InsideSalk

Where cures begin.

THE SALK INSTITUTE FOR BIOLOGICAL STUDIES

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At the Core of Salk's New Training Facility

June 2008
Inside Salk

Suzanne Bourgeois Chronicles the Early Days

Symphony at Salk

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ON THE COVER

Lab Manager Margaret Lutz at work in the new stem cell core facility, which serves as a training center for young scientists at Salk and a shared space where research on human embryonic stem cells is conducted.

Two Salk Researchers Named HHMI Investigators

RESEARCHERS SAMUEL L. PFAFF and **Andrew Dillin** have been selected as new Howard Hughes Medical Institute (HHMI) investigators, the prestigious organization formally announced May 27.

Pfaff, a professor in the Gene Expression Laboratory, is interested in discovering how nerve cells form and correctly wire up, focusing on the fetal development of the spinal cord. Of special interest to him is how motor neurons develop and make connections between the spinal cord and muscles in the body, since these connections are necessary for all body movements.

Spinal cord injuries lead to paralysis because motor neuron function is disrupted. Degenerative diseases such as ALS (Lou Gehrig's disease), spinal muscle atrophy and post-polio syndrome result from the loss of motor neurons.

Dillin, an associate professor in the Molecular and Cell Biology Laboratory, studies the tiny roundworm *Ceanorhabditis* elegans to understand the process of aging by looking at the hormone most widely recognized for its role in diabetes: insulin. The insulin-signaling pathway in worms is not only almost identical to that found in humans, but he discovered how the insulin pathway controls aging without disrupting other physiological processes, such as reproduction and development.

Samuel L. Pfaff

Andrew Dillin

Dillin recently identified a gene that specifically links calorie restriction with prolonged life span. A natural extension of his work on aging is to understand the link between the aging process and age-related diseases, such as Alzheimer's, Parkinson's and cancer.

Clodagh O'Shea

Vicki Lundblad Receives 2008 Pearl Meister Greengard Prize

THE FIFTH ANNUAL PEARL MEISTER GREENGARD PRIZE, an international award to recognize outstanding women scientists, has been awarded to Salk professor **Vicki Lundblad** for her groundbreaking work in telomere biology. She will share the prize with Salk Nonresident Fellow **Elizabeth H. Blackburn,** Ph.D., a professor at the University of California in San Francisco, and Carol W. Greider, Ph.D., a professor at Johns Hopkins University School of Medicine.

Established by Nobel Laureate Paul Greengard, a professor at Rockefeller University, and his wife, sculptor Ursula von Rydingsvard, the prize honors women scientists whose achievements in biomedical research merit international recognition.

Vicki Lundblad

Clodagh O'Shea Receives 2008 Beckman Young Investigator Award

SALK ASSISTANT PROFESSOR Clodagh O'Shea has been named a recipient of the 2008 Beckman Young Investigator award for her work in cancer research. One of her lab's interests lies in developing the next generation of viral vectors and replicating lytic cancer therapies.

O'Shea is also the recipient of the 2007 Young Investigator's Award in Gene Therapy for Cancer. That award was established in 1986 by the Alliance for Cancer Gene Therapy and supports innovative efforts aimed at furthering the development of gene therapy approaches for the treatment of cancer.

Thomas Albright Elected to National Academy of Sciences

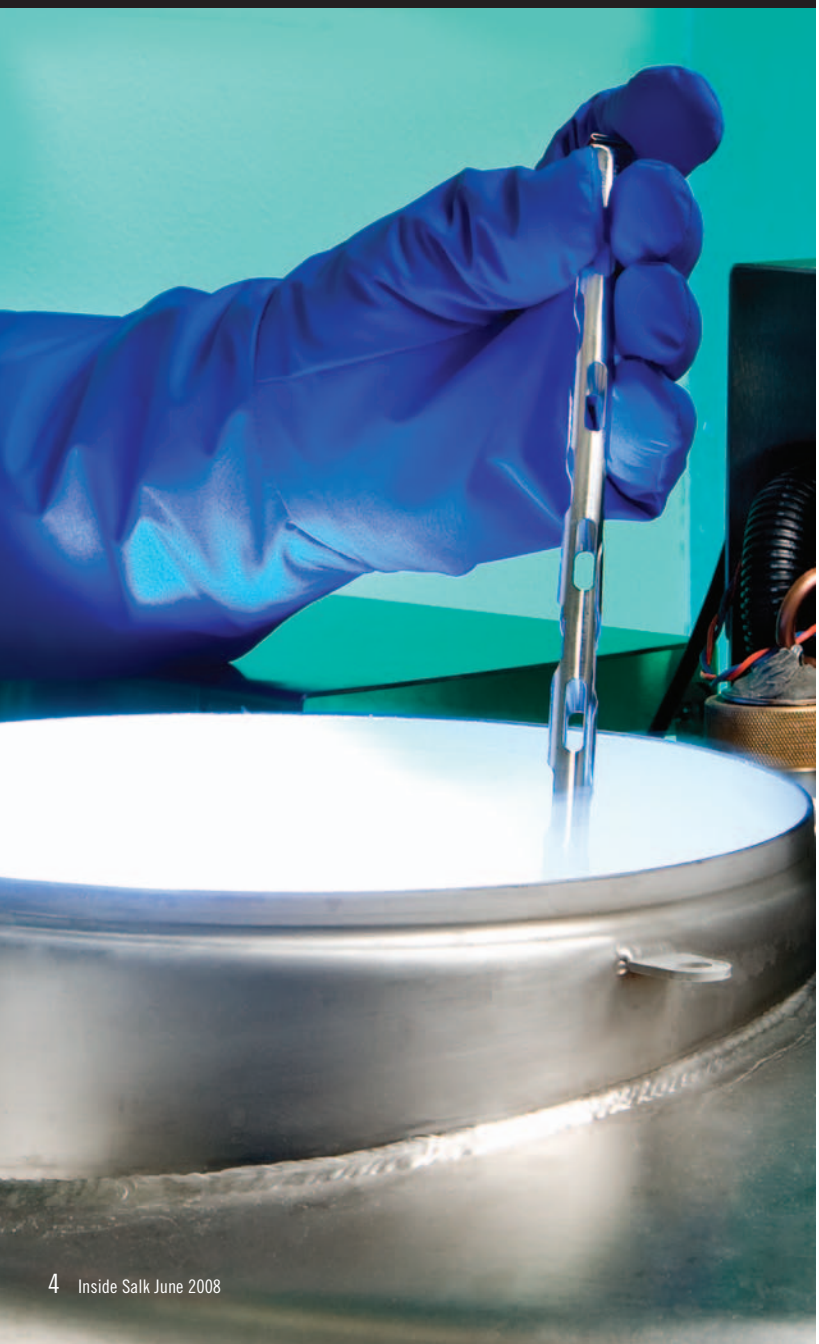
THOMAS ALBRIGHT, PROFESSOR AND director of the Vision Center Laboratory, has been elected a member of the National Academy of Sciences. Election to the Academy recognizes distinguished and continuing achievements in original research and is considered one of the highest honors accorded U.S. scientists.

Thomas Albright

Throughout his career, Albright has sought new avenues to identify how sensory signals in the brain become "integrated" to form neuronal representations of the objects that populate our visual environment and form our conscious experiences of the world. Albright provided the first systematic evidence that humans' perception of motion does not depend on the physical characteristics such as brightness, color or texture of the object that is moving, a feature known as "form cue invariance." He found that single neurons in a brain area specialized for processing motion exhibited robust form-cue invariance, a discovery that came as a surprise at the time.

Stem Cell Core Facility Opens

THE SMELL OF FRESH PAINT and newly delivered furniture still permeated the air as Wenyuan Wang and Qian Wang arrived to feed their human embryonic stem cells (hESC) under the watchful eyes of staff scientist Travis Berggren.



Anand Srivastava

A day earlier, the Wangs — who are not related — had pulled a vial of frozen hESCs from a storage tank filled with liquid nitrogen and placed them in a Petri dish. Bathed in culture medium enriched with nutrients and kept at a cozy 37 degree Celsius (98.6 degrees Fahrenheit), the cells had settled overnight and now were clamoring for fresh nutrients.

"I am not familiar with stem cells and when I look at them through the microscope it is difficult for me to tell whether they are happy or not," says Qian Wang, who mostly works with bacteria and baker's yeast. "It is important to have somebody to guide and teach us until we have enough experience ourselves."

Both Qian and Wenyuan are among the first group of young scientists being trained by Berggren to grow hESC at the Institute's new stem cell core facility. The transformation of the former storage space into a modern stem cell laboratory was made possible by a $2.3 million grant awarded to Salk last summer by the California Institute for Regenerative Medicine (CIRM).

But the newly minted facility is more than just a training center. The 2,000 square-foot lab also serves as shared space for Salk scientists to conduct research on hESCs without the restrictions placed on federally funded stem cell research.

"It is a complete research facility much like the other cores here at Salk," says Berggren, who heads the stem cell core with lab manager Margaret Lutz (see related story on page 7). "There are a limited number of stem cell lines available for research through federal funds, but this facility is completely free of federal funding.

"We now have the space, resources and expertise for Salk researchers to not only learn how to do stem cell culture, but to also carry out experiments with human embryonic stem cells."

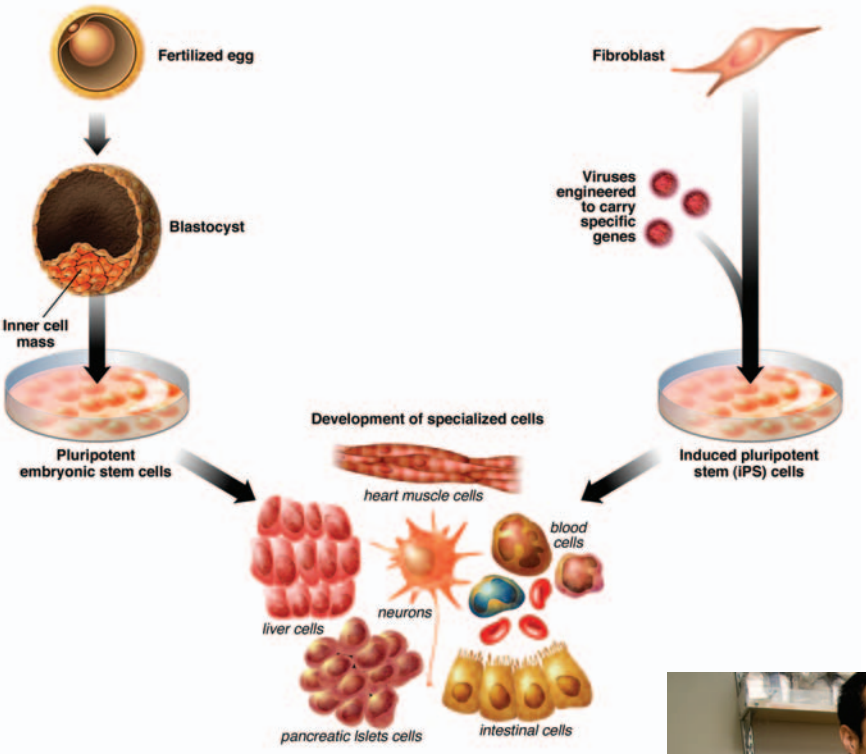
Program Project Director Inder Verma, professor in the Laboratory of Genetics, submitted the grant proposal and planned the facility's layout with Garry Van Gerpen, vice president of Scientific Services.

"When we started planning this facility, about one-third of the Salk faculty expressed interest in working with human stem cells," says Verma. "We envisioned that it would serve as a primer for people to get interested and that it would be a place where they could learn how to grow and manipulate stem cells, and from there they could move forward to do what they like to do."

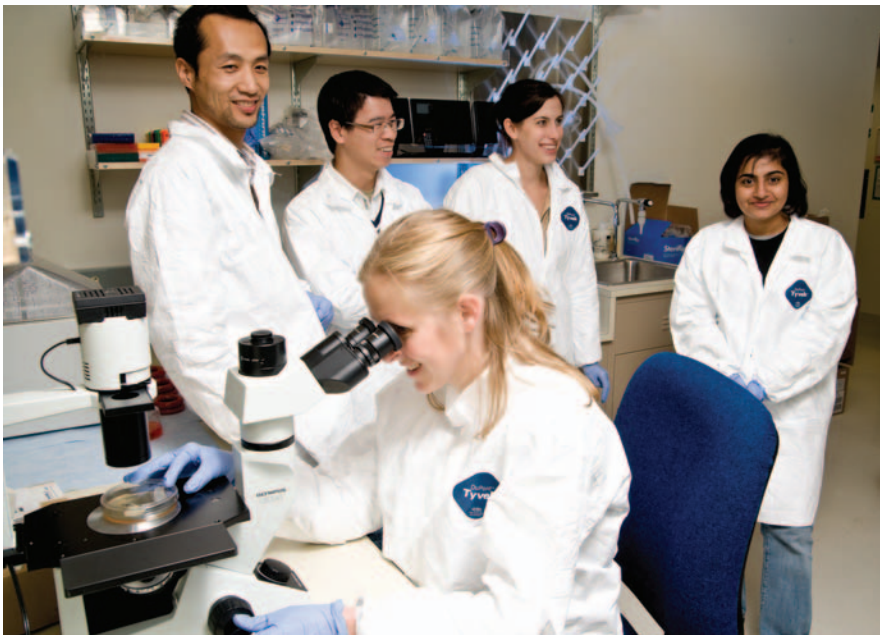
An important aspect of the new facility is the ability it provides to produce lentiviral vectors to deliver genes into cells. Originally developed for gene therapeutic purposes by Verma and his team, the technology will play a central role in the reprogramming of adult human cells (such as skin cells) back into so-called induced pluripotent stem (iPS) cells that appear to mimic hESCs in terms of appearance and behavior.

Its Doors to Salk Researchers

Historically, hESCs have been derived from the inner cell mass of mammalian blastocysts (left). However, recent studies show that human pluripotent stem cells can also be created by using viruses engineered to carry specific genes to reprogram adult human cells (such as skin cells) back into induced pluripotent stem (iPS) cells (right). Illustration by Jamie Simon.



> "We now have the space, resources and expertise for Salk researchers to not only learn how to do stem cell culture, but to also carry out experiments with human embryonic stem cells."
>
> – TRAVIS BERGGREN



Seated at microscope: Kelly Kamp.

Standing, from left: Wenyuan Wang, Qian "Frank" Wang, Margaret Lutz, and Sri Balakrishnan.

A simple skin biopsy can serve as starting material for the generation of iPS cells, raising the hope that one day reprogramming might fulfill the promise of patient specific hESCs in research and medicine without having to negotiate the ethical minefield of working with human eggs and early embryos.

Historically, hESCs have been derived from the inner cell mass of mammalian blastocysts – the balls of cells that develop after fertilization and go on to form a developing embryo.

Since the initial reports of iPS cells caused a media stir last November, several independent studies have confirmed that reprogramming is a valid method for generating human pluripotent stem cells from adult cells.

To turn regular skin cells into versatile stem cells, researchers use viral vectors to slip inside the genes for master regulators Oct3/4 and SOX2 with varying other genes to help the process along. After three to four weeks, a small number of cells will transmogrify into cells that look and act like the pluripotent human embryonic stem cells.

"It won't abolish the need to study human embryonic stem cells right away," cautions Berggren. "A lot of the technical details for reprogramming still haven't been worked out and researchers will need to perform a lot of experiments side by side and directly compare hESCs and iPS cells.

"But with reprogramming looking so promising, this is really the direction we want to move in for the future," Berggren says. "We are planning to establish the methods here at Salk and individual faculty members then will be able to take it wherever they need to."

Stem Cell Research at Salk

There are currently 14 principle investigators who are devoting part of their research to stem cells at the Institute. Here are brief summaries of what each is working to accomplish in their labs.

Juan Carlos Izpisúa Belmonte studies the reprogramming process in murine and human germ stem cells, which spontaneously transform into pluripotent embryonic stem cell-like cells when placed in lab dishes. Since these cells don't require any outside help to override internal growth controls, they are less likely to start dividing uncontrollably.

Senyon Choe tries to identify therapeutically useful messenger molecules involved in hESC self-renewal and maturation to realize the full clinical potential of stem cell therapy.

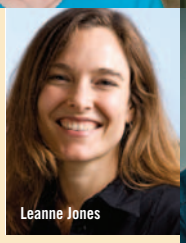
Beverly Emerson suggests that genes are arranged in "neighborhoods" that are surrounded by "fences" that protect the activity in one neighborhood from spilling over into adjacent territory. She wants to identify the fence(s) that border genes that are important to maintain stem cells in their most plastic state.


Senyon Choe


Juan Carlos Izpisúa Belmonte


Beverly Emerson


Kathy Jones


Leanne Jones


Fred H. Gage

Fred H. Gage and lab members have developed protocols that stimulate hESCs to develop into neural stem cells that can then develop into dopamine neurons or cholinergic motor neurons. He will use these cells to explore the cellular and molecular causes for the dysfunction and death of dopaminergic or cholinergic neurons in Parkinson's disease or Amyolateral Sclerosis (ALS), respectively.

Kathy Jones studies how transcription elongation and histone methylation factors function to promote stem cell proliferation, which will help future efforts to direct these cells towards specific developmental fates.

Leanne Jones seeks to uncover the mechanisms that regulate the process of de-differentiation, or reprogramming, to compare these to the mechanisms that endow stem cells with their ability to self-renew. Reprogramming of specialized cells could provide a "reservoir" of cells that could act to replace stem cells lost due to wounding or aging.

Jan Karlseder is interested in how telomeres, the protective "caps" at the end of all 46 human chromosomes, are maintained in stem cells and how this mechanism is disabled once stem cells differentiate.

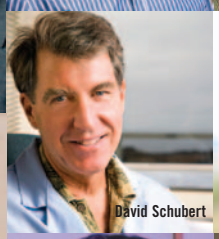
Kuo-Fen Lee investigates the role of stem cells in neurodegenerative diseases. He uses neurons derived from human or mouse embryonic and neural stem cells to study genetic and epigenetic mechanisms underlying the formation of synapses, the connections between nerve cells.

Satchin Panda's work on circadian rhythms has led him to the question of how soon the internal circadian clock starts ticking in developing embryos. He will start his search for cells ticking in unison in stem cells.


Satchin Panda


Samuel L. Pfaff

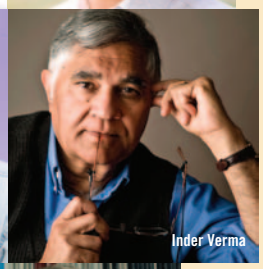
Samuel L. Pfaff wants to discover the molecular signals that coax stem cells to develop into motor neurons, which control our ability to walk, talk, breath or swallow. Over the long term, he hopes to identify small molecule drugs that can help the process along.


David Schubert

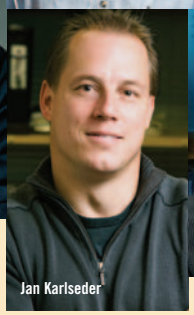

Lei Wang

David Schubert uses human neuronal stem cells to identify both the molecules and the molecular pathways that lead to the differentiation and growth inhibition of human stem cells. The latter is important to prevent embryonic stem cells from turning cancerous, a lethal property they all share.


Kuo-Fen Lee


Inder Verma

Inder Verma's current focus is the reprogramming of human skin fibroblasts into hepatic stem cells and their subsequent differentiation into liver cells.


Jan Karlseder


Wylie Vale

Lei Wang plans to introduce non-natural amino acids to identify unknown factors that govern the development of stem cells into dopamine neurons. Uncovering the mechanisms that regulate the differentiation of embryonic stem cells into dopamine neurons may yield new drug targets and inspire novel preventative or therapeutic strategies for Parkinson's disease.

Wylie Vale and his colleague Peter Gray focus on cripto, the founding member of a small family of vertebrate signaling proteins that function in development. Cripto is highly expressed in hESCs, where it appears to act as an essential cofactor for the maintenance and directed differentiation of these cells.

Travis Berggren Returns to Salk to Head Its Stem Cell Core Facility

HUMAN EMBRYONIC STEM CELLS – FAMED FOR THEIR capability to transform themselves into any type of specialized cell – are a prissy bunch, as any scientist who has tried to grow them in the lab can tell you. The slightest offense causes them to disavow their almighty abilities, or pluripotency in science lingo, and start differentiating into whatever cell type they feel like.

Travis Berggren knows this all too well. He spent five years analyzing the needs of temperamental human embryonic stem cells at WiCell, a private, non-profit stem cell institute headed by scientific director James Thomson after the University of Wisconsin researcher created the first human embryonic stem cell lines nearly 10 years ago.

"Pluripotent stem cells are balanced on a pinnacle and it doesn't take much to have them roll off on either side," says Berggren, Salk's new staff scientist who joined the Institute in September to lead the new stem cell core facility.

Just like any other cell type, stem cells are grown in plastic laboratory culture dishes that contain a nutrient-rich broth known as culture medium – with one important difference: The surface of the dish is typically first coated with so-called feeder cells that provide additional nutrients and signaling factors for the stem cells.

For some experiments and therapeutic applications, however, stem cells need to be grown without the company of feeder cells, which can skew results or contaminate the stem cell sample. Berggren would later help solve this problem with a key discovery at WiCell.

A Different Breed of Cells

Berggren had just finished his doctorate degree in Chemistry at the University of Wisconsin when WiCell was looking for somebody who could set up a mass spectrometry proteomics program for human embryonic stem cells – his area of expertise. Mass spectrometry is used to identify and, increasingly, to precisely quantify thousands of proteins from complex samples.

"In the beginning I naively assumed that the stem cell work would be done by others, but I quickly realized that if you need things to get done, you needed to do it yourself," Berggren remembers.

But that was easier said then done. While mouse stem cells had been around for two decades and the technical details had been all worked out, human embryonic stem cells turned out to be a different breed altogether.

"The defined factors that allowed mouse stem cells to grow in culture didn't work for human cells," says Berggren. "And, somewhat ironically, the feeder cells that are used to grow mouse embryonic stem cells support both types of cells although they signal through different pathways."

So, the young stem cell researcher started by identifying the signal molecules from feeder cells that are directly involved in allowing human embryonic stem cells to grow. Aided by this research, WiCell researchers successfully developed the first chemically defined media for human embryonic stem cells. Other scientists have since developed specially formulated culture media that allow them to grow stem cells without the support provided by non-stem cells.

"While removing a lot of biological variability and inconsistencies, growing cells without feeder cells makes it a lot more challenging.

Travis Berggren

But I have a lot of experience and I am looking forward to establishing this expertise at the Salk," says Berggren.

"On behalf of the Institute's Stem Cell Committee, which includes Salk researchers Fred H. Gage, Chris Kintner, Leanne Jones, Inder Verma and Sam Pfaff, we are delighted to have Travis on board to share his expertise in stem cells so that all of our scientists can take this knowledge into new directions in research," says Juan Carlos Izpisúa Belmonte, chair of the committee.

A San Diego native, Berggren is no stranger to the Institute. After finishing his undergraduate studies at UCSD and a short stint as a commercial fisherman, he worked in professor Wylie Vale's lab at Salk.

"Originally, I wanted to do synthetic organic chemistry but it sounded better on paper and I was glad to get a chance to work in a lab with a biological focus," says Berggren with a laugh.

For his graduate studies, he exchanged the eternal sunshine of Southern California for icy winters along the shores of lake Michigan. "I was just amazed how much your face can hurt," he says, "but the novelty factor wore off quickly and I am very happy to be back."

Remembering Dr. Leslie Orgel (1927-2007)

IN A WORLD OF INTELLECTUALS AND SCIENTIFIC luminaries, **Leslie Orgel** was revered for his ability to reason. He was also admired for his strength of character, his dedication to truth and fairness.

His closest friends and colleagues say they could always turn to the 43-year veteran of Salk's faculty for advice. He had a rare talent for measuring the details of an abstract problem, and he was not afraid to be honest.

"Leslie was not only a friend but a mentor to me," says Inder Verma, a professor in the Salk Laboratory of Genetics, who first met Orgel when he came to the Institute as a research fellow when he was 24 years old. "Leslie was a gentleman first. He did not seek fame but was always in the background. He was totally dependable and we all admired, revered, and respected him with total trust for his judgment."

Gerald Joyce, a professor who teaches and conducts research at The Scripps Research Institute, recalls what he learned while working as a graduate student with Orgel at Salk.

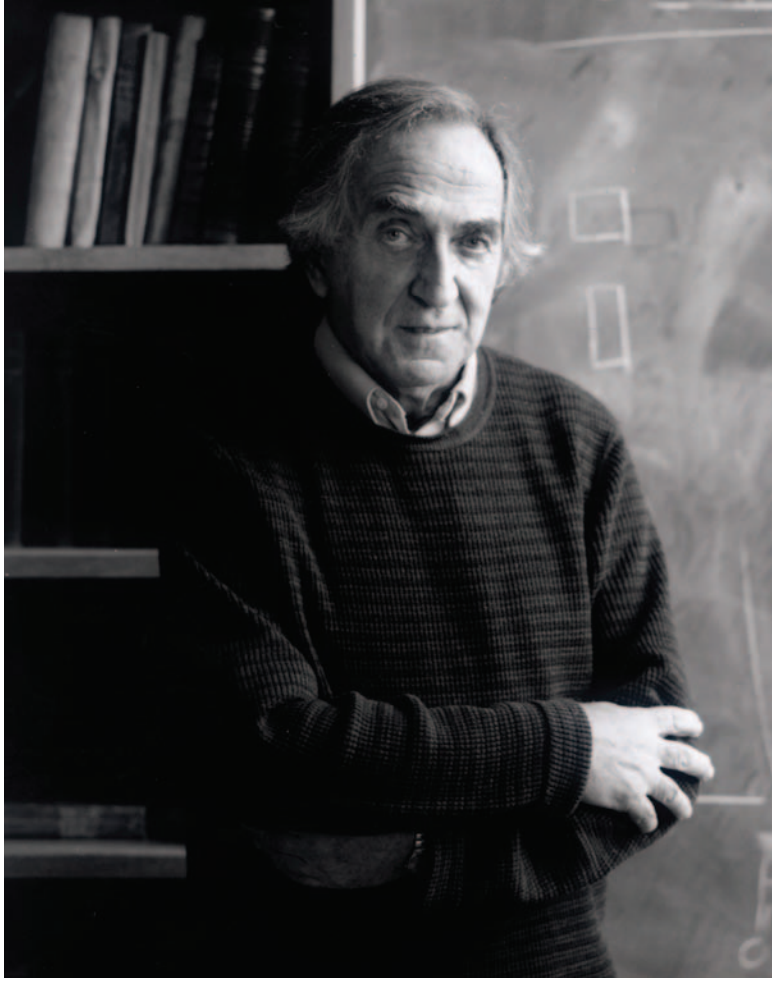
"Sloppy thinking just wasn't allowed in his lab," Joyce says. "He was never caustic or mean, but if you said something that was incorrect, he would say, 'With all due respect…' and then he'd explain exactly why you were wrong. That can be tough for the ego, but once you've been trained like that, it's a whole new way of seeing the world."

Orgel was born into a merchant family in London in 1927. The elder of two children, he earned his bachelor's and doctorate degrees in Chemistry at Oxford University. In the wake of James Watson and Francis Crick's postulation of the double-helical structure of DNA, he went to the California Institute of Technology in 1953 for a research fellowship and began actively taking part in discussions and working groups on the fundamental molecules of life and their origins.

Orgel returned to England in 1955 to continue his work in inorganic chemistry at Cambridge University, but the intellectual challenge that had taken root in California stayed with him. Switching career paths, even within the encompassing field of chemistry, was difficult to do in England so he accepted an invitation to join the founding faculty at the Salk Institute in 1964. Orgel built the Institute's Chemical Evolution Laboratory and remained at its helm for the rest of his career.

At the memorial service following his death from pancreatic cancer last October, fellow researchers and friends celebrated his long list of achievements, which include election to the Royal Society in the United Kingdom and the National Academy of Sciences in the U.S.; a set of simple statements about evolution that are known as "Orgel's Rules," which have been widely accepted as axioms by the scientific community; and collaboration with NASA on the Viking Mars Lander Program and projects related to the search for life on other planets.

They also recalled the parties he and his wife, Alice, an allergist, hosted at their house where they shared fine food and wine and his love and collection of tribal, hand-woven Oriental rugs, which he researched and could discuss in great detail.



> "Leslie was a gentleman first. He did not seek fame but was always in the background. He was totally dependable and we all admired, revered, and respected him with total trust for his judgment."
>
> – INDER VERMA

Orgel remained active in his research until the end. His final scientific paper, submitted posthumously by Joyce, appeared in the January 2008 issue of *PLoS Biology,* published by the Public Library of Science, in which he discusses the possibility of spontaneously generated metabolic cycles in the prebiotic world without the framework of genetics. In Orgel's honor, the Salk Institute has inaugurated The Leslie Orgel Memorial Lecture, the first of which was given in February.

Salk Professor Chronicles the Institute's Early Days

THE STORY OF JONAS SALK AND HIS RACE AGAINST polio has been told and retold many times. But when a flood of new books hit the shelves in 2005 to celebrate the 50th anniversary of the Salk polio vaccine, **Suzanne Bourgeois** was struck by something they all had in common.

"All these books said little or nothing about the Salk Institute and left one wondering what had happened to Jonas Salk subsequently," she says.

"Jonas Salk should be recognized for two major achievements: One is the polio vaccine and the other is the Salk Institute," says Bourgeois, a professor and founder of the Regulatory Biology Laboratory, whose own life history is inseparably entwined with the Institute and reaches back to a time when the Salk Institute was a mere dream in the minds of a handful of scientists.

When it became clear to her that the Salk Institute's history was being overlooked, Bourgeois decided to tell the story that had never been told. Drawing from a unique combination of personal experience, painstaking research and a treasure trove of diaries, she is in the midst of writing a book about the extraordinary events and people that created the Salk Institute.

She has been fascinated with its history since the beginning – keeping pamphlets, booklets and a diary since her mid-20s. "I think I'm probably the only one who has daily records of what happened," she says.

A native of Belgium, Bourgeois went to Paris in 1961 to work in Jacques Monod's laboratory at the Pasteur Institute. Melvin Cohn, a professor at Stanford University and his friend Edwin Lennox, a professor at New York University, arrived in Monod's lab around the same time. Bourgeois recalls Ed and Mel talking a lot about "that mysterious institute that Jonas Salk was planning to build in La Jolla."

Over time, the idea of the Institute evolved and took shape. Salk enlisted a remarkable group of people for the Board of Trustees, with Warren Weaver, who in 1938 had coined the term "molecular biology," at the helm. In addition to Salk, Cohn, Lennox, Renato Dulbecco, a virologist at CalTech, and Jacob Bronowski, a mathematician, signed on as resident fellows. Monod, Francis Crick, who worked in Cambridge at the time, and Leo Szilard, the physicist who had conceived the nuclear chain reaction, took on an advisory role as non-resident fellows.

"What people may not realize is that the first faculty meetings for the Salk Institute were held at the Pasteur Institute in Paris," says Bourgeois. "That's where the founding members discussed what kind of institute they envisioned."

But the person who made the new institute a reality was Basil O'Connor, the founding president of the National Foundation for Infantile Paralysis, which later became known as the March of Dimes. O'Connor had supported the development of the polio vaccine; now he encouraged Salk's new dream and provided the financial foundation for the Institute. His name is inscribed in the stairs that lead up to the Institute's central courtyard.

Construction began in 1962 on land donated by the City of San Diego. The following year, Suzanne and Mel got married and along with the other resident fellows, set up their laboratories in temporary buildings, wooden structures which they lovingly called "the barracks." They moved into the permanent facility in 1966, and almost half a century later, the temporary buildings still house laboratories.

For the past two years, Bourgeois has dedicated most of her time unearthing information that could shine light on the beginnings of the Institute. She's combed through the papers of Szilard and Crick at the UCSD library and was granted permission by Salk's sons to peruse their father's documents.

"I've known the sons of Jonas Salk since they were teenagers and they have been very generous and supportive," she says. "I've also poked around the entire building, the pipe spaces, basements, off-site storage facilities, everywhere."

At one point during her search, she discovered several filing cabinets, some of which were marked "trash." After taking a closer look, she realized she had struck gold. Filed away in the old cabinets were Salk Institute's early archives, which she saved from nearly being destroyed.

Suzanne Bourgeois

"It's a great source of information that is available nowhere else," she says. "I've known everybody involved and it's essential to have this documented chronicle and the view of an insider. It's important to do this while we still have a chance," says Bourgeois.

Roger Guillemin, interim president of the Salk Institute, agrees: "The enormous commitment of time and research combined with her unique perspective as one of the last surviving witnesses assures that Suzanne's personal account will provide a fascinating insight into the history of the Institute from the very beginning."

Bourgeois is working by herself and organizing the vast amount of information she gathered takes time, though. "It's like a huge puzzle and now I have to put all these pieces together," she says.

Researchers Develop Algorithms to Make Sense of and Mimic the Brain

IT'S 3:30 P.M. ON A WEEKDAY AFTERNOON AND MEMBERS of the Salk's Computational Neurobiology Laboratory (CNL) are starting to migrate toward their daily meeting place.

The area has a freshwater fish tank, two long sofas arranged in an L and a round table spread with crackers, chocolate covered almonds and hot tea for everyone.

It's a place where they converge to relax and talk about what's on their minds—a conference, an interesting article, their experiments, and in some cases, their plans to turn research into products that will benefit the public.

Recently, these conversations were about SoftMax, a company acquired in December by wireless communications giant Qualcomm for its proprietary noise reduction technology. The algorithm behind the technology was developed in the CNL and is used to suppress background noise and make phone calls more intelligible.

But what does a basic biological research lab at Salk have to do with cell phones? **Terry Sejnowski,** professor and head of the CNL, explains.

"Our research is primarily focused on learning about the human brain and what it can do, and it's about learning how to make computers that are able to mimic these processes. It's a two-way street."

The noise-reduction algorithm that led to SoftMax is based on independent component analysis (ICA), a type of mathematical formula developed by Tony Bell, a former postdoctoral fellow in Sejnowski's lab. The algorithm solved the cocktail party problem: How to separate out a single sound source from mixtures of recorded signals.

SoftMax independently developed a version of ICA that mimics the human auditory system. It uses a pair of microphones in a cell phone headset, much like a pair of ears, to measure differences in loudness and timing to separate the source of a voice from the background.

"It identifies a speaker's voice from every other sound, and simply intensifies the voice signal while dampening the others," explains Sejnowski, who was on SoftMax's scientific board.

Alternative ICA algorithms for sound reduction exist, he notes, but the SoftMax version is more robust because it can be used with two, 10, or 100 microphones for better sound resolution.

ICA can be used with any type of signal, not just sound. One day, for example, it may help machines read electrocardiograms to reduce the time cardiologists spend with paper recordings and computers. It's already being used to understand what segments of our DNA are being transcribed, and what simply represents interfering background noise.

Philip Low is a postdoctoral fellow in the CNL who has been using electroencephalograms (EEG) to study sleep in birds and humans. With Sleep Parametric EEG Automated Recognition System (SPEARS), an algorithm he created at CNL during his doctorate studies, Low has been able to study brain activity using only two electrodes placed on the scalp, not the dozens that are normally placed all over the head and body in sleep studies.

Furthermore, using SPEARS, he has identified a new range of electrical activity, or "sleep state," that was previously masked by the low frequency waves produced during sleep. This new technology has led Drs. Low and Sejnowski to form NeuroVigil, a company that revolutionizes the way brain electrical activity is both recorded and analyzed.

Through a collaborative consortium with major academic institutions, NeuroVigil plans to perform basic research for the iBrain, an iPod for the brain, which will monitor people's health in real-time.

"I've been very fortunate because the members of my lab are exceptionally talented," says Sejnowski. "We form an eclectic team, with backgrounds in mathematics, physics, electrical engineering, psychology, and even philosophy. But this is what's required to even approach solving the big problems of how the brain works."

Philip Low (from left), programmer Tom Bartol, and Terry Sejnowski.

> "I've been very fortunate because the members of my lab are exceptionally talented. We form an eclectic team, with backgrounds in mathematics, physics, electrical engineering, psychology, and even philosophy. But this is what's required to even approach solving the big problems of how the brain works."
>
> – TERRY SEJNOWSKI

> "I now like molecular biology so much more that I will probably study it in college. I loved the environment and experience at Salk. I will probably come back here one day."
>
> – CHERYL WANG, TORREY PINES HIGH SCHOOL

A student tries her hand at pipetting in a Salk laboratory (top), while a technician (above) gives a brief presentation on the tools of the trade during a lab tour as part of the 18th annual High School Science Day.

High School Science Day Opens Students' Eyes to Careers in Research

THE SALK'S THEODORE GILDRED COURTYARD, WHERE scientists normally discuss ideas and quietly eat their lunch, was alive with boisterous chatter recently when 137 students and teachers gathered to share their first-hand experiences in the labs.

Some students described looking at the fluorescent green heart of zebra fish beating under a microscope while Cecilia Areta of Mira Mesa High School said that dissecting lab mice was an opportunity she would never forget.

"I now like molecular biology so much more that I will probably study it in college," said student Cheryl Wang from Torrey Pines High School. "I loved the environment and experience at Salk. I will probably come back here one day."

The students visited Salk in March for the 18th annual High School Science Day. The program, generously sponsored this year by longtime Salk Board member Charlie Robins, drew students from schools throughout San Diego County to learn more about biological research and explore the possibilities of a career in science.

Organized by Ellen Potter, a neurobiologist who also runs the Institute's educational outreach programs along with science education specialist Dona Mapston and a small army of volunteers, High School Science Day serves as a "demystification" of science – giving students the opportunity to see the work that goes into achieving the milestones cited in their textbooks.

"These are definitely one-of-a kind experiences for San Diego students since Salk laboratories aren't open to the general public," Potter said.

After the welcome meeting, the students were separated into small groups and assigned two laboratories to visit out of the 24 that participated – some of which focus on research in genetics, stem cells, infectious disease and neurobiology. Each student was also provided the opportunity to conduct hands-on experiments and scientific demonstrations led by various Salk scientists and lab technicians.

"This was definitely worth getting up early for on a Saturday," said Deepa Khatri of Mission Hills High School.

The day included a presentation titled "Winning and Losing: Engineering the genome to enhance athletic performance" by Ron Evans, a professor in the Gene Expression Laboratory at Salk, who provided a fascinating look at the Institute's cutting-edge research. The combination of thought-provoking data presented with a slide show liberally sprinkled with amusing graphics sparked a lively question-and-answer session in the young audience that only stopped because time had run out.

"The fact that a world renowned research center would open its doors to us is amazing," said Carrie Biggerstaff, a teacher at West Hills High School. "Most students will not realize how this day has impacted their life until many years from now."

Student Kyle Thompson of Vista High School agreed. "This made me really want to continue on my path toward a career in biology," he said. "I got to see first-hand what my future could be like."

Irwin and Joan Jacobs Establish $10 Million Challenge Fund

CHAIRMAN OF THE SALK'S BOARD OF Trustees Irwin Jacobs and his wife, Joan, have established a $10 million challenge fund to support the creation of 10 endowed chairs for senior scientists at the Institute.

The Joan Klein and Irwin Mark Jacobs Senior Scientist Endowed Chair Challenge will match $1 million for up to 10 individual contributions of $2 million, thus providing each chair with a $3 million endowment. Each $2 million donor will have the right to name the chair they are endowing, which will provide key support for research at Salk.

"As traditional government funding sources that have supported the scientists of the Salk Institute are stagnant or diminishing, the urgency to address our ability to recruit, support, and retain the very finest of the scientific community cannot be overstated," says Salk's Interim President and Nobel Laureate Roger Guillemin. "The creation of 10 endowed chairs will make a transformative difference to the resources available to those whose work is critical to the future of the Institute."

The Challenge was launched in April and will last until 10 chairs are funded or no later than December 31, 2009.

"We are deeply appreciative of Joan and Irwin Jacobs' generosity and vision. The Challenge provides an opportunity to significantly increase the number of endowed chairs at the Institute," says Salk Executive Vice President Marsha Chandler. "This $10 million leadership gift, together with contributions from other philanthropists, will ensure that Salk's extraordinary scientists can continue to carry out their groundbreaking work on our campus."

Irwin, co-founder and chairman of Qualcomm, and Joan provided the lead gift to establish the Crick-Jacobs Center for Computational and Theoretical Biology in 2004 and have since provided additional major gifts for Salk's very successful Innovation Grants program.

Irwin and Joan Jacobs

In choosing to establish the Joan and Irwin Jacobs Leadership Challenge, Irwin Jacobs said: "Salk has drawn together an immensely talented cadre of scientists from all over the world. They bring commitment, creativity, and passion to the discovery process. Currently, the faculty boasts three Nobel laureates, seven Howard Hughes Medical investigators, and 14 members of the National Academy of Science. Through this matching gift, Joan and I are inviting others to support these superb scientists."

Salk Appoints New Vice President of Development

REBECCA NEWMAN JOINED THE SALK INSTITUTE AS ITS new Vice President of Development in February. In her newest role, she oversees the Institute's entire fundraising and communications programs and leads all related strategic planning and donor relation activities.

Rebecca Newman

"We are very happy and fortunate to bring Rebecca Newman to the Institute," said Salk Interim President Roger Guillemin. "She brings more than 25 years of financial endowment development, and campaign and strategic-planning experience from the business and nonprofit industries. Her ability to establish strong relationships with leading philanthropists and some of San Diego's biggest employers in the biotech industry has been key to Rebecca's success as a fundraiser."

Newman joins Salk after serving for six years at UCSD, most recently as Associate Vice Chancellor, Development – a capacity in which she successfully led the university's capital campaign and exceeded its $1 billion goal.

She joined UCSD as Associate Vice Chancellor, Health Sciences Development in 2001 and oversaw what equates to about 50 percent of the campus, including the School of Medicine, the School of Pharmacy, the Cancer Center, the Cardiovascular Center, the Shiley Eye Center, two hospitals and numerous research and clinical programs. Her efforts and that of her team led to increasing the annual fundraising achievement of the Health Sciences from $25-$30 million to an average of $60-$70 million and successfully raising $450 million of the university's $1 billion fundraising goal.

In the spring of 2005, Newman assumed oversight of the fundraising program for the entire university, leading her team to a successful conclusion of the campaign. During her tenure, Newman made numerous contributions to the university's fundraising program, personally securing more than $100 million in gifts — among them the naming gifts for new schools and facilities. She led efforts to enhance the relationships of faculty with the donor community through a philanthropy training program, the creation of salon events, and the establishment of numerous advisory boards.

"It is a privilege for me to be given the opportunity to join the leadership team of the Salk Institute and to work with Interim President Roger Guillemin and Executive Vice President Marsha Chandler," Newman said.

"The beautiful architecture of the campus is the physical embodiment of the sheer excellence of the research being conducted by the world-renowned Salk faculty. I look forward to working with my colleagues and with the Board of Trustees to enhance the philanthropic base of support and to raise awareness of the tremendous impact of the Salk Institute locally, nationally, and internationally."

Waitt Family Foundation Awards $20 Million Grant to Launch Advanced Biophotonics Center

THE SALK INSTITUTE HAS RECEIVED a $20 million grant from Board of Trustee Vice Chairman Ted Waitt to establish an Advanced Biophotonics Center at the Institute. The gift, provided through the Waitt Family Foundation, will pay for build-out of the Center, provide salary support for new faculty and senior technician specialists, and the development and acquisition of some of today's most sophisticated imaging equipment.

"This generous grant by the Waitt Family Foundation provides a major step to create a facility that will help researchers push the boundaries of science even further at Salk," said Inder Verma, a professor in the Laboratory of Genetics.

"The scientific expertise we will gather and the highly advanced instrumentation we will develop will enable our scientists to visually decipher the basic principles behind some of today's most complicated diseases."

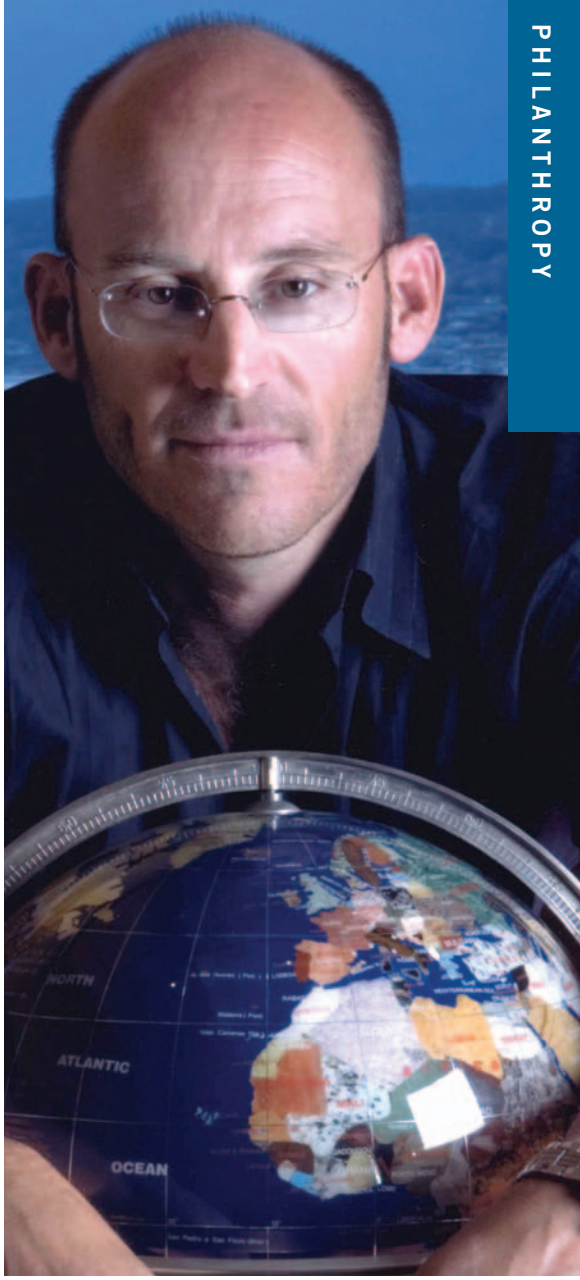
The Waitt Advanced Biophotonics Center will house a convergence of technical advances in several areas: faster cameras, highly powerful microscopes, new light emitting dyes and enough computing power to handle live images occupying up to a terabyte of storage space, all of which allow scientists to detect single photons and record the interaction of molecules to study and understand their function in healthy and diseased cells.

The ability to clearly see cells' minute inner workings will give Salk scientists an even deeper understanding of basic principles of biology and many diseases. This new knowledge, for example, could help explain why some cancer cells are resistant to therapy while others respond. It will also transform the way researchers analyze complex systems such as the brain, and revolutionize the way diseases are treated.

In conjunction with the $20 million grant, the Salk Institute has agreed to establish the Waitt Challenge Grant, which is designed to inspire philanthropic contributions and challenge the Institute to raise up to $20 million that can be applied toward additional funding for the Advanced Biophotonics Center or any other restricted or unrestricted purpose at the Salk.

"The creation of the Advanced Biophotonics Center has the potential to take Salk's already phenomenal science to a new level, and the Challenge Grant has the potential to further cement Salk's solid foundation," said Ted Waitt, co-founder of Gateway, Inc., who has gone on to form multiple enterprises since his retirement from the company.

"We are most grateful for the Waitt Family Foundation's contribution toward this critical component of Salk's forward-thinking initiatives," said Salk Executive Vice President Marsha Chandler. "This grant serves as an extraordinary catalyst for Salk's plan to build a comprehensive biophotonics program that leads technological advances in critical research areas."



Ted Waitt

Trustee Donates $11.5 Million to the Salk Institute

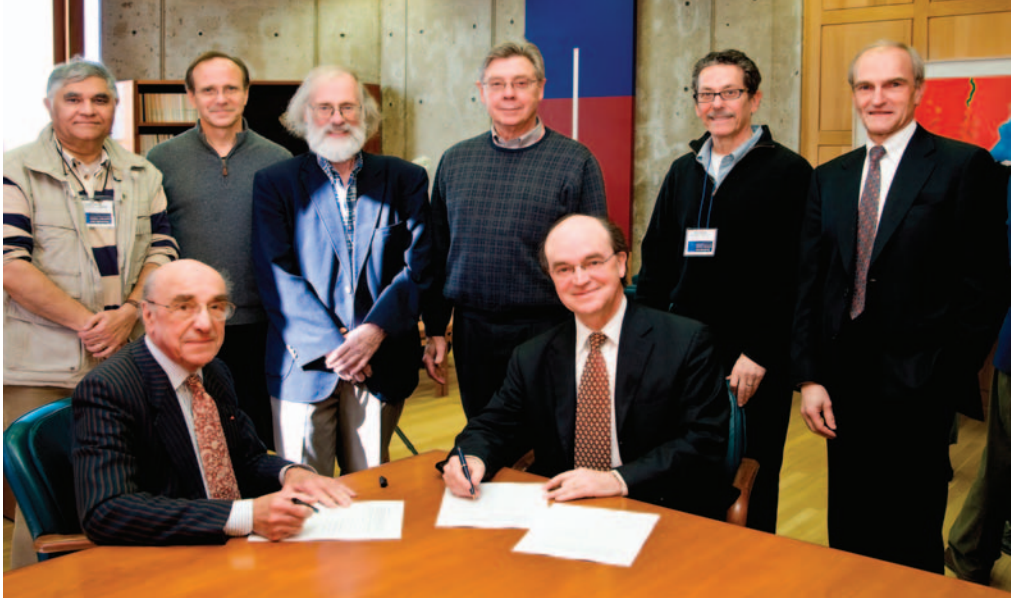
THE NOMIS FOUNDATION, A EUROPEAN FOUNDATION established by Salk Board of Trustee G.H. "Heini" Thyssen, has donated $11.5 million to fund appointments for new investigators specialized in microbial pathogenesis and viral and cellular immunology. The gift, which will launch the Immunobiology and Microbial Pathogenesis program, fulfills a critical component of the Institute's strategic scientific plan.

"The opportunity created by this most generous gift to recruit new scientists who will combine their expertise with that of existing faculty will create a critical mass of investigators that will allow the Salk Institute to contribute in entirely new ways to combating human disease," said Salk Interim President Roger Guillemin. "Additionally, the in-depth study of inflammation has many crossover links to other areas of research, creating opportunities for synergistic benefits."

Under the Immunobiology and Microbial Pathogenesis program, scientists at Salk will take a multi-pronged approach to conducting research on the pathophysiology of disease that arise from chronic infections, and will seek to understand the role of the immune system in preventing microbially induced disease.

The new principal investigators will also work closely with a number of current Salk Institute scientists who are studying the molecular basis of cancer, obesity, and heart disease as well as those studying innate immunity, the first line of defense; and adaptive immunity, the sustained immunity to fight pathogens.

Institute Signs Agreement to Establish Ipsen Life Sciences Program



Seated: Interim President Roger Guillemin and Ipsen Chairman and CEO Jean-Luc Bálingard.

Standing, from left: Salk Professors Inder Verma, Fred. H. Gage, Tony Hunter, Wylie Vale, Ron Evans, and J.P Moreau, head of Research and Development at Ipsen.

SENIOR FACULTY MEMBERS JOINED

Interim President Roger Guillemin and executives from Ipsen to sign a memorandum of understanding that set the framework for creating the Ipsen Life Sciences Program at the Salk Institute.

The agreement will provide Salk with $7.5 to $12.5 million in research grants over the next three to five years. The Ipsen Life Sciences Program will sponsor three categories:

The Target Grant, about $750,000 a year, will support research in pituitary problems that cause acromegaly, a defect in which too much growth hormone is produced. The condition causes disfigurement and gigantism, or excessive growth usually seen first in the hands, feet and face. About 7,000 people in the United States and 19,000 worldwide have developed acromegaly. One of the Institute's goals is to make the first mouse model for acromegaly so scientists can use it to test genes suspected of causing the defect and drugs that may cure it.

The Core Grant, about $1.25 million a year, will be awarded to researchers studying inflammation. Scientists believe inflammation plays a key role in aging, neurodegenerative diseases, metabolic changes and many kinds of cancer.

The Innovation Grant, about $500,000 a year, will give young researchers the chance to explore topics in any category deemed worthy by a selection panel.

John Pizzarelli Trio to Take the Stage During Symphony at Salk

John Pizzarelli

THE CRITICALLY ACCLAIMED JOHN

Pizzarelli Trio will perform with the San Diego Symphony, which will be led by returning guest conductor Thomas Wilkins, on Aug. 23 for this year's Symphony at Salk – A Concert Under the Stars.

Hailed by critics as one of the most accomplished interpreters of the Great American Songbook, John Pizzarelli has cultivated a winning international career by singing classic standards and late night ballads while playing sublime and inventive guitar. His trio is rounded out by pianist Larry Fuller, bassist Martin Pizzarelli, and drummer Tony Tedesco.

A native of Paterson New Jersey, Pizzarelli started playing guitar at age six, following in the tradition of his father, guitar legend Bucky Pizzarelli. John was exposed to all the great jazz music of the era by his father and at 20 began his professional career playing by his side.

In 1982 he formed The John Pizzarelli Trio and toured extensively to rave reviews that often compare Pizzarelli to the jazz icons that inspired him. Pizzarelli has performed for labels including RCA, Chesky, and Stash resulting in over 20 albums as well as collaborative recordings with many pop and jazz icons.

While continuing a busy touring schedule, John has also made numerous stage, screen and television appearances and hosts his own jazz radio program with his wife, Broadway star Jessica Molaskey.

A consummate performer whether performing classic pop, jazz or swing, Pizzarelli continues to set the standard for stylish modern jazz.

Wilkins returns as this year's guest conductor giving the Symphony and audience members another opportunity to enjoy the special energy he brings to every performance. Wilkins began his tenure as music director of the Omaha Symphony in the 2006-'07 season and he is also the resident conductor of the Detroit Symphony. His extraordinary skill and tireless dedication to promote lifelong enthusiasm for music has made him a favorite guest conductor for orchestras throughout the country.

Symphony at Salk is one of about 100 annual performances by the San Diego Symphony, considered one of the leading orchestras in the country. Offering a wide range of concert experiences including the Masterworks, Winter and Summer Pops and the Light bulb Series, the Symphony is committed to providing musical experiences of superior quality for the local community and beyond.

Through a rich mixture of innovative and cultural programming that transcends all ages and cultures, the Symphony makes music an integral part of the cultural and intellectual fabric of San Diego.

Tickets will be available in mid July at $250 each and include a pre-concert champagne reception, seating for the concert, a gourmet supper prepared by Jeffrey Strauss, executive chef and owner of Pamplemousse Grille, wine, refreshments and parking. For more information, visit www.salk.edu.

Support to Salk Comes in Many Different Forms

IT'S BECOME VERY CLEAR TO ME, NOW MORE THAN EVER, that for a leading research institute to survive, let alone thrive, it is necessary to look beyond a reliance on traditional government funding sources, which in recent years have stagnated – and even diminished in some cases. Your philanthropic contributions have never been so crucial to continue Salk's stellar record of scientific discovery to improve human health.

Whether we are training young scientists, equipping our labs with the latest technology, or working toward the latest breakthrough in research, all of our progress is based on your generosity, and no gift is too small to have an impact. At Salk, we are working to steadily increase our donor base, and thankfully, we are beginning to see the fruit of our effort.

I'll give you some examples. Several recent gifts, including a first-time contribution of $20,000 from the David F. and Margaret T. Grohne Family Foundation, have provided Salk researchers unparalleled flexibility to explore their most creative ideas – normally not afforded through government funds.

Newly elected Board of Trustee member Caryl Philips generously supported the Technology and Instrumentation Fund with a $250,000 gift earlier this year, and has since agreed to contribute an additional $250,000 to the same fund, which helps Salk researchers develop and implement cutting-edge technologies – a major component to scientific discoveries.

I am tremendously grateful for the ongoing generosity and vision of our Trustees. G.H. "Heini" Thyssen recently contributed $11.5 million through the Nomis Foundation to launch the Immunobiology and Microbial Pathogenesis program; Irwin and Joan Jacobs have established a $10 million Leadership Challenge Fund to create 10 endowed chairs for senior scientists; and Ted Waitt has just awarded Salk a $20 million grant to launch the Advanced Biophotonics Center and the Waitt Challenge Grant. Each of these extraordinary gifts fulfill important components of the Institute's scientific strategic plan and provide crucial funding to recruit additional scientists whose expertise will provide new collaborative opportunities with existing faculty to combat human disease.

The steady commitment from many of our longtime donors, especially those who are members of the President's Club, constitutes an invaluable base of support. The unrestricted funds received have enabled Salk to remain flexible in addressing emerging priorities and to share its advancements in research by funding scientific seminars and community outreach programs.

Most encouraging is that several of you increased your commitment to become charter members of the Chairman's Circle, a new Annual Fund giving level (starting at $25,000) we launched earlier this year. Your investment demonstrates your confidence in the work of the Institute and helps Salk scientists expand their research into promising new areas of discovery in state-of-the-art laboratories where the next generation of researchers is trained.

While increasingly important, philanthropy is just one component that helps keep the Salk Institute on its course of success. Our Board of Trustees provides leadership and a range of perspectives to the Institute, and I am thankful for their commitment and support of Salk's research and cutting-edge innovation.

Marsha A. Chandler

> "Whether we are training young scientists, equipping our labs with the latest technology, or working toward the latest breakthrough in research, all of our progress is based on your generosity..."

Salk's International Council contributes in myriad ways, from increasing public awareness around the world about the Institute's groundbreaking work, to attracting private support among individual donors, foundations, and corporations. Last, but not least, we are appreciative of Salk's Nonresident Fellows, who offer academic counsel to our faculty. The expertise and renown that each has achieved in their respective fields of research makes their guidance an invaluable asset to our scientific programs.

I am sure that without each of you – our donors, the Board of Trustees, the International Council and Nonresident Fellows – the Salk Institute would be a much different place, and its efforts to move science forward would become increasingly more difficult. Whether through your personal financial commitments, serving as Institute ambassadors, or providing ideas and counsel, your collective support contributes to Salk's mission of scientific excellence and discovery. For that, you have my ongoing appreciation.

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

Salk **Calendar**

JULY 2008

18-22 **DNA Replication Meeting**

AUGUST 2008

15-19 **Protein Phosphorylation Meeting**

23 **Symphony at Salk**

SEPTEMBER 2008

12 **20th Annual Mahajani Symposium: Molecular Targets of Cancer Therapy**

OCTOBER 2008

21-23 **La Jolla Immunology Conference**

For additional information about these and other Salk events, please contact the Development Office at 858.453.4100 x1658

The Floating Paintings, a collection of works by artist Françoise Gilot, widow of Jonas Salk, is currently on display at the Salk Institute. Among the featured acrylic on canvas pieces are: Mother Earth (1982), right; The White Shadow (1986), top from left; Sun Emblem (1980); and Pacific Protection (1984).

These and other works from this collection will remain at the Institute through October.

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