Scripps Florida
2003 – 2013: A Decade of Discovery

2003: The Vision

In October 2003, Florida Governor Jeb Bush announced plans to establish a major science center in Palm Beach County, Florida, focusing on biomedical research, technology development and drug design.

"Scripps is the brand name in biomedical research and we are honored they have chosen Florida to expand their current research facilities," said Governor Bush at that time. "Already known for breakthroughs for cancer and Alzheimer's disease, this new bi-coastal presence will bring even greater opportunities for life-saving and life-enhancing research."

With start-up costs supported by a one-time $310 million appropriation of federal economic development funds by the Florida State Legislature and a generous economic package from Palm Beach County, The Scripps Research Institute was officially established in Florida in 2004, paving the way for other nonprofit organizations and members of the biotech industry to join the region.

2013: 10 Years of Remarkable Accomplishments

Over the last 10 years, Scripps Florida has established deep roots in the Florida community, while fulfilling its mission as a nonprofit organization to advance biomedical research, improve human health and train the next generation of scientists. Some of the highlights include…

Establishing a World-Class Faculty in State-of-the-Art Facilities

- Scripps Florida's 350,000-square-foot permanent facilities, located on a campus in Jupiter, Palm Beach County (adjacent to Florida Atlantic University and Max Planck Florida Institute), provide state-of-the-art tools to conduct biomedical research
- Equipment includes an ultra-high-throughput robotics system—one of only a handful in the world—that can screen up to one million compounds a day for potential drug candidates
- Among Scripps Florida's more than 500 employees are renowned scientists who lead research at the forefront of their fields in cancer biology, chemistry, molecular therapeutics, infectious disease, neuroscience and metabolism and aging

Contributing Critical Scientific Discoveries to Improve Human Health
Scripps Florida's research teams have already contributed a number of major breakthroughs. A few of these include:

- Making advances toward a blood test to diagnose Alzheimer's disease before symptoms appear
- Discovering a compound that might protect brain cells against Parkinson's disease
- Identifying a pathway in the brain that regulates an individual's vulnerability to nicotine addiction
- Uncovering a new mechanism for memory formation
- Showing compulsive eating shares the same addictive biochemical mechanism with cocaine and heroin abuse
- Finding a potential new use for a once-abandoned compound in the prevention and treatment of neuroblastoma, one of the most devastating cancers among young children
- Discovering that a rare natural product has potent pain-killing properties
- Establishing new class of anti-diabetic compounds

Producing Measurable Results
Scripps Florida's research has resulted in:

- More than 100 foreign and domestic patent applications
- 39 technology licenses
- 3 spin-off companies
- More than $347 million in grants from the National Institutes of Health, foundations, individuals and other non-state sources

Anchoring an Emerging Biotech Cluster

- According to Enterprise Florida, before Scripps arrived, the state had 36 biotech companies; today it has more than 200
- According to the 2012 Life Sciences Cluster Report, the biotechnology sector in Florida is expected to expand significantly in the next several years, due in major part to Scripps Florida, which has increased the profile of the region's life sciences community
- Scripps Florida actively collaborates with other local institutions, including Florida Atlantic University, Florida State University, University of Florida, Max Planck Florida and the University of Miami

Offering Advanced Training in Biology and Chemistry

- The Scripps Research Institute's graduate program in biology and chemistry brings to Florida a PhD program ranked consistently in the top 10 in the nation by *US News & World Report*

- The institute has also partnered with Florida Atlantic University in creating a joint program in which students earn both MD and PhD degrees

Reaching Out to Local Students, Teachers and Community Members

- More than 8,000 students, teachers and other community members have participated in Scripps Florida's educational outreach programs
- Funded in part by a grant from the William R. Kenan Jr. Charitable Trust, outreach programs include internships for local students, training for science teachers, weekend workshops and an annual "CELLebrate Science" community event at the Palm Beach Gardens Mall

Thank you for your support!

The Scripps Research Institute thanks the people of Palm Beach County and the State of Florida for their generous partnership in establishing Scripps Florida.

Part 1: New Faculty

Scripps Research Institute Appoints Innovative Neuroscientist

The Scripps Research Institute has appointed Brock Grill as an assistant professor in the Department of Neuroscience. Previously, Grill was a member of the Department of Pharmacology at the University of Minnesota.

"We're extremely pleased to have Brock join our department," said Ron Davis, chair of the Scripps Research Department of Neuroscience. "His innovative work on neuronal and synapse development will help us get to the bottom of how the brain develops, and what exactly goes wrong in conditions of abnormal brain development."

"I'm excited about joining Scripps Florida," said Grill, who lives in West Palm Beach, FL. "The resources here, particularly the drug screening technology, are exceptional and will help tremendously in expanding my research. In addition, Ron Davis is doing a superb job of assembling a great neuroscience faculty—I was onboard very early on after hearing Ron's vision for the department and meeting the talented people he had hired."

Grill received a bachelor's degree in Microbiology from the University of Alberta, Canada, in 1998, and a PhD in Experimental Medicine from the University of British Columbia in 2003. He conducted postdoctoral work at the University of California, Santa Cruz from 2004 to 2007 and Stanford University from 2007 to 2009.

Grill's research is focused on understanding how different events in neuronal development are coordinated on a molecular level. The formation and wiring of the brain requires the intricate interplay of a series of complex molecular events. By unraveling the molecular mechanisms that govern neuronal development in the roundworm *C. elegans*, Grill said he hopes to gain insight into how neurons manage numerous signals from their environment to form a neural network. Such knowledge has tremendous potential to help generate new therapies to treat neurodegenerative diseases, as well as injury to the central nervous system from stroke and trauma.

Scripps Research Institute Appoints NIH Senior Scientist to Cancer Biology Department

The Scripps Research Institute has appointed Christoph Rader as an associate professor in the Department of Cancer Biology and the Department of Molecular Therapeutics.

Before coming to Scripps Florida, Rader was a senior scientist at the National Cancer Institute (NCI) in Bethesda, Maryland. Prior to that, he was an assistant professor on the La Jolla, California, campus of Scripps Research.

"We want to welcome Christoph back to Scripps Research," said John L. Cleveland, chair of the Scripps Research Department of Cancer Biology. "In California, his groundbreaking antibody research helped pioneer a hybrid cancer therapy, and at NIH he was responsible for developing several innovative approaches to antibody drug and target discovery. He's a great addition to our department and to the institute as a whole."

"It's a great pleasure to return to Scripps Research—and to be part of Scripps Florida," said Rader, 46, who lives with his wife and two sons in Jupiter. "The faculty here is terrific, not only in cancer biology, but also in molecular therapeutics and chemistry. What I missed most at the NCI was being able to work more closely with chemists—they were 45 minutes away. Now, chemists are minutes from my office."

Rader has already taken advantage of that proximity, launching collaborations with Scripps Florida chemists William R. Roush and Thomas Kodadek.

Rader's research is focused on developing antibody therapies to treat cancer. "Monoclonal antibody therapy of cancer is a tremendously exciting and rewarding field that thrives on multidisciplinary expertise in biology, biochemistry, chemistry, pharmacology, and medicine," said Rader. "Prompted by current knowledge, we have gone back to the drawing board to design, engineer, test, and deliver the next generation of monoclonal antibodies that target cancer cells with even higher precision and potency. Scripps Florida is an ideal place for hanging our drawing board and developing novel technologies at the interface of chemistry and biology."

Rader studied biochemistry and molecular biology at the University of Bayreuth in Germany (1986-1988) and at the University of Zurich in Switzerland (1988-1995), where he graduated with a diploma in biochemistry in 1991. In 1995, he was awarded a PhD with honors from the University of Zurich for his work on immunoglobulin superfamily molecules.

Rader did postdoctoral work with Professor Carlos F. Barbas III at Scripps California, where he specialized in antibody engineering, phage display, and catalytic antibody technologies. Following his promotion to assistant professor at Scripps Research in 1999, he won the prestigious Investigator Award from the Cancer Research Institute in 2000. Shortly after, he was part of a Scripps Research team that invented the concept of chemical programming of monoclonal antibodies to generate hybrid cancer therapeutics, a cross between traditional small molecules and a certain type of monoclonal antibody. After commercialization, this innovation has brought several new drugs into phase I and II clinical trials for the treatment of various cancers and metabolic diseases.

Rader joined the NCI in 2003 to head the Antibody Technology Section in the Experimental Transplantation and Immunology Branch. In 2007, he received the NCI Director's Intramural Innovation Award for Principal Investigators for a novel chemical programming concept. His achievements include more than 80 publications and 13 patents or patent applications in the area of antibody engineering and conjugation technologies.

Two Noted Scientists Appointed to Metabolism and Aging Department

The Scripps Research Institute has appointed Paul D. Robbins as a professor and Laura J. Niedernhofer as an associate professor in the Metabolism and Aging Department on the institute's Florida campus.

"It is a distinct honor to welcome these two exceptional scientists to the faculty," said Roy Smith, chair of the Metabolism and Aging Department. "They both bring a wealth of knowledge and experience and are involved in research that will help change the way we deal with aging and disease in the future."

Prior to joining Scripps Florida, Robbins was a professor at the University of Pittsburgh School of Medicine; Niedernhofer was associate professor at the University of Pittsburgh and its cancer institute.

Paul Robbins: Focusing on Age-Related Degenerative Diseases

In his research program, Robbins focuses on various biological approaches to understanding and treating age-related degenerative diseases, including cancer, bone healing, and diabetes. He has developed a gene therapy approach to arthritis, and is participating in a clinical trial for osteoarthritis—a project he expects to

continue at Scripps Florida. His laboratory is also studying a novel peptide for bone treatment.

Mostly recently, he has been using genetic and pharmacologic approaches to inhibit NF-κB, a protein factor that controls DNA transcription. NF-kB is involved in a number of key processes, including immune and inflammatory responses, and has been implicated in diseases ranging from cancer and arthritis to various neurodegenerative diseases.

"It's an honor to join the Scripps Florida faculty," Robbins said. "The quality of the research is spectacular, not to mention the collaborative atmosphere and the outstanding facilities. On top of all that, I grew up in Florida, so this is like a homecoming."

Robbins, 54, received a BA in biology from Haverford College, Pennsylvania, in 1980 and a PhD in molecular biology from the University of California, Berkeley, in 1985. He conducted postdoctoral work at the Whitehead Institute at the Massachusetts Institute of Technology from 1986 to 1990.

Robbins joined the University of Pittsburgh School of Medicine as an assistant professor in the Department of Molecular Genetics and Biochemistry in 1990 and was appointed associate professor in 1996. He became a professor in the Department of Orthopedic Surgery in 2001.

Robbins' honors and awards include the Synos Foundation Research Award (2000), the Nicolas Andry Award (2004), the Orthopedic Research Society Kappa Delta Award (2005), and the Juvenile Diabetes Research Foundation Mary Jane Kugel Award (2009).

Laura Niedernhofer: Exploring the Link between Aging and DNA Damage

Niedernhofer is interested in the relationship among DNA, cancer and aging—especially the link between aging and DNA damage. She has focused much of her work on a rare and fatal human disorder known XFE progeroid syndrome. Patients rapidly develop progressive symptoms that are associated with old age such as heart disease, muscle wasting and bone loss.

"I'm thrilled to be joining Scripps Florida," Niedernhofer said. "All of us became scientists because we wanted to change healthcare, and we all have ideas about how to do just that—here we have a chance to get them off the shelf and into practice."

Niedernhofer, 47, received a BS in chemistry from Duke University in 1985 and a master's in physiology from Georgetown University in 1991. She was awarded a PhD in biochemistry from Vanderbilt University School of Medicine in 1996 and an MD from Vanderbilt just two years later. She conducted postdoctoral work at Erasmus Medical Center in the Netherlands from 1999 to 2003.

In 1999, she received a National Science Foundation International Research Fellow Award that was followed the next year by an American Cancer Society Postdoctoral Fellowship. In 2005, she became a Hillman Fellow at the University of Pittsburgh Cancer Institute (2005-2008) as well as being named a New Scholar in Aging by The Ellison Medical Foundation (2005-2009).

Both Robbins and Niedernhofer live in Juno Beach.

Scripps Research Institute Appoints Two Noted Scientists to Cancer Biology Faculty

The Scripps Research Institute has appointed Joseph Kissil as an associate professor and Matthew Pipkin as an assistant professor, both in the Department of Cancer Biology.

"It's a pleasure to announce the appointment of these two terrific investigators who are pushing the envelope in their respective fields," said John Cleveland, a Scripps Research professor and head of the Department of Cancer Biology. "Joe works on regulators that cause lung, pancreas, and liver cancer, and a rare tumor called neurofibromatosis, and upon the tumor microenviroment, while most of Matthew's studies are focused on epigenetic control of cytotoxic T cells and memory T cells, which are essential for immune surveillance in cancer and in combating infectious diseases. The new arenas being tackled by these talented investigators are critical to the future development of new and more effective cancer treatments. We extend a warm welcome to them both."

Joseph Kissil

Prior to joining Scripps Florida, Kissil, 45, was an associate professor at The Wistar Institute in Philadelphia, PA, as well as a member of the Graduate Group in Cell and Molecular Biology at the University of Pennsylvania.

"At Scripps Florida there are few barriers between scientists—you have chemistry, drug metabolism, and basic biology research, all geared to collaboration," said Kissil, who lives in Jupiter. "On top of that, the translational research institute and services such as the high throughput screening core make a fantastic combination."

Kissil received a bachelor's degree in biology from Ben-Gurion University in Israel and a PhD in molecular biology from the Weizmann Institute of Science, Israel. He did postdoctoral work at the Massachusetts Institute of Technology.

In 2001, he received a Young Investigator Award from the Neurofibromatosis Foundation and in 2003, the R.L. Kirchstein National Research Service Award. In 2010, Kissil was named an American Cancer Society Research Scholar.

Kissil's work focuses on the mechanisms that maintain normal tissue balance and how these become deregulated in cancer. Kissil has long been interested in the role

the tumor microenvironment plays in cancer growth and how the deregulation of various signaling pathways, such as those that relay information from the extracellular environment into the cell interior, can contribute to the disease. "We're interested in the molecular basis for disease, particularly cancer," he said. "As we made discoveries, we decided we wanted to take that extra step into translation of the science to potential therapies. To accomplish that, Scripps Florida was the obvious choice."

Matthew Pipkin

Before joining Scripps Florida, Pipkin, 37, held a junior faculty position at the La Jolla Institute for Allergy and Immunology.

Pipkin, a Florida native who now lives in Juno Beach, received a bachelor's degree in microbiology and immunology from the University of Miami in 1998, and a PhD in microbiology and immunity in 2005 from the same institution. He did postdoctoral training at Harvard Medical School.

"It's an honor to become part of Scripps Florida," Pipkin said. "Coming back to Florida was a big draw, and Scripps Florida is at the leading edge of what science and the state has to offer—plus it has an entrepreneurial spirit that I found nowhere else."

Pipkin's research interests are in the study of chromatin, the cluster of proteins that compact the DNA of chromosomes in the cell nucleus; like a meticulous butler, chromatin dynamically packs the DNA in different ways in different cell types to help prevent damage and to help ensure that only certain genes are accessible for transcription as cells become more specialized. His lab specifically focuses on understanding how chromatin regulates accessibility to genes that promote the differentiation of cytotoxic lymphocytes, immune system cells that directly kill cancer cells.

"My research dovetails with the reasons I came to Scripps Florida and to cancer biology," he said. "We want to understand the basics of how chromatin controls gene expression, and how that underlies cell differentiation—cancer is in many ways an aberrant form of differentiation, which at its roots is a gene expression problem and controlled by chromatin. Second, we want to use what we know about cytotoxic lymphocyte differentiation to develop new therapies and vaccines that elicit durable cytotoxic lymphocyte responses. The resources and faculty here will let us try some bold new approaches."

Noted Biochemist Appointed to Molecular Therapeutics Faculty

The Scripps Research Institute has appointed Scott Hansen as an assistant professor in the Department of Molecular Therapeutics. Prior to joining the Jupiter campus

faculty, Hansen was a postdoctoral fellow at the Dana-Farber Cancer Institute at Harvard Medical School.

"We want to welcome Scott to the Scripps Florida faculty and to our department," said Patrick R. Griffin, chair of the Department of Molecular Therapeutics. "His research into the mechanism of lipid control of ion channels adds an important new element to the research programs at Scripps Florida. Scott's experience in membrane protein crystallography is also a great addition to the targets of focus here at Scripps Florida. We look forward to his continued success."

"It's a great honor to become a member of the Scripps Florida faculty," said Hansen, who lives in Jupiter. "What drew me here, aside from the first-rate resources, was the fact that Scripps Florida facilitates serious biomedical research that produces real-world therapies. There are few other institutions that do that."

Hansen, 37, received his bachelor's degree in chemistry from Utah State University in 1999. He held positions at Abbott Laboratories and the California campus of Scripps Research, before pursuing a PhD in biochemistry from the University of California, San Diego (UCSD), winning the Martin D. Kamen Award for best doctoral thesis. Hansen pursed postdoctoral work at The Rockefeller University under Nobel Laureate Rod MacKinnon and as a fellow of the Howard Hughes Medical Institute from 2007 to 2011 before his work at the Dana-Farber Cancer Institute.

Hansen's research is focused on ion channels and lipids, and how they interact. Ion channels function like pores in the lipid membranes of cells, allowing ions or electrically charged atoms and molecules to flow across those membranes. They perform critical roles in the central nervous system as well as the immune system and muscle cells—the heart's rhythmic beating is based on the opening and closing of ion channels.

Ion channel disruption has been blamed for a number of diseases including some forms of epilepsy, cardiac arrhythmias, kidney disorders, and even deafness.

In a paper published last year in the journal Nature, Hansen and colleagues were able to show how a minor component of cell membranes, the phospholipid PIP(2), controls the electrical charge of a cell and thus various ion channels.

"In the cell membrane, lipids act like triggers for ion channels," Hansen said. "In the past, it was thought that lipids more or less just sat there—like dirt holding in a plant. People didn't appreciate how much control lipids had over these channels until we did our study. It was the first time anyone examined how they worked together as a signal."

The most important channels regulated by lipids are in addiction, pain, and cognition. "Those are the areas we're going to focus on," Hansen said.

Scripps Research Institute Appoints Innovative Scientist to Metabolism and Aging Department

The Scripps Research Institute (TSRI) has appointed Anutosh Chakraborty as an assistant professor in the Department of Metabolism and Aging.

Before coming to Scripps Florida, Chakraborty was affiliated with the Johns Hopkins University School of Medicine in Baltimore, MD.

"It is my great pleasure to welcome Anutosh to the department," said Roy Smith, chair of the Department of Metabolism and Aging. "His research at Johns Hopkins was extraordinary and led to new insights into the functions of inositol pyrophophates (IP7) and associated IP6 kinases in cancer and metabolic disorders. At Scripps, he will focus on elucidating related molecular mechanisms regulating glucose and lipid homeostasis and exploiting this information to identify therapeutic targets for diabetes and cardiovascular disease. We look forward to working with him."

"I'm very excited to join the Scripps Florida faculty," said Chakraborty, who lives in Jupiter with his wife, Molee, and 8-year-old daughter, Driptaa. "It's an institute of repute having dynamic and outstanding faculty, not to mention some exceptional resources, particularly the high-throughput screening core. Not too many places have that—it was one of my real points of interest in coming here. In addition to being authorities in their respective fields, the faculty members are very welcoming and I look forward to many productive collaborations."

Chakraborty received his bachelor's degree in Zoology from the University of Burdwan, India, in 1995 and a master's degree in 1997 from the same institution. He was awarded a PhD from the Indian Institute of Chemical Biology in 2005. He conducted postdoctoral work at Johns Hopkins, and then became a research instructor there.

In 1998, Chakraborty was awarded a Lectureship after qualifying in the Joint Council of Scientific & Industrial Research (CSIR), India, and the University Grants Commission National Eligibility Test. He received a Merit Research Grant Award the following year. He ranked second in the nationwide Graduate Aptitude Test in Engineering (GATE), conducted by Indian Institute of Technology (IIT) in 1999.

Chakraborty's research is aimed at understanding the molecular details of the various signaling pathways involved in metabolic diseases, particularly the family of inositol hexakisphosphate kinases (IP6Ks), which play a role in a range of physiological activities from programmed cell death to the regulation of insulin and glucose homeostasis.

In 2008, Chakraborty was a key member of a Johns Hopkins research team that discovered a novel way to develop stronger, less-harmful anticancer drugs—showing that the action of IP6K2, which promotes cell death in response to stress such as commonly prescribed anti-cancer drugs, can be controlled when bound to a

heat shock protein, HSP90. The study was published the journal Proceedings of the National Academy of Sciences.

In 2010, he was the lead author of a study published in the journal Cell that suggested that selective inhibitors of IP6K1 could have strong therapeutic potential in treating type-2 diabetes associated with obesity and insulin resistance—with few adverse side effects. He demonstrated that mice deleted of the IP6K1 gene are protected from age and high-fat-diet-induced weight gain and insulin resistance.

"We believe strongly that IP6K1 may eventually have some therapeutic potential," he said, "While I'm working on the mechanism by which IP6K1 regulates body weight, I am also looking for novel protein targets that we don't know about yet that play important roles in hormonal signaling and adipogenesis. I have used chemical screening approaches to identify modulators of adipogenesis. I plan to extend the approach and I think Scripps Florida is the best place to do that kind of work."

Scripps Research Institute Appoints Two Notes Harvard Scientists

The Scripps Research Institute (TSRI) has appointed Professor Michael R. Farzan and Associate Professor Hyeryun Choe to the faculty on its Florida campus.

Prior to joining Scripps Florida, both were on the faculty at Harvard Medical School.

"It is a pleasure to welcome Michael and Hyeryun," said Peter K. Vogt, executive vice president and chief scientific officer of TSRI. "Both are involved in critical research that will help us advance the diagnosis and treatment of HIV and other devastating viral infections that need to be conquered and defeated."

"I'm honored to join Scripps Florida," Farzan said, "I'm genuinely excited by the compound discovery opportunities at Scripps Florida, and hope to develop new opportunities and new directions for my laboratory. I was drawn to Scripps Florida for its new technologies, and for its investigators with different disciplines."

Choe said, "I'm extremely pleased to become part of Scripps Florida. Over the years, my laboratory has been moving from basic to more translational science, and Scripps Florida has a great reputation in both. I'm looking forward to working with other scientists, particularly medicinal chemists, in developing new therapeutic approaches to viral infection."

Michael R. Farzan

Farzan's research is focused on uncovering the process by which various viruses, including HIV-1 and SARS coronavirus, enter target cells and the immune system's response to this event. Farzan is also working to find ways to enhance these immune responses. For example, his lab identified the cellular receptor for the SARS virus, a key post-translational modification of CCR5 necessary for HIV-1 infection, and a family of innate immune factors that prevent viruses from entering cells.

He has shown that some antibodies mimic certain host receptors, an important finding since such similarities make it more difficult for the virus to escape the body's immune response. Farzan is currently investigating these antibodies, their role in controlling long-term infection, and how to better draw them out. His long-term goal is to find an appropriate combination of antibody and antibody-like molecules to provide long-term protection from HIV-1 infection following a single inoculation.

Farzan received a bachelor's degree from Harvard College in 1984 and a PhD in Immunology from Harvard Medical School in 1997. He was a postdoctoral fellow in the Department of Cancer Immunology and AIDS at the Dana-Farber Cancer Institute in Boston.

Farzan joined Harvard Medical School as an instructor in the Department of Pathology in 1999. In 2002, he was named an assistant professor in the Department of Medicine and, in 2005, an assistant professor in the Department of Microbiology and Molecular Genetics. In 2007, he was promoted to associate professor and, in 2012, to professor.

Among Farzan's honors are the Richard A. Smith Prize for outstanding research at Dana-Farber Cancer Institute, the Burroughs Wellcome Fund Investigators in Pathogenesis of Infectious Disease Award, and a Kavli Fellowship from the National Academy of Sciences and The Kavli Foundation.

Hyeryun Choe

Choe has focused on identifying the processes by which enveloped viruses enter their target cells. That focus has led to the identification of a number of key factors essential for entry of HIV-1, SARS coronavirus and a number of hemorrhagic fever viruses.

Among her significant research is a 2007 Nature paper that reported the identification of a key receptor for pathogenic New World arenaviruses—Machupo, Junin, Guanarito and Sabia, which cause hemorrhagic fever and significant casualties in various regions of South America. The team was also able to show that iron depletion enhances, and iron supplementation slows, infection by these viruses, suggesting iron supplement as a possible treatment.

Choe received a bachelor's degree from Seoul National University in Korea in 1977 and a master's degree in 1980. She was awarded a PhD from Pennsylvania State University in 1984, and subsequently conducted postdoctoral work at Harvard Medical School.

In 1997, Choe was appointed as an instructor at the Dana-Farber Cancer Institute and Harvard Medical School. In 2000, became an assistant professor at Children's Hospital and Harvard Medical School.

Choe was the second most cited scientist for research published in 1996-7 as reported by Thomson Reuters' Essential Science Indicators Science Watch; in 2002, she was named a Prominent Scientist by the Society for Biomedical Research.

Farzan and Choe both live in Juno Beach.

Memory Researcher Joins Florida Neuroscience Faculty

The Scripps Research Institute (TSRI) has appointed Assistant Professor Seth Tomchik as a laboratory head on the Florida campus. Previously, Tomchik was a senior research associate and a member of the Ron Davis laboratory at Scripps Florida.

"It is a genuine pleasure to welcome Seth to our faculty," said Ronald Davis, chair of the Department of Neuroscience. "I have known Seth for many years, and his work has never been less than outstanding. His contributions to the science of memory and learning have enriched Scripps Florida. I fully expect that those contributions will continue to grow."

"I'm honored to become a principal investigator at Scripps Florida," Tomchik said. "I want to thank Ron Davis, who has been an exceptional mentor and advisor, for his support and his thoughtful guidance over the years. I look forward to many more years of friendship and collaboration with him, and all the members of the neuroscience department. It's a great place to do science."

Tomchik, who received a prestigious National Institute of Mental Health Pathway to Independence award in 2010, is focusing his research on how the brain influences both innate and learned behaviors. Like many scientists who study memory, he uses the common fruit fly, Drosophila melanogaster, as a model system to study and decipher the intricacies of neural circuits. Genetic techniques, coupled with in vivo imaging and precise manipulation of neuronal activity, enable him to study how various neurotransmitter pathways are involved in shaping normal behavior and disease.

"When I was at the University of Miami, I looked into sensory coding," Tomchik said, "that is, how sensory input is processed, sent to brain and then returned to the sensory organs to modulate their sensitivity. That's how I became interested in studying learning and memory, to examine how learning modifies the way sensory information flows through neuronal circuits. I want to see how this information gets modified in the fruit fly brain and how it gets disrupted in models of human disease. My ultimate goal is to uncover the pathophysiology of diseases such as fragile X and neurofibromatosis type 1."

Neurofibromatosis type 1 is a tumor disorder that produces tumors within the nervous system, and often results in learning difficulties.

Tomchik received an Honors Program BA cum laude in psychology from the University of Miami in 2001, and a PhD in biology from the same institution in 2005. From 2006 to 2007, he was a postdoctoral fellow at the Miller School of Medicine (University of Miami) and later, from 2007 to 2009, at Baylor College of Medicine. Tomchik received a Robert E. Maytag fellowship in 2002 and a National Institute of Neurological Disorders and Biomedical Discovery Training fellowship in 2007. He joined TSRI in 2009.

Institute Appoints Innovative Biotech Scientist to Cancer Biology Department

The Scripps Research Institute (TSRI) has appointed Mark Sundrud as an assistant professor in the Department of Cancer Biology. Before joining Scripps Florida, Sundrud was a principal scientist and head of discovery biology at Tempero Pharmaceuticals, a GlaxoSmithKline-funded Massachusetts-based biotechnology company focused on developing new therapeutics for autoimmune diseases.

"It's a distinct pleasure to welcome Mark," said John Cleveland, chair of the Department of Cancer Biology. "I fully expect he will be a major contributor to our growing success. His exceptional work in immunology adds depth to the department and will help shed much needed light on the role of immune surveillance in cancer."

"I'm honored to join the Scripps Florida faculty," said Sundrud. "What attracted me—in addition to the high level of science—was the integration of chemistry, molecular therapeutics and exceptional screening resources on one campus. My research interests have always been centered on basic aspects on T cell biology, but always within the context of what's relevant to patients and clinical disease. That will continue to be the focus of my work at Scripps Florida."

Sundrud earned a bachelor's degree in biology and psychology with honors from Concordia College and a PhD in Microbiology and Immunology from Vanderbilt University Medical Center, where he received the Sidney P. Colowick Memorial Award for outstanding graduate research. He went on to complete a postdoctoral fellowship at Harvard Medical School, where he was awarded a fellowship from the Irvington Institute fellowship program of the Cancer Research Institute.

As the head of target discovery at the newly formed Tempero Pharmaceuticals, Inc., Sundrud oversaw the company's early research programs that were focused on defining the mechanisms underlying T cell-mediated inflammation and on developing innovative therapeutic strategies for the treatment of chronic and autoimmune inflammation. Sundrud also served as the scientific manager of a research alliance between GlaxoSmithKline and the Harvard Medical School-affiliated Program in Cellular and Molecular Medicine at Children's Hospital in Boston.

Sundrud was the lead author of a groundbreaking 2009 study, published in the journal Science, which described how halofuginone, a small molecule derived from

the root of the blue evergreen hydrangea, specifically inhibits the development of a unique, inflammatory subset of CD4+ "helper" T cells known as Th17 cells, which have been implicated in a variety of common autoimmune disorders.

In his research program at Scripps Florida, Sundrud, now 34 and a resident of Jupiter, aims to better understand the molecular underpinnings of how inflammatory T cells develop and promote tissue inflammation—with the ultimate goal of applying that knowledge towards the development of new therapies.

"My research has been focused on understanding the metabolic and stress response pathways of Th17 cells so one can restrict inflammation without broadly suppressing the immune system," he said. "But if we switch that around, we may also be able to harness these same T cells and these same pathways to eradicate tumors."

Scripps Research Institute Appoints Immunology Researcher to Faculty

The Scripps Research Institute (TSRI) has appointed Laura Solt as assistant professor at the Florida campus. Previously, Solt was a research associate and a member of the laboratory of Professor Thomas Burris at Scripps Florida.

"It is a pleasure to welcome Laura to our faculty," said Patrick R. Griffin, chair of the Department of Molecular Therapeutics. "In Tom's lab, Laura has been very productive and has made an impact in the understanding of several important nuclear receptors. I look forward to her continued success as a new and independent faculty member and her contributions to our understanding of metabolic and inflammatory disorders."

"I'm honored to become a principal investigator at Scripps Florida," Solt said. "I want to thank both Tom and Pat for their help and support over the past few years. Scripps, and more specifically, the Department of Molecular Therapeutics, has provided a wonderful environment to perform scientific research. I can't think of a better place to build my own lab than here."

Solt received a bachelor's degree in Psychology, with a concentration in Pre-Medical studies, from Boston College in 1998 and a PhD in Immunology from the University of Pennsylvania in 2008 before joining Scripps Florida as a postdoctoral fellow.

Her research is focused on nuclear receptors, a family of protein molecules that are best known for sensing and controlling hormone activity inside the cell; they have been implicated in the progress of a number of cancers, the generation of metabolic syndrome, and several autoimmune diseases. Due to the wide range of physiological and potential pathological consequences of aberrant nuclear receptor activity, this family of proteins is a popular area of research as potential targets for drug development, including for type 2 diabetes, atherosclerosis and metabolic syndrome.

In the Burris lab, Solt was deeply involved in research that led to the development of first-in-class, highly selective compounds that effectively suppress certain types of autoimmune responses, including the severity of multiple sclerosis in animal models. These compounds could provide new and more effective therapeutic approaches to multiple sclerosis and other autoimmune diseases.

"I plan to continue to use those same small molecules we identified, specifically SR1001, in order to better understand the physiology of nuclear receptors," she said. "However, I would like to eventually expand to other compounds or improve upon those in the series so we can gain more insight into each individual receptor's function. The collaborative spirit at Scripps Florida and the resources we have here are exactly what I need to continue my work."

Solt, 36 and a resident of Palm Beach Gardens, is past-president of the Scripps-Florida Society of Research Fellows and one of the founders of the campus's chapter of Network for Women in Science.

Part 2: Grant Awards and Licensing Agreements

Scripps Research Institute Scientist Receives $2.8 Million to Study Critical Cell Signaling Mechanism and Develop Potential Therapeutics

A scientist from the Florida campus of The Scripps Research Institute has been awarded a pair of grants totaling $2.8 million from the National Institute of General Medical Sciences of the National Institutes of Health, and from TargAnox, a Massachusetts-based biotechnology firm.

Kate Carroll, a Scripps Research associate professor, will be the principal investigator for the new projects.

Research funded by both grants will focus on a process known sulfenylation, a relatively new field of research. During periods of cellular stress, caused by factors such as UV radiation or chronic diseases such as cancer, the level of highly reactive oxygen-containing molecules can increase, resulting in inappropriate modification of proteins and cell damage through this process. One oxidant produced naturally in the body, hydrogen peroxide, acts as a messenger that can activate cell proliferation.

In the new research, Carroll will look at cell signaling in sulfenylation and explore ways that it might be modified with potential drug compounds to treat conditions such as lung and breast cancers, as well as be used to diagnose and monitor such diseases.

To explore the process, Carroll and her colleagues have developed a highly selective chemical probe—known as DYn-2— that can detect minute differences in sulfenylation rates within the cell. The new four-year, approximately $1.5 million

NIH grant (award number 1R01GM102187-01) will fund work utilizing that chemical probe to fully define the molecular mechanism through which a key signaling protein, epidermal growth factor receptor (EGFR), is modified by hydrogen peroxide.

"The grant from NIH will let us take a closer look at the basic mechanics of the sulfenylation process and detail how oxidation regulates EGFR," Carroll said. "The TargAnox study uses that work as a spring board into potential treatments."

Carroll said she also plans to investigate additional targets of sulfenylation and to test various compounds that can reverse the process.

Team Receives $2.7 Million to Investigate Major Therapeutic Target

A consortium of scientists from both campuses of The Scripps Research Institute (TSRI) has been awarded $2.7 million from the National Institute of General Medical Sciences of the National Institutes of Health to study the structural rules that govern a large superfamily of proteins that help regulate critical functions such as reproduction, development and metabolism.

The principal investigators for the three-year study will be Kendall Nettles, an associate professor, and Pat Griffin, professor and chair of the Department of Molecular Therapeutics, both on the Florida campus of TSRI. They will work with Professor Ian Wilson and the Joint Center for Structural Genomics on TSRI's La Jolla campus.

The focus of the new project is nuclear receptors, a superfamily of proteins that mediate hormone, lipid and fatty acid activity inside the cell. Nuclear receptors have been implicated in a number of cancers, including prostate, breast and colon cancers. They also represent excellent targets for drug development, including cancer drugs, birth control and anti-inflammatory agents and treatments for diabetes and metabolic syndrome.

Nuclear receptors are ligand-dependent transcription factors that function as scaffold proteins recruiting enzyme complexes to specifically turn genes on and off. Triggering nuclear receptor activity are molecules that include the sex hormones, vitamins A and D, glucocorticoids (which regulate the body's response to stress) and many small molecules involved in metabolism, such as fatty acids, lipids and cholesterols. While several structures of the ligand-binding domain of nuclear receptors have been reported, little is known about the structural rules that allow nuclear receptors to control the function of the enzymes that mediate the receptors' activity. The new study is aimed at filling this gap by obtaining structures of larger domains of nuclear receptors in complex with a subset of interacting proteins.

"We want to look at these proteins—which play key roles in metabolism, cancer, inflammation and bone health and are targets for widely prescribed drugs—and understand their signaling mechanisms through structural biology," Nettles said.

To conduct this research, the team will use x-ray crystallography and nuclear magnetic resonance (NMR), methods that provide a three-dimensional picture of a molecule's atomic structure. The team will draw on the high-throughput screening resources at Scripps Florida, as well as the high-throughput structural biology resources of the Joint Center for Structural Genomics based on the La Jolla, California campus.

The National Institutes of Health project number for the grant is 1U01GM102148-01.

Team Awarded $2.5 Million to Study Inner Workings of Memory Formation

A scientist from the Florida campus of The Scripps Research Institute (TSRI) has been awarded approximately $2.5 million from the National Institute of Neurological Disorders and Stroke to better define how the brain organizes different types of memories among its neurons.

Ronald Davis, a professor and chair of the Department of Neuroscience at TSRI, is the principal investigator for the new study.

The five-year continuation of an earlier grant takes as its research modelDrosophila melanogaster, the common fruit fly. The fruit fly is widely used in these studies because humans and flies share many of the same genes involved in learning and memory.

"Since nearly every neuropsychiatric disorder affects memory formation, these new studies will aid in understanding memory formation in humans—in the normal brain as well as in the diseased brain," Davis said.

The research focuses on the how the brain organizes olfactory or scent memories learned in association with reward conditioning compared to negative conditioning.

The new study has a number of objectives, Davis said, including defining the exact nature of cellular memory traces, the mechanisms for their formation, their duration, and the neurons in which they form.

Aiding current memory research are advances in functional imaging of neural activity in the fly brain, allowing scientists for the first time to see olfactory memory traces as they form—a literal and figurative window into the cellular and systems logic of memory formation.

"Combined with Drosophila's advanced molecular biology and genetics," Davis said, "this imaging technology provides an unprecedented opportunity to dissect the brain's algorithm that underlies Pavlovian conditioning."

The number of the grant is 2R01NS052351-06A1.

$2.1 Million Grant Funds Testing of Potential ALS Treatments

A team led by scientists at The Scripps Research Institute has been awarded $2.1 million by the Department of Defense Congressionally Directed Medical Research Programs to study several compounds with the potential to greatly improve the quality of life for those with amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease (named after the famed Yankee first baseman who died of the condition in 1941).

Philip LoGrasso, a professor on the Florida campus of Scripps Research, will be the principal investigator for the new two-year study, which also involves scientists from Columbia University.

"The potential impact a team effort like this could have on ALS patients may be tremendous, since there are currently no clinically beneficial, neuroprotective drugs for the disease," LoGrasso said. "We're hoping the compounds we're testing will lead to a drug to improve motor function and lengthen patients' lifespan through the prevention of motor neuron death."

LoGrasso and his Scripps Florida colleagues have already identified and validated a series of compounds that inhibit an enzyme called c-Jun N-terminal kinase (JNK, pronounced "junk") with proven neuroprotective effects in a variety of experimental models of human diseases, particularly Parkinson's disease.

JNK has been shown to play an important role in neuronal survival. As such, this kinase is a highly desirable target for drugs to treat neurodegenerative disorders.

Making the new study possible, LoGrasso said, are the cell and animal models of ALS produced by scientists at Columbia University. These models capture the hallmarks of this disease, including selective motor neuron degeneration, and many of the clinical features of the disease. "Given the success in neuroprotection that we've already shown with our proprietary JNK inhibitor in Parkinson's disease, we realized ALS was a perfect alternative candidate—primarily because Columbia had these models of the disease," LoGrasso said.

The team is also trying to develop new compounds that are highly selective for JNK3, a single isoform of JNK that is expressed only in the brain and the heart, thereby enabling tissue-specific inhibition and thus limiting many potential side effects.

The new funding is provided by Department of Defense grant number W81XWH-12-1-0431.

Scientists Awarded $2 Million to Study Tumor-Inhibiting Proteins

Scientists from the Florida campus of The Scripps Research Institute (TSRI) have been awarded just over $2 million from the National Institute of Neurological Disorders and Stroke of the National Institutes of Health to identify proteins that play key roles in tumor cell proliferation and to determine if targeting these proteins could result in the inhibition of tumor growth.

Joseph Kissil, a TSRI associate professor, is the principal investigator for the five-year study.

While normal cells possess mechanisms that inhibit rapid growth, tumor cells find ways to continue their expansion. Signals to grow or stop growing are triggered by a number of conditions, including what is known as "cell-cell contact" when cells reach critical density. The new study is focused on finding out exactly how this cell-cell contact controls growth.

"A lot of things go wrong in cancer, and one of them is known as 'loss of contact inhibition,'" Kissil said. "Normally, cells know to stop proliferating when they get signals from the environment. In cancer, these mechanisms become dysfunctional and that leads to accelerated tumor growth."

A central player in regulating these signals is a protein named merlin, a product of a tumor suppressor gene NF2 (neurofibromatosis type 2); neurofibromatosis is a disease caused by genetic mutations that result in tumors of the nervous system. The NF2 gene also stops functioning in a broad range of tumors, when merlin then becomes incapacitated.

Kissil and his colleagues recently identified proteins known as angiomotins, which are involved in cell movement and new blood-vessel growth, as holding sway over merlin's ability to inhibit tumor cells.

"Angiomotins give us a handle on understanding the process," Kissil said. "This project could be a first step in identifying potential therapeutics that can attack tumor cell growth at its source."

The number of the new National Institutes of Health grant is 1R01NS077952-01A1.

Scripps Florida Scientist Awarded $1.9 Million to Study Food Intake and Metabolism

A scientist from the Florida campus of The Scripps Research Institute has been awarded $1.9 million from the National Institutes of Health to study pathways that regulate how we coordinate the timing of our desire for food throughout the day. These pathways play a key role in maintaining the body's balance between how much we eat and our metabolism and energy expenditure.

Andrew Butler, an associate professor at Scripps Research, is the principal investigator for the new four-year study.

The research focuses on the melanocortin-3 receptor (MC3R, a g-protein coupled receptor) in the central nervous system. The MC3R is one component of the central nervous melanocortin system, which normally responds to signals of nutrient intake. The actions of the central nervous melanocortin system involving MC3Rs are central to the regulation of our metabolism. Attenuated activity of this system has been implicated in a range of metabolic diseases, including obesity and insulin resistance (a precursor to diabetes).

"One function of the melanocortin system is to prevent obesity in humans," he said, "and this system is therefore considered an attractive target for developing drugs against obesity and eating disorders. Unfortunately, very little is known about the functions of melanocortin-3 receptors."

Butler's ongoing research suggests that MC3Rs help synchronize our circadian rhythms (24-hour day-night cycles) with food intake. MC3Rs are also linked to the regulation of glucose production and insulin action during cycles of fasting and feeding.

"Our goal for this new study is two-fold," Butler said. "We want to identify the MC3R signaling pathways involved in regulating behaviors that anticipate feeding, and we want to look at pathways responsible for maintaining metabolic homeostasis."

Beyond forming a better understanding of the functions of MC3R in the central nervous system, Butler said, the ultimate point of the research is to develop new and innovative approaches to prevent and treat metabolic and circadian-rhythm disorders.

Scripps Florida Scientist Awarded $1.6 Million to Develop Innovative Chemical Reactions as Tools for Preparing Rare Natural Products

A scientist from the Florida campus of The Scripps Research Institute has been awarded more than $1.6 million from the National Institute of General Medical Sciences of the National Institutes of Health to develop innovative chemical reactions as tools for the laboratory preparation of rare and structurally diverse natural products with significant therapeutic potential.

"This grant is a continuation of the work we've been doing over the past several years," said Glenn Micalizio, an associate professor at Scripps Florida who is the project's principal investigator. "Our investigations will begin to solidify the significance of the more than 15 new chemical reactions that have been discovered in my laboratory. The central focus of this next phase of the program is on understanding and elucidating the unique power of the chemical tools that have emerged from our studies to provide laboratory access to rare and complex natural compounds."

Micalizio and his colleagues believe that the project has long-term implications for science and medicine. By addressing the limitations and inefficiencies associated with modern chemical science, they hope to establish a firm scientific foundation capable of driving medicinal pursuits for years to come. Compounds targeted in this phase of the project include anticancer, antifungal, analgesic and antibiotic agents whose evaluation as potentially valuable clinical agents is hampered by their low availability from natural sources and the lack of efficient means to accomplish their laboratory synthesis.

"This program, generously supported by the National Institutes of Health, has led to the discovery of a great variety of new chemical reactions (tools for the assembly of molecules) that will undoubtedly have a substantial impact on the manner in which complex molecules can be prepared in the laboratory," Micalizio said. "The extension of this grant provides needed financial support to continue to develop a chemical science that has had, and will continue to have, a profound impact on the process of drug discovery, broadly defined."

The National Institutes of Health grant number is 2R01GM080266-07A1.

Team Awarded Nearly $1.5 Million to Develop New Approaches to Treat Cancer

Scientists from the Florida campus of The Scripps Research Institute have been awarded approximately $1.5 million from the National Institutes of Health to identify and develop new therapeutic approaches against a broad spectrum of cancers.

John Cleveland, professor and chair of the Department of Cancer Biology, and Derek Duckett, associate scientific director of the Translational Research Institute at Scripps Florida, will act as co-principal investigators.

The new three-year grant will allow the Scripps Florida scientists to develop high-throughput screening tests to identify and optimize inhibitors of the "autophagy pathway," the principal recycling center of the cell, which is especially active during times of stress or nutrient loss. During autophagy, various cell components, including damaged proteins and mitochondria, are delivered to the lysosome, which is essentially a bag of enzymes that breaks down cellular waste.

Autophagy is critical to cell survival and defects in the pathway can lead to a number of disorders, including some neurodegenerative and muscular diseases.

"We have shown that impairing autophagy can improve the efficacy of anti-cancer drugs, helping to overcome drug resistance," Cleveland said. "Although there's a lot of interest in generating compounds to act on specific components of the pathway, none exist now. The new grant will, hopefully, help us begin to remedy that situation."

Duckett added, "Our studies have shown that impairing the autophagy pathway increases the sensitivity of cancer cells to conventional therapeutics, so this is a highly practical and productive approach to developing potential treatments."

With the new funding, the scientists will develop a novel biochemical test to identify inhibitors of the UNC-51-like kinase (Ulk1), a critical on-off switch that regulates the pathway. Once identified, these small molecules will also help scientists improve their basic understanding of autophagy, its relationship to cancer, and its use as a target that could enhance the action of conventional anti-cancer therapeutics.

The funding was granted by the National Cancer Institute of the National Institutes of Health under award number CA169142.

Scripps Florida Scientists Awarded $1.4 Million to Develop New Therapeutic Approaches to Chronic Leukemia

Scientists from the Florida campus of The Scripps Research Institute (TSRI) have been awarded more than $1.4 million from the National Cancer Institute of the National Institutes of Health to create a potential new drug to attack the malignant cells that cause chronic lymphocytic leukemia (CLL), which is the most common leukemia in the Western world.

Christoph Rader, a TSRI associate professor, will be principal investigator of the new three-year study. William Roush, a TSRI professor, associate dean of graduate studies and executive director of medicinal chemistry, will be co-principal investigator.

CLL affects approximately 150,000 patients and causes 4,500 deaths per year in the United States alone. While chemotherapy and radiation are used to treat this slow growing form of leukemia, currently there are no therapeutic options for the disease in which physicians can selectively target the malignant cells yet spare normal cells and tissues.

The scientists plan to use the recently discovered cell surface receptor TOSO, which is overexpressed in leukemia cells, to create a rapid and effective entry point for

delivering drugs to these malignant cells while bypassing normal cells as much as possible.

“We want to create carrier-payload combinations to deliver cytotoxic drugs with very specific targeting,” Roush said. “Once we have accomplished that, we expect to optimize potency.”

In addition, the team plans to use an antibody fragment to add a second target to the treatment—the receptor tyrosine kinase ROR1, which is expressed exclusively on leukemia cells.

“This dual-targeting strategy will lay the foundation for further preclinical and clinical investigations in the treatment of this form of leukemia,” said Rader. “We also think that the novel biological and chemical components that come from this study can be easily exploited to develop combinations for diseases beyond CLL.”

The number of the National Institutes of Health grant, which also involves the laboratories of Adrian Wiestner and Terrence Burke at the National Institutes of Health, is 1U01CA174844.

Scripps Florida Education Outreach Receives Boost with $1 Million Grant from Kenan Charitable Trust

Scripps Florida has been awarded a $1 million grant by the William R. Kenan, Jr. Charitable Trust, a North Carolina-based philanthropic foundation with an interest in education, in support of the institute's education outreach programs in Palm Beach County. The four-year grant builds upon several years of continuous Kenan Trust support, which has gradually increased over the past seven years.

The new grant will provide funding through May 2017 for several established programs that each year reach hundreds of students and teachers from middle and high schools throughout Palm Beach County, as well as college undergraduates from across the country. Programs also provide teaching and mentoring experience to the graduate students and postdoctoral fellows who support the initiatives.

Education outreach efforts at Scripps Florida have also been supported by generous gifts from the Mary and Robert Pew Public Education Fund, the Quantum Foundation, as well as the Admiral's Cove Cares Charitable Foundation, the BallenIsles Charities Foundation, and the Berlin Family Foundation.

Esther B. O'Keeffe Foundation Donates $250,000 to Fund Scripps Florida Neuroscience Training Program

The Esther B. O'Keeffe Charitable Foundation has made a $250,000 donation to The Scripps Research Institute (TSRI) to fund neuroscience training and public outreach on the Florida campus.

"We're deeply grateful for the support of the O'Keeffe Foundation," said TSRI President and CEO Michael A. Marletta. "This gift will help us train the next generation of neuroscientists, as well as support a series of presentations on brain function and dysfunction to raise broad community awareness of Scripps Florida's work to understand and combat brain diseases."

"Thanks to the O'Keeffe Foundation, we look forward to connecting with the public and with local policy makers to showcase both what we do and the people involved in our research," added Ronald L. Davis, chair of the Department of Neuroscience at Scripps Florida who will oversee the new fund. "Our scientists-in-training will also benefit from the foundation's support."

The Esther B. O'Keeffe Charitable Foundation was established in 1990 by the late philanthropist Esther B. O'Keeffe, wife of respected surgeon and philanthropist Dr. Arthur O'Keeffe. Their children now carry on the family tradition by serving as trustees of the foundation, which supports a variety of health and medical research causes, as well as a spectrum of arts and cultural programs.

"We are delighted to help contribute to the important scientific and educational work taking place at The Scripps Research Institute," said Clare O'Keeffe, executive trustee of the foundation. "The advances being forged by Scripps Florida scientists are tremendously exciting."

The latest gift from the Esther B. O'Keeffe Charitable Foundation follows gifts totaling more than $3 million to Scripps Florida to fund biomedical research and education. In recognition of the foundation's generosity, last May the Founders Room and the adjoining boardroom on the Florida campus were named the Esther B. O'Keeffe Founders Suite.

The O'Keeffe family's generosity is reflected in the names of many Palm Beach area facilities and programs, including the Esther B. O'Keeffe Art Gallery and Speakers Series at The Society of the Four Arts, pavilions at the Good Samaritan and St. Mary's medical centers, a wing at the Norton Museum of Art, and the American Heart Association's West Palm Beach headquarters. In addition, the Esther B. O'Keeffe Charitable Foundation has supported the Georgia O'Keeffe Museum, Massachusetts General Hospital, Cape Cod Hospital, and many other charities.

BallenIsles Event Raises More than $100,000 for Scripps Florida Prostate Cancer Research

Cancer research on The Scripps Research Institute (TSRI) Florida campus recently received a boost from the BallenIsles Men's Golf Association's annual prostate

cancer awareness and fundraising campaign. The event, which included a silent auction and golf tournament held on the championship-level courses at the BallenIsles Country Club in Palm Beach Gardens, raised a record $104,830.

“This was a significant increase over the fundraising milestone we reached last year and we’re pleased that one hundred percent of the money raised by this tournament and silent auction goes directly to a postdoctoral training fellowship at Scripps Florida, aimed at developing better treatments and, ultimately, a cure for this disease that strikes one out of every six American men,” said BallenIsles MGA/Prostate Cancer Committee Chair Burt Rein.

The prostate cancer research project will be led by Associate Professor Kendall Nettles of TSRI’s Department of Cancer Biology. His team will study novel compounds, identified in collaboration with John Katzenellenbogen of the University of Illinois, that effectively inhibit steroid receptors. “Studies indicate that these agents are effective against many human malignancies, including prostate cancer," said Nettles.

TSRI and Takeda Pharmaceuticals Expand Collaboration

The Scripps Research Institute (TSRI) and the Takeda Pharmaceutical Company have announced plans to expand their recent research collaboration to search for new drug targets for a variety of diseases.

The new agreement extends an initial collaboration launched in 2010 between scientists on the Florida campus of TSRI and Envoy Therapeutics that led to several breakthroughs in identifying potential new compounds for neurological and psychiatric diseases. Envoy was acquired by Takeda Pharmaceuticals last November.

“We’re pleased to expand our partnership with Takeda-Envoy and to push promising drug discovery efforts forward,” said Scott Forrest, TSRI’s vice president for business development. “The high-throughput screening capability at Scripps Florida campus is in increasing demand—both from other research institutes and from industry.”

Scripps Florida’s state-of-the art high-throughput screening facility is part of its larger translational research infrastructure. The facility has expertise in transforming slow, labor-intensive biological and biochemical bench-top experiments into high-throughput screening experiments (“screens”). Fully automated robotic screening platforms then rapidly test more than 650,000 drug-like compounds for pharmacologic activity. After completion of the screens, the facility uses other cutting-edge technologies to support the development of clinically relevant compounds.

Stephen Hitchcock, senior vice president of drug discovery at Envoy said, "We originally came to Jupiter because of Scripps Florida and are thrilled that the potential of our original collaboration has been realized. Now we're moving into new therapeutic areas with different biological targets. The first step is to find small molecules that can validate those targets—and Scripps Florida is amongst the very best places to do that."

Hitchcock said that one intangible factor in the expanded research collaboration was the quality of the people at Scripps Florida. "They have been great collaborators and great friends," he said. "The interaction between our scientists and theirs was a huge factor in expanding our research."

Peter Hodder, who directs the high-throughput screening facility at Scripps Florida, has been collaborating with Hitchcock and Envoy scientists since the company's founding in 2010. "This new effort deepens our commitment to validating novel drug discovery targets via screening-based approaches and also underlines Scripps' intrinsic worth to our partners in early-stage drug discovery research."

Scripps Florida Scientists Awarded Special Collaborative Grant to Develop Anti-Addiction Therapies

As part of an unprecedented national effort to develop new drugs to treat neurological disorders, scientists from the Florida campus of The Scripps Research Institute (TSRI) have been awarded an innovative grant from the National Institute of Neurological Disorders and Stroke to help people break their addiction to nicotine.

Paul Kenny, a TSRI associate professor, is the principal investigator for the new study, which aims to develop anti-smoking drug candidates to the point of Phase I clinical trials, which focus on human safety testing. Also helping to guide the work are TSRI scientists Ted Kamenecka, Patricia McDonald and Michael Cameron.

The new study is part of the National Institutes of Health (NIH) Blueprint for Neuroscience Research Grand Challenge, a collaborative effort that includes the NIH Office of the Director and the 14 NIH institutes and centers that support research on the nervous system. As part of the project, The TSRI scientists will have access to industry-style drug development services and expertise—what the NIH is calling a "virtual pharma" to help develop these new compounds.

"An innovative feature of this grant is the fact that we will have access to a panel of experts to help us advance these compounds into human testing," Kenny said. "The people on the panel are senior industry experts with considerable experience in drug development programs, who are eager for us to succeed. What's more, if the drug is successful in Phase I trials, we will receive help from the NIH in establishing appropriate relationships with industry to advance the drug into the later stages of clinical testing, and eventually to marketing a novel smoking cessation medication."

Kenny and his colleagues will be expanding their already successful investigation of a pair of neuropeptides known as hypocretin-1 and hypocretin-2 (also known as orexin-A and orexin-B), which stimulate hypocretin-1 and hypocretin-2 receptors.

Hypocretin-1 receptor activity is considered critical in maintaining tobacco addiction in human smokers. In a landmark 2008 study in the *Proceedings of the National Academy of Sciences*, Jonathan Hollander and colleagues in Kenny's laboratory showed that blocking hypocretin-1 receptors not only decreased nicotine use in animal models, but also blocked nicotine's stimulatory effects on brain reward circuitries considered critical in motivating tobacco use.

"We have been able to identify novel hypocretin-1 receptor antagonists that demonstrate drug-like properties, meaning that they may eventually be suitable for use in humans. This grand challenge award will allow us to further optimize these compounds and then to test whether they are safe in humans. If this proves to be the case, we believe that they will be highly effective therapeutic agents for tobacco dependence," Kenny said.

Tobacco smoking is a global scourge, killing more than 5 million people each year worldwide, according to the World Health Organization. It is estimated that if current trends continue, by 2020 smoking will become the largest single health problem worldwide. The World Bank estimates that in high-income countries, smoking-related healthcare accounts for between 6 and 15 percent of all healthcare costs, some $160 billion annually.

Nicotine addiction is notoriously hard to break. Even with the most effective smoking-cessation agents available, more than 80 percent of smokers who quit or attempt to quit will relapse.

Part 3: Scientific Accomplishments

Scripps Florida Scientists Identify Critical 'Quality Control' for Cell Growth

Scientists from the Florida campus of The Scripps Research Institute have identified a series of intricate biochemical steps that lead to the successful production of proteins, the basic working units of any cell.

The study, which appears in the July 6, 2012 edition of the journal *Cell*, sheds light on the assembly of a structure called the ribosome, a large and complex protein-producing machine inside all living cells. Ribosomes are the targets of many commercially used antibiotics and represent a promising area of research because of the importance of ribosome assembly and function for cell growth. There are well-established links between defects in ribosome assembly and cancer, making this pathway a potential new target for anti-cancer drugs.

"With important cellular machines like ribosomes, it makes sense that some process exists to make sure things work correctly," said Katrin Karbstein, a Scripps Research associate professor who led the study. "We've shown that such a quality control function exists for ribosomal subunits that use the system to do a test run but don't produce a protein. If the subunits don't pass, there are mechanisms to discard them."

Protein Production Line

As part of the protein-production process called "translation," the ribosome decodes information carried in messenger RNA (mRNA) to produce a protein—a chain of amino acids.

To produce mature, functioning ribosomal RNAs (rRNAs), the body first makes precursor rRNAs that can be processed into mature ones. In human cells, this is done in two stages—the first occurs in the nucleolus, a protein-nucleic acid structure inside the nucleus, and finally in the cytoplasm, the basic cellular stew where protein translation occurs.

In the cytoplasm, these pre-mature ribosomal subunits encounter large pools of mature subunits, messenger RNA, and numerous assembly factors and translation factors that help complete the process.

During the final maturation process, various assembly factors prevent the translation process from acting on the subunits prematurely, which would result in their rapid degradation or in the production of incorrectly assembled proteins, both processes with potentially lethal outcomes for the cell.

Trial Run

While the work of these assembly factors explains how premature translation is blocked, their presence raises another important question, Karbstein said—Does the conversion of inactive assembly intermediates into mature ribosomes require checkpoints to assure that subunits are functional?

In the study, Karbstein and her colleagues were able to show that during this translation-like cycle the newly made ribosome subunit initially joins with its complementary preexisting subunit to form a much larger complex through the influence of a single translation factor.

This large ribosome complex contains no messenger RNA, which is blocked by assembly factors, and thus produces no protein. Once the major functions of the smaller ribosome subunit have been inspected and approved, another translation factor breaks up the complex and actual protein production occurs.