had a clue” that these findings would have serious implications for human cancer and the aging process, Lundblad said. Ironically, she pointed out, “in today’s NIH environment, with the focus on immediate medical relevance, it is not clear this research would have been funded.” She added: “that’s why support by private philanthropy for basic research is so crucial.”

Beyond the issue of ongoing support for basic science, Lundblad says this award-winning work had another key element deserving mention: the scientists were going against the scholarly tide in performing their early telomerase experiments. Remembering her first taste of that scientific creativity and its results, she said: “It is a phenomenal place to be, when you know you are heading in the right direction, and everyone else is looking elsewhere.” But going against conventional wisdom requires a free-wheeling environment.

“I came to the Salk exactly because of its support for that environment” of intellectual risk-taking, Lundblad said. Of course, taking such risks means dealing with failure, and Lundblad laughs: “I’ve had some spectacular failures.” But such failures are hugely instructive – and “if you aren’t failing occasionally, then perhaps you aren’t taking enough risks.”

Today, both Lundblad and colleague **Jan Karlseder**, an associate professor also in the Molecular and Cell Biology Laboratory at Salk, continue to aggressively probe the mysteries of telomeres, working with yeast, worms and human cells to unlock the next big question in telomere biology: how are these natural chromosome termini protected against the cell’s tendencies to get rid of DNA ends?

And Lundblad reports that, decades after the first pivotal insights that resulted in this year’s Nobel Prize in Medicine, excitement about telomere research in Salk laboratories is extremely high. Enmeshed in what one scientific colleague calls “venture science,” Lundblad and Karlseder are both caught up in the challenge of the research and “still losing sleep at night.”

Salk Service Awards Ceremony Honors More Than 140 Staff Members During Luncheon

Event to Become Annual Tradition at the Institute

THE INSTITUTE HOSTED ITS FIRST EVER Salk Service Awards Ceremony in honor of more than 140 staff members who had achieved between 10 and 45 years of employment. The Sept. 9 luncheon took place at the Institute where President **Bill Brody**, Academic Council Chair **Greg Lemke** and Master of Ceremonies **Walter Eckhart** thanked those in attendance for their hard work over the years.

"Our strength is the dedicated service of all of you," Brody said. "You are the reason why Salk is so successful."

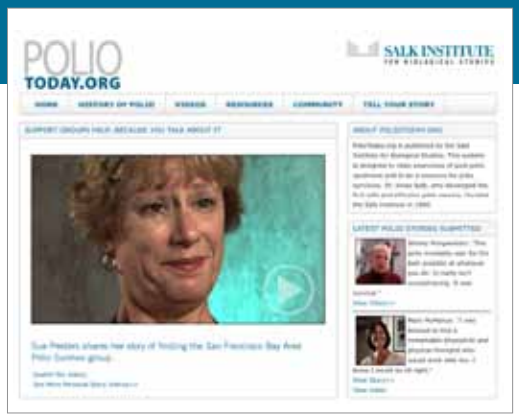
Lemke spoke about non-academic departments at the Institute and gave examples of how each contributed to research before saying: "It takes more than the cadre of scientists to reach the level of our success. It takes the work of a broader group of people who are represented here today."

After the luncheon each of those being honored were called by name and invited to the stage where they were photographed with Brody and Lemke. The Hypotheticals, a singing group composed of Salk employees and scientists, provided comical entertainment with spoofs of television show tunes from the decade in which each group of honorees began their employment at Salk.

The ceremony, which will be an annual event moving forward, concluded near the Institute's Theodore Gildred Court, where Executive Vice President **Marsha Chandler** unveiled a series of red bricks that had been engraved with the names of those who had achieved 25 years or more of service.

"This is a new tradition to honor those of you who have served the majority of your careers at Salk," Chandler said. "The names engraved on these bricks represent a truly special group. They are members of the Salk family who have shown steadfast dedication to your work and to the Salk Institute, and for that we thank you."

Shedding Light on the Latest Ravages of Polio in America:



Salk Institute Launches Website for Polio Survivors

THE SALK HAS LAUNCHED POLIOTODAY.ORG – a resource for polio survivors intended to raise awareness of the crippling post-polio syndrome (PPS), a serious neuromuscular condition that can strike an estimated 40-50 percent of people decades after they were first infected with poliovirus.

The World Health Organization estimates there are about 10-20 million polio survivors worldwide. Characterized by extreme fatigue and renewed weakness or paralysis in the limbs, PPS is often misdiagnosed because its symptoms resemble other crippling neurodegenerative diseases. The severity of paralysis during the original polio infection (decades earlier) does not seem to play in role in whether or when PPS strikes, and the syndrome is typically gradual in onset.

"I have had patients who had very mild cases of polio, or don't even remember having had polio when they were young, end up with post-polio syndrome," says Dr. Jacquelin Perry, renowned orthopedic surgeon and world authority on gait analysis who treats PPS patients at Rancho Los Amigos National Rehabilitation Center in Downey, California.

PPS mimics other debilitating diseases, and because there is no single diagnostic test to confirm it, it is considered a disease of exclusion – meaning it requires specialized testing by well-trained physicians who rule out all other possibilities to achieve a proper diagnosis. That diagnostic complexity and confusion, coupled with the fact that the U.S. polio survivor population is now elderly (or close to it), has relegated the PPS community to relative obscurity.

"People suffering from PPS seem to exist in the shadows, far from broad public awareness of the disease and its terrible manifestations," says Susan Trebach, Salk Institute Senior Communications Director. "Our goals are to heighten awareness and understanding of PPS, encourage people to seek proper diagnosis and treatment, and facilitate the growth of online communities of polio survivors around the world."

PolioToday.org features video testimonials from polio survivors who share recollections of their personal battles with polio when they were young, their more recent diagnosis and management of PPS, and how they are coping with their condition. There is an expert opinion video page featuring several clips by UCLA Neurologist Dr. Susan Perlman, a PPS specialist who explains the cause of PPS and provides relevant information.

"Polio survivors have searched for a way to actively connect to one another for years," says polio survivor Gladys Swensrud from San Diego, California. "This exciting Salk Institute site, PolioToday.org, offers not only a forum for the distribution of important polio and post-polio related information, but it also creates a much needed link for polio survivors worldwide to connect with one another using modern social networking capabilities."

Rick Van Der Linden, a polio survivor from Hemet, California adds:

"The best part of the site is that it's been developed just for us. It allows us to communicate with and learn from one another. It's the best thing going on the Web for the polio survivor community."

Since going live in August, with no mainstream public announcement of any kind, the Community section of the site is already attracting attention as polio survivors, some from as far away as Australia, have signed up to participate in various discussions that have been posted. Under the Emotional Stress and PPS discussion topic, for example, members describe the ways they control the anxiety and depression associated with PPS.

"It is amazing to see people openly discuss their deepest health concerns related to PPS as well as how they found us in the first place," says Mauricio Minotta, the Salk Communications Director leading the website project.

"It is especially gratifying to receive comments, either on Twitter or YouTube, from people who tell us how much they appreciate this new internet resource," Minotta says.

The Resources page provides users with a growing list of polio survivor groups around the country and PPS and polio-related literature from other organizations such as Post-Polio Health International, the World Health Organization and Rotary International Polio Eradication.

Most of the activity on PolioToday.org to date has been generated through connections made on Twitter, YouTube and Facebook.

> **"The best part of the site is that it's been developed just for us. It allows us to communicate with and learn from one another."**

Plant Biology Lab Remembers Founding Scientist Chris Lamb

THE SCIENTIFIC COMMUNITY WAS SADDENED THIS summer when **Chris Lamb**, the founding scientist and director of the Salk Institute's Plant Biology Laboratory, died suddenly at age 59 in Norwich, England.

A world-renowned researcher who pioneered studies in the molecular mechanisms that underlie how plants defend themselves against pathogens, Lamb was recruited by former Salk President Frederic de Hoffmann from Oxford in 1983 to establish what would become an extraordinary Plant Biology program at the Institute.

In an interview last year for an *Inside Salk* cover story (Oct. '08 issue) in celebration of the Plant Biology Laboratory's 25th anniversary, Lamb recalled his thoughts in deciding to take de Hoffmann up on the offer to establish a lab at the Salk.

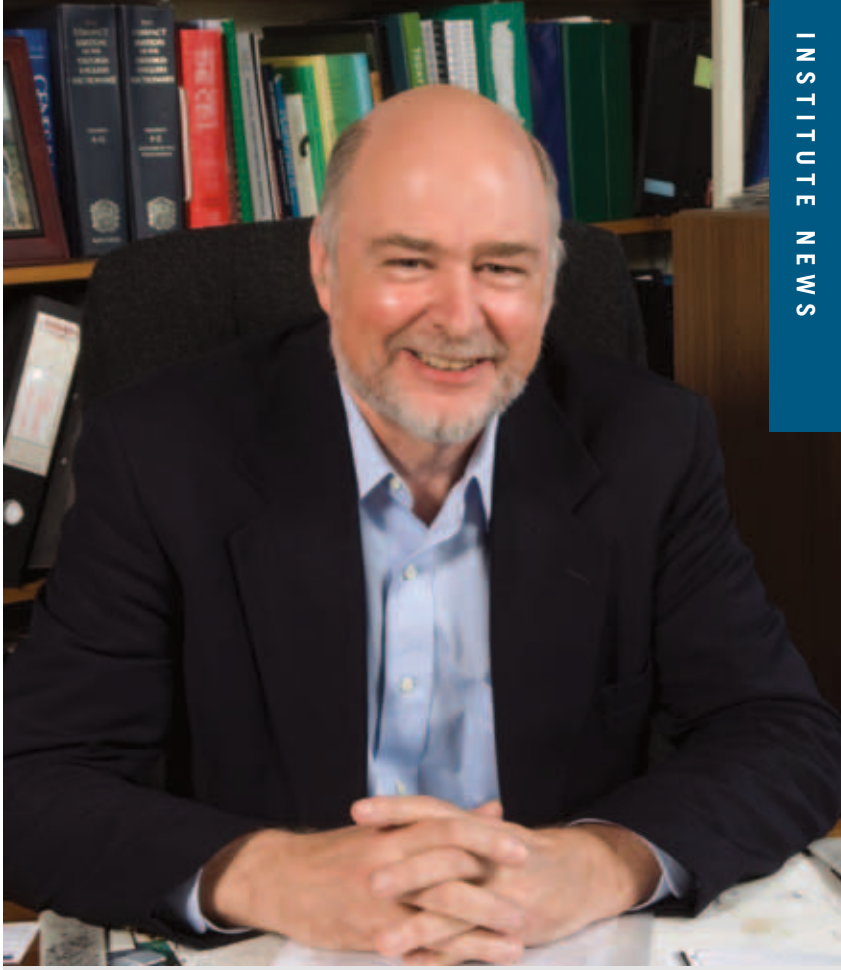
"This seemed a fantastic, if somewhat risky, opportunity," Lamb said. "Fantastic because of Salk's great prestige and reputation in biomedicine and neurobiology. Risky, but exciting, because I would be starting something from ground zero."

Lamb left Oxford and headed for La Jolla, where he spent the next 15 years conducting some of the groundbreaking work that led him to become one of the most respected leaders in plant biology research.

"Chris had a good sense of the big picture," said Joanne Chory, professor and director of Salk's Plant Biology Lab, who was recruited to the Institute by Lamb in 1988. "He was focused and analytical, and always knew how to move things forward.

"Lamb had a real sense of the beauty of plant biology," she said. "Beyond his superb science, he will be remembered as the founding faculty member of the Salk program and as an international voice for the discipline."

Lamb returned to England in 1998 to lead the John Innes Centre, one of the world's leading institutions of plant research. He promoted a culture of excellence there, and was recently named a Fellow of the Royal Society in recognition of his scientific achievements.



Chris Lamb

> "Lamb had a real sense of the beauty of plant biology…Beyond his superb science, he will be remembered as the founding faculty member of the Salk program and as an international voice for the discipline."
>
> –JOANNE CHORY

From left: Joseph P. Noel, Chris Lamb, Jeffrey A. Long, Detlef Weigel, Joanne Chory, James Umen, Joseph R. Ecker at the 25th Anniversary Celebration of Salk's Plant Biology Lab last October.

In 2000 Lamb returned to Salk for a visit, saying he'd come back to California "for a dose of optimism." Chory said he remained very fond of the Salk and spoke of how it had influenced him.

Likewise, Lamb influenced the San Diego research landscape. Today, there are 16 Plant Biology principal investigators across the mesa (Salk, UCSD and Scripps), seven of whom are members of the National Academy of Sciences.

"Chris' legacy in La Jolla is not just his own science, but the scientists he identified and mentored who have made La Jolla one of the top places for plant science in the world," Chory said. "We are deeply saddened by this loss."

A Spanish Gathering for International Council

MORE THAN 31 MEMBERS OF SALK'S International Council gathered in Barcelona this spring for three days of scientific presentations and activities designed to update them on the most recent developments at the Institute.

Some of Salk's leading scientists provided overviews of their promising discoveries in stem cell research and advancements in studies related to metabolism, cancer and therapeutics for chronic disease.

Highlights from some of the group's activities included a tour of the charming medieval town of Sitges, a Gaudi architectural tour and an elegant dinner and flamenco show hosted by the Spanish government.

The Salk's International Council is made up of business executives who serve as ambassadors of the Institute in an effort to help raise the Institute's profile around the world as they share Salk's latest discoveries with their circle of influence.

To learn more about the Salk Institute International Council, contact Allyson Collins, director of Development Administration, at 858-4100 x2005 or e-mail: acollins@salk.edu.

At left: Hotel Casa Fuster, site of the meeting.

From left: Sukuma Jayananda, Frederik Paulsen, Ellen Schwickart, Sukum Nawapan, Stephanie Still and Carl-Otto Still.

Discovery Roundup

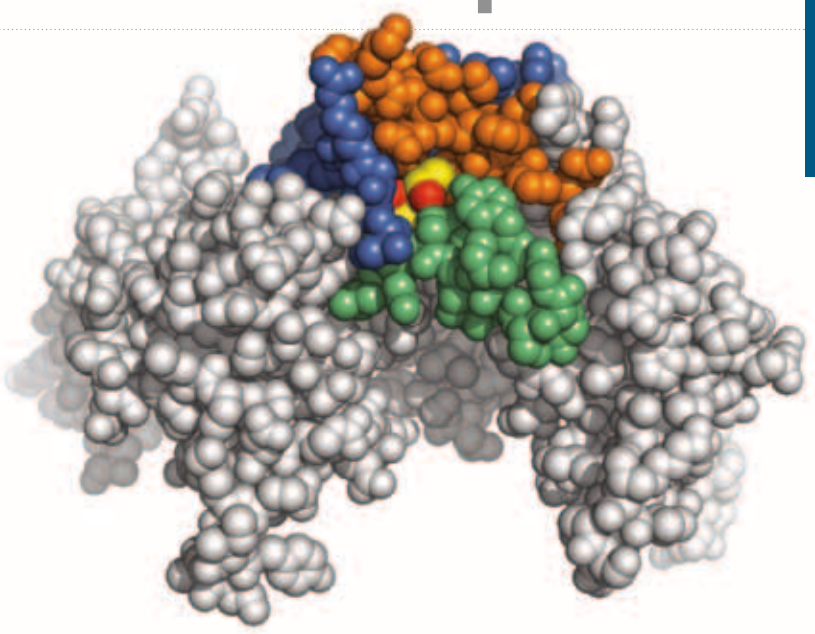
Site for Alcohol's Action in the Brain Discovered

ALCOHOL'S INEBRIATING EFFECTS MAY BE FAMILIAR TO many, but the molecular details of its impact on brain activity remain a mystery. A new study by researchers at the Salk Institute provides a better understanding how alcohol alters the way brain cells work.

Their findings reveal an alcohol trigger site located physically within an ion channel protein; their results could lead to the development of novel treatments for alcoholism, drug addiction, and epilepsy. **Paul Slesinger** and his team now show that alcohols directly interact with a specific nook contained within a channel protein. This ion channel plays a key role in several brain functions associated with drugs of abuse and seizures.

Previous research by Slesinger and his group focused on the neural function of these ion channels, called GIRK channels. GIRK channels open up during periods of chemical communication between neurons and dampen the signal, creating the equivalent of a short circuit.

Having the location of a physical alcohol-binding site important for GIRK channel activation could point to new strategies for treating related brain diseases. Using this protein structure, it may be possible to develop a drug that antagonizes the actions of alcohol for the treatment of alcohol dependence.



X-ray crystallography revealed a binding site for alcohol in an ion channel.

Alternatively, "If we could find a novel drug that fits the alcohol-binding site and then activate GIRK channels, this would dampen overall neuronal excitability in the brain and perhaps provide a new tool for treating epilepsy," says Slesinger.

Why Some Tumors Don't Respond to Radiation and Chemotherapy

A TIGHTLY CONTROLLED SYSTEM OF CHECKS and balances ensures that a powerful tumor suppressor called p53 keeps a tight lid on unchecked cell growth but doesn't wreak havoc in healthy cells. In their latest study, scientists at the Salk Institute suggest just how finely tuned the system is and how little it takes to tip the balance.

When unprovoked, at least two negative regulators—the related proteins Mdm2 and Mdmx—prevent p53 from unleashing its power to kill. But just slightly increasing the amount of available Mdmx, which grips p53 and renders it inactive, the Salk researchers discovered, made mice remarkably resistant to the harmful effects of radiation but very susceptible to the development of oncogene-induced lymphomas.

"Our experiments emphasize how subtle and precarious the balance is," says postdoctoral researcher and first author **Yunyuan V. Wang**. "A slight shift of balance and the mice survive the equivalent of Chernobyl but are in big trouble when an oncogene is activated."

Their findings could explain why some tumors don't respond to radiation or chemotherapy, and provide novel routes for the development of new anti-cancer therapies.

As a powerful tumor suppressor, p53 turns on genes that either halt cell division to allow time for repair of damaged DNA or, when all rescue attempts prove futile, to prevent cells with genetic defects from dividing, as this would fuel the development of cancer. Consequently, before any tumor cell can start proliferating willfully, it needs to escape from p53's iron fist.

"One way or another, p53 function is compromised in all cancers. Either p53 itself is mutated or there is a problem with one of the proteins that regulate p53's activity," says the study's leader **Geoffrey M. Wahl**, a professor in the Gene Expression Laboratory. "Our hope is that we can develop small molecule drugs that will activate p53 in those tumors where it is still functional but inactivated by one of its negative regulators."

Discovery Roundup

Tumor suppressor pulls double shift as reprogramming watchdog

A COLLABORATIVE STUDY BY RESEARCHERS at the Salk Institute uncovered that the tumor suppressor p53, which made its name as "guardian of the genome," not only stops cells that could become cancerous in their tracks but also controls somatic cell reprogramming.

Although scientists have learned how to reprogram adult human cells such as skin cells into so-called induced pluripotent stem cells (iPSCs), the reprogramming efficiency is still woefully low. The Salk study, published in the Aug. 9 advance online edition of *Nature*, gives new insight into why only a few cells out of many can be persuaded to turn back the clock.

"Although we have been able to reprogram specialized cells for a while now, there had been nothing known about the control mechanisms that prevent it from happening spontaneously in the body and why it has been so hard to change their fate in a Petri dish," says **Juan-Carlos Izpisúa Belmonte**, a professor in the Gene Expression Laboratory, who worked closely with **Geoffrey M. Wahl**, also a professor in the Gene Expression Laboratory.

Their findings bring iPSCs technology a step closer to fulfilling its promise as source of patient-specific stem cells but also force scientists to rethink the development of cancer.

"There's been a decade-old idea that cancer arises through the de-differentiation of fully committed and specialized cells but eventually it was discarded in favor of the currently fashionable cancer stem cell theory," says Wahl. "Now that we know that p53 prevents de-differentiation, I believe it is time to reconsider the possibility that reprogramming plays a role in the development of cancer since virtually all cancer cells lose p53 function in one way or another."

Growth Factor Keeps Brain Development on Track

SALK SCIENTISTS REPORT THAT FGF10, A MEMBER OF THE FIBROBLAST GROWTH factor (Ffg) family of morphogens, lets brain stem cells know when it's time to get to work, ensuring they hit their first developmental milestone at the right moment.

Their findings not only add new insights into brain development and a novel function for Fgfs, but also reveal a possible mechanism for the selective expansion of specific brain areas over the course of evolution, such as the greatly increased size of the frontal lobe in humans.

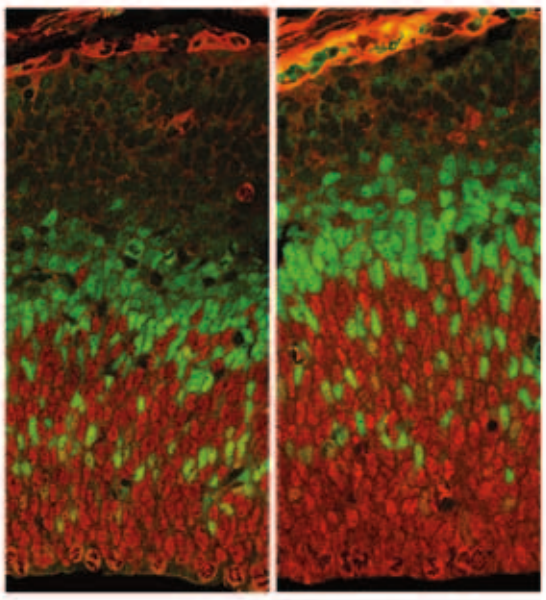
During embryonic brain development, stem cells in charge of building the cortex—the largest brain structure and seat of most higher cognitive functions—pass through a series of tightly regulated stages: from omnipotent stem cell to cortical progenitors cells capable of producing neurons.

"The timing of each of these transitions has critical implications for brain development, since minor changes in the proportion of progenitors exhibiting one or the other division mode at early stages will result in substantial changes in the number of neurons and the size of the cortex," says **Dennis O'Leary**, a professor in the Molecular Neurobiology Laboratory, who led the study.

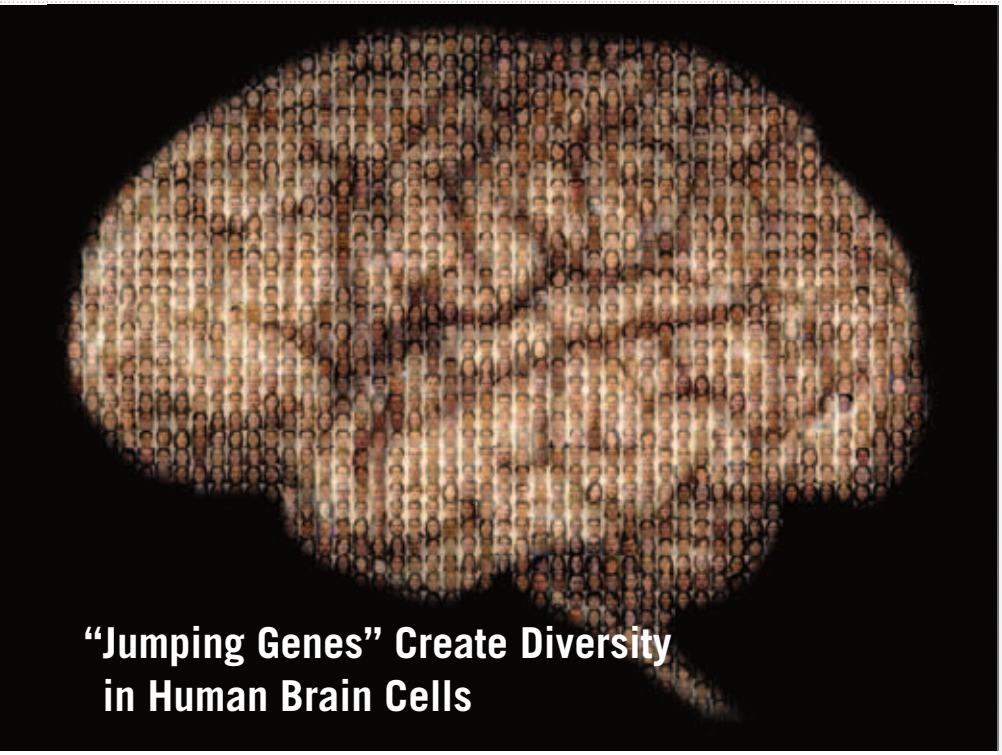
Early in corticogenesis, stem cell-like progenitor cells known as neuroepithelial cells undergo symmetric cell division, producing two identical progenitors to expand the pool of neuroepithelial cells. Later on, they differentiate into more mature progenitor cells referred to as radial glia, which then divide asymmetrically to produce a pair of unlike daughter cells: one radial glia to maintain the pool of progenitor cells and a cortical neuron or a basal progenitor. The latter will migrate outward and then produce neurons to establish the superficial layers of the cortex.

But little is known about the mechanisms that mediate the critical transition period that bridges the early expansion phase of neuroepithelial cells and the later neurogenic phase, which produces all the neurons that will eventually form the six layers of the cortex.

"These findings demonstrate a direct mechanism employed during normal development to regulate brain size," says O'Leary. "These findings also have potential implications for how cortical areas have evolved. Selectively expanding the progenitor pool by Fgf10 regulation of the timing of radial glia differentiation could account for the selective expansion of the frontal cortex, which has been greatly expanded in humans and is thought to be important for evolving what are considered typically human traits."



Without Fgf10 (right), neuronal stem cells fail to differentiate on time. As a result, they keep multiplying and generate a bigger pool of radial glia (shown in red).



"Jumping Genes" Create Diversity in Human Brain Cells

Rather than sticking to a single DNA script, human brain cells harbor astonishing genomic variability, according to Salk scientists. The findings could help explain brain development and individuality, as well as lead to a better understanding of neurological disease.

The team, led by **Fred H. Gage**, a professor in the Salk's Laboratory of Genetics, found that human brain cells contain an unexpected number of so-called mobile elements—extraordinary pieces of DNA that insert extra copies of themselves throughout the genome using a "copy and paste" mechanism.

"This is a potential mechanism to create the neural diversity that makes each person unique," says Gage. "The brain has 100 billion neurons with 100 trillion connections, but mobile pieces of DNA could give individual neurons a slightly different capacity from each other."

In earlier work, Gage had already shown that mobile pieces of DNA known as LINE-1 elements (short for Long interspersed element 1) randomly add extra copies to the genome of mouse brain cells. But whether or not the same process, colloquially referred to as "jumping," held true for neurons in human brains had been a matter of some debate.

When postdoctoral researcher and first author **Nicole Coufal** measured matched samples (brain versus other body tissues) from numerous individuals, she found that some brain samples had as many as 100 extra copies per cell.

"This was proof that these elements really are jumping in neurons," explains Coufal. Strikingly, it also means that not all cells are created equal—humans are true chimeras since the DNA in their brain cells is different from the DNA in the rest of their cells.

Nicotinic Receptor May Help Trigger Alzheimer's Disease

FOR CLOSE TO A DECADE, PHARMACEUTICAL researchers have been in hot pursuit of compounds to activate a key nicotine receptor that plays a role in cognitive processes. Triggering it, they hope, might prevent or even reverse the devastation wrought by Alzheimer's disease.

A new study from the Salk Institute, however, suggests that when the receptor, alpha-7, encounters beta amyloid, the toxic protein found in the disease's hallmark plaques, the two may actually go rogue. In combination, alpha-7 and beta amyloid appear to exacerbate Alzheimer's symptoms, while eliminating alpha-7 seems to nullify beta amyloid's harmful effects.

These findings, reported recently in *The Journal of Neuroscience*, may shed new light on the processes leading to Alzheimer's and could have important implications for researchers seeking to combat the disease.

Intrigued by earlier studies showing that beta amyloid seemed particularly drawn to the alpha-7 nicotinic receptors, researchers in the lab of **Stephen F. Heinemann**, in the Salk Molecular Neurobiology Laboratory, sought to determine whether the alpha-7 receptors actually modulate the effects of beta amyloid in Alzheimer's disease.

Hypothesizing that the alpha-7 nicotinic receptors mediate beta amyloid effects in Alzheimer's disease, Heinemann's team crossed mice engineered to lack the gene for alpha-7 with a mouse model for Alzheimer's disease, which had been genetically engineered to overexpress amyloid precursor protein (APP), an antecedent to beta amyloid. They then put the offspring through a series of memory tests.

Surprisingly, those with both mutations—too much APP and no gene for alpha-7—performed as well as normal mice. The Alzheimer's mice, however, which had the alpha-7 gene and also overexpressed APP, did poorly on the tests. Pathology studies revealed the presence of comparable amounts of plaques in the brains of both types of mice, but in those lacking the alpha-7 gene, they appeared to have no effect. Similar disparities were evident in measurements of the synaptic function underlying learning and memory.

Longtime Donor Ruth Hamill Bequeaths $250K to Institute

WHEN SHE WASN'T TAKING HER DAILY TWO-MILE WALK NEAR HER HOME or meeting with friends from her sewing club, you might catch Ruth Hamill playing a game of tennis or volunteering with Meals on Wheels. But when she received invitations to the Salk Institute over the years, she wouldn't pass up the chance to hear presentations on scientific research, yet another one of her longtime interests.

"I invited her to come hear a scientist speak at one of Salk's events in the 1990s because I knew she was interested in biomedical issues and research in general," said Ruth's friend and attorney for nearly 20 years Richard Muscio, who previously served on Salk's Planned Giving Advisory Committee.

"After that first meeting, she just fell in love with the place," he said. "Ruth loved hearing new ideas. She was just fascinated by the depth and breadth of knowledge and the creativity of Salk's researchers."

The science of cognition was of particular interest to Ruth, more so after her husband, King, developed Alzheimer's disease and passed away in 2006. The couple supported Salk research as members of the President's Club and eventually decided to include the Institute in their estate plan, which resulted in a $250,800 unrestricted contribution when Ruth passed away in March.

Ruth is survived by her two sons, Rick and Dean, who are very supportive of their parents' philanthropic endeavors, Muscio said.

> "Ruth loved hearing new ideas. She was just fascinated by the depth and breadth of knowledge and the creativity of Salk's researchers."

King and Ruth Hamill

Institute Establishes Presidential Chair to Honor Irwin M. Jacobs

THE SALK INSTITUTE HAS ESTABLISHED the Irwin M. Jacobs Presidential Chair based on an endowment from Qualcomm and its employees. The Chair commemorates Jacobs' decision to step down as chairman of Qualcomm's Board of Directors and recognizes his ongoing dedicated leadership of the Salk Institute's Board of Trustees.

The Presidential Chair will be Salk's largest endowment of its kind and will provide $4 million to the Institute when fully funded. The inaugural chair-holder will be the Salk President, **William R. Brody**.

"Endowing a chair that will help ensure superb leadership at the Salk seemed a very fitting way to honor Irwin," said **Paul E. Jacobs**, chairman and CEO of Qualcomm. "His legacy is linked to the attraction and development of the world's finest executive talent, and his instincts are always to motivate, encourage and promote groundbreaking research."

"Irwin Jacobs' exemplary leadership of the Salk Board has been critical to enhancing the Institute's international renown," said Salk Executive Vice President **Marsha Chandler**. "This Presidential Chair is the perfect recognition of Irwin's inspiring guidance and commitment to the Salk's future."

Irwin Jacobs and his Qualcomm cofounders redefined how the world thinks of telecommunications and information technology. More than 20 years after its start, Qualcomm is a leading innovator of advanced wireless technologies, products and services.

"We are pleased and proud to play a role in the ongoing excellence of the Salk Institute," said Paul Jacobs. "Salk discoveries are transforming our understanding of human health, and this is an outstanding way to support one of Irwin's major passions."







Nearly 700 people gathered for an exceptional evening that raised $784K for basic research.

Broadway Veteran Bernadette Peters Dazzles Symphony at Salk Audience

EVEN A TORRENTIAL MORNING RAINSTORM failed to dampen excitement for the 14th annual Symphony at Salk concert held Aug. 22 at the Institute's cliff-top courtyard overlooking the Pacific Ocean. Mother Nature was quickly upstaged by a spectacular evening of music that combined the talents of multi-award winning performer Bernadette Peters and the San Diego Symphony led by returning guest conductor Thomas Wilkins.

Nearly 700 people gathered at the Institute to enjoy an exceptional evening of dining and entertainment at the sold-out fundraiser that raised more than $784,000 — a new record — to benefit the Salk's groundbreaking research and its community outreach programs.

Peters dazzled the audience with her amazing vocal range that ensured every song was delivered to ultimate effect. She performed an eclectic mix of selections that showcased her versatility whether she was strutting through the Broadway belter "Ain't Nothing Like a Dame," heating things up with "Fever," or singing the sweet and poignant ballad "Shenandoah."

Peters easily connected with the audience between songs, delighting them with playful conversation and racy banter that kept the show at a lively pace until her exhilarating finale, which included a haunting rendition of "I Honestly Love You" and "Some Other Time."

Her show was preceded by a rousing performance by the San Diego Symphony under the skillful direction of Maestro Wilkins playing selections by Franz von Suppe, Gabriel Faure and a stirring rendition of Johann Strauss Jr.'s "Emperor Waltzes."

A champagne reception kicked off the festivities as guests mingled in the eucalyptus grove and bid on several unique items offered at the event's first-ever silent auction. Prior to the start of the concert, they also enjoyed a delectable meal prepared by critically acclaimed award-winning chef and owner of Pamplemousse Grille Jeffrey Strauss, who catered the event for the second year in a row.

» WEB EXTRA

To see more images from this event, visit **www.salk.edu/insidesalk/symphony09**

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Salk **Calendar**

NOVEMBER 2009

1 Breathing & Sleep Symposium

5–6 Transitional Mechanisms of Early Lymphocyte Development Symposium

11 Stem Cell Meeting on the Mesa 2009

17–18 4th Annual Peptide Therapeutics Symposium

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

A group of high school students spent eight weeks at the Salk where they worked with scientists on various experiments as part of the Summer Internship Program.