

THE SCRIPPS RESEARCH INSTITUTE

# ENDEAVOR



*Breakthroughs  
of 2007*

THE SCRIPPS RESEARCH INSTITUTE

# ENDEAVOR

VOLUME TEN / NUMBER TWO

WINTER 2007/08

## FEATURES:



- 06 HOW TO SAVE THE PLANET:**  
NEW APPROACHES TO PREVENTING  
THE SPREAD OF FUTURE EPIDEMICS



- 12 ON THE CUSP OF REGENERATION:**  
SHENG DING UNLOCKS THE SECRETS  
OF STEM CELLS



- 16 THE NEW WORLD:**  
CORINNE LASMEZAS EXPLORES THE  
STRANGE LANDSCAPE OF PRION DISEASES



- 22 GETTING CREATIVE WITH CHEMISTRY:**  
PHIL BARAN FOLLOWS HIS PASSION

## ALSO:

- 01** PRESIDENT'S LETTER
- 26** GRADUATE AND POSTDOCTORAL STUDIES
- 28** INTERVIEW WITH GERALD JOYCE
- 31** FINANCIAL HIGHLIGHTS
- 32** NAMES OF SCRIPPS FLORIDA  
FACILITIES TO RECOGNIZE DONORS

---

ENDEAVOR IS A PUBLICATION OF  
*THE SCRIPPS RESEARCH INSTITUTE*

This issue of *Endeavor* features some of the many scientific breakthroughs of 2007 from investigators at The Scripps Research Institute.



Richard A. Lerner, M.D.  
*President*

## *Year in Review : 2007*

---

01

PRESIDENT'S LETTER

It is my pleasure to report on another extraordinary year at The Scripps Research Institute. In 2007, construction began on the permanent Scripps Florida campus in Jupiter, Palm Beach County; scientists at the institute continued to push the boundaries of discovery; and new collaborations positioned Scripps Research to thrive in the future.

PRESIDENT'S LETTER

Left: Palm Beach County Commission Chair Addie Greene, former Florida Governor Jeb Bush, and Florida Governor Charley Crist share in the Scripps Florida celebration. Right: The crowd applauds the dedication of the new campus.



The Scripps Florida campus was dedicated to “increasing human knowledge, advancing biomedical science, educating the researchers of the future, and improving the health of humanity.”

## SCRIPPS FLORIDA ADVANCES

In March, Scripps Research officially dedicated its Florida campus in Jupiter to “increasing human knowledge, advancing biomedical science, educating the researchers of the future, and improving the health of humanity.”

At the ceremony before some 400 Scripps Florida employees and guests at the construction site on Florida Atlantic University’s Jupiter campus, I had the opportunity to again thank the people and leaders of Palm Beach County and the State of Florida for their contribution toward the establishment of Scripps Florida.

We were honored to have with us to share in this celebration Palm Beach County Commission Chair Addie Greene, former Governor Jeb Bush, and Governor Charlie Crist. Each has been instrumental in bringing Scripps Florida to where it is today and contributing to its future positive impact on the community, science, and human health.

Construction on the first phase of Scripps Florida—three buildings totaling 350,000 square feet of laboratory and administrative space—is currently proceeding according to schedule. The buildings are expected to be ready for occupancy in early 2009. Some 220 researchers, technicians, and administrative staff are currently at work in two temporary buildings and several trailers adjacent to the construction site. The buildings will be turned over to Florida Atlantic University when the new permanent facilities open.

In 2007, we welcomed two new students to our graduate program in Florida. We were also proud to graduate our first student completing his thesis on the Florida campus. Chemistry student Porino Va marched down the aisle with 26 of his California colleagues to receive his doctorate of science as part of the Kellogg School of Science and Technology’s commencement celebration.

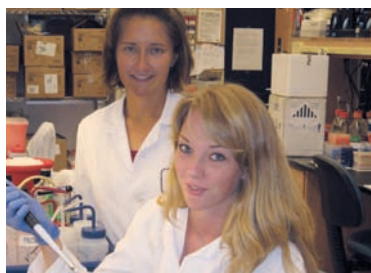
We have also continued to expand our education outreach efforts in Florida. Scripps Florida’s summer internship program, modeled on the La Jolla program and now in its third year, hosted nine students and three high school teachers, thanks to support from the William R. Kenan, Jr. Charitable Trust. The Science Saturday program gave more than 300 Palm

Beach County high school students an opportunity to use modern biotechnology tools. The hands-on Introduction to Science lesson has provided information to middle schools on what the world is made of and how it fits together. In addition, work has begun on a permanent exhibit at the South Florida Science Museum, illustrating how bioscience is shaping our lives and our future.

## BREAKTHROUGHS OF 2007

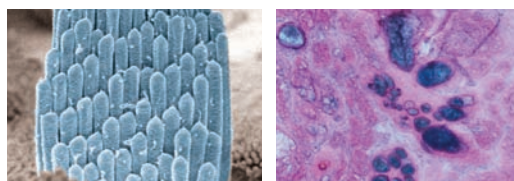
Conducting innovative science is central to The Scripps Research Institute’s mission as a leading biomedical research institution, so I am delighted to take this opportunity to highlight a few of our researchers’ many scientific accomplishments in 2007. In addition to the work featured in this issue of *Endeavor*—research on organic chemical synthesis, prions (a cause of “mad cow” and related diseases), stem cells, and methods to predict and prevent potential pandemics such as the “bird flu”—this year the institute’s scientists:

- + *Developed an innovative dual action anthrax vaccine-antitoxin combination.* Associate Professor Anette Schneemann, Ph.D., Associate Professor Marianne Manchester, Ph.D., and colleagues developed a new and highly effective agent that provides protection against anthrax by combining a fast-acting anthrax toxin inhibitor with a vaccine in a single compound. The immune response generated in rats protects against lethal toxin exposure after only one injection, and is faster and stronger than any currently available vaccine.
- + *Solved the structure of the HIV capsid protein.* Professor Mark Yeager, M.D., Ph.D., Research Associate Barbie Ganser-Pornillos, Ph.D., and colleagues published a detailed molecular model of the full-length HIV CA protein—a viral protein that forms a cone-shaped shell around the genome of HIV. This structure reveals a never-before-seen molecular interaction that may be a weakness at the core of the virus.
- + *Developed a combination therapy that obliterates new vessel growth in tumors and certain types of eye disease.* Professor Martin Friedlander, M.D., Ph.D., and colleagues achieved complete inhibition of new blood vessel growth in animal models of a highly vascular brain tumor and of neovascular eye diseases with little or no effect on



High school students learn about life in the lab through summer internships in California and Florida.

2007



Left: Scientists showed that two key proteins in the ear join together at the precise location where the energy of motion is turned into the electrical impulses of hearing. Right: Researchers found that the growth of skin tumors is restricted by the presence of cells undergoing senescence, which permanently halts cells' proliferation.

normal tissue vasculature. This combination therapy provides a whole new range of treatment options for patients with neovascular diseases.

- + *Revealed a pivotal hearing structure.* Professor Ulrich Mueller, Ph.D., and colleagues showed that two key proteins join together at the precise location where energy of motion is turned into electrical impulses in the ear. These proteins, cadherin 23 and protocadherin 15, are part of a complex of proteins called “tip links” that are on hair cells in the inner ear.
- + *Developed a monoclonal antibody that destroys the addictive drug methamphetamine in vitro.* Professor Kim Janda, Ph.D., and colleagues developed a new monoclonal antibody that destroys the highly addictive drug methamphetamine. The new antibody, called YX1-40H10, converts the drug methamphetamine into a benign substance, pointing to an entirely new way to treat the global epidemic of abuse.
- + *Revealed a mechanism behind nicotine dependency.* George Koob, Ph.D., chair of the Committee on the Neurobiology of Addictive Disorders, Research Associate Olivier George, Ph.D., and colleagues identified one neurobiological mechanism that contributes to nicotine dependence, and to the anxiety and craving experienced upon withdrawal. The findings may lead to drugs that could help smokers quit.
- + *Unveiled a new chemical tool that captures previously unseen molecules.* Julius Rebek, Ph.D., professor at Scripps Research and director of its Skaggs Institute for Chemical Biology, and colleagues described a new chemical tool that effectively pauses the formation of certain intermediate products never before seen, allowing them to be identified and studied. The technique will improve basic understanding of chemical processes, and may also aid biosynthesis studies, drug development, and pollutant detection.
- + *Identified a new pathway to target for drugs to prevent or treat cancer.* John L. Cleveland, Ph.D., professor and chair of the Department of Cancer Biology, and colleagues showed that targeting the autophagy pathway (an ancient cell survival pathway that cells use to survive conditions of metabolic stress) can prevent and cure cancer in mouse models of malignant lymphoma and leukemia.
- + *Revealed a new function of the protein kinase pathway in tumor suppression.* Associate Professor Peiqing Sun, Ph.D., Professor Jiahuai Han, Ph.D., and colleagues discovered a surprising new function of a well-known signaling pathway

that, when activated, can inhibit tumor development. This finding may lead to the development of drugs that can serve as an effective cancer therapy by artificially activating this pathway in cancer cells.

- + *Unveiled a drug target for parasitic diseases.* Professor Paul Wentworth, Jr., Ph.D., and colleagues furthered the ongoing search for better treatments for devastating parasitic diseases such as Chagas' disease and African sleeping sickness. The group now understands better a critical DNA-protein binding event that, if blocked, can kill the parasites that cause the diseases. The researchers are already working to screen drugs that will block this mechanism.
- + *Pinpointed specific neurons involved in memory formation.* Associate Professor Mark Mayford, Ph.D., and colleagues unlocked one of the secrets of how memory is formed. Working with a unique breed of transgenic mice, the study showed the same neurons activated during fear conditioning are, in fact, reactivated during memory retrieval. The findings could help uncover precisely how drugs such as antidepressants work in the brain, allowing clinicians to better evaluate treatment options.
- + *Discovered a chemical pathway that causes mice to overeat and gain weight.* Professor Tamas Bartfai, Ph.D., Research Associate Manuel Sanchez-Alavez, Ph.D., and colleagues discovered a pathway that appears to play a critical role in the onset of obesity. The team showed that mice genetically altered to lack a molecule known as the EP3 receptor tend to be more active during their normal sleep cycle and to eat more. Further research could lead to better understanding of obesity and to new treatments.

#### NEW GRANTS SUPPORT FORWARD-LOOKING WORK

In recognition of their potential for future breakthroughs, Scripps Research scientists received a number of new grants this year. In addition to support for individual research programs, these included funding for several consortiums and other notable projects.

A \$17 million, five-year grant from the National Eye Institute (NEI) will support the development of the use of adult stem cells as a therapy for treating the most common types of vision loss, including diabetic retinopathy, age-related macular degeneration, glaucoma, and



*Immunologist Richard Ulevitch, Ph.D., is the principal investigator of the new \$51 million contract.*



Cindy Ehlers, Ph.D., has been awarded a prestigious 10-year MERIT award for her research on risk and protective factors for alcoholism.

retinitis pigmentosa. The team, led by Friedlander and including the Scripps Research groups of Laura Crisa, M.D., Glen Nemerow, Ph.D., Wolfram Ruf, M.D., Gary Siuzdak, Ph.D., Bruce Torbett, Ph.D., and William Balch, Ph.D., will conduct the extensive and detailed pre-clinical work necessary for moving the potential therapy forward.

A \$51 million, five-year contract from the National Institute of Allergy and Infectious Diseases (NIAID) will support the study of innate and adaptive immune responses to a number of dangerous pathogens, including the influenza virus, smallpox, and anthrax. The project, led by Richard Ulevitch, Ph.D., professor and chairman of the Department of Immunology, and including scientists at the Institute for Systems Biology in Seattle, WA, the Australian National University, in Canberra, AU, and Stanford University in Palo Alto, CA, will develop innovative approaches to improving vaccines and immunotherapeutics.

A prestigious, 10-year MERIT grant to Associate Professor Cindy Ehlers, Ph.D., from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) will support research on risk and protective factors for alcoholism in Southwest California Indians. This population has a five-fold greater risk for developing alcohol dependency than the general population. In work funded by a separate three-year, \$1.5 million grant from the NIAAA and National Center on Minority Health and Health Disparities, Ehlers will help design, implement, and evaluate a program to build services and to prevent underage drinking in Native American young people.

**PRIVATE GIFTS ACCELERATE RESEARCH**

In addition to government-sponsored grants and our corporate partners, we are grateful for the generosity of our many donors, whose gifts accelerate the progress of research on our campuses and leave a powerful legacy for future generations.

Always notable is the ongoing gift from Aline and Sam Skaggs through the Skaggs Institute for Research and their family foundation, the ALSAM Foundation. The \$100 million commitment created the The Skaggs Institute for Chemical Biology at Scripps Research to

improve human health by supporting research at the interface of chemistry and biology.

In 2007, philanthropist and entrepreneur Mark Pearson gave \$3 million to establish the Pearson Family Chair, an endowed position in alcohol and addiction research whose first recipient will be Professor Barbara Mason, Ph.D. The Pearson Family Chair builds on Pearson's previous gift of \$3 million in 2003, which created the Pearson Center for Alcoholism and Addiction Research. The center, co-directed by Mason and Professor George Koob, Ph.D, combines the latest biomedical research with new clinical treatments to fight the devastating, costly, and deadly diseases of alcohol and drug addiction.

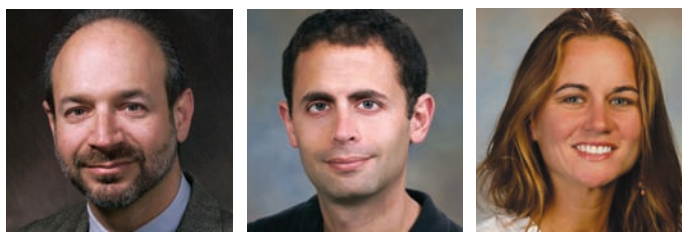
The result of another far-reaching act of generosity, in 2007 the institute received the final payment from the estate of Norma and Frank Sugg, a California couple who included Scripps Research as a beneficiary of their will. The \$1.6 million gift from proceeds from the sale of the Suggs' home as well as other assets will support research on leukemia.

Long-time Scripps Research friend and supporter Daniel Koshland, Jr., Ph.D., gave \$100,000 to the Scripps Research Kellogg School of Science and Technology this year, forming the basis for a new student fellowship, the Koshland Graduate Fellowship in Enzyme Biochemistry. Sadly, Dan passed away in July at the age of 87. An original thinker whose work changed the field of biochemistry, he will be remembered not only for his exemplary science, but also for his deep commitment to the next generation.

**NEW CORPORATE COLLABORATION BEGINS**

2007 marked the first full year of our new research collaboration with Pfizer Global Research and Development. Under the terms of the agreement, Pfizer will pay Scripps Research \$100 million over a five-year period, during which time scientists from Pfizer and the institute will work together to identify and perform specific projects of mutual interest. The agreement aims to advance scientific knowledge of uncured diseases and novel ways to treat them, making full use of emerging technologies and resident talent from both organizations.

Conducting innovative science is central to The Scripps Research Institute's mission.



Left: Bruce Beutler, Ph.D., was awarded the 2007 Balzan Prize. Center: Benjamin Cravatt, Ph.D. was elected as a fellow of the AAAS. Right: Kristin Baldwin, Ph.D., won a Pew Scholarship in the Biomedical Sciences.

In a separate initiative, Pfizer is funding eight postdoctoral fellowships in chemistry at the institute.

AWARDS AND HONORS

In 2007, Scripps Research investigators, postdoctoral fellows, and graduate students were again lauded by numerous awards. To mention only a few, this year's honors include:

- + *Balzan Prize.* Bruce Beutler, M.D., chair of the Genetics Department, was awarded the prestigious 2007 Balzan Prize for his work with Jules Hoffmann of the Academie des Sciences in Paris. The International Balzan Prize Foundation of Italy and Switzerland cited the researchers "for their discovery of the genetic mechanisms responsible for innate immunity. They have worked in close cooperation to develop a new vision of the molecular defense strategy deployed by animals across a wide evolutionary spectrum against infectious agents. Their work has led to very promising medical applications."
- + *Honorary Doctorate of Science from the University of Oxford.* In June, I received an honorary doctor of science degree from the University of Oxford for my research "in the field of catalytic antibodies which has shown that antibodies can be employed as enzymes—research which has relevance for such conditions as atherosclerosis and Alzheimer's disease."
- + *AAAS Membership.* Professor Benjamin Cravatt III, Ph.D., was elected as a fellow in the American Association for the Advancement of Science (AAAS) "for the development of innovative chemical proteomic technologies to annotate enzymatic pathways in mammalian systems." Cravatt also won the 2007 Young Investigator Award from the Linda and Jack Gill Center at Indiana University, Bloomington.
- + *Humboldt Research Award.* Professor Chi-Huey Wong, Ph.D., was selected as the recipient of a Humboldt Research Award in recognition of lifetime achievements in research by the Alexander von Humboldt Foundation. In addition, in 2007 Wong received the F.A. Cotton Medal from Texas A&M; an honorary degree from Technion-Israel Institute of Technology; and an Honorary Fellowship from the Chemical Research Society of India.

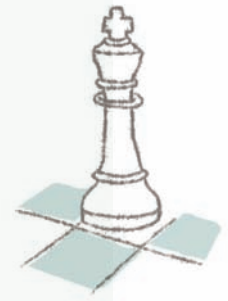
- + *Distinguished Scientist Award.* Professor Francis Chisari, M.D., won the Hepatitis B Foundation's Distinguished Scientist Award for his "seminal work in the immunopathology of hepatitis B, which has contributed significantly to the current understanding of the disease and advanced medical research towards finding a cure."
- + *Scientist of the Year.* Professor William Roush, Ph.D., executive director of Medicinal Chemistry and associate dean of Scripps Florida graduate studies, was named Scientist of the Year by the South Florida Science Museum in the first of the museum's annual series of awards.
- + *Distinguished Achievement Award.* Professor Linda Curtiss, Ph.D., received the American Heart Association's Council on Arteriosclerosis, Thrombosis, and Vascular Biology Distinguished Achievement Award for "immense contributions to the council for many years."
- + *Ernest Guenther Award.* Professor Dale Boger, Ph.D., won the Ernest Guenther Award in the Chemistry of Natural Products from the American Chemical Society "in recognition of contributions to the total synthesis of complex biologically active natural products and key analogs used to define their mode of action."
- + *Burroughs Wellcome Fund Prize.* Associate Professor Dorian McGavern, Ph.D., won a prestigious award from Burroughs Wellcome Fund, which named him one of 15 new Investigators in Pathogenesis of Infectious Disease. These highly competitive awards are given to early career scientists.
- + *Pew Scholarship in the Biomedical Sciences.* Assistant Professor Kristin K. Baldwin, Ph.D., was named one of 20 exceptional researchers selected as 2007 Pew Scholars in the Biomedical Sciences by the Pew Charitable Trusts and the University of California, San Francisco.

I extend my sincerest thanks to trustees, donors, friends, faculty, staff, postdoctoral fellows, and students for their efforts making 2007 another exemplary year at The Scripps Research Institute.

Richard A. Lerner







*“Our work will put high-throughput screening into the hands of the worldwide scientific community.”*

RICHARD LERNER, M.D.

## How to Save the Planet

07

NEW APPROACHES TO PREVENTING THE SPREAD OF FUTURE EPIDEMICS

Led by Scripps Research President Richard A. Lerner, M.D., Nobel laureate Sydney Brenner, M.D., Ph.D., and Assistant Professor Tobin J. Dickerson, Ph.D., a group of scientists from The Scripps Research Institute created a breakthrough methodology in 2007 that, once fully developed, could make the world a bit safer.

The new methodology, called “checkmate analysis,” can be used to rapidly and accurately predict how viruses—including the avian influenza H5N1, a dangerously virulent strain of “bird flu”—could mutate in response to attacks by the immune system. The study was published by the journal *Proceedings of the National Academy of Sciences* in July.

The team’s revolutionary approach can also take the process one step further, predicting which antibodies or small molecule therapeutics might best neutralize these deadly viral mutations before they develop into global epidemics.

If, as Arthur C. Clarke once observed, any sufficiently advanced technology is indistinguishable from magic, this could come pretty close.

### CHANGING THE DYNAMIC

Throughout the course of an infection, new viruses and new neutralizing antibodies are selected and discarded, as the microbe and the host struggle for dominance. But instead of anticipating the next

viral mutation, the immune system operates largely in a reactive mode. Vaccines and other treatments are also designed to defend against what the virus has done rather than what it *might* do. The new methodology devised by Lerner and colleagues changes that dynamic.

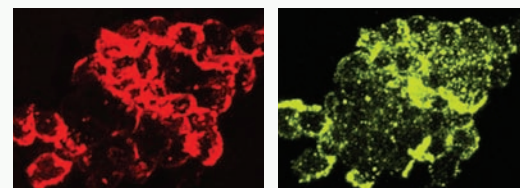
“Our new ‘checkmate analysis’ allows scientists to explore all the possible routes that a virus might take to escape an immune response or a small molecule therapy,” Lerner says. “The result is a detailed chemical map of the trajectories of viral escape and antibody response.”

The new method starts with large libraries of mutant viral proteins and immune system antibodies that are expressed on a phage surface. (Phages, also called “bacteriophages,” are single-stranded DNA viruses, which infect only bacteria.) These two factions are then used to challenge each other.

Because of its simplicity and low cost, this innovative approach could well be within the reach of almost any biomedical laboratory on the planet—from a lab in the Arctic to a research hospital in Africa—providing an inexpensive firewall to help block the rise of viral pandemics.

“Currently, high-throughput screening is limited to those who have access to expensive equipment,” Lerner says. “Our work will put high-throughput screening into the hands of the worldwide scientific community.” →

The team used some elegant chemistry to express the influenza virus protein hemagglutinin on a phage surface, shown here agglutinating red blood cells.



Which was the idea from the start, according to Dickerson, and it was Lerner who first proposed the concept, as part of a significantly larger picture.

Another manifestation of his broad vision is Project Checkmate, a collaboration between IBM and Scripps Research announced in 2006 that combines high performance computing systems such as IBM's BlueGene supercomputer (280.6 *trillion* calculations per second) with advanced predictive methods developed by Scripps Research scientists in California and Florida. The ultimate goal is to ready defensive maneuvers—antibodies, drugs, and vaccines—against flu strains which may have pandemic potential, but which haven't yet materialized.

#### THERE AT THE BEGINNING

The study by Lerner, Brenner, Dickerson, and their Scripps Research colleagues, including Professor Kim Janda, Ph.D., was conceived around the same time as part of the drive to devise new strategies in the deadly game we play against pathogens.

"There are a number of different pieces for what is ultimately a model for global prediction," Dickerson says. "Our portion of it came about when four of us—Richard Lerner, Sydney Brenner, Kim Janda, and I—were discussing how one could develop and implement a system that allows prediction in a test tube. I thought it was achievable, so we decided to see what we could do."

Before the team's *PNAS* study, which was supported by the National Institutes of Health and the Skaggs Institute for Chemical Biology, no one had succeeded in expressing functional viral proteins on phages. While methods for generating combina-

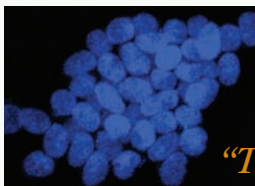
torial small molecules and antibody libraries were well established (thanks in large part to pioneering work by Lerner in the late 1980s), the expression of functional viral proteins on phages posed additional challenges. These proteins are frequently assembled in cell membranes and often composed of various subunits, as is the case with hemagglutinin (HA), a glycoprotein on the influenza virus surface that enables the virus to bind and enter host cells.

The team bridged this technological gap using some elegant chemistry to design a new system, which they then successfully applied to expressing hemagglutinin on the phage surface.

A sample protocol, the study suggested, might involve starting with a population of hemagglutinin-containing phages plus a similar population of antibodies or small molecules that prevent binding. The hemagglutinin would be mutated and the viral escape variants (which preserve binding capacity) selected. These new viral mutations could then be used to screen for new antibodies or small molecules that can bind and hold the escaped mutants.

Once the scientists had conceived of the virus protocol, they realized it had even broader applications, including single molecule drug screening. Dickerson was talking with Lerner when the possibility came up: "The question was, what else could we use the protocol for—because it seemed like we were missing something. I was thinking of ways to probe biological processes, but it was Lerner who asked, 'Why can't we use it for drug screening?' Ultimately, it's the same experiment."

Janda said he expects that the method, which Scripps Research is seeking to patent, will gain widespread use, particularly in commercial applications.



*“The goal for most drug companies is efficiency, cost-effectiveness, and speed in churning out things that are useful, and I think [our Checkmate method] has all the things you need.”*

KIM JANDA, PH.D.

“The goal for most drug companies is efficiency, cost-effectiveness, and speed in churning out things that are useful,” Janda says, “and I think this has all the things you need.”

#### TEAMWORK

The teams that Lerner has assembled for the Checkmate projects are impressive, broad in scope, and highly collaborative—a recognized strength of the institute, and one that can bring a number of different disciplines to bear on major scientific challenges.

“We have structural biology, glycomics, animal modeling, immunology, biochemistry, and organic chemistry components,” Dickerson says. “These are well coordinated and well integrated teams—the very thing that makes Scripps Research the unique place that it is.”

It’s worth noting the collaboration involved both senior scientists and those at the beginning of their careers. Dickerson, a former student of Kim Janda, is a 2004 graduate of the Scripps Research Kellogg School of Science and Technology.

“I was lucky to be in the right place at the right time,” Dickerson says. “My senior colleagues have been very supportive and let me take this to its logical conclusion. When we were discussing it, it was clear that this was a very large, very global idea, but the nuts and bolts were not quite so obvious.”

Authors of the *PNAS* study also included former postdoctoral fellow Kathleen McKenzie and Kellogg School student Amanda Hoyt, as well as Malcolm Wood, director of the Scripps Research Electron Microscopy Facility.

And, of course, there’s Sydney Brenner, who

was based for many years at Cambridge, England’s Laboratory of Molecular Biology (LMB), and who is currently affiliated with The Molecular Sciences Institute, The Salk Institute, the Scripps Research Worm Institute for Research and Medicine (WIRM), as well as other institutions. Born in Germiston, South Africa, a graduate of Oxford University, and a self-described mediocre medical student, he arrived formally at The Scripps Research Institute in 1992 when he was 65-years-old.

“It became imperative,” he wrote in his Nobel autobiography, “for health reasons that I spend the winter months in a warmer climate and Richard Lerner made this possible by giving me a part-time appointment in The Scripps Research Institute in La Jolla, California. Here I found I could pursue new interests in chemistry and especially in the interface between chemistry and biology.”

That was also the year Lerner and Brenner collaborated to publish a study on a combinatorial chemistry technique to tag polymers with individually coded DNA molecules for more effective identification in drug screening—essentially an elegant way to keep track of things that quite often got lost. This technique was termed “encoded combinatorial chemistry” and is now a subject of intense study.

Speaking at the Nobel banquet in 2002, where Brenner was honored with H. Robert Horvitz, Ph.D., and John Sulston, Ph.D., for discoveries concerning genetic regulation of organ development and programmed cell death, Brenner said he had received a letter from a Chinese student asking how he, too, could win the Nobel Prize. Among the things Brenner suggested, was “...choos[ing] excellent colleagues who are willing to join you in the



## 1918 Flu Pandemic

The deadly “Spanish Flu” took more lives than World War I and became the largest and deadliest influenza outbreak in recorded history—unmatched in its magnitude even though two similar outbreaks occurred in 1957 and 1968.

hard work you will need to do.”

The fruitful collaborations with Lerner and other Scripps Research scientists seem to be a case of taking your own good advice.

### ADDING COMPUTATION

Collaboration is also the name of the game in the related endeavor, Project Checkmate. To date, some powerful players have been attracted to the project, which seeks to use a combined experimental and computational approach against a virus, such as a “bird flu” pathogen.

“Project Checkmate addresses a major global health threat, that harnesses the combined resources of both Scripps campuses, Mt. Sinai, and IBM,” says Scripps Research Professor Ian Wilson, D.Phil., who heads the project. “It’s a tremendously exciting opportunity to apply our combined skills and resources to such an important medical problem.”

In addition to those involved in the recent paper, the team includes Professor Dennis Burton at Scripps Research, who is examining antibodies that could cross-neutralize different strains and subtypes of influenza virus; Peter Palese, a renowned influenza virologist at Mount Sinai; Professor James Paulson at Scripps Research, who is investigating receptor binding specificity; and, of course, Wilson and his group, who are looking at crystal structures of viral components and are generating libraries of influenza strains. Researchers at Scripps Florida are well positioned to work with IBM using the institute’s high-throughput screening capabilities as well as its expertise in bioinformatics.

Computationally, preliminary work is being conducted at IBM to see how much computation power will be needed for the initial research. Long-term funding for the project is still under review at the National Institutes of Health.

The idea behind the initiative is to create continual feedback between data from the real world and a computer algorithm that models viral evolution.

“We know, for example, how the 1968 pandemic has evolved over the last almost 40 years, so we can therefore look at the 1968 pandemic at an early stage, and see if we can find ways to predict how the virus has already evolved,” said Wilson. “In addition, we can try to evolve the virus in the test tube. Once we make predictions, we can set up experiments as a reality check to see: 1) do we get a viable virus? 2) does it infect? and 3) does it transmit? All these are really important considerations. When new information comes in about how an existing virus is changing, we can again see if our predictions have been correct. If not, we change the algorithm to better emulate what is actually happening in nature.”

Has anyone tried this strategy before? “Not on this scale and magnitude,” says Wilson. “This is a completely new approach to try to predict in advance what will happen to an emerging virus. Usually, you are working after the event, not before.”

### BACK TO THE FUTURE

Richard Lerner seems to have a knack for new approaches. Described variously as a research chem-

*“This is a completely new approach to try to predict in advance what will happen to an emerging virus. Usually, you are working after the event, not before.”*

IAN WILSON, D. PHIL.

ist, an entrepreneur, and a visionary, Lerner is best known scientifically for his pioneering work with catalytic antibodies (simultaneously with Scripps Research Professor Peter Schultz, Ph.D., then at the University of California, Berkeley), which showed that antibodies can be employed as enzymes. This year, Lerner was awarded an honorary degree from Oxford University for this work, adding to his long list of accolades.

Lerner’s other scientific achievements have spanned a remarkably wide range, including unique insights into protein and peptide structure, the identification of a sleep-inducing lipid, and the discovery that human antibodies generate a product with the chemical signature of ozone (a highly reactive molecule never before considered part of biology), which may help explain diseases such as atherosclerosis. In addition, 2007 was the 40th anniversary of Lerner’s landmark study showing a particular antibody—the anti-glomerular basement membrane (GBM) antibody—causes a type of inflammatory kidney disease in humans.

That anniversary also coincides with the 20th anniversary of Lerner’s appointment as head of Scripps Research. When Lerner became head of the institute (then called the Research Institute of Scripps Clinic), the La Jolla group was a well-respected but small research organization. But Lerner, a Stanford M.D. who had been a postdoc at the institute before becoming a faculty member there, had a larger vision.

In much the same way that he gathered the members of the Checkmate teams, as president of

the institute, Lerner quickly recruited top scientific talent, notably faculty working at the frontiers of science and at the intersection of chemistry and biology. Over the last two decades, Scripps Research has become one of the largest nonprofit research organizations in the world. Laboratory space in La Jolla has expanded roughly three-fold to more than one million square feet. The number of staff at the institute has increased from 700 to more than 3,000. The institute has expanded geographically as well, now including the Jupiter, Florida, campus.

Scripps Research also now boasts of a graduate school ranked among the top-ten nationally in its fields of biology and chemistry by *U.S. News & World Report*. The school, named the Kellogg School of Science and Technology, produces a caliber of scientists that speaks for itself—innovators like Tobin Dickerson, and two other alumni featured in this issue of *Endeavor*, Phil Baran and Sheng Ding.

The recent Checkmate projects represent the fruits of Lerner’s 40 years of research, and 20 years of leadership, talent scouting, and team building. But the projects also reflect a focus on the future—the future evolution of viruses, new directions in science and drug development, and a continual renewal of enthusiasm for discovery and exploration.

“One of the most rewarding parts [of the Checkmate project is] the conversations that started all this are still going on and the project continues to evolve and grow,” says Dickerson.

ERIC SAUTER AND MIKA ONO BENEDYK



*“Even as a young student I thought about how amazing it is that a creature develops from basically nothing to become a complicated entity... I wanted to understand how this happens.”*

SHENG DING, PH.D.

## On the Cusp of Regeneration

SHENG DING UNLOCKS THE SECRETS OF STEM CELLS

In Greek mythology, the Hydra is a creature that terrifies humans because of its uncanny ability to regrow its heads after they are cut off. Today, the idea of regeneration has moved out of the realm of frightening myth into hopeful reality as scientists increasingly are finding ways to enable the body to repair itself.

The Scripps Research Institute’s Sheng Ding, Ph.D., a chemist at the forefront of regenerative medicine, is studying how stem cells can assist the body’s own healing processes. In two recent breakthroughs, the Ding lab has generated a new type of embryonic stem cell and also developed a chemical method to “reprogram” adult mouse somatic cells to become embryonic stem cells, thus opening up important research avenues.

### UNLIMITED POTENTIAL

The excitement generated by embryonic stem cells derives from the fact that these cells are pluripotent—capable of differentiating into the different cells in the body—and “immortal”—even after months in culture dishes, they maintain the ability to develop into muscle, cartilage, nerve, bone, blood, brain, and other specialized cell types. Stem cells hold the promise of providing an infinite supply of specific cell types for basic research and for transplantation therapies for neurodegenerative diseases, spinal cord injuries, and cancers.

Since the first human embryonic stem cells were derived in 1998, a major research obstacle has been that these cells are much more difficult to work with than mouse embryonic stem cells. It also appears that they have very different properties, so that findings in mice are not necessarily relevant to humans.

Now, after small molecule manipulation, the Ding lab has created a new kind of pluripotent embryonic stem cell—human cells that mirror key features of mouse embryonic stem cells, essentially wiping out the problem of species specificity.

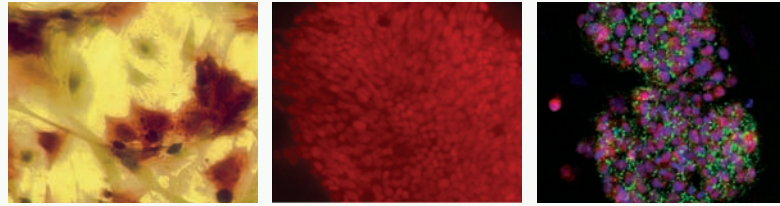
“Our latest research shows that the problem scientists faced working with human embryonic stem cells was one of ‘stage’ rather than ‘species,’” Ding says. “With the creation of this new cell type, most of the differences we thought existed between the organisms are not there. Now, scientists can continue research with mouse embryonic stem cells, and also work with human embryonic stem cells with the same ease, and be confident that all information gained from mouse research pertains to humans. This opens up huge new research potential.”

### A UNIQUE PERSPECTIVE

As a chemist working in stem cell research, Ding approaches his work from a unique perspective. He believes the potency of stem cells can ultimately best be harnessed not through actual cell therapy—



Sheng Ding, Ph.D., hopes that one day scientists will be able to use one chemical cocktail to revert specialized cells back to an earlier developmental stage, then a second cocktail to differentiate the cell into the type needed for therapy.



implanting stem cells themselves at the site of the defect or injury—but by using specific small molecules (drugs) to coax stem cells into the desired cell type and function.

There are clear advantages to this approach, Ding says. He points to the multiple steps required in bone marrow transplantation as an example of the difficulties of cell-based therapy. First, a suitable donor must be found. Then, the patient must go into the hospital to receive the transplant. Before transplantation, the patient's own bone marrow must be irradiated in order to create a tissue environment that allows stem cells to repopulate. And in the end, many such transplants prove ineffective. In drug-based stem cell therapy, on the other hand, drugs would be used to boost the function of stem/progenitor cells that already exist in the body and are responsible for normal tissue maintenance.

“We are searching for those small molecules, which would eventually be turned into drugs, that could boost progenitor cells' capability to regenerate damaged or injured tissue,” Ding says. “I believe such drugs will be developed and that they will be preferable to the cell transplantation approach.”

Ding uses a metaphor to describe the role of chemicals in guiding stem cell function. “Think of a rock sitting on top of a cliff. When pushed, the rock starts rolling down the mountain. There are many twists and turns, and depending on forces that the rock encounters along the way it can wind up in a ditch or in a stream or rolling further down the mountain. In the same way, small molecules can intervene to determine what stem cells will become. The challenge lies in understanding which chemicals are needed to guide the cells to preferred directions.”

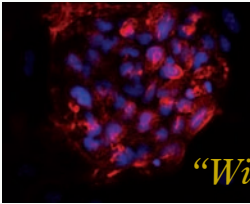
#### GOING BACKWARD, MOVING FORWARD

Another groundbreaking aspect of Ding's work has to do with “dedifferentiation,” or the reprogramming of cells from a specialized state back to an embryonic stem cell. In addition to cell transplantation, one aim of dedifferentiation is to develop cell lines from patients who suffer from genetic diseases, such as Huntington's disease, spinal muscular atrophy, muscular dystrophy, and thalassemia. Such lines would be invaluable tools for understanding specific diseases and testing potential drugs to treat them. The other goal, of course, would be to repair disease-damaged tissue.

Several years ago, Ding, in collaboration with the laboratory of Scripps Research Professor Peter Schultz, Ph.D., discovered a small molecule, dubbed “reversine,” that could revert muscle cells back into mesenchymal progenitor cells (cells that develop into connective tissues, such as bone, cartilage, fat, and skeletal muscle.) Following up on this work, Ding has now discovered a way to use small molecules to reprogram specialized cells all the way back to the pluripotent embryonic stem cell state. Until now, the only way scientists knew how to do this type of reprogramming was by using four specific oncogenes, or cancer causing genes. When these oncogenes are used to dedifferentiate cells, tumors inevitably result. “Obviously, this is not a viable outcome,” Ding says.

So far, Ding has been able to replace two of the four oncogenes with chemicals. “This is the proof of principle we were looking for,” he says. The idea would be to develop one chemical cocktail to revert specialized cells back to an earlier developmental stage, then a second cocktail to differentiate the cell into the type needed for therapy.





*“With the creation of this new cell type, most of the differences we thought existed between the organisms are not there.”*

SHENG DING, PH.D.

#### A LIFELONG FASCINATION WITH DEVELOPMENT

Ding has always been captivated by the idea of how multicellular organisms develop from a single cell.

“Even as a young student I thought about how amazing it is that a creature develops from basically nothing to become a complicated entity that contains all sorts of cells that perform very different functions,” he says. “I wanted to understand how this happens.”

After emigrating to the United States from China in 1996, Ding enrolled at Cal Tech. He majored in chemistry, but his interest in developmental biology continued. After graduation, Ding came to Scripps Research to pursue his Ph.D. In 1999, while a Howard Hughes Medical Institute predoctoral fellow in the Schultz lab, Ding set out to assemble molecules that could spur embryonic stem cells to become neurons. He was looking for “signaling” molecules that move between and inside of stem cells, instructing them to differentiate into specific cell types. Ding and his colleagues designed more than 50,000 small molecule “keys” and tried them all. Eventually, one of those compounds fit, and proved particularly effective in stimulating mouse embryonic stem cells to become neurons.

More recently, Ding has used large-scale screens to investigate the genetic networks that control adult stem cell differentiation, the process by which stem cells develop into specialized cell types. The ability of these cells to proliferate and differentiate into a variety of mature cell types makes them integral to regenerative medicine.

Ding is a member of the San Diego Consortium for Regenerative Medicine, a collaboration organized in 2006 comprised of four of the nation’s pre-eminent research institutions, all based in San Diego—Scripps Research, Burnham Institute

for Medical Research, Salk Institute for Biological Studies, and the University of California, San Diego. The consortium was created as a result of the 2004 passage of the California Stem Cell Research and Cures Initiative, which led to the formation of the California Institute for Regenerative Medicine (CIRM). CIRM will manage \$3 billion in state funds to support stem cell research in California. Ding provides chemistry and technology expertise in stem cell research, as well as collaborating with consortium scientists.

#### SUN, MOUNTAINS, AND SCIENCE

In the decade that Ding, a native of Beijing, has lived in Southern California, he has found an environment that has energized him personally and scientifically. At 32, he has his own 15-person lab, one that buzzes with a sense of excitement that comes from conducting cutting-edge research. Married, with a one-year-old son, Leo, Ding finds the California climate, sun, and natural beauty conducive to creativity. An avid mountain climber, Ding relishes travel around the United States and around the world. An amateur photographer, he has an abiding interest in experiencing new cultures.

Though Ding acknowledges that many questions and obstacles remain in understanding the mechanisms of action of stem cells, he is confident that a chemical approach to stem cell regulation will pave the way for the development of drugs that can regenerate and repair tissue.

“The time frame I’m thinking of is perhaps 5 to 10 years,” he says. “I see a day, not that long from now, when it will be possible to go into a pharmacy and buy a drug that will enable one’s stem cells to regenerate.”

ANNA SOBKOWSKI



*“Our findings open new avenues for the development of neuroprotective strategies.”*

CORINNE LASMÉZAS, D.V.M., PH.D.



## The New World

CORINNE LASMEZAS EXPLORES THE STRANGE LANDSCAPE OF PRION DISEASES

When Corinne Lasmézas, D.V.M., Ph.D., started out in science, she fell almost immediately into the unexplored territory of bovine spongiform encephalopathy (better known as mad cow disease) and has been there ever since, turning out paper after paper on the incurable and deadly disease that attacks cattle and, rarely, humans. While her focus hasn't changed, her range has gotten bigger over the years, expanding outward from the disease itself to encompass the source of the infection: prions.

Her most recent paper, published by *PloS Pathogens* late last summer, broke new ground. For the first time, she was able to pinpoint small clumps of abnormal prions called oligomers as the primary cause of the widespread death of neurons in transmissible spongiform encephalopathies like mad cow disease or the human form of the illness, Creutzfeldt-Jakob disease. Such intermediate-stage protein aggregates are also likely to be the cause of other devastating neurodegenerative conditions.

“Our new work demonstrates that the prion-induced neurodegeneration mechanism we uncovered in prion diseases is similar to that of other diseases such as Alzheimer's, Huntington's, and Parkinson's,” says the Paris-born Lasmézas, now a professor on The Scripps Research Institute's Florida campus. “The degree of this commonality is remarkable, and our findings open new avenues for

the development of neuroprotective strategies that directly target abnormal prion protein oligomers.”

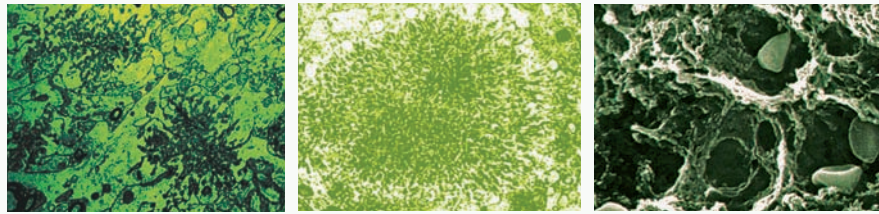
### AIMING HIGH

A groundbreaking piece of science, made all the more remarkable coming from a young woman whose initial goal was to become the second French female astronaut in space. (The first, Claudie Haigneré, spent roughly two weeks aboard the Mir space station in 1996.)

“What I really wanted to become was an astronaut, but I was short-sighted and couldn't train as a pilot,” she says. “So I changed dreams early on. I was always interested in biology, fascinated by it. I also liked animals, so I thought, ‘Medicine for animals, that's perfect.’ Maybe they will need to do experiments with animals in space and that would be one way to get there.”

The space thing, she admits now, was something of an obsession, one that did not abate even after two years of hard-to-get-into French veterinary school. Before she received her veterinary degree, she applied to study aeronautic and space medicine at the University of Toulouse (founded in 1229 and one of the oldest universities in Europe), where she earned a second diploma. This piling on of activities was part of Lasmézas' makeup long before she headed down the road to research. →

This electron micrograph shows a deposit of abnormal prion protein (two left panels), and spongiform lesions (right panel) in the brain of a patient afflicted with the human genetic prion disease Gerstmann-Sträussler-Scheinker syndrome.



*“I wanted to know, what is this agent that causes these holes in the brain that can’t be cured?”*

CORINNE LASMÉZAS, D.V.M., PH.D.

“I was always very busy in school—study, swimming, music,” she says. “I was too busy to be a typical teenager.”

Lasmézas was born in the 13th arrondissement in Paris—she admits to being 30 something. Her mother was German; her father, French, with a family of Spanish origin. Although she learned German from her mother, she is only now learning to speak Spanish. To complete this kind of globalized American-style gumbo, she met her husband—who is Russian—in the United States and recently gave birth to their first child. And, yes, she’s also learning to speak Russian.

After graduating from the University of Toulouse, she worked as a veterinarian in Paris for a few months while trying to find a way into the French scientific system. Although she liked veterinary work—she took care of race horses, trotters—she didn’t intend to be a horse doctor her whole life.

She soon learned of an army researcher, Dominique Dormont, M.D, who was studying mad cow disease and looking for a veterinarian to work in his laboratory.

#### MAD COWS AND ENGLISHMEN

Bovine spongiform encephalopathy (BSE) was first identified in 1985 in a veterinary laboratory in Surrey, one of the counties that borders on London in the southeast of England. To date vastly more devastating in Europe than in the United States, by 2001 the disease had led to the destruction of nearly five million cows in Britain alone. Public concern

over the spread of the disease turned to outright panic in 1996 when it became clear that the infectious agent of BSE was capable of infecting and killing people who had mistakenly eaten tainted beef; the human form of mad cow was called variant Creutzfeldt-Jakob disease.

By 2007, this prion disease had killed more than 160 people in Britain, more than 20 in France, and a few in several other countries around the globe. Three cases have been confirmed in the United States.

“In the early ‘90s, there were two emerging diseases to study, AIDS and prion disease,” Lasmézas says. “In the beginning, no one knew mad cow was transmissible to humans, but it was a rare and strange disease because no one could find what caused it. There were very few people working on it, so, I thought, this is my area—I wanted to know, what is this agent that causes these holes in the brain that can’t be cured?”

Lasmézas jumped into the fray.

Between 1990 and 1996, she worked on spongiform encephalopathies at the Commissariat à l’Énergie Atomique just outside Paris; in 1997, she became a principal investigator and by 2002 was the head of her own laboratory. Before arriving at Scripps Florida in 2005, she had published more than 30 papers and contributed more than a dozen articles about the disease to a number of international journals.

During that time, her focus shifted from the disease to its cause—prions. →

## A Primer on Prions

For more than a century, accepted scientific dogma held that only bacteria, viruses, fungi, and parasites could cause infectious diseases. During the past 25 years, however, evidence accumulated of an infectious disease of another kind.

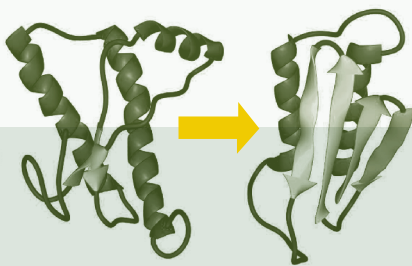
Termed “transmissible spongiform encephalopathies” (TSEs), these include fatal neurodegenerative diseases of humans and animals—Kuru and Creutzfeldt-Jakob disease in humans, scrapie in sheep and goats, mad cow disease in cattle, and chronic wasting disease of deer and elk. The cause most likely lies with abnormally folded infectious proteins—dubbed “prions”—with the bizarre ability to cause their normal counterparts to change their shape, transforming them into deadly biological bullets with a latent capacity to kill. It is possible that prions need to be associated with another molecule to be infectious. A susceptible person eating prion-tainted beef could succumb to a dementia-like disease years, even decades, later.

Prions—the word is a combination of “proteinaceous” and infectious—were discovered by Stanley Prusiner, M.D., of the University of California, San Francisco, who received a Nobel Prize for his work in 1997. Prusiner’s work was at first treated with incredulity—how could proteins that are not able to reproduce without DNA and RNA actually replicate in the body of a human or animal? The question is still not fully answered.

Humans who eat meat from infected cattle or who otherwise absorb the abnormal protein may contract the human form of mad cow, variant Creutzfeldt-Jakob disease. Creutzfeldt-Jakob, named for the German scientists who first diagnosed it, is a neurological disease that most often strikes older people, causing dementia, memory loss, hallucinations, seizures, and eventually, death. Variant Creutzfeldt-Jakob causes psychiatric symptoms, ataxia, late dementia and is also fatal, but strikes much younger people, often in their 20s and 30s. Since prions are misshapen copies of a normal protein, the body does not mount a typical immune response against them.

One complicating factor in containing an epidemic of mad cow or related diseases is that prions are nearly indestructible, very resistant to proteases—the enzymes in the body that can normally break down proteins—and are killed only at extremely high temperatures or with very strong chemicals, methods that harm living tissue.

Currently, there is no vaccine to protect against infection, and no known drug stops the progress of the spongiform degeneration once it begins—which makes the research on prions by Scripps Research scientists all the more pressing.



Infected prion proteins cause their normal counterparts to change their shape to the toxic form.

*“Chronic wasting disease concerns me because it’s spreading and the infectious agent is very resistant in the environment. In instances where you have farm-raised elk and deer, once the pastures are contaminated it’s very hard to get rid of...”*

CORINNE LASMÉZAS, D.V.M., PH.D.

*(continued from page 18)*

Infectious prions (from *proteinaceous infectious particles*) are unique pathogens associated with some 20 different diseases in humans and other animals. Prions, thought to be composed solely of protein, have the ability to reproduce, despite the fact that no nucleic acid genome has yet been found. (See “Primer on Prions.”) These infectious proteins start out as individual molecules or monomers, but then clump together. Oligomers are an intermediate state of aggregation. The fibril end-stage consists of much larger clumps or sheets of proteins.

But it is the intermediate stage that kills, as Lasmézas’ most recent study shows.

“When we look at the brain of an individual or an animal affected by a prion disease,” Lasmézas noted, “we often don’t find neurons dying in the same region as large fibril deposits (also called plaques). One theory suggests that these large fibril deposits may actually be the brain’s way of containing the toxicity of the intermediate-stage oligomers.”

#### CALL TO ACTION

Lasmézas was working on understanding how prion disease makes the jump from the cow to human infection when she was asked to come to Scripps Florida by Charles Weissmann, M.D., Ph.D., a pioneer in modern biomedical research, including prion diseases. Weissmann himself had joined Scripps Florida in 2004.

“I met Charles Weissmann many times at in-

ternational conferences and he was a reference in the field,” she says. “When he asked me to set up a lab in his Department of Infectology, it was such an honor, I was thrilled.”

Of course, by the time she arrived at Scripps Research, Lasmézas was a known quantity due to her work in France, which strongly suggested that bovine spongiform encephalopathy is transmissible to humans, and which established models to study the pathogenesis of prion diseases in primates and rodents.

Starting around 2000, Lasmézas and her colleagues had also published a series of papers, primarily in *The Lancet*, delineating the ways and means the disease was working its way into the human population and in the body and calling for action to keep it from spreading further.

Lasmézas does worry about prion disease in the United States, but not so much from mad cow disease as from chronic wasting disease, which affects deer, elk, and moose. So far, this disease has been reported in 11 states and two Canadian provinces, according to the Centers for Disease Control.

“Chronic wasting disease concerns me because it’s spreading and the infectious agent is very resistant in the environment,” she says. “In instances where you have farm-raised elk and deer, once the pastures are contaminated it’s very hard to get rid of. Not only are the numbers increasing, but the disease is spreading geographically.



We don't know about transmission to other species because it's still too early. But we do know we don't want it to turn out like mad cow in the U.K. and wake up to find out it's a catastrophe."

What makes diseases like chronic wasting and mad cow problematic in terms of tracking human infection, she said, is the fact that incubation in humans takes a long time, in some cases up to 50 years. This lag time also complicates following up the possibilities of human-to-human transmission from blood transfusions and other therapies using human products, as she eloquently argues in a 2006 *Lancet Neurology* commentary, entitled appropriately "Of mice and men ...and vCJD."

#### A LONG ADVENTURE

While keeping the big picture in mind, Lasmézas does not lose sight of the practical side of her research.

"I'm focused on fundamental issues now," she says, "looking at the mechanism of prion disease. I'm also keeping up my interest in devising therapies. Even though there are so many questions of mechanism, we always try to find molecules to cure these diseases."

Scripps Research offers her a unique platform for therapeutic development, she said, because of the institute's multiple molecular libraries and rapid screening technologies. She maintains her scientific connections to France and to her European

colleagues; her recent paper was an international collaboration made up of scientists from France, Germany, and the United States.

"The whole study took a tremendous amount of time," she says. "This was a well thought out collaboration—when my colleagues in Europe had things to add, they simply jumped in. From both a human and a scientific perspective, it was a very long but very good adventure."

She has clearly adapted to the United States, something that seems to come as a surprise to her because she did think long and hard about making the change. It was a great opportunity but it also meant leaving everything, including family and friends, behind.

"I did have something of a reputation of behaving like a crazy scientist, so when I told my Parisian friends that I was moving to Florida, they said, 'Now we have confirmation that you are really crazy.'"

But she made the move, built a laboratory, produced a breakthrough study, and started a brand new life in a brand new world.

"I have to give most of the credit to Charles Weissmann," she says, "He was one of the main reasons I came here because I wanted to work with him. Scripps has a worldwide reputation and that is important, too, especially from a collaborative perspective. Also, when you think about it, Florida is really one of the nicest places in America."



*“We focus on creating beauty, inventing new science, exploring uncharted realms of chemistry, and educating students.”*

PHIL BARAN, PH.D.

## Getting Creative With Chemistry

PHIL BARAN FOLLOWS HIS PASSION

Today, the field of chemistry is little burdened by the question of whether a particular chemical compound can be produced. Given enough time and money, available techniques allow synthesis of just about anything.

The more contemporary question is whether a given compound can be produced well—because available methods are often so complex as to be prohibitively expensive, and so inefficient as to yield barely enough product for scientists to study. Such limitations can have chilling effects on biomedical research, specifically testing the efficacy of potential new drugs.

At an age when most researchers' careers are just ramping up, 29-year-old Phil Baran, Ph.D., is already a standout in the field of organic chemical synthesis, making great strides in developing innovative ways to synthesize chemicals well. As a tenured associate professor in the Department of Chemistry at The Scripps Research Institute, his laboratory's work has already advanced an array of biomedical studies by synthesizing promising potential drugs and creating new chemicals. But Baran is looking for something more.

### EXPLORING UNCHARTED REALMS

As the candidate drug pipelines at major pharmaceutical companies are drying up, it could be

increasingly important to explore new compounds derived from nature as potential new drugs. However, what truly drives Baran is the more basic desire to create. Results that could ultimately save lives are a bonus.

“We focus on creating beauty, inventing new science, exploring uncharted realms of chemistry, and educating students,” says Baran, “That’s the idea. You want to follow your passion.”

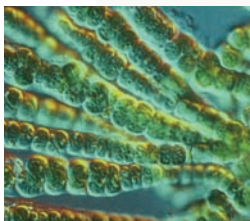
As a result, though much of Baran's work has important practical applications, it's the chemistry that is his primary focus when choosing new challenges. The benefits, he says, are sure to follow from there.

“He’s one of the few professors that in picking targets for his syntheses, shifts focus away from biological activity,” says Ian Seiple, one of Baran's students and a Ph.D. candidate in the Scripps Research Kellogg School of Science and Technology. “He really looks for opportunities to do some elegant, unique, or developmental chemistry with the natural products he synthesizes.”

The concept of creativity in chemistry, particularly the synthesis of compounds, is a stretch if you believe that chemists simply take known reactions and put them in a new order to make a new molecule. But that's not reality, according to Baran. In his view, the field involves so many unknowns it can still be considered in its infancy. →







The Baran lab used this blue-green algae in its recent *Nature* study, which presented new techniques for dramatically simplifying the synthesis of natural products with anticancer and antibacterial promise.

Baran found his passion for creating early on. “In high school I discovered the joy of mixing things to see what happens and eventually found out you can get paid for doing that,” he says.

Once his goal was fixed, Baran began working toward it at top speed. By the time he graduated from high school, at the ripe old age of 16, he already had an associate’s degree, which allowed him to complete his undergraduate degree in just two years at New York University. He would go on to become the youngest graduate ever of the Scripps Research Kellogg School at 23 after completing his dissertation with K.C. Nicolaou, Ph.D., chair of the Department of Chemistry.

After a postdoctoral fellowship at Harvard University, Baran returned to Scripps Research as a faculty member.

Not surprisingly for someone so driven, those working with him in the lab say his excitement about the research is contagious. “He’s made it very clear that he doesn’t want this to be just another organic chemistry lab,” says Noah Burns, another Ph.D. student in the Baran group. “He wants it to be something that stands out.”

#### THE BEAUTY OF SIMPLICITY

Baran recently made headlines with a seminal paper in the March 22, 2007, issue of *Nature*. The *Nature* work presented new techniques for dramatically simplifying the synthesis of marine natural products that have shown anticancer and antibacterial promise.

Specifically, the paper described chemical syntheses in which Baran and his colleagues were able to avoid the use of protecting groups—extraneous molecules used during the production of a compound of interest to shield its more reactive portions and prevent unwanted reactions. Protecting groups are used ubiquitously in chemical syntheses, but they add new levels of complexity and reduce efficiency, often leading to high production costs

and low output. The Baran team showed that it was possible to avoid the use of protecting groups in many cases by thinking of innovative ways to put all a compound’s reactive portions to use in producing the intended final product.

Despite the attention the *Nature* paper has brought to the lab, Baran says the protecting group work is but one small step in his lab’s overall goal of transforming chemical synthesis from the often mysterious pursuit it now is, to something much more predictable.

“Right now, our ability to predict what happens in a flask is hopelessly behind what actually happens,” he says.

Ultimately, Baran would like to see the day when most natural products are as easy to make as genetic sequences of amino acids currently are. He envisions a computer program that would enable researchers to enter a chemical formula and receive a reliable scheme for how the compound could be efficiently produced.

Toward that end, the Baran group focuses not simply on developing novel methods for producing specific compounds, but rather on new methodologies that can be broadly applied. Indeed, the *Nature* paper went beyond describing the team’s experimental work to include a list of guidelines for generally increasing the efficiency of chemical syntheses. This touched on everything from the suggestion to favor the strategic implementation of reactions that form carbon-to-carbon chemical bonds whenever possible to a reminder to use reactions that minimize change of oxidation state.

#### SIDE EFFECTS

Despite (or perhaps because of) the group’s focus on methods, the work is showing numerous practical benefits in biomedical research. In the process of synthesizing compounds, the team often creates analogs, or slightly altered versions, of compounds that have already shown therapeutic



*“I don’t believe if I had gone to work in any other lab  
I would have learned as much...”*

NOAH BURNS, Ph.D. candidate in the Baran lab

value and these they hand off to other groups for analysis. Baran has also collaborated with organizations such as Genentech and Burnham Institute for Medical Research to produce needed compounds, typically natural products isolated from marine organisms.

Target molecules often show great promise but come from sources that would be difficult or impossible to collect in sufficient quantities to support initial studies of their efficacy as disease treatments, much less in the quantities needed to support clinical trials. Short of decimating a marine ecosystem (and in some cases even if that were an option), researchers can typically only isolate milligrams of a given natural product from marine species. In contrast, Baran’s work often leads to the production of gram quantities of these products. In some cases, other research groups have been able to reveal a product’s promising medical bioactivity only because he has produced the synthetic product.

The Genentech project involves compounds isolated last year from a sea squirt, or marine tunicate, showing potential for killing colon cancer cells in laboratory experiments. The Burnham work focuses on compounds isolated from marine sponges that demonstrate an enticing penchant for blocking the movement of cancer cells.

Another applied research project involves a collaboration between Baran and his neighbor at Scripps Research, Benjamin Cravatt, Ph.D., chair of the Department of Chemical Physiology. The researchers are working to synthesize a version of a compound, this time discovered in marine bacteria, that includes a chemical tag. This “tagged” version of the compound helps the Cravatt group to decipher its interactions within cancer cells. Besides better means for producing important chemical compounds, another natural by-product of Baran’s work is new insights into how molecules are produced in nature. “We don’t necessarily try to mimic nature,” he says. “Instead, we first imagine

what she’s doing and then we work to prove that an invented biosynthetic pathway is feasible.”

#### HUMAN TRANSFORMATIONS

Recently, Baran was recognized by the American Chemical Society’s National Fresenius Award, given each year to an outstanding chemist under 35 who has made “substantial, nationally recognized scientific contributions.” He was also profiled in *Chemical & Engineering News* and the journal *Science*. In the latter, his postdoctoral advisor, Nobel laureate Elias J. Corey at Harvard University, called Baran “an off-the-scale youngster who towers above everyone else in his age group.”

But Baran doesn’t have much time to bask in the glory. He has work to do—not only organic chemistry *per se*, but also training students and others in his lab group, now numbering almost 30. Throwing himself into the task, Baran has created a rigorous program he compares to Navy SEAL training. While his students confirm that extremely hard work is a prerequisite—most spend at least 12 hours a day in the lab—they say the benefits are clear.

“I knew coming to work in this lab I was going to be pushed harder than I would in other places,” says Burns, “but it’s been very rewarding, and I don’t believe if I had gone to work in any other lab I would have learned as much as I will doing my Ph.D. with Phil. He really wants us to think about problems in new ways and that’s a really cool part of the learning experience.”

While Baran finds the discoveries that result from his research a high point, he says he counts success as a teacher as the greater prize. “For me, the most exciting and rewarding thing has been watching students go from naïve and not so focused to brilliant, independent researchers who are creative, imaginative, and able to think outside the box,” he says. “That has been the best.”

MARK SCHROPE

# Graduate and Postgraduate Studies

## Kellogg School Celebrates Graduates' Hard Work, Determination, and Skill

*In a joyful ceremony Friday, May 18, The Scripps Research Institute celebrated its 15th commencement, graduating 27 Ph.D. students—among them the first from Scripps Florida. Speaking at the event was University of California, San Diego (UCSD) Chancellor Marye Anne Fox, Ph.D., who also received an honorary degree.*

### Top Ranked Program

After a colorful procession of students and faculty across the oceanside La Jolla, California campus, Scripps Research President Richard Lerner, M.D., offered welcoming remarks and Professor Jeffery Kelly, Ph.D., dean of graduate and postgraduate studies, spoke about the Scripps Research Kellogg School of Science and Technology, emphasizing its reputation for excellence.

Kelly noted that, from its inception, the program was able to attract the very best students because of the power of its mission—to train the next generation of scientists as individuals capable of bringing together the principles of various scientific disciplines, in Kelly's words, "the skill set required to solve the complex problems of today and especially tomorrow."

Since the graduate program opened its doors in 1989, it has expanded greatly in both size and reputation. The Kellogg School currently trains more than 225 doctoral students, who attend classes, complete lab rotations, and write dissertations that offer original contributions to their fields.

The continuing quality of the Kellogg School is highlighted by stellar rankings from various organizations, including *U.S. News & World Report*, which this year again ranked the program among the top ten nationally in both biology and chemistry.

### A Florida First

And Scripps Florida is now an integral part of the program's accomplishments, as confirmed by the first graduate from the Florida program, Porino Va.

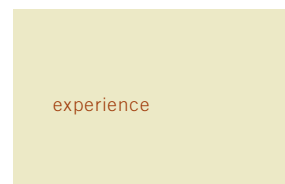
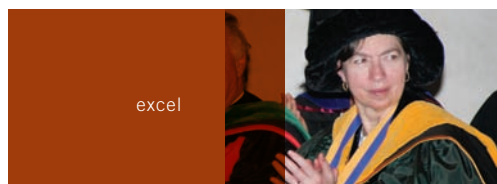
"The first student to complete the requirements for the Ph.D. degree at Scripps Florida...is a milestone event for Scripps Florida and the Kellogg School of Science and Technology," noted William Roush, Ph.D., professor, executive director of Medicinal Chemistry, and associate dean for Florida graduate studies, who was Va's advisor.

Va, who transferred to Scripps Florida with the Roush lab in 2005, will go on to postdoctoral studies in the laboratory of Scripps Research Professor Dale Boger, Ph.D., in La Jolla, California. He is delighted with his decision to complete doctoral work at Scripps Florida. "I feel very fortunate to have the honor of being Professor Roush's first Scripps Florida Ph.D. graduate," he said. "The facilities and the science being conducted at Scripps Florida are truly world-class."

### The Importance of Collaboration

As the ceremony continued, Fox—a physical organic chemist who is UCSD's seventh chancellor and the first woman to be permanent chancellor of that institution—congratulated the graduates and addressed the audience.

She stressed the importance of collaboration in the sciences, which brings together the unique strengths of different individuals. Fox also spoke about the importance of taking risks. "Failure is not the opposite



of success,” she said, advising the graduates to try new things. Rather than avoiding failure, she recommended ensuring the survival of the exceptional.

After Fox’s address, the graduating students’ advisors stepped up to the stage to speak about the scientific and personal accomplishments of each graduating student. Audience members applauded long and loud in recognition of the new graduates’ hard work, determination, and skill.

### New Collaborations Provide New Opportunities

*It’s not easy making the transition from student to faculty member, but thanks to two new collaborations, Scripps Research scientists at the beginning of their careers have a helping hand.*

#### JUST

One new program, the Joint University of San Diego-Scripps Training Program (JUST) funded by the Fletcher Jones Foundation offers Scripps Research graduates and postdoctoral fellows the opportunity for mentored teaching experience.

“We’re excited to launch this partnership with USD,” says Professor James Williamson, Ph.D., associate dean of the Scripps Research Kellogg School of Science and Technology. “The initiative fills a gap for our junior scientists whose career plans include teaching and research at an undergraduate institution.”

In addition to its more than 200 graduate students, Scripps Research trains 700 to 800 postdoctoral fellows, who spend several years after receiving their doctoral degree honing their skills in a mentor’s lab. The new program offers two positions. The JUST Fellowship, currently held by Ola Ghoneim, Ph.D., provides two years of stipend and a small budget for teaching and research expenses; the fellow team-teaches the first course with a USD faculty member, then transitions to solo teaching responsibilities. The JUST Internship, currently held by Kim Reynold, Ph.D., and Anita Pottekat, Ph.D., provides a modest teaching stipend for one semester.

The Fletcher Jones Foundation, has provided separate support to both Scripps Research and USD. This funding has included two endowed fellowships at the Kellogg School.

#### Leadership Training

Another initiative, the San Diego Lab Management Symposium, was born from a collaboration among the postdoctoral offices and societies of institutions on the Torrey Pines Mesa—Scripps Research, Burnham Institute for Medical Research, Salk Institute for Biological Studies, and UCSD.

The intensive, two-day seminar gave graduate students, postdoctoral fellows, and junior faculty an inside look at elements of scientific leadership, including effective hiring strategies, time management, communication, start-up budgets, and mentoring.

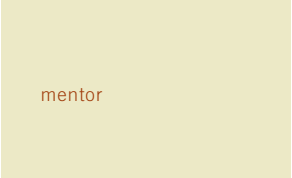
“There is no group willing to work harder than the people who attended this course,” said Scripps Research Associate Professor Marianne Manchester, who was the faculty advisor for the event, “so it was especially rewarding to see them take in the specifics of what to do and how to do it—like a curtain being pulled aside for them to see their future as a new principal investigator.”



learn



photo by Michael Balderas



mentor



## Creating Momentum: An Interview with Gerald Joyce



Gerald Joyce, M.D., Ph.D., dean of the faculty for The Scripps Research Institute, speaks with Mika Ono Benedyk of *Endeavor* about the process of building up Scripps Florida, the challenges of federal funding, and the importance of philanthropy going forward.

**ENDEAVOR:** *Could you reflect on developments relating to the Scripps Research faculty in the last year?*

**JOYCE:** The big picture is that we have hit a good, steady state in terms of size in La Jolla and we are chomping at the bit to expand into the new buildings in Florida. In Florida, we are currently crammed into two temporary buildings and a number of trailers, but anyone can log onto our website and see the new buildings going up. Barring any major hurricanes, we will be taking occupancy of those buildings ahead of schedule. Even if something slips, by the beginning of 2009 we will be in 350,000 square feet of permanent space on a gorgeous new campus. What that means is we are poised for a major push in hiring new faculty in Florida.

**ENDEAVOR:** *What is the process for recruiting new faculty?*

**JOYCE:** It's different for Florida and California. People already know how

great Scripps in California is; we just let them come and see for themselves what they already know. In Florida, we know how great Scripps Florida is, but people on the outside don't necessarily know. Many people still remember some of the difficulties getting the campus rolling. While the original site was abandoned for complex reasons, we now actually have a superior site in Jupiter—closer to restaurants, theaters, the arts, schools... So we have potential recruits visit the Florida campus with an open mind. So far, every person who has visited has been blown away with what we have on the ground already and what is being built.

It is hard to think of a place other than the Howard Hughes Medical Institute's Janelia Farm (outside of Washington, D.C.) where a whole campus is going up for biomedical research right now. There are campuses putting up new buildings or new centers, but ours is a whole new campus at an absolutely top quality level, with outstanding technology including a world-class screening center. Those who are forward thinking want to be a part of Scripps Florida; they want to be involved in the build-out and stand on top of this wonderful technology platform that we have put in place. Sometimes we encourage a follow-up visit to La Jolla, so potential recruits appreciate how the two campuses work together

and how the quality of Scripps permeates both campuses at the same level of distinction.

**ENDEAVOR:** *Recruiting so many faculty sounds like a big job.*

**JOYCE:** Yes. We are fortunate that our existing department chairs in Florida—John Cleveland, Pat Griffin, and Charles Weissmann—all are taking a strong role in recruiting, not only for individuals in their departments, but also for fellow department chairs. My hope is that the department chairs we bring in will be natural builders with a level of charisma to help create their departments. We are trying to get the ball rolling and expect it will pick up its own momentum as more people come on board.

**ENDEAVOR:** *Could you speak to the new departments that were created at the institute this year?*

**JOYCE:** While there were some issues intrinsic to La Jolla, the bigger picture is that we are trying to establish what I like to call sister department relationships between the Florida campus and the La Jolla campus. The idea is to promote good scientific interactions and collaborations and cement the sense that this is one Scripps—two campuses, but one Scripps. We are not like the University

---

It is all about the science and the high quality performance of that science.



of California, which has separate campuses with separate governance, and governance on top of that. Richard Lerner is the president of all of Scripps; I am the dean of faculty for all of Scripps; we have one graduate program for all of Scripps. We are looking for every way we can to cement relationships between individuals and departments between the two campuses.

**ENDEAVOR:** *How does the sister department relationship work?*

**JOYCE:** The idea is to create easy pathways of communication and collaboration by bringing departments together based on scientific discipline. Of course, it ultimately comes down to the level of the individual faculty and how they collaborate for their science.

To give one example, in La Jolla, we have an absolutely world-class Department of Immunology, and in Florida we have the Department of Infectology, which will blossom and expand in the new building. To me that is a natural partnership. The top-class infectious disease group in Florida will tell us about all the nasty bugs that are trying to get us, and the top-class immunology department in California will tell us how we are going to defend against those nasty bugs.

Similarly, the Department of Cancer

Biology in Florida will complement the Department of Molecular and Experimental Medicine, which has a strong oncovirology program, in California. This past year, Pat Griffin's Department of Molecular Therapeutics in Florida and Ben Cravatt's Department of Chemical Physiology in California were born as sisters. We are planning two new departments in Florida. One of them will involve neuroscience, and will have three siblings in California—the Molecular and Integrative Neuroscience Department; the Committee on Neurobiology of Addictive Disorders; and the Department of Neurobiology. The other department in Florida will likely focus on metabolism and aging, and have a natural sister in the Department of Cell Biology.

Chemistry is somewhat of a special case. We already have what we believe is the greatest department of chemistry in the country. We do not need to have two of those; we just want to expand what we have. K.C. Nicolaou will be the chair of all of chemistry, including faculty in Florida, and the go-to person on the ground in Florida will be Bill Roush.

**ENDEAVOR:** *Do you think the distance between the campuses poses a problem?*

**JOYCE:** Some might say it is impossible to truly connect the two campuses given

the physical distance, but it is not impossible—just watch us. First of all, the modes of communication now are completely different than they were even ten years ago, with web-based teleconferencing, electronic documents passing back and forth, and so on. For example, I lectured the graduate students last Friday in La Jolla in the Committee Lecture Hall, but I was being piped live via video to the students in Florida. And if Bill Roush gives a lecture in Jupiter on medicinal chemistry, then that is piped to students in La Jolla. Second, I think Scripps has an edge for maintaining connections between the two campuses because the culture of collaboration is already there. If we can put chemistry and biology together to create the new discipline of chemical biology, we can certainly deal with the logistics of two campuses that are 2,500 miles apart.

**ENDEAVOR:** *How does philanthropy fit into the picture?*

**JOYCE:** The philanthropy side is going to be key for both campuses. In Florida, startup funding comes from the Scripps Florida Funding Corporation, but that will end. To become self-sustaining will take a mix of funding sources.

The first is federal and nonfederal grants, the traditional source of fund-

---

Our faculty's biggest concern right now is to keep their programs thriving in an era of constrained resources.

ing for an academic research institution, especially funding from the National Institutes of Health [NIH]. The second is commercial connections. The productive relationship we enjoy with Pfizer applies to both campuses. The commercial side also provides the potential for a royalty stream from the drugs that come out of discovery efforts, but that takes some time.

The third source, an essential one, is philanthropy. I would expect that the good citizens, foundations, and corporations of Florida realize they have an absolutely world-class biomedical research institute in their backyard, making progress toward curing the diseases that the population suffers from and providing a nucleus for business development in South Florida. Because we are new, a philanthropist or foundation can play a key role in building the institute, not just layering a little something onto a cake that is already baked, but really being a key force.

**ENDEAVOR:** *Aren't we in a challenging federal funding environment these days?*

**JOYCE:** Yes, it is no secret that it is a tough time to get grants, probably the toughest since the mid-'70s. There was a period from 1998 to 2003 when the overall NIH budget doubled, but then the budget hit a wall and has remained basically flat since. Unfortunately, this actually means a decline in real dollars, not just because of inflation, but also because the cost of

research has escalated even faster than the inflation rate. Furthermore, during the era when the budget was doubling, the NIH made commitments to a number of large programs. While Scripps has benefited from some of those, they have pinched at the money available for investigator-initiated research. In addition, many universities across the country expanded their biomedical research capacity during the boom times, so now there is more demand on fewer dollars. You put those factors together—a flattening budget, an increased cost of doing science, an increased level of what you might call scientific earmarks for large programs, and increased demand—and what is left over is a really tight pool.

This poses a challenge for our faculty, but they are incredible athletes. By that I mean they know how to keep their scientific program going because it matters to them more than anything. They cannot let the research go on hiatus because they would lose momentum; they would lose the talent that is in their lab; they would lose the cutting edge. What they have done is to spend more time, beyond the seeming number of hours in the day, to find resources to keep their science going. That means more applications for federal grants, looking to nonfederal sources, and participating in more of the large strategic initiatives with program-specific sources of funding.

But it is a challenge. In a place like Scripps, we depend on grant support for everything we do. What we see now is

that when faculty members put in their renewal applications at the NIH, even for successful programs, there seems to be an almost automatic denial of the first application. Then, faculty have to go in for a reapplication, or even a re-reapplication. For us that is very dangerous because it means that the research program stops for six to nine months during each reapplication phase. Our faculty's biggest concern right now is to keep their programs thriving in an era of constrained resources.

**ENDEAVOR:** *What can we do to respond?*

**JOYCE:** I think philanthropy is the missing piece. Philanthropy can basically keep the students and postdocs employed during the fallow times when grants are up for renewal. Philanthropy can mean we do not have to lose momentum, and do not have to turn these people away from the science that they want to do. Philanthropy can also fill in the gaps in support for emerging fields, high-risk but potentially high-impact studies, and translation of research from the lab to the clinic. It is pretty hard to find a place where you can get more leverage for your philanthropic contributions than a place like Scripps. We run a tight ship. There is a very small administrative layer—it is all about the science and the high quality performance of that science. I think philanthropists would be pleased to know that they are getting maximum leverage for their contributions.



# Scripps Research Financial Highlights

FISCAL YEARS ENDING SEPTEMBER 30

## Sponsored Programs (millions)

05		327.4
06		322.6
07		308.5

## Total Assets (millions)

05		567.4
06		632.3
07		763.3

■ Investments  
 ■ Property  
 ■ Other

## Net Assets (millions)

05		419.8
06		483.1
07		525.6

## Asset/Debt Ratio (millions)

05		(567.4/60.6) 9.4
06		(632.3/58.9) 10.7
07		(763.3/57.2) 13.3

## Net Income (millions)

05		63.4
06		63.3
07		42.5



### *Naming Opportunities*

#### DRUG DISCOVERY BUILDING

*First floor* Lobby, Seminar Room

*Second floor* Conference room

*Research Suites* Ultra High Throughput Robotics, Magnetic Resonance, Mass Spectrometry, X-Ray, Medicinal Chemistry, Chemical Biology, Discovery Biology, Drug Metabolism & Pharmacokinetics, Synthetic Chemistry



## Names of Scripps Florida Facilities to Recognize Donors

Scripps Florida is embarking on a drive to raise funds to endow the operation and maintenance of its striking new campus in Jupiter, Florida.

### GIFT FROM ALEX AND RENATE DREYFOOS NAMES CENTRAL ATRIUM

Scripps Research Trustee Alex Dreyfoos has been involved with the construction of the institute's new campus in Jupiter from its earliest conceptual design. Now, as the project moves toward the construction crew's traditional "topping-off" ceremony, Mr. Dreyfoos has agreed to Scripps Research's request to name the central building atrium in recognition of his attention to the project and his and his wife Renate's \$1 million founding gift.

The Renate and Alexander Dreyfoos Atrium will welcome visitors to the 350,000-square-foot campus, as well as to the impressive masonry and steel structure housing Scripps Florida's advanced technology laboratories and a library, auditorium, and classrooms to serve the whole campus.

The support of Alex Dreyfoos means as much to the project as his monetary contributions. In Palm Beach County, where he has lived since 1968, he has become synonymous with civic leadership. The Scripps Florida architects, Zeidler Partnership, are well known to Alex Dreyfoos; he worked closely with the firm's senior partner, Eberhard Zeidler, throughout the design and construction of the Kravis Center for the Performing Arts in West Palm Beach, for which Mr. Dreyfoos was founding chairman. Other projects in the region also bear the Dreyfoos name, including the county's arts magnet high school.

Mr. Dreyfoos's charitable works extends to Massachusetts Institute of Technology (MIT), from which he graduated in 1954; MIT recently recognized his generosity by naming its new Frank Gehry-designed laboratory building in his honor.

Mr. Dreyfoos has established and owned a number of businesses in Palm Beach County over the years. These have included Photo Electronics Corporation, which provided the anagram name (WPEC) for the West Palm Beach-based CBS affiliate Channel 12 television station that he bought from legendary Florida businessman and fellow philanthropist John D. MacArthur. Mr. Dreyfoos's real estate firm, The Dreyfoos Group, owned and operated the Sailfish Marina in Riviera Beach.

As an inventor, Mr. Dreyfoos's early work in the electronic applications of photography led to his election as a fellow of the American Academy of Arts and Sciences--and to Hollywood's 1970 Academy Award from the Academy of Motion Picture Arts and Sciences for his invention of the Video Color Negative Analyzer. His energies are currently focused on an innovative yacht he helped to design for ocean cruising with his wife Renate.

#### HEADQUARTERS AND ADVANCED TECHNOLOGIES BUILDING

*First floor* Science Education Pavilion, Auditorium, Lakeside Plaza

*Second floor* Founder's Suite, Library

*Third floor* Scripps Florida Headquarters

*Research Suites* Microscopy, IT/Informatics, Genomics, Protein Sciences



Renderings courtesy of Zeidler Partnership

#### BIOMEDICAL RESEARCH BUILDING

*Second floor* Atrium, Lounge

*Research Suites* Cancer Biology, Infectology, Cell Biology, Neurobiology

### FOUNDERS' FUND COMMEMORATES EARLY BENEFACTORS

Scripps Florida is embarking on a drive to raise funds to endow the operation and maintenance of its striking new campus in Jupiter, Florida. Called the Founders' Fund, it will commemorate early benefactors for this important new biomedical research institute, sister campus to the renowned Scripps Research Institute in La Jolla, California.

If you are interested in having your name, or a loved one's name commemorated on the new Scripps Florida campus or on the California campus, please go to [www.scripps.edu/philanthropy/buildings.html](http://www.scripps.edu/philanthropy/buildings.html) for further details (and see a list of naming opportunities, above). For Florida, contact Barbara Sufas Noble at (561) 656-6400 or [bsnoble@scripps.edu](mailto:bsnoble@scripps.edu). For California, contact Wendy Scott Keeney at (858) 784-7083 or [wkeeney@scripps.edu](mailto:wkeeney@scripps.edu).

### SCRIPPS FLORIDA DESIGN AND CONSTRUCTION UPDATE

With each passing week, the Jupiter construction site becomes an ever-more-visible part of the Florida landscape. "On time and on budget" has been the project's mantra since vertical construction on the site began in January 2007. Construction is expected to be completed by 2009.

The three buildings, housing more than 350,000 square feet of space, promise to be impressive additions to the architecture of South Florida. The project's design pays homage to the state's tradition of a bright color palette. Four dominant colors will connect the buildings to one another in shades of silver, cool green, grey-blue, and terra cotta.

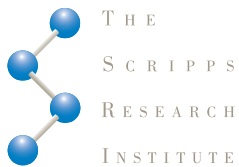
The design's most striking feature will be a 8.4-ton galvanized steel tower rising from the Dreyfoos atrium to a point 134 feet above the ground, more than 12 stories tall. The twisting shape of the spire is intended to evoke the double-helix shape of human DNA. The tower, which was engineered to withstand 140 mph hurricane winds, will be visible from Interstate 95, making it a landmark for those driving along one of the most heavily traveled highways on the East Coast.

The design team, led by Eberhard Zeidler, consists of architects from two award-winning firms, Zeidler Partnership and Bohlin Cywinski Jackson and Partners.

Check out progress on the construction of the permanent Scripps Florida campus at [www.scripps.edu/florida/watchusgrow](http://www.scripps.edu/florida/watchusgrow).

#### Editor's Note

This year, donor recognition lists have moved from *Endeavor* to the Scripps Research *Annual Philanthropy Report*, which will be published shortly. To receive a copy of this new publication, contact Wil Burfitt, (858) 784-2037 or [burfitt@scripps.edu](mailto:burfitt@scripps.edu).



THE  
SCRIPPS  
RESEARCH  
INSTITUTE

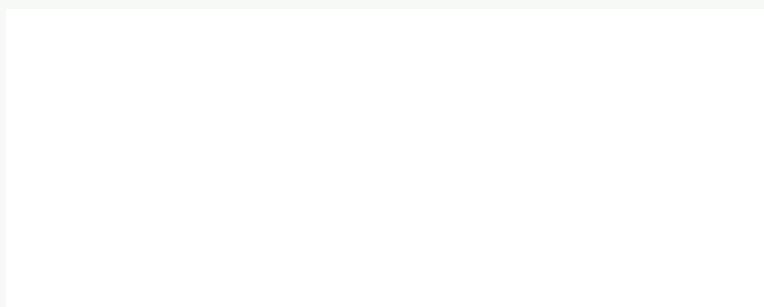
NON-PROFIT  
U.S. POSTAGE  
**PAID**  
PERMIT 751  
SAN DIEGO, CA

---

A PUBLICATION OF  
THE SCRIPPS RESEARCH INSTITUTE

---

Office of Communications—TPC30  
10550 North Torrey Pines Road  
La Jolla, California 92037  
[www.scripps.edu](http://www.scripps.edu)



PUBLISHER:  
*Keith McKeown*

EDITOR:  
*Mika Ono Benedyk*

DESIGN:  
*Octopus Ink*

COVER ILLUSTRATION:  
*Penelope Dullaghan*

PORTRAIT PHOTOGRAPHY:  
*Dana Neibert*

EDITORIAL PHOTOGRAPHY:  
*Kevin Fung*  
*Randy Smith*

PRINTING:  
*Precision Litho*

