

InsideSalk

Where cures begin.
Salk Institute 3 | 13

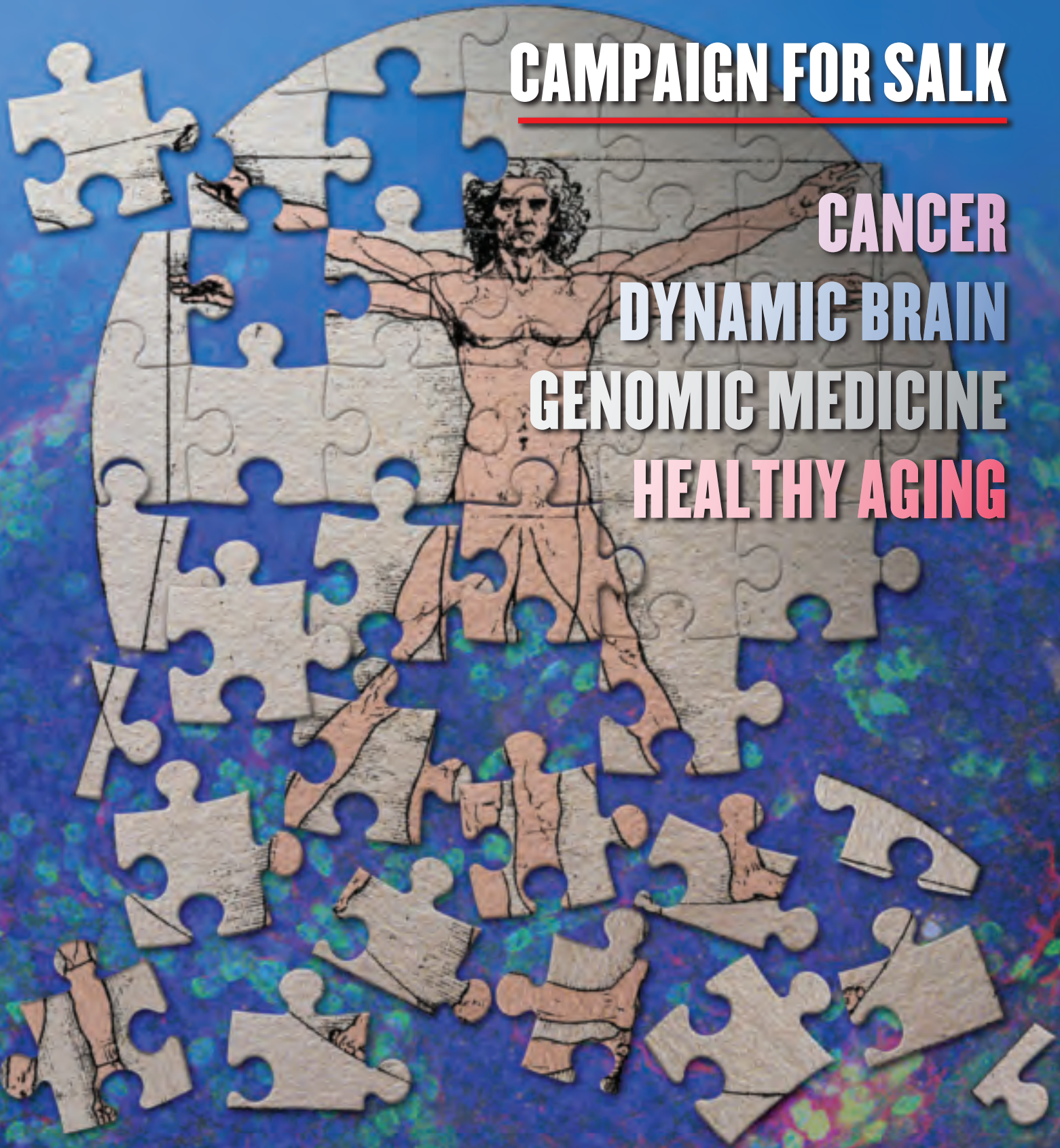
CAMPAIGN FOR SALK

CANCER

DYNAMIC BRAIN

GENOMIC MEDICINE

HEALTHY AGING



March 2013

Inside Salk



The Campaign for Salk



Next generation: Charisse Crenshaw



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

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

Rebecca Newman
Vice President,
External Relations

Stacie Spector
Chief Communications Officer

Christopher Emery
Director, Scientific Communications

Andy Hoang
Director, Media Relations

Karen Heyman
Staff Writer

Sarah Lifton
Copy Editor

Scott Edwards
Contributing Writer

Liz Hincks
Web Editor

Joe Belcovson
Photographer

Mike Sullivan
Videography

Kat Kearney
Media Specialist

Rhiannon Bruni
Contributing Writer

Diane Wilson
Proofreader

studio L.
Graphic Design

Visit the Salk Institute at www.salk.edu

3 EXECUTIVE MESSAGE

LEAD STORY

4 The Campaign for Salk

INSTITUTE NEWS

13 Scientists brief the media on the Campaign for Salk

14 One on one with...Daniel C. Lewis

16 Salk scientists awarded new chairs created as part of the Joan and Irwin Jacobs Chair Challenge

17 Salk holds second Women & Science event

18 From bench to runway

19 The art in science; the science in art

20 Step into Discovery

Parting shots

21 Two more Salk faculty elected as AAAS Fellows

22 Creative projects receive Innovation Grant Awards

Tom Albright named president of Academy of Neuroscience for Architecture

23 Salk researchers receive prestigious NARSAD Young Investigator Grants

Salk investigator receives 2012 Ray Thomas Edwards Foundation Career Development Award

24 Two Salk researchers selected for 2012 Life Sciences Research Foundation Fellowships

Salk Scientists score National Institutes of Health Director's New Innovator Award

DISCOVERY ROUNDUP

25 More than 3,000 epigenetic switches control daily liver cycles

26 Aggressive brain tumors can originate from a range of nervous system cells

27 Salk scientists pinpoint key player in Parkinson's disease neuron loss

28 Salk study finds diabetes raises levels of proteins linked to Alzheimer's features

29 What can the water monster teach us about tissue regeneration in humans?

Chromosome "anchors" organize DNA during cell division

30 Cold viruses point the way to new cancer therapies

NEXT GENERATION

31 Good luck keeping up with Charisse Crenshaw

PHILANTHROPY NEWS

34 Celebrating Salk science, President's Club-style

35 Salkexcellerators

36 International Council enjoys science and music at Salk

37 Insider's View

38 Get Involved

CALENDAR

Back Cover

InsideSalk is printed on recycled paper.

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





William R. Brody

Dear Friends,

THIS IS A TIME OF REMARKABLE FIRSTS AT THE SALK INSTITUTE.

In January, we publicly launched the first-ever *Campaign for Salk*, a major fundraising effort with a goal of raising \$300 million to support Salk research. Soon afterward, we received an extraordinary gift of \$42 million from the Leona M. and Harry B. Helmsley Charitable Trust for a Center for Genomic Medicine, the single largest gift in the Institute's history. And next month, on April 13, we celebrate Step into Discovery day, an event featuring a rare open house of Salk laboratories and the inaugural Walk for Salk, a 5K fundraising walk along the beautiful Torrey Pines mesa.

Each of these firsts, which you will read about in this issue of *Inside Salk*, help support the important work of Salk's scientists, who are in the business of breaking new scientific ground. Every day, they probe the frontiers of knowledge, and their work expands our understanding of how our bodies function and how, when we become sick, we might better heal them.

The Salk Institute was founded on a legacy of historic discovery. The Walk for Salk will take place a day after the 58th anniversary of Jonas Salk's announcement of the polio vaccine. April 23rd is the 60th anniversary of the discovery of DNA. Salk shares many connections to this scientific milestone, including several Nobel laureates, among them **Francis Crick**, co-discoverer of the double helix, who came to Salk to take up the challenges of neuroscience. These anniversaries underscore the fact that many years of research go into making life-changing discoveries.

At Salk today, our scientists continue to follow Dr. Salk's example, working long hours in the laboratory to lay the groundwork for the medicine of the future. Using powerful new technologies and collaborating in innovative ways, they are seeking cures and preventive treatments for cancer,

“ We received an extraordinary gift of \$42 million from the Leona M. and Harry B. Helmsley Charitable Trust for a Center for Genomic Medicine, the first gift of its size in the Institute's history. ”

diabetes, neurodegenerative disorders, aging and associated conditions. With your help, these historic firsts for Salk will translate into scientific firsts that benefit human health.

Thank you for your continued support and commitment. 🙏

William R. Brody, M.D., Ph.D.
President, Salk Institute
Irwin M. Jacobs Presidential Chair



ON THE COVER

Scientists have discovered details about the human body that were unimaginable when Leonardo da Vinci drew his iconic Vitruvian Man more than 500 years ago. The Campaign for Salk is a visionary effort to complete the puzzle of what makes us tick and how to cure the diseases that attack our health and vitality. Cover by Jamie Simon



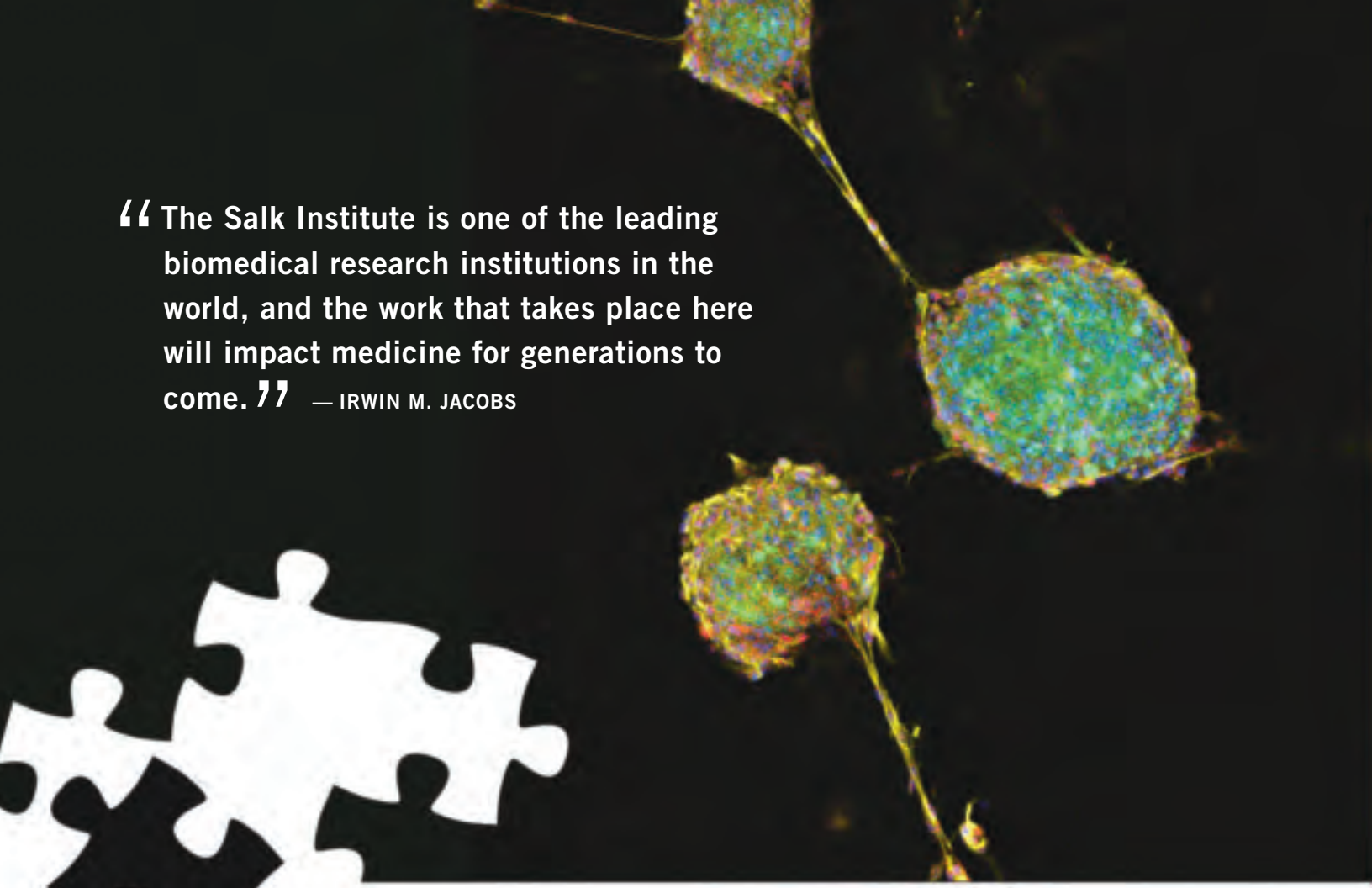
“ At Salk, even the buildings are designed so that you bump into colleagues regularly, which leads to surprising collaborations. ” — RONALD M. EVANS



The Campaign for Salk

WHEN HISTORIANS LOOK BACK TO THE early decades of the 21st century, they will discover an era of astounding technological advances and dramatic upheavals—political, social and economic. At the Salk Institute, we believe they will also find a period of remarkable scientific progress, a time when science overcame barriers to curing the world's most devastating medical conditions.

Thanks to advances in imaging, genomics, stem cells, computational analysis and disease modeling, biomedical science is progressing far faster than even just a decade ago. These breakthroughs hold tremendous promise for explaining what happens in our bodies when we are healthy or sick, for producing new therapies and for helping to address the crisis in healthcare as the population ages and the burden of chronic disease grows.



“The Salk Institute is one of the leading biomedical research institutions in the world, and the work that takes place here will impact medicine for generations to come.” — IRWIN M. JACOBS

The blue, green, red and yellow in this image indicate that these neurons are producing proteins typical of immature nerve cells, evidence that they have reverted to a stem cell-like state. Salk scientists found that mature cortical neurons are capable of reverting to this immature state and developing into an aggressive type of brain tumor that was previously thought to only develop from neural stem cells or glia, another type of cell in the brain.

Image: Courtesy of Dinorah Friedmann-Morvinski

To ensure that this vital work continues, the Salk Institute recently launched its first-ever Campaign for Salk, a \$300 million fundraising effort to support research in the most promising areas of science. The campaign focuses on significantly increasing the Institute's unrestricted endowment and garnering support for four major initiatives where private philanthropy can have a powerful impact on human health: Cancer, Genomic Medicine, Healthy Aging and the Dynamic Brain.

“The Salk Institute is one of the leading biomedical research institutions in the world, and the work that takes place here will effect medicine for generations to come,” says **Irwin M. Jacobs**, chairman of Salk's board of trustees and co-founder of the technology company Qualcomm. “Salk scientists are working at the cutting edge of biological research, and their discoveries help us to understand a wide range of diseases. The Campaign for Salk, to support this unique institution, is a campaign for everyone.

The public launch of the campaign in January was the culmination of several years of planning and preparation and followed a “quiet phase” of campaign fundraising. During that time, Salk's faculty identified the areas where investments in scientific expertise, technology and ideas will have the greatest impact.

“The Campaign for Salk represents a common vision for the future of research at the Institute, developed by some of the most talented scientists of our time,” says **Marsha A. Chandler**, Salk's executive vice president. “The Salk Institute is a leader in neuroscience, cancer, genomic medicine, plant biology, aging research and many other areas of biological science. The campaign builds on this foundation of excellence to carry science and medicine far beyond what is currently possible.”

Already the campaign has generated record levels of contributions. In 2012, the Institute received over \$50 million from individuals, corporations and foundations, bringing the total raised during the quiet phase of the campaign to approximately \$150 million. Soon after the public launch in January, the Institute announced an additional gift, the largest in Salk's history and one of the largest ever to an independent research institution: an award of \$42 million from the Leona M. and Harry B. Helmsley Charitable Trust to establish the Helmsley Center for Genomic Medicine.

Rebecca Newman, Salk's vice president of external relations, says the landmark gift and extraordinary level of giving by other Salk donors has given the Institute terrific momentum as it enters the public phase of



HEALTHY AGING

THANKS TO ADVANCES IN NUTRITION AND HEALTHCARE, people are living and remaining active longer than ever before. By the time all baby boomers are 65 or older, the senior population in the United States will have grown from today's 40 million to about 72 million. While living longer is a gift of modern society, it also brings a higher risk for diseases such as cancer, heart disease, stroke and diabetes and the burden of healthcare costs that skyrocket in our later years. Salk researchers explore how age-related changes in one cellular pathway have a cascade of effects throughout cells and organs. They investigate how molecular wear and tear on neurons leads to neurodegenerative diseases such as Alzheimer's and Parkinson's. With their in-depth knowledge of age-related diseases and biological pathways, Salk scientists are uniquely prepared to uncover the common biological mechanisms of aging, thereby helping people stave off disease and enjoy a high quality of life in their advanced years.



CANCER

CANCER IS THE SECOND LEADING CAUSE OF DEATH IN THE United States, surpassed only by heart disease. More than 1.6 million new cases will be diagnosed in 2012, and more than 577,000 Americans will die of it—approximately 1,500 people a day. Although the five-year relative survival rate for all cancers diagnosed is 67 percent, up from 49 percent in 1975–77, survival statistics vary greatly by cancer type and stage at diagnosis, and the need for more research remains great. Identifying the cellular pathways of growth and metabolism in tumors, developing intelligent nanomachines that diagnose and destroy cancers, and unraveling how cancers override the shortening of telomeres, the protective caps on the end of chromosomes, are just some of the promising areas that Salk scientists have identified for further research. Using new technological tools, they will model cancer's many variations, leading to an ability to design therapies that target the pathways and mutations that produce a cancer.



DYNAMIC BRAIN

WE ARE ON THE CUSP OF A REVOLUTION IN NEUROSCIENCE.

In the past, scientists were limited to studying one neuron at a time, but the nervous system is all about connections. Now, a more sophisticated neuroscience is emerging at the Salk Institute, one capable of explaining how billions of neurons work in unison to allow us to think, feel and move. Salk scientists are pioneering advances such as new imaging technologies, stem cell techniques and the ability to control neuron function with light. At the same time, they are working across traditional boundaries of neuroscience, merging molecular neurobiology, neurophysiology and computational and behavioral neuroscience. This new, all-encompassing approach is revealing critical details of the nervous system's molecular and cellular machinery and allowing us to study multiple living neurons simultaneously for the first time in history. Salk scientists are mapping the brain's circuitry, modeling human disease in the laboratory and exploring the genetic links to cognition and behavior—work that lays the groundwork for prevention and treatment of neurological diseases and injuries such as Alzheimer's, schizophrenia, spinal cord damage and blindness.



GENOMIC MEDICINE

WITH A COMPLETE MAP OF HUMAN DNA—THE GENOME—

scientists now have the unprecedented ability to explore the genetic aspects of disease. This information promises to revolutionize medical care by allowing doctors to tailor treatment to individual patients based on their genomic profile, with the goal of minimizing side effects and maximizing efficacy. Scientists in Salk's new Helmsley Center for Genomic Medicine, will identify the common genes and signaling pathways that are activated in all chronic illnesses. They will chart how genes and biological pathways work together as networks to generate tissues, organs and physiological states and how the activity of these networks is altered in the case of disease. Identifying the common genomic basis for chronic conditions such as diabetes, inflammation and cancer will uncover new potential targets for therapies. Understanding how gene networks control stem cell development will allow researchers to manipulate genes to make stem cells useful for studying disease and regenerative medicine. And exploring how disease alters the epigenome, which influences genetic activity, will further explain why patients with similar genetic profiles respond differently to treatment.



Salk researchers Joe Feeney and Anna Bartlett in the Genomic Analysis Laboratory.

“The Campaign for Salk represents a common vision for the future of research at the Institute, developed by some of the most talented scientists of our time.”

— MARSHA A. CHANDLER

the campaign. “We are incredibly gratified by the generosity of people who understand the importance of Salk scientists’ work,” she says. “We still have a long way to go to reach our fundraising goal of \$300 million, but already the campaign is helping our researchers pursue their most unconventional and promising ideas.”

The Campaign for Salk comes at a pivotal time in the history of science. In the past, biomedical researchers in the United States received the bulk of their funding from the National Institutes of Health (NIH). Federal funding from NIH now accounts for less than half of Salk’s budget, however, compared to two-thirds of the budget just ten years ago. Given the looming federal deficit, it appears the trend of declining public funds for science will continue into the foreseeable future. With government support waning, private philanthropy—a mainstay of Salk since its inception—is becoming ever more essential to scientific discovery.

The Campaign for Salk was conceived to address both the decline in federal funding and the emergence of new technologies that are rewriting the rules of molecular biology research. These technologies are allowing

scientists to discern what’s happening at the deepest molecular level in our bodies and make sense of the bewildering complexity of our physiology. We are essentially a collection of nested biological machines—organs, cells, genes, proteins—that operate together to allow us to eat, breathe, walk and think. At the core of these systems is the intricate web of biochemical interactions of proteins and other biological molecules, such as DNA and RNA. Thanks to new imaging techniques and methods for measuring the rapidly fluctuating chemical reactions taking place in cells, we are now able to see individual molecules and to record the biochemical activity of cells in real time.

“This ability to understand cells at a small scale is revealing the big picture of how they operate as complex systems,” says **Inder M. Verma**, one of the directors of Salk’s Helmsley Center for Genomic Medicine and holder of the Irwin and Joan Jacobs Chair in Exemplary Life Science. “This is crucial to developing better therapies, since you can’t understand how a machine works—or how to fix it—without mapping out all the gears, switches and wires.”



ELEMENTS OF DISCOVERY

THE SALK INSTITUTE IS DETERMINED TO ACCELERATE ITS PACE OF DISCOVERY, WITH THE ULTIMATE goal of bringing the world new therapies and cures and keeping people active and free of debilitating conditions in their later years. Toward this end, the Institute has identified four areas where investment will have the greatest impact.

ENDOWED FACULTY CHAIRS

Competition to recruit the world's top scientists is fierce. One of the best ways to attract and retain faculty is through endowed chairs, which generate ongoing funding to support salaries and laboratory infrastructure. Contributions to increase the number of endowed chairs will enable Salk to attract outstanding new faculty with expertise in high-priority research areas.

The Joan Klein Jacobs and Irwin Mark Jacobs Senior Scientist Endowed Chair Challenge was created by Dr. and Mrs. Jacobs to encourage donors to establish endowed chairs for senior scientists. For every \$2 million that a donor contributes toward an endowed chair at the Institute, Joan and Irwin Jacobs will add \$1 million to achieve the \$3 million funding level required to fully endow a chair for a Salk senior scientist. To date, 17 chairs have been established as a result of this program.

POSTDOCTORAL AND GRADUATE STUDENT FELLOWSHIPS

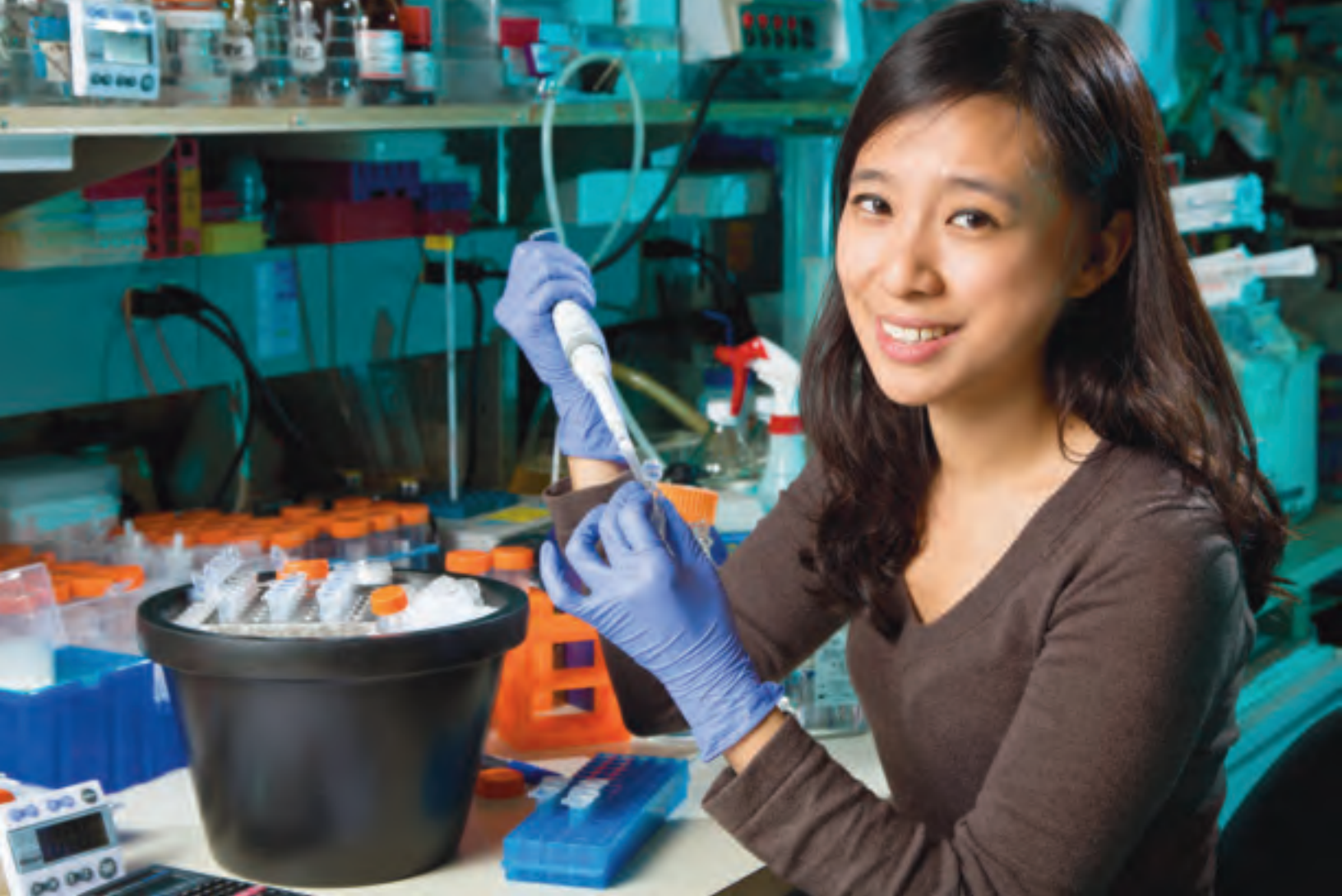
Postdoctoral and graduate fellows—gifted young scientists who work with senior scientists on complex projects—are essential to every laboratory, but cuts in federal research budgets have severely limited funding for these positions. For this reason, the Salk Institute is seeking contributions to support postdoctoral and graduate student fellowships.

RESEARCH TECHNOLOGY

Dramatic advances in imaging, computing and high-throughput DNA sequencing are profoundly impacting biomedical research, allowing investigators to see cellular details and map complex bodily systems in ways never before possible. The Institute is seeking funding to assure Salk scientists continued access to the state-of-the-art technology that will be critical to their success.

INNOVATION GRANTS

The Institute's success has been built on bold, innovative investigations that yield high-impact discoveries, but shrinking federal funding is being directed toward more conservative approaches, leaving Salk scientists unable to pursue some of their most creative ideas. Through the Campaign for Salk, donors can support crucial proof-of-concept research, enabling scientists to go on to compete for traditional funding.



Nasun Hah, a researcher in Ronald M. Evans's Gene Expression Laboratory at Salk.

As Salk scientists record highly detailed information about how our biological systems function, new computational approaches for analyzing these data are pinpointing which components—genes, molecules, cellular pathways—are linchpins for multiple systems and the common links between various diseases.

Ronald M. Evans, a professor in Salk's Gene Expression Laboratory and co-director of the new Helmsley Center for Genomic Medicine, notes that the Institute was founded and built with a philosophy of encouraging scientists from different fields to work together. This makes it fertile ground, he says, where interdisciplinary research can crack tough interconnected biological problems.

"When Jonas Salk envisioned the Institute, he saw people working together who normally wouldn't—infectious disease experts working

with neuroscientists, for instance, or cancer researchers working with physicists," says Evans, holder of the March of Dimes Chair in Molecular and Developmental Biology. "At Salk, even the buildings are designed so that you bump into colleagues regularly, which leads to surprising collaborations. Integrating expertise from different fields allows you to tackle a disease from many angles. At Salk, interaction leads to inspiration, and that is where the chemistry for new discoveries begins."

A leading priority of the Campaign for Salk is fostering even closer collaborations between the Institute's laboratories by recruiting outstanding scientists working at the cutting edge of genomics, neuroscience, aging, plant science, cancer research and other promising areas of biomedical research. These new faculty will integrate existing areas of expertise and enhance understanding of the body's various systems.

In addition to recruiting faculty, endowed fellowship programs will attract talented early career scientists to work in Salk laboratories. This will simultaneously bring fresh ideas to the Institute and train the next generation of highly effective scientists.

Young researchers will also bring the technical savvy needed to incorporate emerging technologies into Salk laboratories. "This will help fulfill another major thrust of the campaign, which is to acquire advanced technologies that allow our researchers to look deeper and more comprehensively at how the body operates, both when it's healthy and in the case of disease," says Salk president **William R. Brody**.

The Campaign for Salk will raise money for establishing endowed technology funds to allow the Institute to invest in crucial new equipment as technology evolves. It will also seek support

Right: Salk faculty celebrating the opening of the Helmsley Center for Genomic Medicine.



salk
Where things begin.
and
THE LEONARD AND HARRY D.
HELMSLEY
CHARITABLE TRUST

Celebrate
A New Partnership

THE CENTER
FOR
GENOMIC
MEDICINE

Campaign for Salk Cabinet

CHAIR

Irwin Mark Jacobs

CO-CHAIRS

Howard Newman

Darlene Shiley

HONORARY CO-CHAIRS

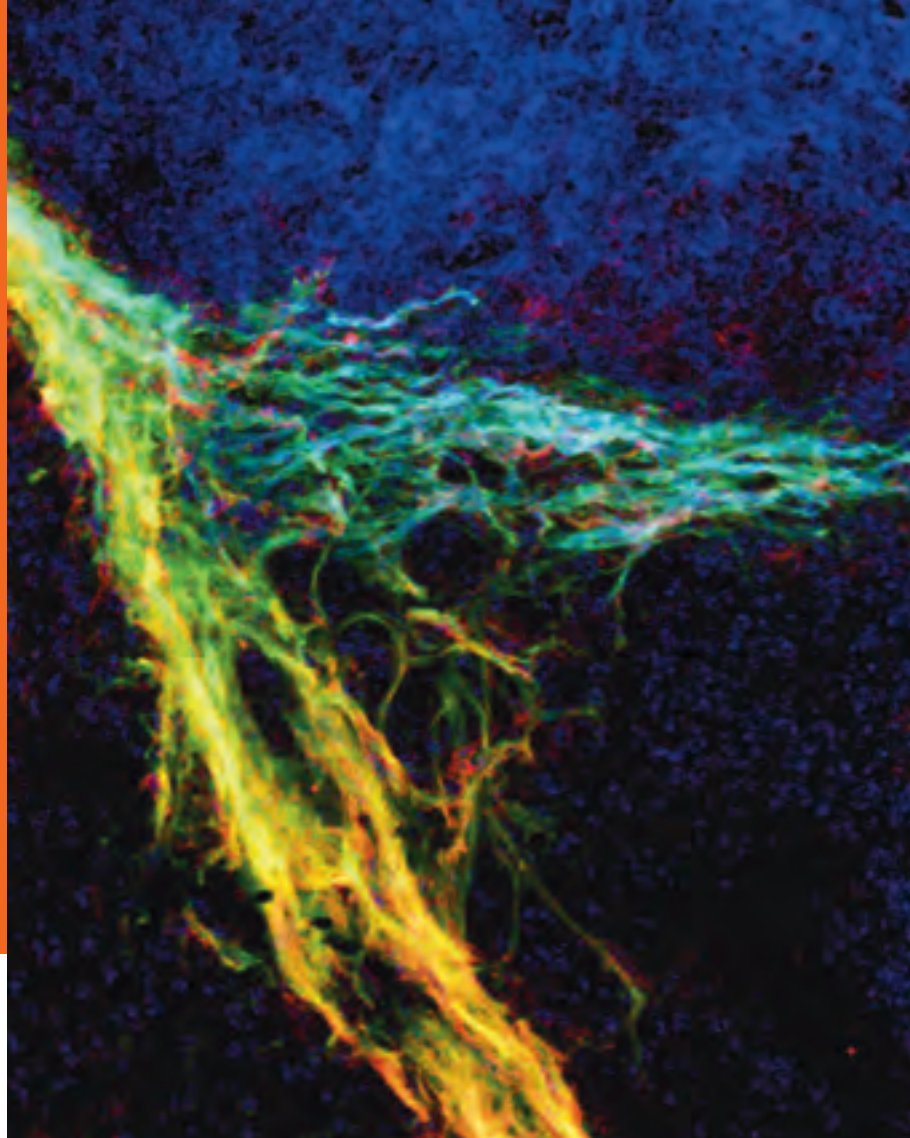
Françoise Gilot-Salk

Corinne Mentzelopoulos

Heini Thyssen

Nerves (in green) that control body movements emerge from the spinal cord of a mouse (upper left, in cross section) and connect to muscles in the base of the leg. Salk researchers discovered that a combination of genes direct nerves to split in the leg (lower right) to make the proper connections with their target muscles during early development.

Image: Courtesy of Dario Bonanomi, Salk Institute for Biological Studies



“The work we’re doing now, both the science and the fundraising that supports it, plants the seeds for the therapies of tomorrow. That’s what the Campaign for Salk is all about.” — WILLIAM R. BRODY

for one-time purchases of equipment and facilities essential to launching the primary research initiatives. By providing seed grants and the leveraging funds necessary to obtain larger grants, the campaign will foster adventurous research projects that cross many subdisciplines. Brody offers Salk’s new Helmsley Center for Genomic Medicine as an example of cutting-edge research made possible through private philanthropy.

Supported by the Leona M. and Harry B. Helmsley Charitable Trust, the new center brings together scientists working in computational biology, cancer, inflammation, metabolic disease and regenerative medicine to decode the common factors underlying chronic diseases and find therapies that target these factors.

For instance, Salk researchers are finding that the cellular pathways involved in inflammation play a role in a range of diseases, including diabetes, heart disease and cancer. This suggests that developing

treatments that address inflammation could help prevent and treat a broad range of disorders.

To accomplish this, the center will recruit new faculty with expertise in the hottest areas of biomedical research and will fund innovative studies in metabolism and physiology, stem cells and cancer. The Helmsley Charitable Trust gift also establishes several shared core facilities that provide Salk scientists with access to technologies they couldn’t afford to purchase for a single laboratory.

“Thanks to the Helmsley Charitable Trust and investments from a number of generous supporters, we are off to a great start in revolutionizing how science is conducted at the Salk and around the world,” Brody says. “The work we’re doing now, both the science and the fundraising that supports it, plants the seeds for the therapies of tomorrow. That’s what the Campaign for Salk is all about.” 🏢



Ronald M. Evans, professor and director of the Gene Expression Laboratory and holder of the March of Dimes Chair in Molecular and Developmental Biology talked about the Genomic Medicine Initiative at the press announcement for the Campaign for Salk – the Institute's \$300 million fundraising campaign.

Scientists brief the media on the Campaign for Salk

ON NOVEMBER 8, THE INSTITUTE EMBARKED ON A NEW CHAPTER IN ITS 53-YEAR history, when it announced its first-ever major fundraising campaign. At a press conference held in the Institute's courtyard, **William R. Brody**, president of the Salk Institute, and **Irwin M. Jacobs**, chair of the Salk board of trustees, were joined by Salk scientists **Fred H. Gage**, **Tony Hunter**, **Ronald M. Evans**, **Martin W. Hetzer** and **Jennifer Ehren** to speak about the campaign and the critical role it will play in securing the future of Salk science.

The Campaign for Salk is a six-year, \$300 million initiative to raise private resources to support the advancement of biological research in areas such as cancer, Alzheimer's and Parkinson's disease, obesity and diabetes, aging, spinal cord injuries, vision, ALS and crop yields. It focuses on four major scientific initiatives—Cancer, Healthy Aging, Dynamic Brain and Genomic Medicine—and will help the Institute accelerate the pace of discovery leading to new therapies for today's most complex diseases; it will also help Salk recruit and retain the world's brightest scientists and secure the future of research over the next several decades.

Nearly \$200 million of the \$300 million goal has already been raised in gifts from individuals and foundations since the quiet phase of the campaign began in 2009. 📄

» Watch the video

www.salk.edu/ismar13/video2



Dan and Martina Lewis

One on One with...

Daniel C. Lewis

Daniel C. Lewis gives back to the science that helped save his life

THE PREVIOUS ISSUE OF *INSIDE SALK* FEATURED an interview with Salk professor **Tony Hunter**, whose discovery of tyrosine kinases, enzymes that regulate cellular growth, ultimately led to the cancer-fighting drug Gleevec.

One of the people who benefited from Hunter's discovery was **Daniel C. Lewis**, the newest member of Salk's board of trustees. In 2004, Lewis was diagnosed with chronic myeloid leukemia, which before Gleevec had only a 50 percent cure rate. Now Lewis's cancer is under control.

Before joining the board, Lewis had been a member of Salk's International Council for over ten years. Lewis and his wife, Martina, recently established the Daniel and Martina Lewis Chair, currently held by **Geoff M. Wahl**, a professor in the Institute's Gene Expression Laboratory.

As the former president of Booz & Company, where he worked for 32 years, Lewis traveled all over the world, but he grew up in the northern Illinois city of Rockford,

where a winter temperature of 30 degrees Fahrenheit is considered warm. It's no wonder he chose to retire in temperate La Jolla. From their home, he and Martina enjoy a sweeping coastal view, which includes Salk's iconic towers.

But "retirement" is something of a misnomer. In addition to serving on Salk's board of trustees, he is also a trustee at Fairleigh Dickinson University, where he received an MBA. Lewis also serves on the Executive Council of the College of Technology at Purdue University, his undergraduate alma mater, and is a member of the World Economic Forum. When he does take part in an activity associated with retirement—fishing—it's in competitions for marlins the size of Volkswagen Beetles.

As a beneficiary of a key Salk discovery and a prominent contributor to Salk, Lewis shared his unique perspective on the Institute, the Campaign for Salk and its promise for impacting human health.

“ I genuinely think there’s a special process that has been perfected at Salk by breaking down departmental boundaries and using shared services. ”

— DANIEL C. LEWIS



The 500-pound marlin

How did you become involved in the Salk Institute?

I had two major things in my life that brought me to Salk. Joe [C. Arnold] Kalman, my mentor at Booz, was on the Salk International Council. Joe was a very direct mentor. He said, “You’re a very senior guy. You live in La Jolla. You need to be involved in something as important as the Salk Institute.” He introduced me to Salk, I attended some scientific presentations, visited some labs, and I was hooked.

The second major thing was that I found I had leukemia, and the form of leukemia I have is the kind that was cured by Tony Hunter’s tyrosine kinase work. My health is fine now. Gleevec is unique in the world of cancer; it’s been very successful. There are now some subsequent drugs, because these cancers never stay still, they mutate. But I’m blessed to have had this cancer at a time when the research had been done. Gleevec had been approved as a drug in 2000, and I was diagnosed in 2004. I’ve had quite a few years now of basically cancer-free life as a result of the drug, and that endeared me even more to Salk and made me feel closer in many ways.

After I retired, my wife and I decided to give back in a bigger way than we’d been giving. **Geoff Wahl** is the first holder of the oncology chair we donated. That was one of the chairs made possible by **Irwin and Joan Jacobs**. Their matching grant was the difference between doing it and not doing it.

As the former president of the world’s oldest management consulting firm, do you have advice you can give to scientists about project management?

I specialized in commercial aviation, which includes the global airlines and airplane manufacturers, so my expertise is quite different. In manufacturing, they rely on well-tested and proven scientific laws and principles. By contrast, Salk’s focus is on basic research, which writes or rewrites the rules. Much of the methodology is crafted by scientists’ shared experience in how to ask the right kinds of scientific questions and set up the right kinds of experimentation. I genuinely think there’s a special process that has been perfected at Salk by breaking down departmental boundaries and using shared services, like the scientific facilities cores—things that make it a particularly effective place to do research.

By the way, speaking of “oldest,” did you know that Booz was founded the same year that Jonas Salk was born? We’re both celebrating centenaries next year.

San Diego has a strong tradition of biotech entrepreneurship. Do you have any guidance for scientists who may be thinking of creating startups?

The people who ought to be giving that advice are Bill Brody and Irwin Jacobs!

I don’t believe there’s a better management combo you could have put together for Salk. It’s really a phenomenal thing and a blessing to have two very prominent, successful innovators team up in a way that has paid big dividends for Salk. I think Salk is a unique place; it’s very professionally and efficiently run. What the trustees can do is ask questions and bring all kinds of different experience and serve important roles in fundraising.

We hear your hobby is sport fishing.

When you do the kinds of things that I’ve been doing in a professional career, you really only have time for one great passion, and this is it! I have a sport fishing boat in Cabo San Lucas, and I fish in marlin tournaments. In one respect, ocean fishing for marlin is not that different from any other kind of fishing—it’s not that difficult to reel them in, if you’ve got the right kind of gear. The hard part is getting them to bite in the first place, and you’ve got a lot more area to cover!

I once brought in a 762-pound blue marlin. It’s a pretty good size, but they get bigger. My goal is to land a 1000-pounder. I have a 500-pound marlin on my wall; it’s the only one I’ve ever mounted. Most of the time, we release these fish, because it’s incredibly important to preservation.

Is there a link among your interests?

The common thread is passion. And the other common thread is leadership. Both of those skills are required to be able to compete, whether it’s in business or science or fishing.

One final question, do you have specific recommendations for the Campaign’s success?

I think education is key. While people know Jonas Salk’s name and how he was essentially able to eradicate polio, the science has moved on in an incredible way, so that the discoveries today are groundbreaking in so many places, from plant biology to neurogenetics. The Campaign is showing what an important asset Salk is to the San Diego community and beyond. Salk is a very special place. The best way to get people to give money to Salk is to get them to Salk. 🏠



Marsha A. Chandler, Edward M. Callaway, Audrey Geisel

“The donors who endow these chairs know that they are ensuring the excellence of the Salk’s research today and in the future.”

– WILLIAM R. BRODY

Salk scientists awarded new chairs created as part of the Joan and Irwin Jacobs Chair Challenge

ON NOVEMBER 16, EDWARD M. CALLAWAY AND JOSEPH P. NOEL were honored at the Board of Trustees Luncheon and Recognition Ceremony and selected as the inaugural holders of two new endowed chairs. Colleagues and patrons convened at the special reception to celebrate with the scientists, who were heralded for their contributions to research.

The Audrey Geisel Chair in Biomedical Science and the Arthur and Julie Woodrow Chair were both created under the Joan Klein Jacobs and Irwin Mark Jacobs Senior Scientist Endowed Chair Challenge. In 2008, the Jacobses established a challenge grant to encourage donors to establish endow chairs for senior scientists. For every \$2 million that a donor contributes toward an endowed chair at the Institute, Joan and Irwin Jacobs will add \$1 million to achieve the \$3 million funding level required to fully endow a chair for a Salk senior scientist. To date, 17 chairs have been established.

Edward M. Callaway, a professor in the Systems Neurobiology Laboratories, was appointed the inaugural holder of the Audrey Geisel Chair in Biomedical Science. Geisel, one of San Diego’s most renowned philanthropists, began her commitment to Salk in 1978 as a member of the Women’s Association of Salk Institute, helping to increase awareness about the importance of basic research, providing support for the Salk Scholars Fund, and raising funds for many projects. A longstanding patron of the Institute, Mrs. Geisel is also one of the founding donors for Symphony at Salk.

Callaway’s research has revealed important insights into the organization and function of neural circuits in the visual cortex and enhanced our understanding of how these circuits give rise to perception and behavior. His lab has pioneered novel molecular, genetic and viral tools for revealing the detailed structure and function of neural circuits, including a method that allows scientists to trace a single neuron’s connections to its neighbors. Callaway’s current studies capitalize on these and related tools to explore the neural circuit mechanisms that underlie the function of the cerebral cortex.

Joseph P. Noel, director of Salk’s Jack H. Skirball Center for Chemical Biology and Proteomics, is the inaugural holder of the Arthur and Julie Woodrow Chair. Woodrow created the chair in memory of his late wife and

has been an active supporter of the Salk for over a decade, both as a Partner in Research and a member of the Chairman’s Circle.

Noel explores the roots of biological diversity at the chemical level and seeks to understand the natural chemical factories that plants and microbes use to produce a vast array of compounds that allow them to survive and prosper in the challenging ecosystems found all over the earth. Through this research, he seeks to harness and alter the biosynthetic pathways needed to produce complex molecular scaffolds that will expedite the development of effective medicines and provide new strategies to increase the nutrition and sustainability of the world’s food supply.

“We are proud of these two exceptional scientists and this well-earned recognition for their scientific leadership,” said Salk president **William R. Brody**. “The donors who endow these chairs know that they are ensuring the excellence of the Salk’s research today and in the future. We thank Audrey Geisel and Arthur Woodrow for their crucial support and Joan and Irwin Jacobs for their continued generosity.”

From left to right: Darlene Shiley, Arthur Woodrow and Bill Brody. Seated: Joseph Noel





From left: Catherine Rivier and Darlene Shiley

salk women & science

Where cures begin.

Women & Science participants Heather Virdo and Luanne Bas.




Salk holds second Women & Science event

MORE THAN 60 COMMUNITY AND BUSINESS LEADERS

assembled at the Salk Institute on November 27 for the second Salk Women & Science event, which featured **Catherine Rivier**, professor emerita of the Clayton Foundation Laboratories for Peptide Biology, speaking about her groundbreaking research on hormones. The ongoing program is designed to provide a vibrant forum for women to interact with female scientists as they discuss the latest discoveries in research and technology.

Rivier gave a presentation of how information about stressors, such as exposure to alcohol or stimulation of the immune system, is transmitted to the brain, as well as where in the brain the information is received and how the brain mounts appropriate endocrine responses. The event also featured remarks by **Darlene Shiley**, vice chair of the Salk board of trustees and co-chair of the Campaign for Salk.

The next Salk Women & Science event will be held Tuesday, March 19 from 4–6 p.m. For more information, contact **Betsy Reis**, director of donor relations, at 858.453.4100, x1426 or email: breis@salk.edu. 

» Watch the video

www.salk.edu/ismar13/video1



Geoff Wahl (center), professor in Salk's Gene Expression Laboratory and holder of the Daniel and Martina Lewis Chair, with members of his lab at the San Diego Salk/Bloomingdale's *Ready, Set, Pink!* event.

From bench to runway

SCIENTISTS AT THE SALK INSTITUTE WALKED THE RUNWAY AS models at Bloomingdale's *Ready, Set, Pink!* event on October 25 in San Diego.

The annual event raises awareness and funds for breast cancer research. Bloomingdale's selected Salk as its beneficiary, with 10 percent of all purchases made at Bloomingdale's that day donated to the Institute.

Claire Johns from the Gene Expression lab and Chemical Biology and Proteomics lab member **Charisse Crenshaw**, who is featured in this month's *Next Generation*, slipped into evening gowns, cocktail dresses and casual wear for the *Ready, Set, Pink!* fashion show, seamlessly assuming the role of models and strutting the runway with style. 📺

Claire Johns and Charisse Crenshaw take a walk down the runway and strike a pose with Salk executive vice president Marsha A. Chandler.





Tom Albright (third from left) and fellow panel experts discuss creativity and science at The Art in Science—The Science in Art forum. Photos by Kevin Berne.


The art in science; the science in art

A DISCUSSION AT THE INTERSECTION of technology and creativity took place at the Mandell Weiss Forum on November 11, when the public was invited to take part in a conversation with scientists and theater artists at “The Art in Science—The Science in Art.” In partnership with the Salk Institute, Sanford-Burnham Medical Research Institute and The Scripps Research Institute, La Jolla Playhouse hosted the free forum, in conjunction with their world premiere musical *Yoshimi Battles the Pink Robots*. The production had incorporated

consultations with biotech and medical experts to help craft a tale about a woman in a love triangle facing a life-threatening illness.

Salk scientist **Thomas D. Albright**, professor and director of the Vision Center Laboratory, and holder of the Conrad Prebys Chair in Vision Research, participated as one of the experts on the panel. Albright is a leader in research into the mechanics of visual information processing, studying how the brain perceives motion, form and color and how this contributes to knowledge, behavior and consciousness.

“There’s an obvious relationship between understanding the visual system and the appreciation and creation of art,” he said.

In particular, the audience and authorities on science and art discussed whether a theatrical experience can broaden the mind, just as new methods in research and medicine work to change the thought process, expand frontiers and alter what is considered possible. 



Kimiko Glenn (“Yoshimi”) and the cast of La Jolla Playhouse’s world-premiere production of *YOSHIMI BATTLES THE PINK ROBOTS* (Nov 6 – Dec 16, 2012), story by Wayne Coyne and Des McAnuff, music and lyrics by The Flaming Lips, directed by Des McAnuff.

“There’s an obvious relationship between understanding the visual system and the appreciation and creation of art.” – TOM ALBRIGHT

Step into Discovery

walk for salk explore salk

Where cures begin Tours, activities, talks

SATURDAY, APRIL 13, 2013

THE MOST IMPORTANT LEG OF ANY RELAY RACE is the first one. Without it, the team never crosses the finish line.

At Salk, the basic research we do is that first step to discovering new cures.

Without us there is no second step.

Join us on **Saturday, April 13**, for the inaugural **5K Walk for Salk** and **Explore Salk**, a free community open house with exclusive behind-the-scenes lab tours and an opportunity to interact with world-renowned scientists.

Your support will go directly to the heroes in the labs who are researching cancer, Alzheimer's, Parkinson's, healthy aging, diabetes, obesity, plant biology and our education outreach programs.

Entry fee for the **Walk for Salk** is \$35, which includes breakfast, t-shirt, water bottle and bag. Children under 12 are free.

Registration for **Explore Salk** activities is free.

For more information, please visit:
www.salk.edu/stepintodiscovery
or call 858.597.0657

“Basic research is why I’m still alive.”

– Jennifer Ehren, Salk scientist and cancer survivor




Several winners from the Salk Photography Contest stand in front of the other side of the camera.

Back row, left to right: Anirvan Nandy, Gerald Pao, Gianfranco Candela, Stan Helms. Front row, left to right: Marito Hayashi, Suvasini Ramaswamy, Florian Sweeney, Ruben Alvarez Rodriguez

Parting shots

A RECEPTION WAS HELD OCTOBER 17 TO CONGRATULATE THE winners of the Salk Employee Photography Contest and celebrate the opening of the accompanying exhibition.

Last year, Salk employees were invited to participate in a photography contest that highlighted the Institute through their eyes. Inspired by themes such as “Reflections,” “Breakthrough,” “Workspace,” “Impact,” and “Light,” contestants captured images of Salk from their own unique

perspectives. Each month one photo was selected as a People’s Choice finalist based on the number of online votes from the Salk community. At the end of the contest, a jury, made up of six employees from departments across campus, selected the top photos. The winning images from the juried competition and the people’s choice are currently on display in the Salk foyer. 



Joseph R. Ecker

Two more Salk faculty elected as AAAS Fellows

JOSEPH R. ECKER AND JOSEPH P. NOEL


have been named 2012 Fellows of the American Association for the Advancement of Science (AAAS), the world's largest general scientific society and the publisher of the journal *Science*. Election as an AAAS Fellow is among the highest honors in American science. Scientists are selected by their peers for "scientifically or socially distinguished efforts to advance science or its applications," according to election administrators.

"We are very proud of these investigators and the distinguished research that they have conducted at the Institute," says Salk president **William R. Brody**. "We congratulate them on their election as AAAS Fellows and look forward to their many more scientific accomplishments in the future."

Joseph Ecker, a professor in the Salk's Plant Molecular and Cellular Biology Laboratory, is a Howard Hughes Medical Institute–Gordon and Betty Moore Foundation investigator, a member of

the National Academy of Sciences and holder of the Salk International Council Chair in Genetics. He was honored for his contributions to the genomics/epigenomics of plant and human cells, particularly for the development of new tools that enable genome-wide analyses.

Joseph Noel, professor and director of Salk's Jack H. Skirball Center for Chemical Biology and Proteomics, is a Howard Hughes Medical Institute investigator and the inaugural holder of the Arthur and Julie Woodrow Chair. Noel was selected for his contributions to the understanding of plant metabolism, especially the evolution, biochemistry and structures underlying the biosynthesis of specialized metabolites, including polyketides and terpenes.

Ecker and Noel are among 702 new members who were honored during the 2013 AAAS annual meeting in Boston on February 16. The elections bring the Salk's current total of AAAS Fellows to 16. 

“We are very proud of these investigators and the distinguished research that they have conducted at the Institute.”

– WILLIAM R. BRODY

Joseph P. Noel





Martyn D. Goulding
Professor, Molecular Neurobiology Laboratory



Shreekanth Chalasani
Assistant Professor, Molecular Neurobiology Laboratory



Xin Jin
Assistant Professor, Molecular Neurobiology Laboratory



Christopher R. Kintner
Professor, Molecular Neurobiology Laboratory


Creative projects receive Innovation Grant Awards

FOUR FACULTY MEMBERS HAVE BEEN selected as the latest recipients of Salk Innovation Grants. The program encourages scientific innovation by supporting risk-taking projects that are unlikely to be funded by traditional sources. The grants were awarded through the Innovation Research Fund, which was established in 2006 by Irwin Jacobs, chairman of the Salk board of trustees.

The competition is held twice each year; in the most recent round, the four projects were chosen from a field of ten. **Martyn Goulding**, in collaboration with **Edward Callaway**, will extend Callaway's work on tracing neural circuits. **Shreekanth Chalasani's** lab will develop

a method to do rapid 3D imaging of neuronal activity in the worm *C. elegans*, established as a model organism for neurobiology by Salk Nobel laureate **Sidney Brenner**. **Xin Jin**, who is developing a way to make wireless brain recordings, will seek to understand how mice learn under natural conditions. **Chris Kintner** will perform a genome-wide analysis of an essential step in the process of gene expression.

From its inception, the Innovation Research Fund has proven the value of well-targeted money at an early stage of research. Thirty-four projects were supported and completed between 2007 and 2011, and so far, a \$5.4 million investment has been leveraged to obtain

\$28 million of new research funding, with results reported in 15 publications, including the high-impact journals *Cell*, *Nature*, *PNAS* and *Neuron*. One of the early triumphs was Callaway's success in showing that a modified rabies virus could be used to label partner cells across neuronal synapses—a technique that allows for the identification of cells that form a circuit within living brain tissue. Even before the results were published, more than 30 laboratories had requested the modified virus, demonstrating that developing innovative tools can have as much of an impact on biomedical research as breakthrough results. 

Tom Albright named president of Academy of Neuroscience for Architecture

Academy melds architecture and neuroscience in conceptualizing brain-based buildings


THOMAS D. ALBRIGHT, PROFESSOR AND DIRECTOR of the Salk's Vision Center Laboratory, is the newly appointed president of the Academy of Neuroscience for Architecture (ANFA). His term began in January 2013.

ANFA grew out of a 2003 American Institute of Architects (AIA) conference. In September 2012, the organization hosted more than 150 scientists and architects at its first annual conference held at Salk, where it announced its new grants program. The awards are intended to encourage both architects and neuroscientists to explore ways to incorporate the latest ideas in brain research into building design; cross-disciplinary teams may receive up to \$50,000.

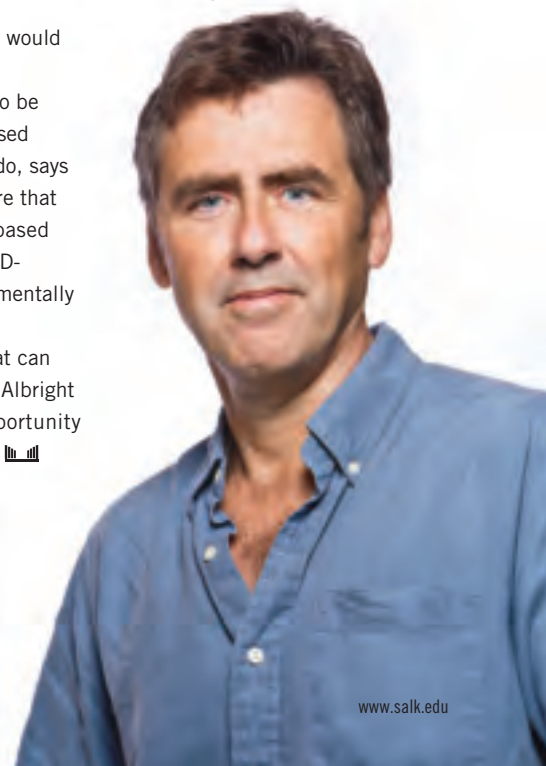
"Good architects have lots of intuitions, and that's why good architecture works," says Albright. "Our hope is that we can identify principles backing up those intuitions that are more deeply rooted in knowledge about how the brain works. We'd like to be able to

identify, for example, what particular elements would give you a better space for learning."

While there is a great deal that still needs to be studied and tested to develop an "evidence-based architecture," what ANFA ultimately hopes to do, says Albright, is create a certification that will ensure that a building's architecture has followed brain-based principles of design, in the same way that LEED-certified buildings conform to the best environmentally based practices.

"There are things that architects can do that can tap into the natural organization of the brain," Albright says. "As a neuroscientist, I welcome the opportunity to share these ideas with other professionals." 

Thomas D. Albright, professor and director of the Salk's Vision Center Laboratory and Conrad T. Prebys Chair in Vision Research, was appointed president of the Academy of Neuroscience for Architecture.

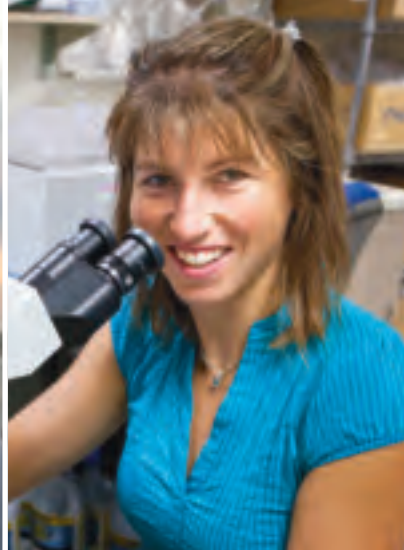




Jiwon Choi



Euseok J. Kim



Kristen J. Brennand



Xin Wang

Salk researchers receive prestigious NARSAD Young Investigator Grants

FOUR SALK RESEARCHERS HAVE BEEN awarded highly competitive NARSAD* Young Investigator Grants from the Brain and Behavior Research Foundation. The program, which has been the driving force behind thousands of scientific achievements, provides resources to young scientists conducting innovative neurobiological research that may otherwise not get funded.


Jiwon Choi and **Euseok J. Kim**, researchers in **Edward Callaway's** Systems Neurobiology Laboratories; **Kristen J. Brennand** in **Fred Gage's** Laboratory of Genetics; and **Xin Wang**, who works

in **Terry Sejnowski's** Computational Neurobiology Laboratory, all received the grants.

Out of the 1,030 applications received, only 202 researchers were selected.

Since 1987, the Brain and Behavior Research Foundation has given nearly \$300 million in over 4,000 NARSAD grants to more than 3,300 scientists around the world. The grants are among the most competitive in biomedical research because of the great ability and career success of the applicants.

"The NARSAD Young Investigator Grants have led to groundbreaking and important new

research that has improved the lives of people living with mental illness through enhanced treatments and therapies and a better understanding of the causes of mental illness," said Benita Shobe, president and CEO of the Brain and Behavior Research Foundation. 


* NARSAD is an acronym for National Alliance for Research on Schizophrenia and Depression, the former name of the Brain & Behavior Research Foundation

Salk investigator receives 2012 Ray Thomas Edwards Foundation Career Development Award

HU CANG, ASSISTANT PROFESSOR IN THE WAITT Advanced Biophotonics Center, has been named the recipient of the prestigious Ray Thomas Edwards Foundation Career Development Award. Only one three-year grant is conferred annually, aiming to foster the development of a promising early career biomedical researcher and to help him or her make the transition to becoming an independent investigator.

Cang will receive Edwards Foundation funding to support his research project, "Developing a Single Molecule Light-Sheet Fluorescence Microscopy to Image Intracellular Amyloidogenic Process," which seeks to

design a unique lens system for optical microscopes that achieves the same resolution as electron microscopes.

The Ray Thomas Edwards Foundation was established in 1997 to provide financial support for basic research in the biomedical sciences. Funded by an endowment from the late Ray Edwards, the foundation supports a range of programs designed to train and support San Diego's future scientific leaders and provides much-needed resources for young researchers. The foundation has also provided funds to endow the Roger Guillemin and Francis Crick Nobel lecture series at the Salk. 

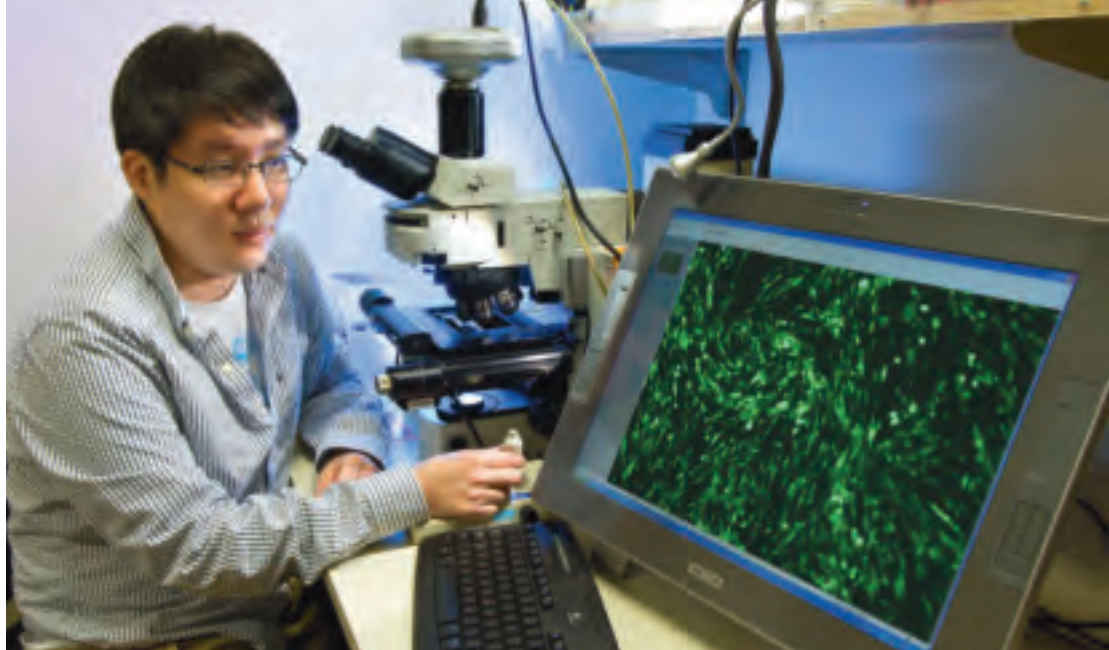
Hu Cang

Assistant Professor, Waitt Advanced Biophotonics Center





Yusuf Tufail, postdoctoral researcher, laboratory of Axel Nimmerjahn, Waitt Advanced Biophotonics Center



Euseok Kim, postdoctoral researcher, laboratory of Edward Callaway, Systems Neurobiology

Two Salk researchers selected for 2012 Life Sciences Research Foundation Fellowships

YUSUF TUFAIL AND EUISEOK KIM, HAVE BEEN AWARDED LIFE Sciences Research Fellowships from the Life Sciences Research Foundation (LSRF). They are two of only 50 finalists selected by the foundation's Peer Review Committee, from over 950 candidates.

Tufail, a postdoctoral researcher in the Waitt Advanced Biophotonics Center was chosen for the extremely competitive program based on his proposal titled "The role of astrocyte-interneuron communication in modulating cerebellar brain dynamics."

Kim, a scientist in Salk's Systems Neurobiology Laboratories was a recipient of a fellowship for his proposal entitled "Fine-scale connectivity analysis of ontogenetic neuronal clones using novel trans-synaptic viral tracers."

This is the thirtieth year the three-year postdoctoral fellowship awards have been issued by the LSRF, which was established in 1981 as an alternative means for guiding monies from industry, foundations, agencies and other donors to the non-targeted support of outstanding young scientists. Since the inception of the program, the LSRF has gained support from a wide variety of sponsors, which provide resources to an individual chosen by the LSRF board on the basis of the merit of the proposed research and the quality of the applicant's past performance. By fostering partnerships between research-oriented companies and academic institutions for their mutual benefit, the LSRF provides the framework for patrons to help fund the very best innovative early career researchers. 📊

Salk scientists score National Institutes of Health New Innovator Awards

SALK RESEARCHERS BJÖRN F. LILLEMEIER AND AXEL NIMMERJAHN have been named recipients of the prestigious 2012 National Institutes of Health (NIH) Director's New Innovator Award.

The NIH Director's New Innovator Award is a highly selective program drawing hundreds of applicants from the nation's top scientific institutions. Established in 2007, it addresses two primary goals: stimulating innovative research and supporting promising new investigators. It supports exceptionally creative young scientists who propose innovative projects with the potential for extraordinary impact. Only 51 scientists received the honor this year.

Lillemeier and Nimmerjahn will each receive \$1.5 million over five years, part of a group of young investigators who have been awarded approximately \$155 million to pursue visionary science with the potential to transform scientific fields and speed the translation of research into improved health.



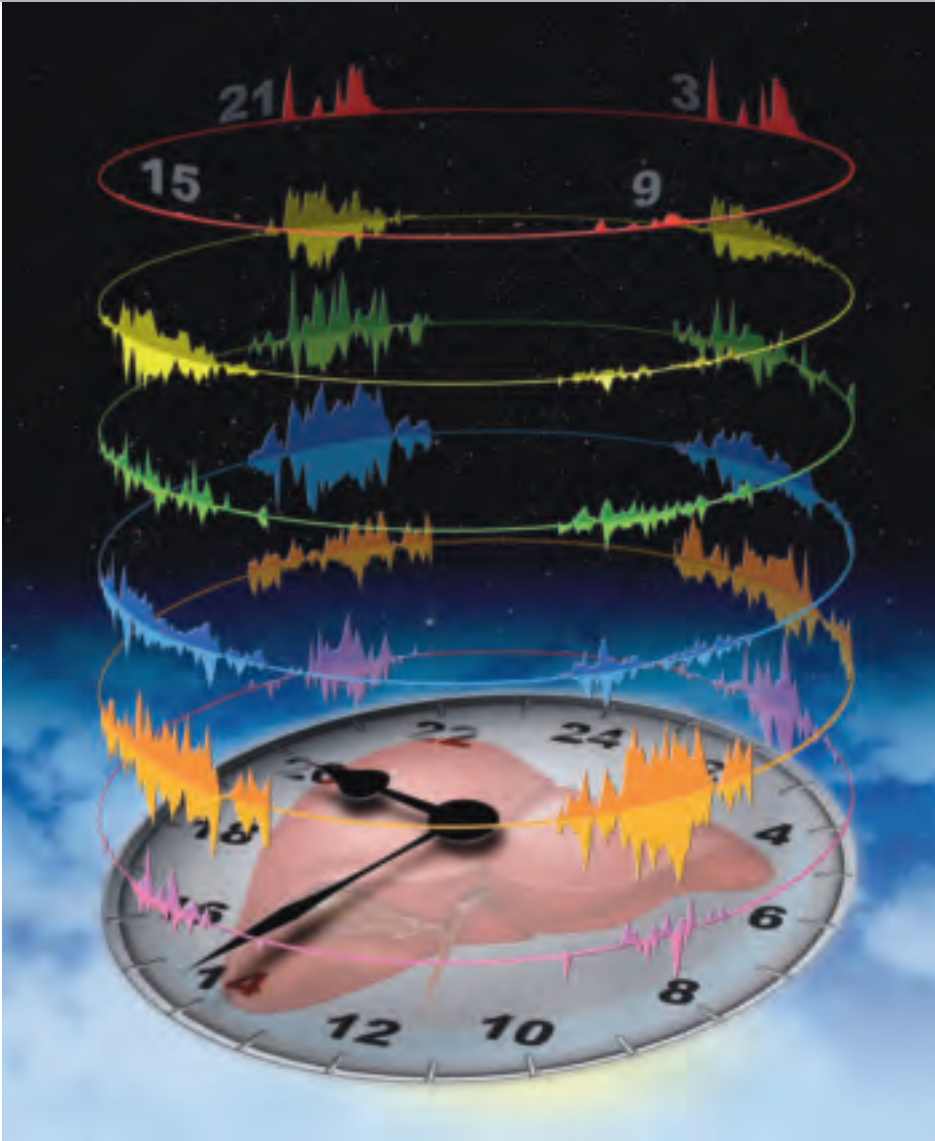
Björn F. Lillemeier
Assistant Professor
Nomis Foundation Laboratories for Immunobiology and Microbial Pathogenesis and the Waitt Advanced Biophotonics Center



Axel Nimmerjahn
Assistant Professor
Waitt Advanced Biophotonics Center

"It is extremely rare that a scientist would receive such an honor in his career, and even more exciting that an institute is fortunate enough to have two recipients selected for an NIH Director's New Innovator Award at the same time," said **William R. Brody**, Salk president. "We are very proud of Björn and Axel and grateful for NIH's support of young researchers who pursue innovative and bold science." 📊

Discovery Roundup



Thousands of epigenetic switches in the liver control whether genes turn on or off in response to circadian cycles. The figure illustrates daily changes, every six hours, in five different features of chromatin associated with the timed expression of a gene (red track on top).

More than 3,000 epigenetic switches control daily liver cycles

Salk findings may help explain connections between dietary schedules and chronic disease

WHEN IT'S DARK, AND WE START TO FALL asleep, most of us think we're tired because our bodies need rest. Yet circadian rhythms affect our bodies not just on a global scale, but at the level of individual organs, and even genes.

Now, Salk scientists have determined the specific genetic switches in mice that sync liver activity to the circadian cycle. Their finding gives further insight into the mechanisms behind health-threatening conditions such as high blood sugar and high cholesterol.

"We know that genes in the liver turn on and off at different times of day and they're involved in metabolizing substances such as fat and cholesterol," says **Satchidananda Panda**, co-corresponding author on the paper and associate


professor in Salk's Regulatory Biology Laboratory. "To understand what turns those genes on or off, we had to find the switches."

In the case of humans and other vertebrates, a brain structure called the suprachiasmatic nucleus controls circadian responses. But there are also clocks throughout the body, including our visceral organs, which tell specific genes when to make the workhorse proteins that enable basic functions in our bodies, such as producing glucose for energy.

In the liver, genes that control the metabolism of fat and cholesterol turn on and off in sync with these clocks. But genes do not switch on and off by themselves. Their activity is regulated by the "epigenome," a set of

molecules that signal to the genes how many proteins they should make, and, most importantly from the circadian point of view, when they should be made.

To their surprise, the Salk scientists discovered that among those epigenetic switches was chromatin, the protein complex that tightly packages DNA in the cell nucleus. While chromatin is well known for the role it plays in controlling genes, it was not previously suspected of being affected by circadian cycles.

Panda and his colleagues, including **Joseph R. Ecker**, holder of the Salk International Council Chair in Genetics, reported their results in *Cell Metabolism*. 

Discovery Roundup



From left: Postdoctoral researcher Dinorah Friedmann-Morvinski and Inder Verma, professor in Salk's Laboratory of Genetics.

Aggressive brain tumors can originate from a range of nervous system cells

SCIENTISTS HAVE LONG BELIEVED THAT GLIOBLASTOMA MULTIFORME (GBM), the most aggressive type of primary brain tumors, begins in glial cells that make up supportive tissue in the brain or in neural stem cells. In a paper published in *Science*, however, Salk researchers reported that the tumors can originate from other types of differentiated cells in the nervous system, including cortical neurons.


"One of the reasons for the lack of clinical advances in GBM has been the insufficient understanding of the underlying mechanisms by which these tumors originate and progress," says **Inder Verma**, a professor in Salk's Laboratory of Genetics and the holder of the Irwin and Joan Jacobs Chair in Exemplary Life Science.

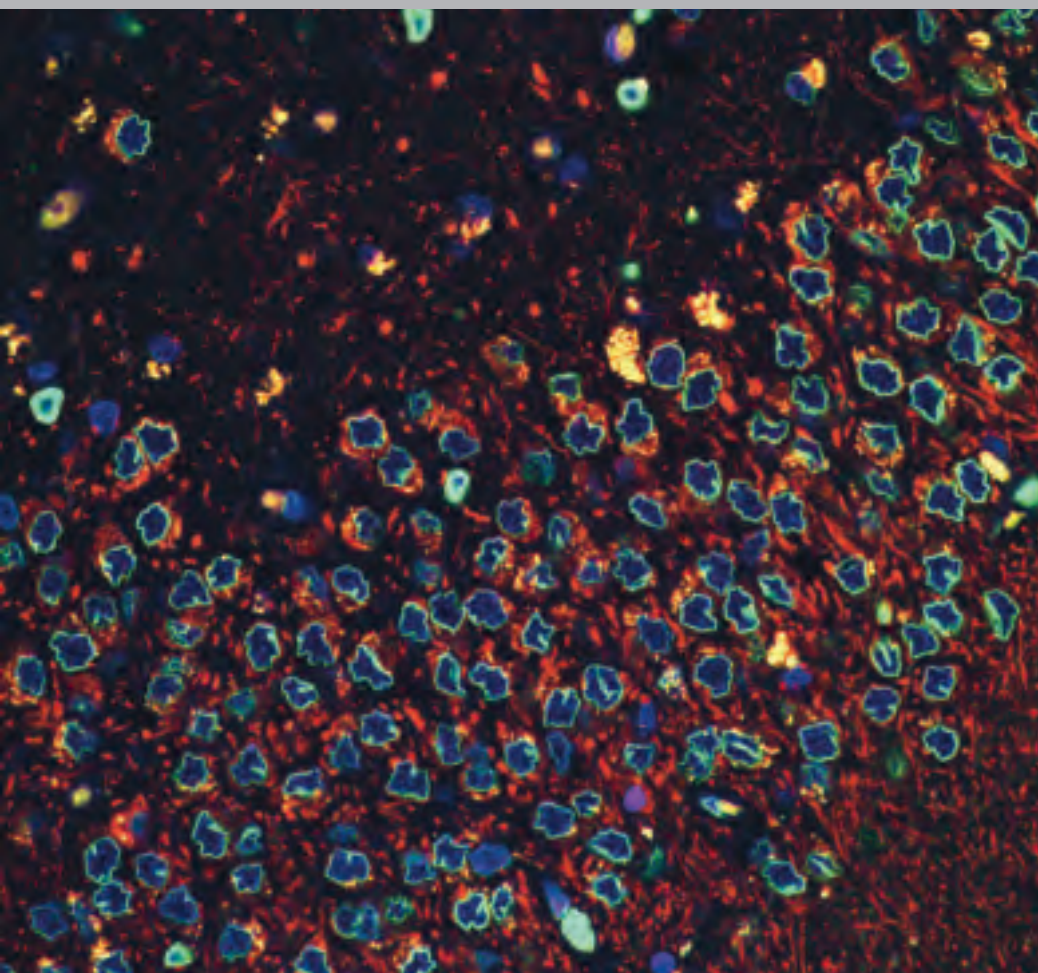
To better understand this process, Verma's team harnessed the power of modified viruses, called lentiviruses, to disable powerful tumor suppressor genes in mice that regulate the growth of cells and inhibit the development of tumors. With these tumor suppressors deactivated, cancerous cells are given free rein to grow out of control. The modified viruses target two genes—neurofibromatosis 1 (NF1) and p53—that, when mutated, are implicated in severe gliomas like GBM. Using sophisticated analytical

techniques, they discovered that neurons genetically converted by the lentiviruses are capable of forming malignant gliomas.

"Our findings," says lead author **Dinorah Friedmann-Morvinski**, a postdoctoral researcher in the Laboratory of Genetics, "suggest that, when two critical genes—NF1 and p53—are disabled, mature, differentiated cells acquire the capacity to reprogram [dedifferentiate] to a neuroprogenitor cell-like state, which can not only maintain their plasticity, but also give rise to the variety of cells observed in malignant gliomas."

GBM is one of the most devastating brain tumors that can affect humans. Despite progress in genetic analysis and classification, the prognosis of these tumors remains poor, with most patients dying within one to two years of diagnosis. The Salk researchers' findings suggest potential new targets to treat these deadly cancers.

"Our results offer an explanation of recurrence of gliomas following treatment," says Verma, "because any tumor cell that is not eradicated can continue to proliferate and induce tumor formation, thereby perpetuating the cycle of continuous cell replication to form malignant gliomas." 



The Salk researchers found that a common genetic mutation involved in Parkinson's disease deforms the membranes (green) surrounding the nuclei (blue) of neural stem cells. The discovery may lead to new ways to diagnose and treat the disease.

Salk scientists pinpoint key player in Parkinson's disease neuron loss

BY REPROGRAMMING SKIN CELLS FROM Parkinson's disease patients with a known genetic mutation, Salk researchers have identified damage to neural stem cells as a powerful player in the disease. The findings, reported in *Nature*, may lead to new ways to diagnose and treat the disease.

The scientists found that a common mutation to a gene that produces the enzyme LRRK2, which is responsible for both familial and sporadic cases of Parkinson's disease, deforms the membrane surrounding the nucleus of a neural stem cell. Damaging the nuclear architecture leads to destruction of these powerful cells and decreases their ability to spawn functional neurons, such as the ones that respond to dopamine.

The researchers checked their laboratory findings with brain samples from Parkinson's disease patients and found the same nuclear envelope impairment.

"This discovery helps explain how Parkinson's disease, which has been traditionally associated with loss of neurons that produce dopamine and subsequent motor impairment, could lead to locomotor dysfunction and other common non-motor manifestations, such as depression and anxiety," says **Juan Carlos Izpisua Belmonte**, a professor in Salk's Gene Expression Laboratory, who led the research team. "Similarly, current clinical trials explore the possibility of neural stem cell transplantation to compensate for dopamine deficits. Our work provides the platform for similar trials by using patient-specific corrected cells. It identifies degeneration of the nucleus as a previously unknown player in Parkinson's."

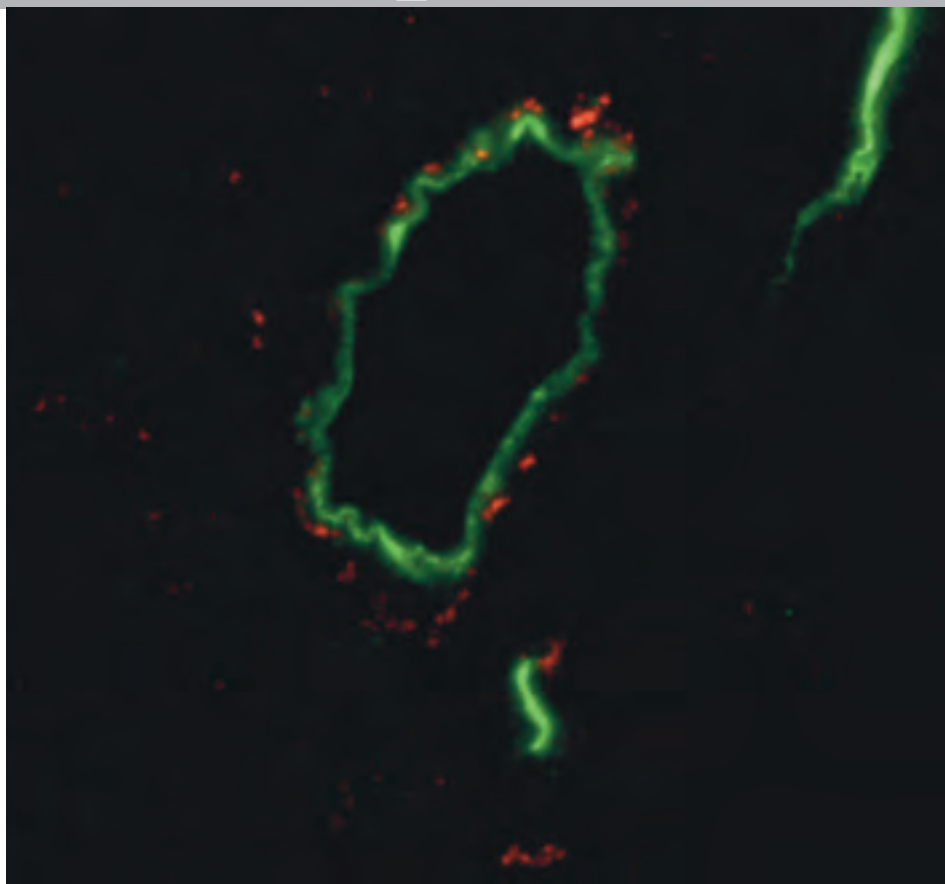
Although the researchers say that they don't yet know whether these nuclear aberrations cause Parkinson's disease or are a consequence of it, they say the discovery could offer clues about potential new therapeutic approaches.

For example, they were able to use targeted gene-editing technologies to correct the mutation in patients' nuclear stem cells. This genetic correction repaired the disorganization of the nuclear envelope and improved overall survival and functioning of the neural stem cells. They were also able to chemically inhibit damage to the nucleus, producing the same results seen with genetic correction. "This opens the door for drug treatment of Parkinson's disease patients who have this genetic mutation," says Izpisua Belmonte.

The new finding may also help clinicians make better diagnoses. "Due to the striking appearance in patient samples," Izpisua Belmonte says, "nuclear deformation parameters could add to the pool of diagnostic features for Parkinson's disease." ■

Discovery Roundup

“We show that type 1 diabetes increases vascular-associated amyloid beta buildup in the brain and causes accelerated brain aging.” — PAMELA MAHER



This microscope image shows blood vessels in the brain of a mouse (green) surrounded by amyloid beta peptides (red), a component of the amyloid plaques found in the brains of Alzheimer's patients. Salk researchers found that these peptides accumulate in the brains of diabetic and aged mice, a finding that may help explain the connection between diabetes and Alzheimer's.

Salk study finds diabetes raises levels of proteins linked to Alzheimer's features

GROWING EVIDENCE SUGGESTS THAT THERE MAY BE A LINK between type 1 diabetes and Alzheimer's disease, but the physiological mechanisms by which diabetes impacts brain function and cognition are not fully understood. Now, in a study published in *Aging Cell*, Salk researchers show, for the first time, that diabetes enhances the development of aging features that may underlie early pathological events in Alzheimer's.

The Salk team found increases in two hallmarks of Alzheimer's—accumulations of amyloid beta (Aβeta) and tau protein—in the brains of diabetic mice, especially in cells surrounding blood vessels. Aβeta, the misfolded peptide that is thought in part to cause Alzheimer's disease, aggregated inside astrocytes, star-shaped brain cells that, upon interaction with Aβeta, release inflammatory molecules that can destroy neurons. Previously, this had not been shown in mouse models of type 1 diabetes.


“Our study supports and extends the links between diabetes, aging and Alzheimer's,” says author **Pamela Maher**, a senior staff scientist in Salk's Laboratory of Cellular Neurobiology. “We show that type 1 diabetes increases vascular-associated amyloid beta buildup in the brain and causes accelerated brain aging.”

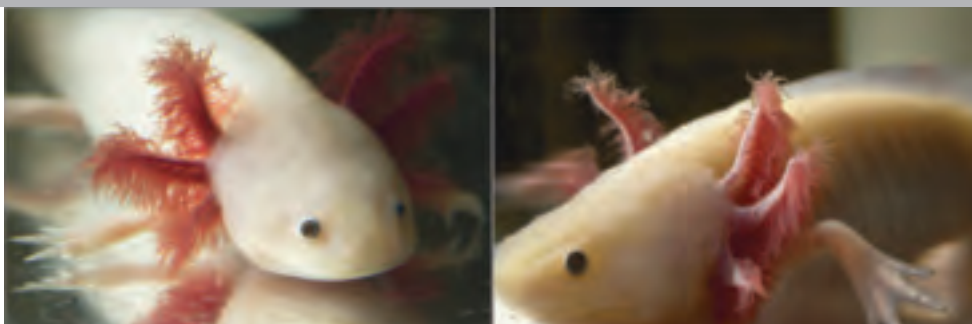
To examine the contributions of diabetes to Alzheimer's-related pathology in the aged brain, the Salk researchers induced type 1 diabetes

in two sets of mice. One set, known as SAMP8 mice, undergo accelerated aging and develop early deterioration in learning and memory, as well as a number of brain alterations similar to those found in Alzheimer's. The other set, SAMR1 mice, which in this study came from the same gene pool as the SAMP8 mice, age normally.

Using these mice, Maher and her colleagues addressed how type 1 diabetes interacts with age to contribute to Alzheimer's-related pathology. They showed that diabetes elicits a wide range of pathological changes in the brains of both strains of mice, which are exacerbated by premature aging.

The Salk study is the first to show that these modifications are similar to those seen in old nondiabetic SAMP8 mice and to identify unique pathological changes, such as increases in markers for inflammation, in aged, diabetic SAMP8 mice. Unlike most mouse studies of Alzheimer's, Maher's mice were not engineered to produce high levels of human Aβeta or tau, so all of their observations came from naturally occurring Aβeta and tau.

The findings suggest that the neurovascular system may be a good candidate for new therapeutic targets to treat Alzheimer's in the early stages of the disease. 



Salk research shows that in the axolotl, a Mexican salamander, jumping genes have to be shackled, or they might move around in the genomes of cells in the tissue destined to become a new limb and disrupt the process of regeneration.

What can the water monster teach us about tissue regeneration in humans?

BASED ON TWO NEW STUDIES BY SALK researchers, regeneration of a new limb or organ in a human will be much more difficult than the mad scientist and supervillain, Dr. Curt Connors, made it seem in the Amazing Spider-Man comics and films.


As those who saw the recent movie, *The Amazing Spider-Man*, will know, Connors injected himself with a serum made from lizard DNA to successfully regrow his missing lower right arm—that is, before the formula transformed him into a reptilian humanoid.

But by studying a real lizard-like amphibian, which can regenerate missing limbs, the Salk researchers discovered that it isn't enough to activate genes that kick-start the regenerative process. In fact, one of the first steps is to halt the activity of so-called jumping genes.

In research published in both *Development, Growth & Differentiation* and *Developmental Biology*, the researchers showed that in the Mexican axolotl, an immature tadpole-like form of a salamander, jumping genes have to be shackled, or they might move around in the genomes of cells in the

tissue destined to become a new limb and disrupt the process of regeneration. They found that two proteins, piwi-like 1 (PL1) and piwi-like 2 (PL2), perform the job of quieting down jumping genes in the axolotl—a creature whose name means water monster and who can regenerate everything from parts of its brain to eyes, spinal cord and tail.

“What our work suggests is that jumping genes would be an issue in any situation where you wanted to turn on regeneration,” says the studies’ senior author, **Tony Hunter**, a professor in the Molecular and Cell Biology Laboratory and director of the Salk Institute Cancer Center.

“As complex as it already seems, it might seem a hopeless task to try to regenerate a limb or body part in humans, especially since we don’t know if humans even have all the genes necessary for regeneration,” says Hunter. “For this reason, it is important to understand how regeneration works at a molecular level in a vertebrate that can regenerate as a first step. What we learn may eventually lead to new methods for treating human conditions, such as wound healing and regeneration of simple tissues.” 

Chromosome “anchors” organize DNA during cell division

FOR HUMANS TO GROW AND TO REPLACE and heal damaged tissues, the body’s cells must continually reproduce, a process known as “cell division,” by which one cell becomes two, two become four, and so on. A key question in biomedical research is how chromosomes, which are duplicated during cell division so that each daughter cell receives an exact copy of a person’s genome, are arranged during this process.

Now Salk scientists have discovered a new characteristic of human cell division that may help explain how our DNA is organized in the nucleus as cells reproduce. They found that telomeres, molecular caps that protect the ends of the chromosomes, move to the outer edge of the cell’s nucleus after they have been duplicated.

“What we discovered is that telomeres not only protect our chromosomes; they also help organize our genetic material in the nucleus,” says **Jan Karlseder**, a professor in the Molecular and Cell Biology Laboratory and holder of the Donald and Darlene Shiley Chair. “This is important because the three-dimensional

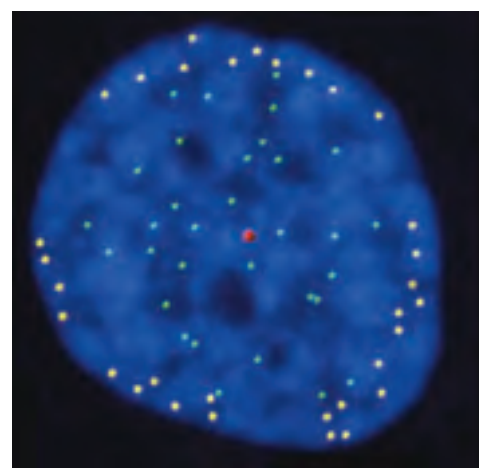
position of DNA in the nucleus influences gene expression profiles and how the genome morphs over time.”

Previous studies on human cells have shown that telomeres change position during cell division, suggesting they might play a role in organizing DNA in the nucleus. But these studies provided only isolated snapshots of telomeres at various stages of the cell cycle.


In their new study, Karlseder and his team used advanced time-lapse live-cell confocal microscopy to track telomere movement in real time throughout the cell cycle. They also recorded the movement of chromatin, a combination of DNA and proteins that forms chromosomes.

The scientists found that the telomeres move to the periphery of the nuclear envelope of each daughter cell nucleus as they assemble after mitosis, the stage of cell division during which the cell’s DNA is duplicated to provide each daughter cell with its own copy.

“The tethering of telomeres to the nuclear envelope may serve as an anchor point to reorganize chromatin after each cell division, so that our DNA is correctly situated for gene



This image shows telomeres (yellow), protective caps on the ends of chromosomes, moving to the outer edge of a cell’s nucleus (blue).

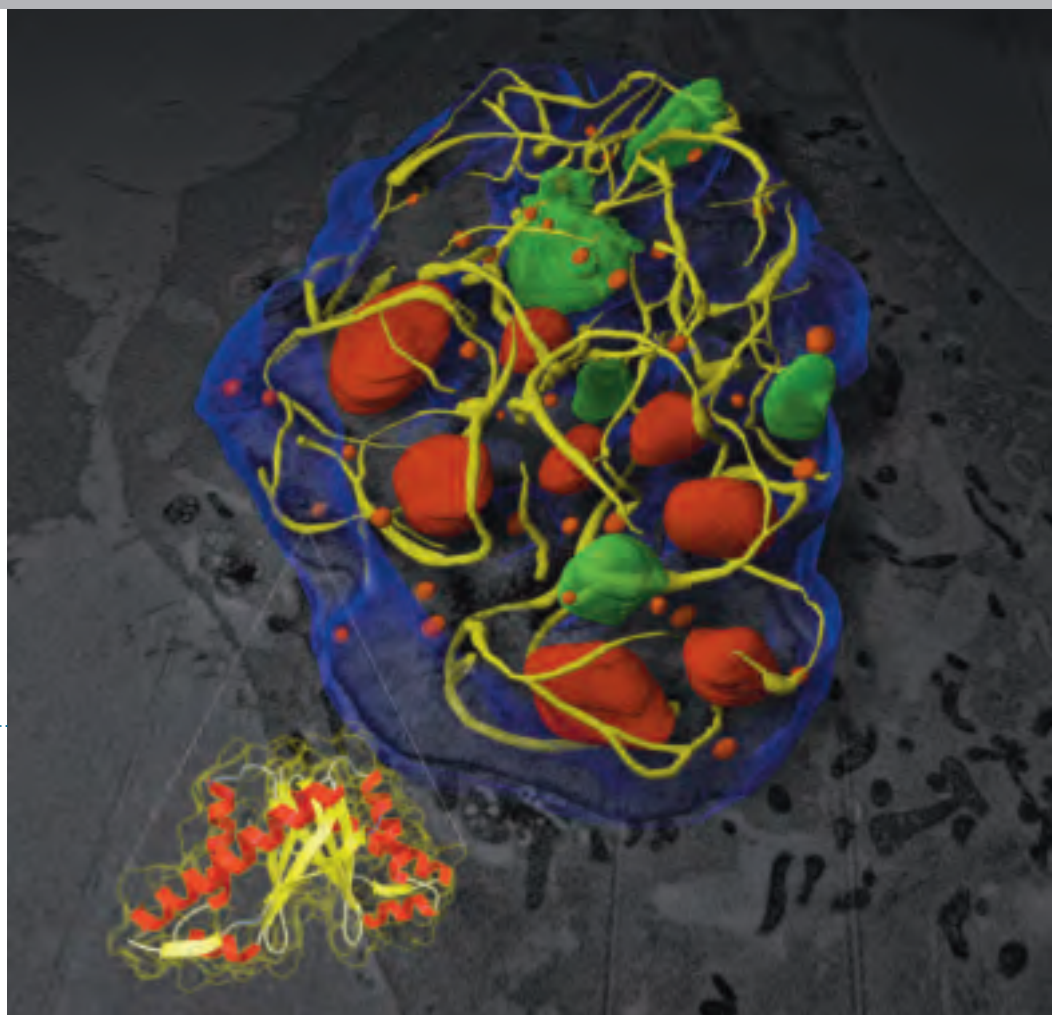
expression,” Karlseder says. “This tethering could also play a role in the maintenance of telomeres, thereby influencing aging, cancer development and other disorders associated with DNA damage. We plan to explore these possibilities in future experiments.” 

Discovery Roundup

» Watch the video

www.salk.edu/ismar13/video3

Salk researchers discovered that a small protein produced by cold viruses disables large cellular machines involved in growth, replication and cancer. These proteins accomplish this by forming a three-dimensional web inside a cell's nucleus (yellow) that traps these components. The findings point the way to new approaches to targeting and destroying tumors.



Cold viruses point the way to new cancer therapies

COLD VIRUSES GENERALLY GET A BAD RAP, which they've certainly earned, but new findings by a team of Salk scientists suggest that these viruses might also be a valuable ally in the fight against cancer.

Adenovirus, a type of cold virus, has developed molecular tools—proteins—that allow it to hijack a cell's molecular machinery, including large cellular machines involved in growth, replication and cancer suppression. The scientists identified the construction of these molecular weapons and found that they bind together into long chains (polymers) to form a three-dimensional web inside cells that traps and overpowers cellular sentries involved in growth and cancer suppression. The findings, published in *Cell*, suggest a new avenue for developing cancer therapies by mimicking the strategies employed by the viruses.


"Cancer was once a black box," says **Clodagh O'Shea**, an assistant professor in Salk's Molecular and Cell Biology Laboratory, who

led the study. "The key that opened that box was revealing the interactions between small DNA tumor virus proteins and cellular tumor suppressor complexes. But without knowing the structure of the proteins they use to attack cells, we were at a loss for how these tiny weapons win out over much larger tumor suppressors."

O'Shea's team studied E4-ORF3, a cancer-causing protein encoded by adenovirus, which prevents the p53 tumor suppressor protein from binding to its target genes. "Most cellular polymers and filaments form uniform, rigid chains," O'Shea says. "But E4-ORF3 is the virus's Swiss army knife—it assembles into something that is highly versatile. It has the ability to build itself into all sorts of different shapes and sizes that can capture and deactivate the many defenses of a host cell."

In collaboration with scientists from the National Center for Microscopy and Imaging Research at the University of California, San Diego, O'Shea's team used new techniques to

reveal the ultrastructure of the remarkable polymer that E4-ORF3 assembles in the nucleus—something that previously had proven difficult since the polymer is effectively invisible using conventional electron microscopy.

The findings may help scientists develop small molecules—the basis for the vast majority of current drugs—capable of destroying tumors by binding and disrupting large and complex cellular components that allow cancer cells to grow and spread. Understanding how viruses overcome healthy cells may also help scientists engineer tumor-busting viruses, which offer a new and potentially self-perpetuating cancer therapy. Such modified viruses would destroy only cancer cells, because they could only replicate in cells in which the p53 tumor suppressor has been deactivated. When a cancer cell is destroyed, it would release additional copies of the engineered viruses, which would seek out and kill remaining cancer cells that have spread throughout the body. 

A woman with dark hair tied back, wearing a white long-sleeved shirt and black pants, is captured in a dynamic yoga pose on a grassy hill. She is leaning forward with her arms extended high above her head, palms facing each other. Her legs are spread wide in a lunge-like position. The background features a vast, calm ocean under a clear blue sky, with the sun low on the horizon, creating a soft, golden light. The overall mood is serene and focused.

The **next** generation:

Good luck
keeping up with
Charisse Crenshaw

“I believe the broader your interests are, the more fundamental are the connections you’re likely to recognize.”

– CHARISSE CRENSHAW

CHARISSE CRENSHAW STUDIED GYMNASTICS AS A CHILD BEFORE

switching to ballet and jazz, ran track in high school, and as a graduate student led her Harvard laboratory volleyball team to such heights that they moved up an entire competitive bracket. But that’s just for starters. She also practices yoga, is a classical soprano, a fashion model and active in her church. All that on top of being a postdoctoral researcher in the laboratory of Salk plant biochemist **Joseph P. Noel**.

Just reciting her schedule can leave other people breathless, yet she sees her activities as essential to her science. “I believe the broader your interests are, the more fundamental are the connections you’re likely to recognize,” says Crenshaw. “Pursuing vocal training, captaining our lab volleyball team, and serving my church family was like cross-training for my brain in graduate school. When I myopically stopped doing some of the other things I loved, I actually felt less smart. Having hobbies outside of the lab should be a requirement for scientists!”

As a woman, a scientist, a black American and a person of faith, Crenshaw has been at the center of many flashpoint topics in American society. Much of her life, both personally and professionally, has been spent challenging other people’s assumptions. As a biochemist now studying plant biology, she finds one of the most persistent assumptions is the idea that if it’s natural, it’s good for you.

“That’s not always true!” she counters, “Plants don’t play around! They kill all the time!”

The reason, she explains, is that plants can’t run away from their predators or towards each other to mate. As a result, they’ve developed sophisticated biochemical communication systems, with an extraordinary array of molecular compounds. “The plant natural product family I study has 30,000 known compounds, and we barely understand what they do,” she says.

But if plants can be more dangerous than we realize while sniffing organic produce at the farmers’ market, they can also be more beneficial than even the most ardent natural advocate can dream. “Not a lot of people realize that the vast majority of drugs on the market have their origins in plants, as well as microorganisms, such as fungus, which have an intricate relationship with plants,” says Crenshaw. “As a biomedical researcher, there’s a huge incentive to get to know more about natural products.”

Among those products are the “terpenes,” a large group of volatile chemicals created by plants. Their functions range from light scents that attract pollinators to heavy resins that trap predators. “Terpenes are why pine trees smell ‘piney’ and lemons smell ‘lemony,’” explains Crenshaw.

Most famous among the medically relevant terpenes may be paclitaxel, a chemical produced by the Pacific yew tree, known by the trade name Taxol®. In the 1960s, it was found to successfully treat several



types of cancer. While Taxol is potent, it is far from perfect: It is costly to prepare, challenging to administer, and worst of all, has potentially dangerous side effects. Unfortunately, it is so molecularly complex that it is hard to modify to overcome these problems.

This is where Crenshaw’s work as a biochemist in Noel’s lab comes in. “We’re currently trying to determine how the puzzle of Taxol and the other over 30,000 terpenes fits together. The basic puzzle pieces are enzymes. If we can predictably engineer these enzymes, we could tap into the vast unknown reservoir of terpenes that are out there for treating disease but currently are impossible to find,” she says. “Our ultimate goal is to use new technological advances to engineer at the nanoscale and produce tailor-made synthetics that can be used for a lower-cost cancer treatment.”

Crenshaw came to Noel’s lab after graduate work in biochemistry at Harvard. She hails from Bakersfield, where her family moved from Brooklyn when she was seven. Her father, a former internist, felt a calling to the ministry and left medicine to become a pastor in California. Her mother still practices in Bakersfield as an obstetrician/gynecologist.

With two doctors for parents, it’s no surprise Crenshaw’s earliest memories involve science. “My dad thought every 4-year-old should know an atom was made from protons, neutrons and electrons,” she says of her parents’ approach to raising a smart and curious child.



Crenshaw leads a scientific demonstration for this year's Aaron Price Fellows.

“I hope just by being myself and working hard, I can prove to kids that successful scientists can come from any background...” — CHARISSE CRENSHAW

Crenshaw had never known any Ph.Ds growing up, so she thought medical school would be the answer to her ravenous scientific curiosity. But as a pre-medical undergraduate at the University of California, Los Angeles, her questions were answered by professors offering disclaimers about the limits of current knowledge. She was horrified. “I thought, ‘What?! I haven’t even gotten to medical school—and we’ve run out of information!’”

Realizing how much was left to discover was both scary and exhilarating. She couldn’t picture herself telling patients that their conditions had no known cures. She realized that the answers she sought for herself and those with illnesses could only be found through basic biomedical research. So she turned to biochemistry. “I realized I needed to study the molecules themselves,” she says, “and understand why they worked and why they malfunctioned.”

Recently, she’s taken on a new challenge, sharing her enthusiasm for science with children through the Aaron Price Fellows Program and Salk’s Educational Outreach Program, which provides San Diego middle and high school students with hands-on science education. She feels most inspired when speaking to younger children, because she knows that many are interested in science but are turned off by stereotypes of scientists that they don’t identify with. “I know I defy most of those stereotypes,” she says. “I hope just by being myself and working hard, I can prove to kids that successful scientists can come from any background, because it’s our intellectual honesty and curiosity that bind us together.” 📖



Crenshaw walks the runway at Bloomingdale's *Ready, Set, Pink!* (For more on the event, see page 18).




Standing from left: Brian Devine, Silvija Devine, Michel Mathieu, Judy Hodges, Richard McDonald. Seated, from left: Clifford Schireson, Helene Kruger, John Venekamp, Alice Orgel

Celebrating Salk science, President's Club-style

MORE THAN 60 SALK PRESIDENT'S CLUB MEMBERS

gathered at the Institute on December 6 for the group's annual holiday luncheon. The program featured a presentation by Salk Cancer Center director and professor **Tony Hunter**, titled "What Tumor Viruses Have Taught Us About Cancer." Hunter described how his discovery of a key chemical reaction that regulates a wide variety of cellular events has resulted in new cancer therapies, including Gleevec, which is used by many thousands of patients to treat leukemia and other cancers. President **William R. Brody** outlined how the Campaign for Salk will generate funding to ensure Salk scientists the resources they need to continue making groundbreaking discoveries in light of declining federal funding.

President's Club members provide critical support for Salk scientists, whose research is leading to transformational diagnostics, therapies and cures. President's Club supporters receive a number of benefits, including special invitations to engage with Salk scientists. To learn more, please visit www.salk.edu/support or call 858.453.4100 x1405. 





Left to right: Trent and Trish Douglas, Joanna Roddis, George and Kristin Trikas

salkexcellerators

San Diego Salkexcellerators gain insights into metabolism and cancer research

THE SAN DIEGO SALKEXCELLERATORS

gathered at the Institute on November 7 for a private reception and presentation by **Reuben Shaw**, titled “Treating Cancer with Diabetes Drugs...and other Adventures in Basic Biomedical Research.” Shaw, an associate professor in the Molecular and Cell Biology Laboratory and the Dulbecco Laboratory for Cancer Research, serves as the Salkexcellerator faculty liaison.

Postdoctoral researcher **Rob Svensson**, who joined the Shaw lab in summer 2011, spoke

first, about the rigorous academic and professional hurdles that up-and-coming scientists face as they make their way from biology students to principal investigators. Shaw’s talk outlined his laboratory’s findings about the molecular pathways involved in the development of both cancer and type 2 diabetes—a connection that his group discovered is far closer than previously known.

Salkexcellerators are the next generation of community members committed to

supporting scientific discovery through the Salkexcellerators Fund. The program provides a social and educational forum through a year-round calendar of events with Salk scientists in La Jolla and in New York City. For more information, please visit www.salk.edu/support/salkexcellerators or call 858.453.4100 x1405. 📶

From left to right: Salk scientists Dan Egan, Erin Toyoma, Rob Svensson, and Portia Lombardo





William R. Brody and Karen Joy Davis dazzle the audience playing 191.

International Council enjoys science and music at Salk

THE ANNUAL MEETING OF THE SALK

International Council, which took place at the Institute this year, showcased Jonas Salk's vision for a research facility dedicated to the best of both art and science.

The 70-person meeting kicked off Wednesday, January 23, with "Bio 101," a 2½-hour basic biology overview. It set the stage for the next two days, which featured a true insider's look at the Institute, including in-depth scientific talks and laboratory tours. Salk researchers discussed in detail the scientific issues behind the initiatives of the Campaign for Salk.

A highlight of the event was the first concert ever given in the Auditorium at Salk, a classical piano recital on Thursday night by award-winning concert pianist Karen Joy Davis. She performed on "191," the world-famous Steinway grand piano that was recently gifted to the Institute by Salk trustee **Conrad Prebys**. For Brahms's Hungarian Dances (No.1 in G minor and No. 5 in F# minor), she was joined by a surprise guest artist, Salk president **Bill Brody**.

In addition to scientific and artistic offerings, this year's gathering celebrated **Lidia Garcia-Campmany**, who works in **Martyn Goulding's**

Molecular Neurobiology Laboratory, and is the first postdoctoral researcher supported by the new Jonas Salk Endowed Fellowship. The fellowship's endowment is nearly at its goal of \$1.5 million.

The council is made up of more than 50 distinguished men and women who are world-wide leaders in business, medicine, law, the arts and community affairs. 📊

Lidia Garcia-Campmany discusses research with International Council members Jo Norris and Mary Jane Salk.

From left to right: Carl Hahn (IC member, Germany), Amedee de Georges (special guest), Stephanie Blank (special guest), Cedric Bardy (research associate in Gage Lab), Ed Streim (IC member, NY)





Insider's View

William R. Brody, M.D., Ph.D.
President, Salk Institute
Irwin M. Jacobs Presidential Chair

WITH ALL THE EMPHASIS ON COST CONTROL BY THE CONGRESS, THE BIG ELEPHANT

in the room that has not yet been tamed is the rapid rise of costs for the care of Medicare recipients. Recently I spoke to the vice dean for clinical investigation at Johns Hopkins School of Medicine, and he echoed the sentiment that Medicare patients with five or more chronic ailments are consuming a large fraction of Medicare costs and sapping the energy of the healthcare delivery system.

Patients arrive with a chart outlining multiple problems—diabetes, high blood pressure, heart failure and arthritis, for example—then drop a grocery bag full of medications into the doctor's lap. There simply isn't enough time in the day to sort through which of the patient's problems require focused attention by the doctor and which are not germane to the current visit. The interactions between the myriad drugs are so complex that often it is difficult to separate a problem caused by a drug interaction from one that results from the chronic disease itself. On top of that, the various diseases themselves interact in often unknown ways.

Simply put, we need a far better understanding of the relationships between diseases—and that is where Salk comes in. At the Salk Institute, scientists focus on the basic mechanisms of how cells work in health and disease. Although many of our scientists are exploring the frontiers of specific diseases, such as cancer, Alzheimer's, diabetes and so forth, they also realize that the various pathways by which cells or organs function in one disease may also be active in others. Salk scientists have helped to discover pathways in diabetes that also play a significant role in cancer, for instance, leading to the speculation that one of the most commonly used drugs to treat type 2 diabetes, metformin, may also play a role in reducing the risk of developing certain types of cancers.

The recent award of \$42 million from the Leona M. and Harry B. Helmsley Charitable Trust resulted from a free-form discussion among Salk scientists. They considered the similarities among various types of chronic diseases, and postulated that understanding chronic inflammation may be a key to unraveling common pathways underlying these illnesses.

Such an audacious idea is far too risky to be supported by the National Institutes of Health without a lot of data to support the hypothesis. The generous support and keen input from the Helmsley Charitable Trust in developing this grant allows us to bring together scientists at Salk working in different areas, from stem cells to genetics, metabolism to immunology, cancer to neurodegenerative disease. The unique fabric of collaboration without boundaries at Salk, combined with a Helmsley Charitable Trust's willingness to support novel ideas, will make groundbreaking discoveries possible. ■■■

Salk Science LEADS TO DISCOVERIES.

IMPACTING HUMAN HEALTH BEGINS AT THE SALK.

Scientific discovery at the Salk Institute is made possible through annual contributions from individuals, organizations, corporations and foundations. Your support will accelerate the pace of breakthroughs in understanding disease and pave the way to new drug therapies. To learn more, please visit **www.salk.edu/support** or call 858.453.4100 x2068.

Get INVOLVED

FRIENDS OF SALK

Unrestricted gifts, in any amount, provide funding where it is most needed and allows our scientists to conduct critical early-stage research. Contributors up to \$2,500 receive *Inside Salk* magazine and invitations to annual events.

SALKEXCELLERATORS

The Salkexcellerators program is focused on making Salk science accessible to a younger generation of business professionals, entrepreneurs, and volunteers. Donors receive *Inside Salk* magazine and invitations to private receptions and lectures with Salk's renowned scientists. Salkexcellerators meet in La Jolla and New York City, and engagement ranges from \$500 to \$5,000.

PRESIDENT'S CLUB

President's Club donors fulfill a central role for the Institute and provide the flexibility to respond to Salk's greatest needs. Contributors of \$2,500 – \$25,000 enjoy unique opportunities to interact with our scientists in the lab and receive Salk publications.

CHAIRMAN'S CIRCLE

Chairman's Circle visionary donors support the Institute's mission with unrestricted annual gifts of \$25,000 and above. Their generous support fills a vital need for the Institute by providing the world's finest minds in science with the resources to pursue discoveries at the frontier of human knowledge. Donors are invited to exclusive lab tours and special events with senior researchers that provide opportunities to discuss specific areas of interest. Donors receive Salk publications and individual reports on the impact of their gifts.

SPECIAL PROJECTS

If you have a special interest in one of Salk's areas of research, such as cancer, aging, diabetes, neuroscience, genetics, vision or plant biology, you may designate your gift to support investigations in that field. You may also elect to support the work of a young scientist with a fellowship or Salk's education outreach programs. You will be privy to exclusive updates and invitations.

PARTNERS IN RESEARCH

Salk's legacy society, Partners in Research, welcomes those who have included Salk in their estate plans. Charitable gift planning is a powerful way of ensuring your legacy lives on, and it can maximize tax and other financial benefits to you, your family, and the Institute. Partners in Research members receive special communications and are invited to events throughout the year.

A photograph of the Salk Institute building, a modern structure made of large concrete blocks with rectangular windows. In the foreground, three people are standing on a paved courtyard, engaged in conversation. The sky is blue with some clouds.

When you support Salk...

You support progress everywhere.

Scientific discovery at the Salk Institute is made possible through contributions from individuals, organizations, corporations and foundations. Your support will accelerate the pace of breakthroughs in understanding disease and pave the way to new drug therapies. To learn more, please visit www.salk.edu/support or call **858.453.4100 x2068**.

STREET ADDRESS

10010 North Torrey Pines Road
La Jolla, California 92037-1002

Telephone: 858.453.4100

Fax: 858.552.8285

www.salk.edu

NONPROFIT ORG.

U.S. POSTAGE

PAID

PERMIT NO. 611

SAN DIEGO, CA

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

Salk Calendar

APRIL

3 Back to Basics -
"Diabetes and the Obesity Epidemic"

12 Salk Polio Vaccine Anniversary

13 Step into Discovery/5K Walk for Salk
& Explore Salk Open House

17 San Diego Salkexcellerators
Reception & Lab Tour

22-24 New York Salkexcellerators

May

15 San Diego Salkexcellerators
Reception & Lecture

15-17 41st Annual Tax Seminar
for Private Foundations

20 Professional's Event

31 Biophotonics Symposium

JULY

23 Women & Science Event

AUGUST

24 Symphony at Salk

© Françoise Gilot, 2012

A Rose

39 3/8 x 32 inches

From the collection of F. Gilot

Follow us on:



facebook.com/salkinstitute



twitter.com/salkinstitute

