THE SALK INSTITUTE FOR BIOLOGICAL STUDIES

CELEBRATING 40 YEARS

INSIDE SALK

The Secret Life of Plants

For the past two decades, Salk professor Joanne Chory has been unraveling the secret life of plants — specifically, the molecular cues that underlie their growth and development.

The results of her basic research may yield new agricultural techniques that could help the world feed its ever-growing population.

In recent research, Chory and her colleagues in the Salk Institute's Plant Molecular and Cellular Biology Laboratory have filled in two significant gaps in our understanding of the molecular pathway that allows steroid hormones to stimulate plants to be larger and more fruitful.

The Salk scientists recently revealed that a protein protruding from the outer surface, or membrane, of a plant cell is the receptor that recognizes a steroid hormone essential to the growth and development of plant cells. Once the protein receptor, which was previously cloned (copied for laboratory study) by Chory's team and named BRI1 ('bry-one'), recognizes the hormone, a series of biochemical activities occur inside the cell. At the other end of this chemical pathway, inside the plant cell, the Salk team has also now uncovered the transcription factors that turn on key genes controlling the cell's growth. Chory's lab reported their findings in papers

Joanne Chory

Plant steroid hormones bind to proteins that project to the outside of the plant cell, like a key in a car ignition.

published in *Nature* and *Cell* in January.

Although plants and animals both use steroid hormones to control growth and development, animal steroid hormones such as testosterone and estrogen turn on cells by binding to receptors inside the cell. By contrast, plant steroid hormones, called brassinosteroids, bind to proteins that project to the outside of the plant cell, like a key in a car ignition. Until the publication of Chory's research, the nature of the 'keyhole' was unknown, and it was also unclear how the 'sparkplug' worked, i.e., how the resulting signal turned on the key genes that control growth and sexual maturation.

By a combination of genetic and biochemical techniques, Chory and colleagues finally proved that the 'keyhole' is BRI1, a protein that protrudes from the plant cell membrane.

At the other end of the signalling pathway, the team revealed that one of the 'sparkplugs' that fires the genetic engine inside the cell is a protein called BES1, a member of a completely new family of plant-specific transcription factors. Transcription factors transcribe a gene's DNA blueprint into proteins, each of which performs a specific function in the plant.

The latest findings are the outcome of work that started with a major discovery in Chory's lab almost 10 years ago. In 1996, the team definitively showed that brassinosteroids are involved in the plant cell's response to natural and artificial light. The Salk researchers' results were published in *Science*. Since then the lab has focused on discovering the molecular mechanisms of how brassinosteroids operate.

"It was satisfying after all these years that BRI1 turned out to be what we thought it was — the receptor for the steroid," said Chory. "Genetics originally led us to the right gene, and follow-up biochemical studies allowed us to show that the protein made by this gene actually bound the steroid. We are hoping that these discoveries will have a significant impact on crop yield."

This *Arabidopsis* plant is a 'dwarf' because its cells are not making the steroid hormones essential for growth and development.

Our Future Determined by Just Three Genes?

What was the most important turning point in your life? There is only one right answer, according to Salk Institute geneticist Juan Carlos Izpisúa Belmonte. Quoting the famous embryologist, Lewis Wolpert, Belmonte says that while most people may consider birth or marriage as the most crucial events, in reality the central event in anyone's life is the point in embryonic development when his or her basic body plan is established.

The incredibly complex process by which cells in the developing embryo migrate into the right places at the right time to form organs is called pattern formation.

Belmonte's team has now discovered that three key genes make the difference between healthy, properly aligned body organs and deformed organs in the wrong place. The findings appeared in *Genes & Development* in January.

Juan Carlos Izpisúa Belmonte

The three genes that are essential to pattern formation are called *wnt4a*, *silberblick/wnt11* and *wnt11-related*. These genes code for three crucial signaling proteins that cells use to communicate with one another as they form into organs. Two and one-half years ago, the Salk researchers began systematically blocking a wide variety of genes implicated in the development of the large, transparent embryo of the zebra fish. They observed that simultaneously blocking *wnt4a*, *silberblick/wnt11* and *wnt11-related* prevented the heart, gut, liver and pancreas from lining up as they normally should, along the midline of the body.

SURPRISING COMPLEXITY

The scientists were surprised at their findings. "It's a complex pathway, much more complex that we are used to," said senior research associate Angel Raya, co-author of the paper.

The discovery of this novel genetic pathway has important implications for stem cell research. While scientists are making headway on changing the fate of stem cells so that they will become replacement nerve or heart tissue cells, the greater struggle will be to persuade these cells to form new whole organs.

"Our results give insight into how cells migrate to form tissues and organs," said Belmonte. "That's the second level of complexity we need to understand if stem cell therapy is to reach the clinic. These genes control cell behavior, rather than cell fate."

Eavesdropping on Brain Cells

For more than 40 years, it has been an article of faith for brain researchers that nerve cells (neurons) with similar functions stick together. That thinking may be refined, thanks to work by Salk researcher Ed Callaway published in *Nature* in February.

Callaway and colleagues showed that neighboring neurons keep secrets that they share only with trusted friends. Neurons are, in fact, organized into precisely interwoven sub-networks, like neighborhood cliques.

"This might not make for the friendliest neighborhood, but it probably makes the brain smarter and allows more sophisticated computations than are possible in a fully connected network," said Callaway.

Previous studies of the brain's architecture, in particular Nobel-Prize winning work by Wiesel and Hubel at Harvard in the 1960s, showed that thousands of brain cells with similar functions are organized into vertical slices called 'functional columns.' However, neuroscientists have remained puzzled about why so many neurons are needed to apparently carry out the same function.

FINE-SCALE CONNECTIONS

Callaway and associates Yumiko Yoshimura and Jami Dantzker used glass microelectrodes to record from neurons in fine slices of rodent brain tissue. By eavesdropping on two neighboring neurons simultaneously, they determined whether both neurons were receiving the same messages.

"The thousands of neurons in these columns are not the same," said Callaway. "There are fine-scale connections within the columns so that neurons right next to each other could be involved in very different functions."

The fact that the brain's circuitry is organized on a much finer scale than previously suspected highlights the need for methods that can tease out different sub-networks. The Salk team is now using gene expression to reveal chains of interconnected neurons.

These approaches could help answer basic questions about brain disorders such as schizophrenia or depression, said Callaway: "It's necessary to understand how the circuitry works normally if you're ever going to figure out what goes wrong with it."

Ed Callaway

...neighboring neurons keep secrets that they share only with trusted friends.

Melanopsin can absorb light and trigger an electrical signal that resets the biological clock.

Biological Clock Uses System 'Borrowed' from Flies

"Sleep is the golden chain that ties health and our bodies together," wrote Shakespeare's rival, Thomas Decker. This still holds true four centuries later, as weary jet-lagged travelers will testify. Now Salk researcher Satchin Panda has discovered a molecular switch that controls our sleep-wake cycles and the results are surprising: we are using ancient 'technology' borrowed from insect vision. The study, carried out while Panda was at the Genomics Institute of the Novartis Research Foundation (GNF), appeared in *Science* in January.

Satchin Panda

Sleep-wake cycles are controlled by a biological, or circadian, clock in the suprachiasmatic nucleus of the brain. When time zones or seasons change, a light sensor in our eyes resets the clock, in a process called photoentrainment. According to Panda, impaired photoentrainment prolongs jet lag and may lead to depression and other disorders in shift workers and people at high latitudes.

Scientists have believed for some time that the re-set switch resides in specialized light-sensitive nerve cells in the retina that contain a unique photopigment called melanopsin. These specialized cells in the retina act as a 'sixth sense' distinct from the regular visual system.

NEW FINDING, ANCIENT 'TECHNOLOGY'

Panda and his GNF colleague Tim Jegla have now confirmed that melanopsin can absorb light and trigger an electrical signal that resets the biological clock. Remarkably, the mechanisms involved differ from those of normal human vision.

"In fact, the melanopsin photoresponse is akin to that of lower animals such as insects," said Jegla. "We should be able to tap into years of research on fly vision for more clues to how melanopsin signals our biological clock."

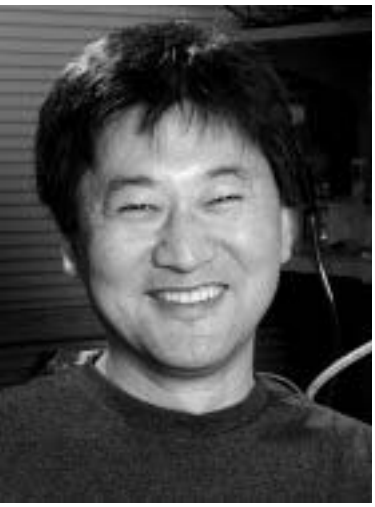
Hard on the heels of Panda's discovery, research by others suggests a novel role of melanopsin-containing cells in conveying color and light intensity information to the brain. Such findings expand the scope of Panda's work beyond circadian light entrainment into a deeper understanding of higher visual processes in humans and other mammals.

"Fascinating, Pure Breakthrough Discovery"

To law-enforcement agencies, cocaine and marijuana differ greatly from Prozac® and aspirin, but to the biochemist these drugs are all members of the same family: substances whose actions are mediated by crucial and mysterious molecules in the membranes of our cells called membrane proteins.

Now Senyon Choe and Roland Riek and their colleagues have discovered a remarkable 'partner' protein called Mistic that will allow large-scale production of human membrane proteins. This advance should benefit drug discovery as well as the basic biological sciences. The research appeared in *Science* in February.

"Although membrane proteins, as the 'gatekeepers' of a body cell's outer wall, are central to medical research, little is known about them because they are almost impossible to recreate as isolated proteins in the laboratory," said Tarmo Roosild, the lead author of the study.



Senyon Choe

Roland Riek

Unlike proteins that exist freely inside the cell, which can be studied relatively easily by inserting genes into bacteria such as *E. coli* and thus creating multiple copies of them, membrane proteins need to be inserted into a cell membrane to function properly. There was no easy way to do this until the Salk team discovered Mistic. Like a host drawing a reluctant guest into a cocktail party, Mistic appears to automatically fold into place within the cell membrane bringing the 'guest' protein into the *E. coli* membrane along with it.

The auto-inserting ability of Mistic gives researchers a new tool that could revolutionize membrane biology and become an intense focus of interest since more than half of all blockbuster prescription drugs target just two classes of membrane proteins: ion channels and G-protein coupled receptors (GPCRs). Using Mistic, Choe's group has now successfully created dozens of such important human membrane proteins, allowing the scientists to understand for the first time the molecular workings of key potassium channels, cancer-causing growth factor receptors, and GPCRs.

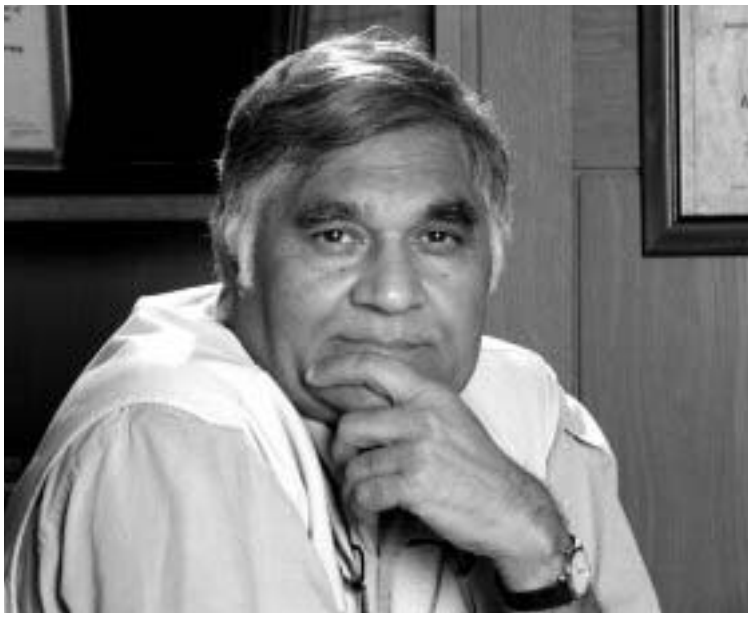
"Figuring out how to produce these proteins abundantly using Mistic is probably the most fascinating, pure breakthrough discovery we have ever made in my 12-year old laboratory at the Salk," said Choe.

Gene Therapy Clears 'Silt' of Alzheimer's

In 1901, a 51-year-old Frankfurt housewife named Auguste started accusing her husband of having an affair with every woman he met. Five years later this unfortunate lady's brain was on Alois Alzheimer's postmortem table, and a new disease was born: Alzheimer's disease.

Damaging protein deposits such as those Alzheimer saw in Auguste's brain might eventually be treatable with gene therapy, according to Salk scientists Inder Verma and Robert Marr. Their findings appeared in the *Proceedings of the National Academy of Sciences* in January.

In Alzheimer's disease protein fragments called amyloid-beta peptides 'silt up' the brain. A transporter molecule called apolipoprotein E (apoE) appears to be associated with the amount of amyloid in the brain, and whether you get Alzheimer's or not can depend on which version of the apoE gene you carry. People with the apoE4 gene are prone to late onset Alzheimer's. Conversely, the apoE2 gene appears to be protective against Alzheimer's. However, until the Salk research, the question remained: was apoE2 actively clearing amyloid, or was the 'protective' effect simply a consequence of not having the 'bad' version of the gene, i.e., apoE4?



Inder Verma

THE PROTECTIVE GENE

Verma and Marr, working with colleagues at Lilly Research Laboratories, infused the apoE genes into the brains of mice that were genetically engineered to develop Alzheimer's. They found that within 5 weeks to 3 months apoE2 reduced amyloid-beta deposits by 50 to 70%. By contrast, infusions of the apoE4 gene more than doubled the amyloid deposits. This demonstrated that the apoE2 gene was able to clear deposits, even in the presence of the naturally occurring 'bad' apoE gene.

"This study is scientifically interesting because it suggests that apoE2 is having an active, protective effect in Alzheimer's rather than just a passive role due to the lack of apoE4," said Robert Marr. "It also suggests the very real possibility of apoE2 as a therapy for Alzheimer's."

Doing the Math on the Visual System

Biologists often feel frustrated that they cannot explain their complicated world in neat mathematical terms, unlike their colleagues in physics or chemistry. Now Salk scientist Greg Lemke has come up with a rare exception: a set of mathematical equations that exactly describes how nerve cells (neurons) from the retina of the eye grow to the correct places in the brain.

Lemke's *Nature* paper in October, 2004 solved mathematically "probably the grandest, oldest problem in developmental neurobiology," as the researchers wrote in their report, which rapidly became among the most downloaded papers in neurobiology.

During development, neurons from the retina are wired to neurons in the brain in a pattern that precisely mirrors our picture of the outside world. This wiring process is controlled by molecular messengers on the cell surface called ephrin-As and their receptors, EphAs. Ephrin-As repel nerve fibres with EphAs, so neurons with least ephrin-A connect to neurons with most EphA. Thus neurons spread themselves evenly across a retinal 'gradient' of EphA.

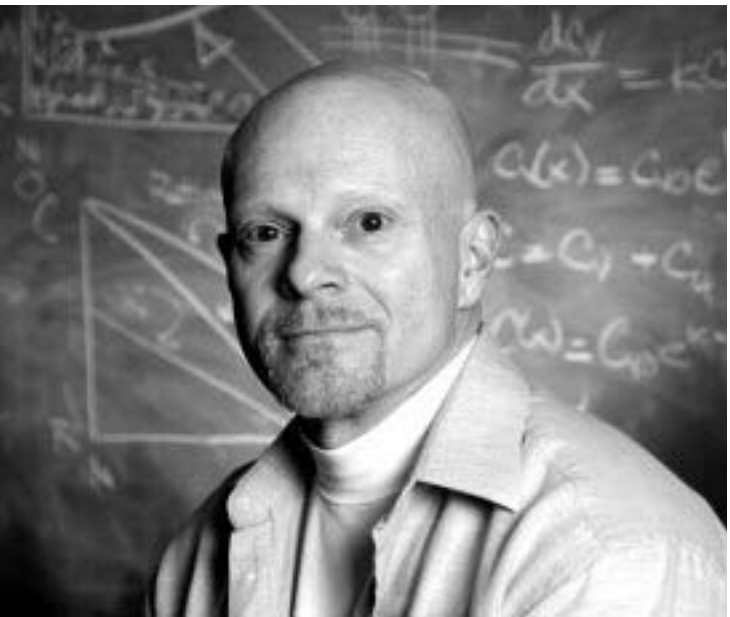
"IT WAS STUNNING"

How do the neurons know where they are in the gradient? In an earlier paper, Lemke and colleagues showed that neurons find their spot by comparing themselves to their neighbors. What matters is not the absolute, but the relative, difference in the amount of EphA that each neuron has on its outer surface.

"If you and I were two cells in the retina," explained Lemke, "and you had seven EphA receptors and I had 14 EphA receptors, what matters is not that I had seven more than you, but rather that I had twice as many as you."

Lemke and colleagues Michael Reber and Patrick Burrola have now come up with the mathematical equations that describe this 'relative signaling' process. They tested these equations by manipulating the EphA gradient in genetically engineered mice and found that the manipulated cell 'map' turned out to be exactly as per their mathematical predictions.

Greg Lemke



"It was stunning," said Lemke,"because there is almost no other example of this in biology where people have been able to measure the components well enough. Mapping of this sort occurs over and over in the body so understanding how these maps form is a very basic and a very old problem. Now we have real numbers on this."

Joseph P. Noel

Sascha du Lac

Prestigious HHMI appointments go to two Salk Institute researchers

■ Sascha du Lac and Joseph P. Noel, both basic research scientists at the Salk, were selected for the prestigious position of Howard Hughes Medical Institute (HHMI) investigator.

Du Lac focuses on how the brain learns to stabilize an image on the retina of the eye and compensate for head movement. This simpler form of motor learning provides du Lac with a model system to unravel the more complex cellular and molecular mechanisms in the brain that are modified by experience. A systems neuroscientist, du Lac hopes that her research will improve scientific understanding about how these critical mechanisms operate within the context of neural circuits to mediate adaptive changes in behavior.

In plants and microbes, the biochemist Noel searches for the roots of biological diversity at the chemical level. Through this research, he hopes to harness and alter the biosynthetic pathways needed to produce complex molecular scaffolds that will expedite the development of effective medicines.

The two Salk scientists are among the 10 California-based researchers selected as new HHMI investigators. With du Lac's and Noel's appointments, the Salk Institute's 57-member faculty will have seven scientists who are HHMI investigators. Du Lac and Noel are among 43 researchers nationwide newly designated as HHMI investigators. These 43 researchers increase the HHMI's total investigators nationwide to almost 350.

Their HHMI appointments will bring du Lac and Noel additional resources that will help expedite their basic research and enable them to move quickly and directly into promising new avenues.

"In the course of research, a scientist often bumps into an unexpected, puzzling finding," explained du Lac. "Pursing that finding can lead to a spectacular discovery."

"The HHMI funding will give us the latitude, the leeway, to follow new ideas and findings right away, and not set them aside until additional funding can be acquired," added Noel.

Such non-government funds and philanthropic donations enable Salk scientists to pursue the highly innovative research that accelerates the pace of scientific discovery and for which Salk scientists are known.

Du Lac, the institute's Hearst Endowment Associate Professor in Systems Neurobiology, gives credit to the Salk's highly collegial scientific environment for enabling her to develop tools for performing integrated analyses of motor learning and memory storage at the behavioral, circuit, cellular and molecular levels.

The HHMI biography about du Lac states, "Scientists who are knowledgeable about her research view du Lac as poised to make the links across levels of analysis to provide a plausible explanation, in terms of molecules, cells, and circuits, for one form of behavioral learning."

Noel's basic research studies in the Salk Institute's Jack Skirball Chemical Biology and Proteomics Laboratory, is unraveling the structure and function of the enzymes that plants and microbes use to produce three important classes of natural compounds, polyketides, terpenes and hybrid polyketide-terpene chemicals.

A Professor at the Salk, Noel seeks to understand the natural chemical factories plants and microbes use to produce a vast array of compounds that allow them to survive and prosper in the multitude of challenging ecosystems found all over the earth.

Such compounds already have played an important role as sources of new pharmaceutical drugs such as the anti-cancer drug Taxol.

THE PRESIDENT'S CLUB

The President's Club is the leadership giving program for the Salk's annual fund that each year raises $4 million in individual gifts, ranging from $1,000 to $1 million, to support talented young Salk Institute scientists' early steps into exciting new research territories. These contributions also support: University of California at San Diego graduate students' training in Salk labs; symposia and seminars that bring together scientists from Salk and neighboring research institutions to share information and ideas; and High School Science Days, Mobile Science Labs and other activities that foster in today's high school students the passion for science that may persuade them to become the next generation of scientists. In addition, thanks to gifts to the President's Club, Salk researchers can have access to the advanced equipment and core facilities essential for 21st century biological sciences.

We are grateful to all President's Club members and acknowledge the following donors for gifts during July 1, 2004 to March 18, 2005:

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Stuart Rubaloff endows new Research Discovery Fund

■ Salk supporter **Stuart Rubaloff** has set up a $1 million endowment fund through his estate. The Stuart Rubaloff Endowed Research Discovery Fund will support the studies of upcoming young researchers working on emerging areas of the biological sciences.

Explaining his support for the Salk, Mr Rubaloff said: "Here is an organization that is actually in the trenches of developing new concepts that may increase our lifespan, our quality of life. At Salk I was introduced to scientific ideas that I could barely comprehend but I knew I wanted to be part of it."

Mr. Rubaloff, a retired engineer, was especially struck by the importance of supporting young scientists as they begin their careers.

The endowment route appealed to him because, once the needs of his family had been met, "I want to be in charge of distributing my estate to where I think it should go," said Mr. Rubaloff. "Some people leave all their money to save animals. I would rather save human beings."

Rich Murphy (left) with Stuart Rubaloff

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Tony Hunter awarded Wolf Prize

Tony Hunter, the Salk Institute's American Cancer Society professor of molecular and cell biology, will be honored by the State of Israel with its highest award for achievements benefiting humankind.

Hunter, whose 1979 discovery of a cell signaling mechanism revolutionized basic research on cancer, will share the prestigious 2005 Wolf Prize in Medicine with Anthony Pawson of Mount Sinai Hospital, Toronto, Canada, and Alexander Levitzki of the Hebrew University of Jerusalem.

On Sunday, May 22, the President of the State of Israel, Mr. Moshe Katsav, will present the award to Hunter at a special ceremony at the Knesset (parliament).

The vaccine developed by Jonas Salk, M.D., and launched in 1955 has saved millions of children and adults from the crippling and often fatal disease, poliomyeltis. Five years later, Dr. Salk founded the institute that today bears his name.

Smithsonian exhibit celebrates 50 years of polio prevention

■ *Whatever Happened to Polio?* is the title of a new exhibit that will open to the public at Smithsonian's National Museum of American History in Washington, D.C., on April 12 to celebrate the 50th anniversary of the first safe, effective polio vaccine.

The exhibit, which will close later this year, is sponsored by the Salk Institute, March of Dimes, International Rotary Club, and the Smithsonian Institution.

"The celebration of Jonas Salk's contribution does not end with the vaccine," said Jerome Kohlberg, chairman of the Salk Institute's Board of Trustees.

"It continues on with the wondrous work at the Institute he founded."

"Thank you, Dr. Salk" celebration

■ On the morning of April 12, hundreds of Salk scientists, graduate students and staff will begin their day at the Institute by celebrating the 50th anniversary of the vaccine that has saved them — and millions of others — from becoming crippled or dying from poliomyelitis or polio.

The Salk Institute has named its celebration, "Thank you, Dr. Salk," because these words were written on the many hand-made signs posted in store windows throughout the United States in response to the dramatic April 12, 1955 announcement in Michigan that the polio vaccine developed by Jonas E. Salk, M.D., was safe and effective.

Virtually overnight, Jonas Salk became an international celebrity. He leveraged his fame to assemble some of the greatest minds in science to found in 1960 the basic research institute that today bears his name.

In 1965, just 10 years after Salk developed the polio vaccine, the Institute's lab facility — designed by the famous architect Louis Kahn — opened its doors.

Salk talks DNA at the Fleet

■ On March 26, the Salk's Mobile Science Lab volunteers participated in *DNA Day* at San Diego's Reuben H. Fleet Science Center, which provides science education for the public through workshops, IMAX movies, and exhibits. The event was part of the Fleet's ongoing weekend series of talks.
A group of Salk researchers and scientists from other San Diego institutions discussed how studying DNA helps to diagnose illnesses, offers hope of more effective disease treatments, and allows us to identify and prosecute criminals.

The Salk's Mobile Science Lab was originally developed to teach middle school children about science and was featured in the February 9th edition of the *San Diego Union*. The mobile lab expanded its reach last February when it formally partnered with the Fleet to improve public understanding about science. The Salk Mobile Science Lab visits the center three times a year.

Salk inspires Price Fellows students

■ A group of 40 San Diego high school students visited the Salk on January 22 for a behind the scenes view of the Institute. During their trip, students were treated to talks by Salk staff members who discussed their career paths and current positions, and were provided with an architectural tour of the facility. Students also toured the Institute's Molecular Neurobiology Lab with Timothy Hendricks, the Molecular and Cell Biology Lab with Gina Yanochko, and the Systems Neurobiology Lab in the company of Vivian Ciaramitaro.

The students were participating in the Aaron Price Fellows Program, a charity that strives to teach teenagers about the relevance and significance of various local government institutions. Students in the program have the opportunity to observe the inner workings of a diverse array of organizations in the San Diego area. The Salk has hosted Price Fellows students annually since 1999 to help them learn about and appreciate the Institute and its research.

Above: Postdoctoral fellow Gina Yanochko, shown while preparing growth media to nurture cells in lab cultures, provided the high school students with a tour of the Molecular Cell and Biology Lab.

Tony Basurto raises thousands for WalkAmerica

■ The WalkAmerica kickoff luncheon last month honored Tony Basurto, the senior stockroom attendant in the Salk's Purchasing Department, for raising $10,000 for the March of Dimes at WalkAmerica 2004. Basurto also independently organized a post-walk raffle whose proceeds accounted for $2,000 of his sizeable March of Dimes contribution. He was the first-ranked walker for the San Diego-Imperial Division and came in 15th for the entire state of California. His efforts will help the March of Dimes continue its support of families affected by birth defects, and its programs to educate the public about healthy pregnancy and raising healthy children.

Basurto participated in WalkAmerica for the first time in 2003 and raised $3,200. Following his success in 2004, he says that each year he aims to surpass his previous fundraising goal. To honor his efforts, March of Dimes gave him a $400 travel voucher and presented him with a special award at last month's luncheon.

Below: Tony Basurto, honored by March of Dimes

New Vice President Communications Appointed

The Institute's new Vice President of Communications is **Cathy Yarbrough**, whose 30-year career has included leadership positions at Novartis Pharmaceuticals, NIH's Human Genome Project, national American Heart Association, and Emory University's Yerkes National Primate Research Center. Before joining Salk in January, she was Vice President of Communications and Public Affairs at Rockefeller University in New York City.

"In Broadway terminology, the Salk is a 'triple threat'," said Yarbrough. "Of course, Salk is not a performer who can sing, dance and act. Instead it's that rare research institution with the triple strengths of a stellar faculty, who are among the best and brightest in biological sciences; a president and senior administrative team who want to provide the resources that will help the Institute's talented scientists do their work; and an enviable research environment that nurtures everyone's creativity and dedication. I am very proud to be here."

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Staffing Announcements

Elizabeth Powell, a San Diego attorney, has joined Institute Relations as Major Gifts/Planned Giving Officer. "These kinds of gifts make an impact that will last for generations, providing the donor a wonderful sense of helping a greater good," said Powell. "Being involved with this is very rewarding to me personally."

Also new to the Salk is Senior Major Gifts Officer **Pam Becker**, following five years as a lobbyist for the American Society of Mechanical Engineers and seven years as Director of Development for the College of Engineering, San Diego State University. "I was attracted to the Salk because of its fabulous reputation for doing good things and doing them well," said Becker.

Eowyn Bates has been promoted to Development Officer after two years with the Institute's Development Department. Bates joined the Salk after a varied career in the not-for-profit sector. "I'm looking forward to further developing our relationship with our donors and showcasing the outstanding basic science that the faculty does here," she said.

Plant Biotechnology: Unconscionable that People Must Suffer from Hunger and Malnutrition

Joanne Chory's important work showing how hormones regulate plant growth (see page 1) brings to mind one of the unfortunate realities of today's revolution in biological research: DNA-based molecular biology has been invaluable in helping us understand human diseases, but the technology has not yet realized its exciting potential to resolve starvation and malnutrition, the leading causes of death worldwide. Overwhelming evidence suggests that gene transfer can be used safely and economically to improve the quality and volume of the world's food supply, and yet millions of malnourished people are not benefiting from this technology because of fear, misinformation, and politics.

The principle behind the genetic engineering of plants is similar to cross breeding, which farmers and scientists have been doing safely for centuries. In cross breeding, hundreds of unidentified genes are exchanged from one plant to another, and the resulting hybrids are grown for several generations to obtain the traits being sought. Genetic engineering simply accelerates and improves this process by allowing scientists to transfer single genes of known function, one at a time, into recipient plants, thereby allowing selective improvements to plant species.

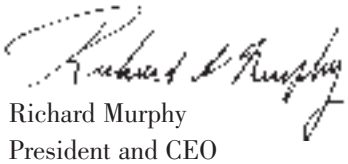
A case in point is "Golden Rice," a strain engineered by Swiss scientist Ingo Potrykus to help solve the problem of vitamin A deficiency in underdeveloped countries. According to Potrykus, 400 million people who rely on rice as their main dietary energy source suffer from vitamin A deficiency, 6000 of these die daily, mostly children, and 500,000 go blind annually.

To solve the problem, Potrykus and his colleagues introduced into rice a series of genes that result in the production of β carotene, which is converted by the body to vitamin A. Golden Rice can be made available free of charge to individuals running small farms since patent rights have been waived. A single seed in the hands of an experienced farmer could result in 20,000 tons of product within two years without the use of pesticides or additional agrochemicals. Furthermore, seeds from one crop could be used to grow the next, making the crop self-renewing. Yet, despite five years of successful field safety testing, Golden Rice is still not available to the people who need it. Governments have opposed its distribution for reasons ranging from misinformation, fear and public pressure, to apathy. The assumption, unproven by facts, is that the risks of distributing Golden Rice and other genetically engineered foods outweigh the benefits.

The American experience proves otherwise. In 2004, genetically engineered varieties accounted for 85% of the US soybean crop, 45% of the corn crop, and 76% of cotton. Currently available or on their way to being produced are grains, fruits, and vegetables that are environmentally friendly by being pesticide resistant or herbicide tolerant, edible vaccines, plants that detoxify polluted soils or produce complex chemicals, and plants that are salt tolerant to grow on the 30% of the worlds irrigated lands that today are unusable.

When recombinant DNA technology was first launched in the mid-1970s, a public outcry ensued as to its dangers. Remember Cambridge, Massachusetts Mayor Al Vellucci's point that "God knows what's going to crawl out of the laboratories" if biotechnology-based research were carried out at Harvard? Scientists wisely took control of the controversy by recommending safe methods of carrying out recombinant DNA research, and 10 years later, when it became clear that the research could be done safely, the self-imposed restrictions were lifted.

Scientists need to go on the offensive again to convince world leaders that genetic engineering of crops can be used to improve the health of people around the world. Scientists know that the technology can be made attractive for investments, accessible to the people who need it, and safe. They also know that the benefits of plant biotechnology far outweigh the risks and that allowing innocent people to suffer from hunger and malnutrition, when the technology is available to help them, is unconscionable.



Richard Murphy
President and CEO

CELEBRATING 40 YEARS

INSIDE SALK

In 1960, just five years after developing the first safe, effective vaccine against polio, Jonas B. Salk, M.D., founded the institute that today bears his name. Home to 11 Nobel laureates since its founding, the Salk Institute for Biological Studies is a world leader in basic research on the biological principles governing life at all levels, from the individual cell to an entire population. For more information: www.salk.edu.

1964 construction at the Salk Institute

Calendar

APRIL 12
50th Anniversary of Polio Vaccine
(events at Smithsonian Institution, Washington, D.C., and Salk Institute, La Jolla)

APRIL 16
Salk Institute High School Science Day
Salk Institute, La Jolla

MAY 11–13
Tax Seminar
Salk Institute, La Jolla

AUGUST 27
Symphony at Salk 2005
Salk Institute, La Jolla

Please note: the above represents a selected list of events. For additional information about these and other Salk events, please contact Institute Relations at 858.453.4100 ext. 1200.

SALK INSTITUTE
FOR BIOLOGICAL STUDIES

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

MAILING ADDRESS
Post Office Box 85800
San Diego, California 92186-5800

Telephone: 858.453.4100
Fax: 858.552.8285
www.salk.edu

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