Agenda Item #: 9:30 AM

PALM BEACH COUNTY
BOARD OF COUNTY COMMISSIONERS

WORKSHOP SUMMARY

Meeting Date: **August 27, 2013**

Department: **Administration**

I. EXECUTIVE BRIEF

Motion and Title: **Staff recommends a motion to receive and file:** the Scripps Florida Annual Report for Year Ending June 30, 2012.

Summary: The Board of County Commissioners (BCC) directed Staff to provide a comprehensive update on the status of the County's Grant Agreement with The Scripps Research Institute. This Workshop presentation will focus on the County and Scripps' obligations under the Grant Agreement, Scripps Phase II – Briger, and the Scripps 2012 Annual Report. Countywide (HF)

Background and Policy Issues: On January 24, 2012, the BCC received and filed a Ground Lease Agreement between Palm Beach County and the Scripps Research Institute for 70 acres. On May 2, 2006, the BCC approved the Grant Agreement with The Scripps Research Institute which included the Ground Lease Agreement as an Exhibit. On February 28, 2006, the BCC approved an Agreement (R2006-0423) for the Donation and Purchase and Sale with The Lester Family Investments, L.P., Richard Thall, Robert Thall, Peter L. Briger, Paul H. Briger, and the David Minkin Florida Realty Trust for 70 acres of property on the Briger site in Palm Beach Gardens.

Attachments:
1. Staff Presentation
2. Scripps Florida Annual Report for Year Ending June 30, 2012

Approved By: Shannon R Berg 8-6-13
Assistant County Administrator **Date**

II. FISCAL IMPACT ANALYSIS

A. Five Year Summary of Fiscal Impact:

Fiscal Years	2013	2014	2015	2016	2017
Capital Expenditures					
Operating Costs					
External Revenues					
Program Income					
In-Kind Match (County)					
NET FISCAL IMPACT	0	0	0	0	0

# ADDITIONAL FTE POSITIONS (Cumulative)					

Is Item Included In Current Budget? Yes _____ No _____
Budget Account No.:

Fund _____ Dept _____ Unit _____ Object _____ Program Code/Period _____

B. Recommended Sources of Funds/Summary of Fiscal Impact:

C. Departmental Fiscal Review: _____

III. REVIEW COMMENTS

A. OFMB Fiscal and/or Contract Development and Control Comments:

8/9/2013
OFMB

8/9/13
Contract Development and Control
8-9-13

B. Legal Sufficiency:

8/12/13
Chief Assistant County Attorney

C. Other Department Review:

_____
Department Director

(THIS SUMMARY IS NOT TO BE USED AS A BASIS FOR PAYMENT)

Scripps Program Update

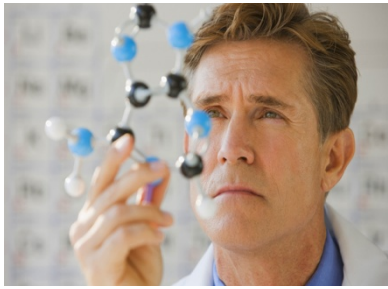
Board of County Commissioners
August 27, 2013

Shannon R. LaRocque, P.E.
Assistant County Administrator

Overview

- **Grant Agreement**
  - County Obligations
  - Scripps Obligations
- **Scripps Phase II/Briger**
  - County Requirements
  - Ground Lease
- **Scripps 2012 Annual Report**
- **Florida Regional Medical Center**



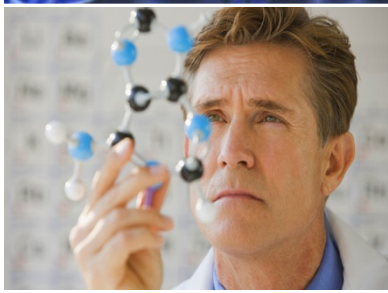


Grant Agreement

Executed May 2006

- **County Obligations**
  - $189 Million for Construction
  - Purchase 70 acres on Briger
    - 30 acres – Donated by Lester Family
    - 40 acres- Purchased for $16 M
    - Deed Restricted
  - Obtain Approvals for 70 acres
    - Development Approvals
    - Environmental Permits



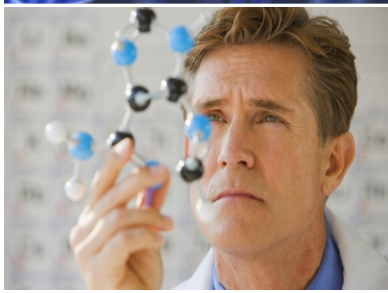


Grant Agreement

Executed May 2006

- **Scripps Obligations**
  - Construct 364,000 SF permanent facilities
  - Deposit $5 Million in Escrow Account
  - Execute Ground Lease on Briger
  - Shall create/relocate
    - 545 jobs
    - December 2013
  - Shall strive to create/relocate
    - 2,777 jobs
    - February 6, 2021
  - Work cooperatively to create/relocate
    - 6,500 jobs



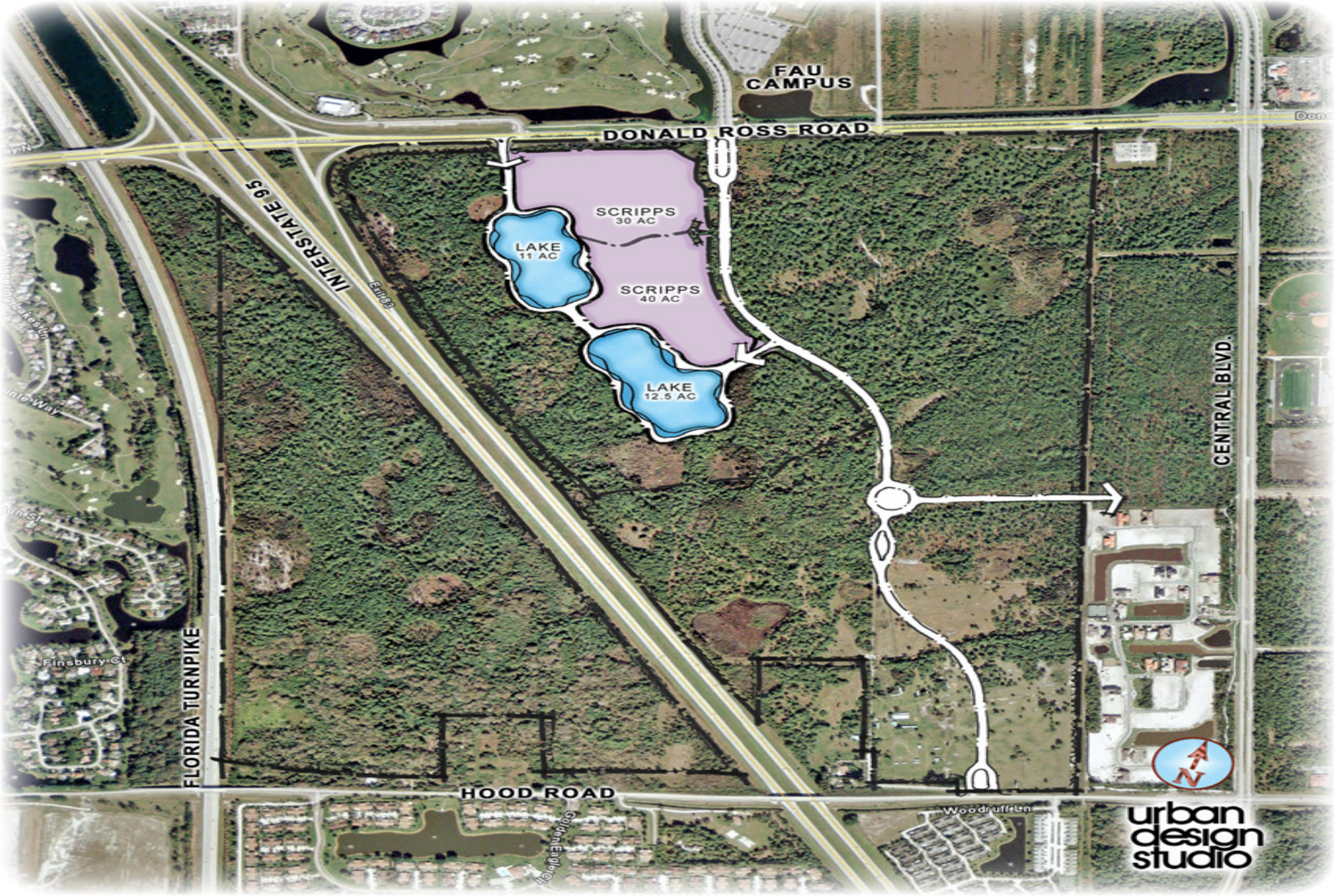


Scripps Phase II – Briger Site

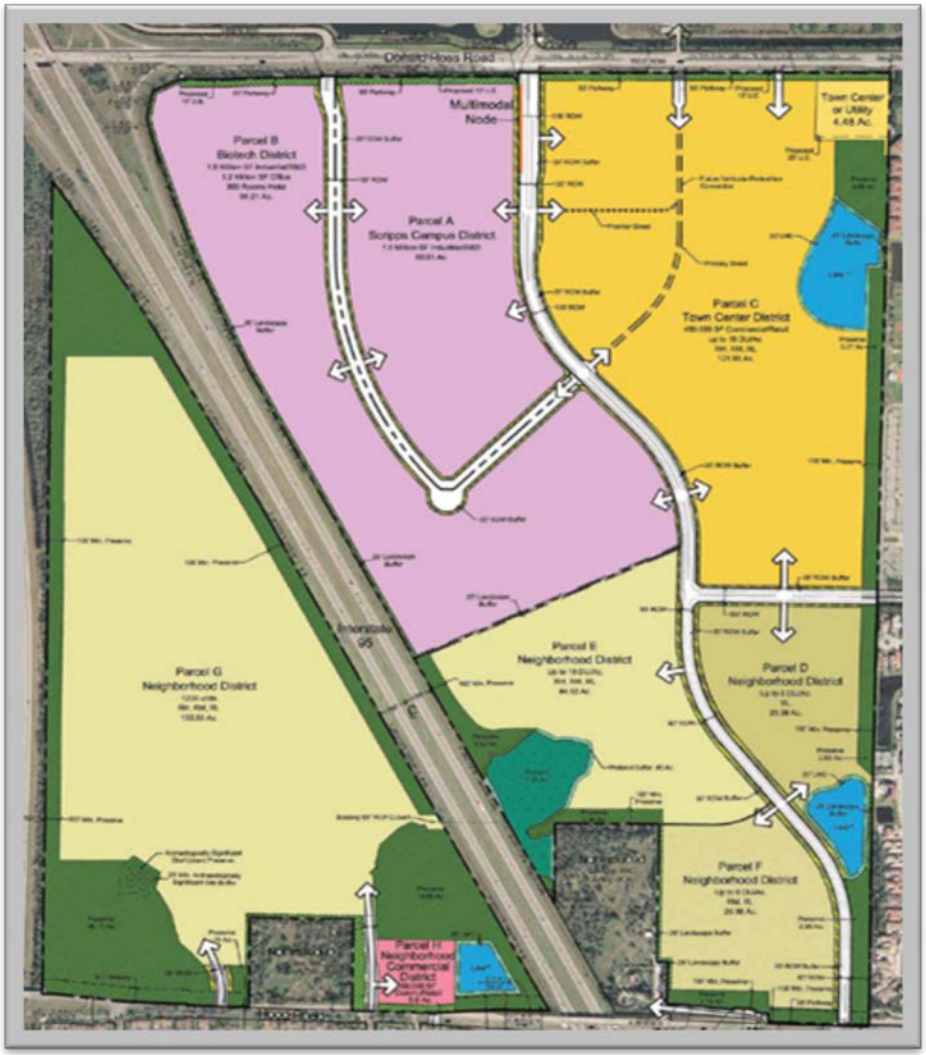
- 681 Acres
- City of Palm Beach Gardens
- Last large infill parcel
- 70 Acres – County
- 1.6 M sf - Scripps

The Scripps Research Institute

BRIGER TRACT



Scripps/Briger Master Plan



- 681 acres
- Biotech & Ancillary Uses
  - 4 M SF
  - 1.6 M SF (County Land)
  - 2.4 M SF (100 acres)
- Residential Use
  - 2,700 units
  - Mix of SF & MF
- Town Center
  - 450,000 SF commercial/residential
  - Pedestrian oriented

Scripps Phase II/Briger

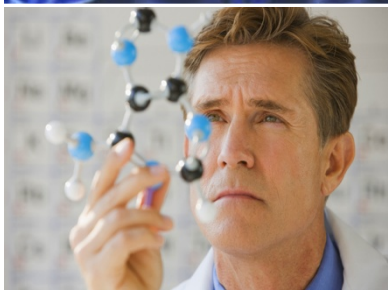
County Progress

- ✓ Development of Regional Impact
- ✓ Comprehensive Plan Amendment
- ✓ Planned Community Development District
- ✓ Zoning
- ✓ Department of the Army Permit
- ✓ South Florida Water Management District Environmental Resource Permit
- ✓ Northern Unit of Development formed
- ✓ Water/Sewer Capacity Reservations

Briger Ground Lease

- Approved in May 23, 2006
  - Exhibit to the Grant Agreement
- Executed January 9, 2012
  - BCC Receive and File January 24, 2012
- Expires February 6, 2021
  - Convey property to Scripps for $1.00

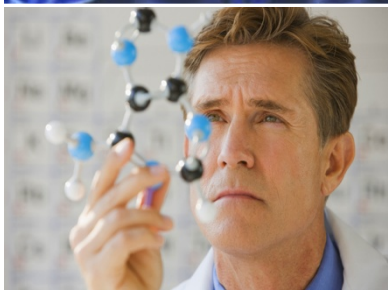




Briger Ground Lease

- Annual Rent
  - $1.00/Year
- “Triple Net”
  - No expense to the County
- Allowable Use
  - Biomedical Research Facility
  - Biomedical and other scientific research, training and education

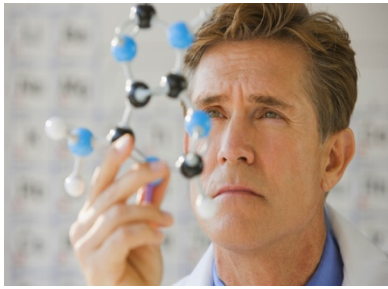




Briger Ground Lease

- Improvements
  - Scripps Responsibility
- Lease Assignment
  - Not Assignable
  - Subleasing permitted, consistent with permitted use
- Early Option to Purchase
  - $1.00
  - Reached Job Creation goal and maintained for two years





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THE SCRIPPS RESEARCH INSTITUTE

2012 Highlights

Research Grants

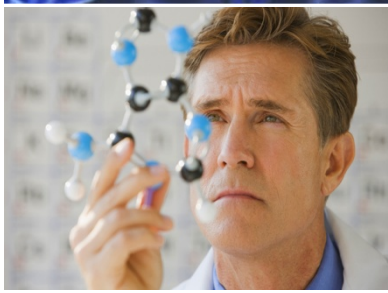
June 2011 – June 2012

- Scientists awarded 54 research grants
- $55 Million awarded

To date:

- Scientists awarded 240 research grants
- $275 Million awarded



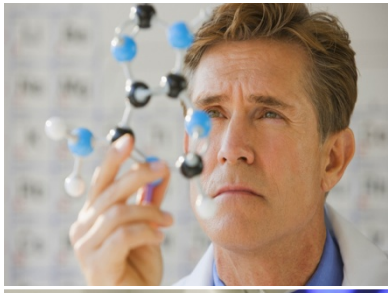


2012 Highlights

Research Grants

Diverse Research Ongoing	
$8.4 Million	New Anti-Smoking Treatments
$4.2 Million	Type 1 Diabetes Research
$3.85 Million	Cancer Therapies
$3.4 Million	HIV/AIDS Research
$3.0 Million	Effective Pain Treatment
$2.2 Million	Study Hepatitis C
$2.0 Million	Study Lymphoma
$1.5 Million	HIV Inhibitors
$1.0 Million	Disease & Aging Research
$700,000	Cocaine Addiction
$500,000	Parkinson’s Disease



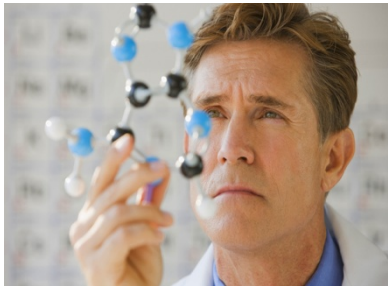


2012 Highlights

Scientific Accomplishments

- Define cellular pathways essential to removing damaged mitochondria (energy producing machines of the cell)
  - ***Potential cancer therapies***
- Establish new class of anti-diabetic compound
  - ***Better treatments for diabetes patients***
- New role for gene in maintaining steady weight
  - ***Combat obesity and diabetes***





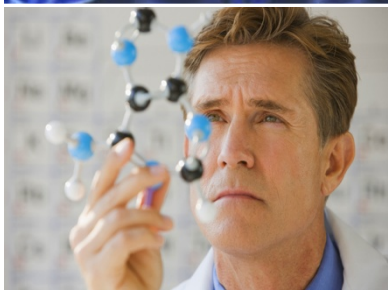
2012 Highlights

University Collaboration

Educational Collaboration

- Florida International University
- University of Florida
- University of Central Florida
- University of Miami
- Florida State University
- Nova Southeastern University
- University of South Florida
- Max Planck Florida Institute



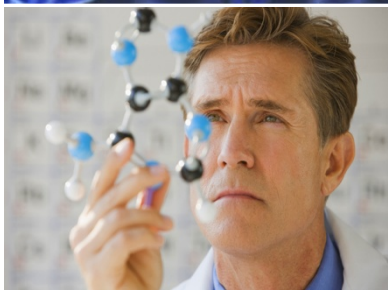


2012 Highlights

Scripps Kellogg School

- Bi-coastal Ph.D. Program
- Reaccreditation in 2011
- 30 Graduate students enrolled
- 5 completed Ph.D. Program
- 8 Undergraduates from Florida colleges/universities





2012 Highlights

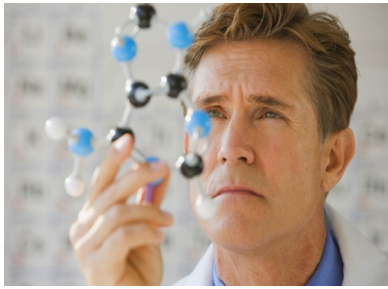
Employment

As of June 2012

440 people employed

- Faculty – 41
- Research faculty – 9
- Staff scientists – 28
- Research associates – 160
- Scientific support – 96
- Administrative support - 106





Florida Regional Medical Center

Florida Regional Medical Center

Collaborative Partnership

- Scripps Florida
- Tenet Healthcare

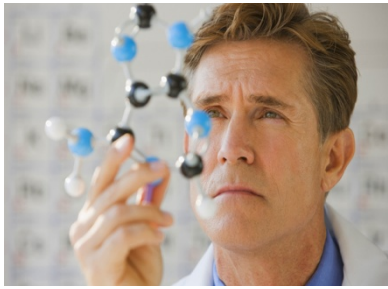
Goal

To enhance the progression of medical research and education and training of physicians and surgeons into point-of-care patient applications in the hospital setting

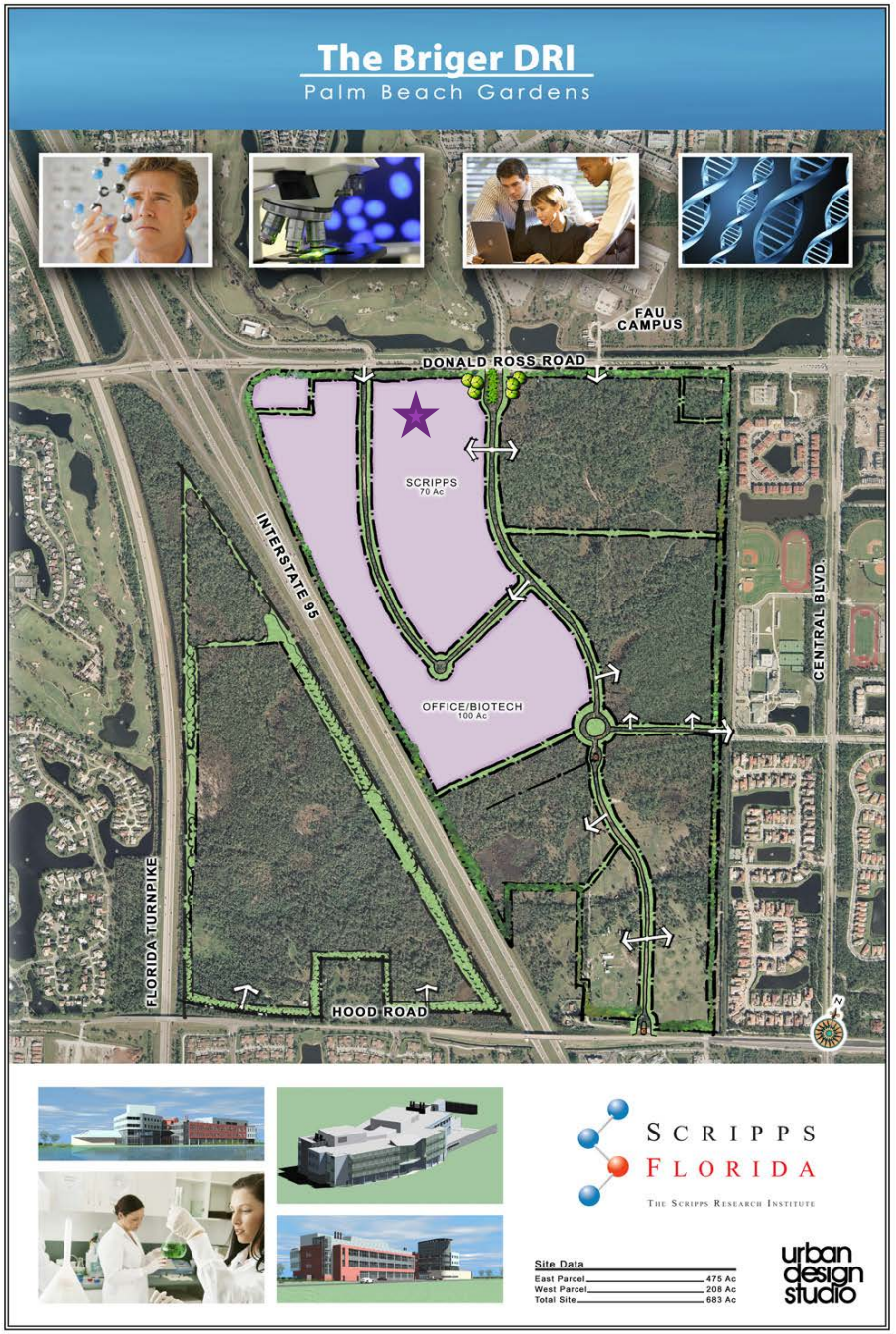
Florida Regional Medical Center

- Academic Medical Center
  - Phase 1 – 80 beds
  - Phase 2 – 80 beds
- Governance
  - Governing Board
    - Scripps
    - Palm Beach County Official
    - Tenet Healthcare
  - Academic Advisory Committee
    - Oversee all academic and medical education programs relating to clinical and translational research, residences, and internships





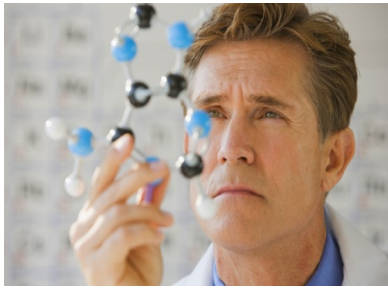
Florida Regional Medical Center



Thank You

Questions?





SCRIPPS FLORIDA™

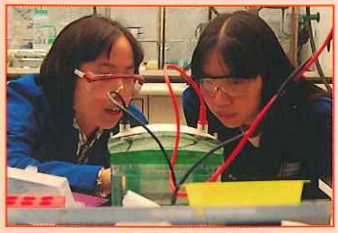
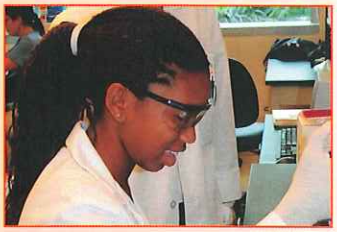
THE SCRIPPS RESEARCH INSTITUTE

ANNUAL REPORT

FOR YEAR ENDING: JUNE 30, 2012









SCRIPPS FLORIDA ANNUAL REPORT
FOR THE YEAR ENDING JUNE 30, 2012

PART I – SUMMARY OF ACCOMPLISHMENTS FOR YEAR ENDING JUNE 30, 2012

Part 1: New Faculty and Scientific Administration

Scripps Research Appoints Noted Autism Researcher to Neuroscience Faculty

The Scripps Research Institute has appointed Damon Page, PhD, as assistant professor in the Department of Neuroscience.

Page, 36, will work on the Scripps Florida campus in Jupiter. Prior to his appointment, he was a senior analyst at the Allen Institute for Brain Science in Seattle, Washington.

"Damon's research on autism makes a valuable addition to our department," said Ron L. Davis, chair of the Department of Neuroscience. "His discovery of genes that can cause autism-like symptoms is a breakthrough in the complex origins of the disease and offers new potential therapeutic targets to investigate. We're delighted he is joining us."

"This is a wonderful opportunity to be part of a dynamic, highly collaborative organization, with a breadth of basic and translational research that meshes perfectly with my research," Page said. "Scripps Florida is a unique place to explore the basic science of how the brain develops and then to use that knowledge to develop potential new treatments for autism."

Page, who lives in Jupiter, received his bachelor's degree in biology from Eastern Oregon University in 1999 and his PhD from the University of Cambridge in 2002. He was a postdoctoral fellow at the MRC Laboratory of Molecular Biology from 2002 to 2004 and the Massachusetts Institute of Technology (MIT) from 2004 to 2009; he worked as a research scientist at MIT from 2009 to 2010.

It was during his stint at MIT that Page led a groundbreaking study that resulted in the discovery of a novel mechanism whereby two autism risk factors interact to shape autism-like symptoms in an animal model. That discovery showed for the first time that genes acting in two distinct molecular pathways implicated in autism can interact to significantly influence the severity of symptoms. The study pointed to the intersection of these pathways as a potential new target for therapeutic development.

Autism is a complex neurodevelopmental disorder that impairs the normal development of social and communication skills, among other facilities. Autism is the most severe form of autism spectrum disorders; milder forms include Asperger syndrome. According to the National Institutes of Health, six children out of every 1,000 have autism spectrum disorder, with males four times more likely to be afflicted than females.

"There are a number of risk factors for autism," Page said, "but at present we don't understand how these interact in the developing brain to cause the disorder. My aim is to shed light on this problem, but, more importantly, to apply what we learn in the laboratory to help individuals and families affected by the disorder."

For more information, see Page's faculty web page at http://www.scripps.edu/research/faculty/page

Noted Scientist Joins Scripps Research Neuroscience Faculty

The Scripps Research Institute has appointed Srini Subramaniam, PhD, as an assistant professor in the Department of Neuroscience. Subramaniam, who investigates the signaling networks involved in neurodegenerative diseases, was a research associate in neuroscience at Johns Hopkins University prior to joining Scripps Research.

"It's a great honor to join the Scripps Florida faculty," he said. "When I first visited, I was impressed with the science and the people—they were all highly focused, highly energized. Many are working on the same types of problems I am but taking different paths, so the possibility of collaboration is exceptional."

"Srini is a dynamic researcher who will continue to make remarkable inroads in the science of neurodegenerative diseases," said Ron Davis, chair of the Department of Neuroscience. "We want to extend a warm welcome to him and his family."

Subramaniam received a bachelor's degree in chemistry, botany, and zoology in 1992 from the University of Bangalore, India, and a PhD in neuroscience in 2004 from the University of Heidelberg, Germany, graduating summa cum laude. He also received the German Anatomical Society's Wolfgang-Bargmann Prize, and the Young Investigator Award from the University of Heidelberg.

During his graduate studies, Subramaniam founded the Samatva Trust for Rural Education in Bangalore. The trust's goal is to support children who excel in school but cannot pursue further education due to lack of financial support. More than a thousand students have benefited from the scholarship program. For more information, please visit www.samatvatrust.org

Subramaniam completed his postdoctoral work at Johns Hopkins University. In 2010, the Johns Hopkins School of Medicine honored him with the Daniel Nathan Research Award.

At Scripps Florida, Subramaniam's laboratory will focus on finding target genes involved in neurodegenerative diseases such as Huntington's, Parkinson's, and Alzheimer's and developing novel therapeutics to treat them.

Subramaniam, who led the Johns Hopkins research team, uncovered the cause of brain specific damage that occurs in Huntington's disease, a hereditary neurodegenerative disorder that affects some 30,000 Americans. In Huntington's disease the selective brain region called striatum is damaged and the cause for this selectivity was unknown. In 2009 article in the journal Science,

Subramaniam and his colleagues pinpointed a protein known as Rhes that is prevalent in the striatum as responsible for striatal damage in Huntington's disease; Huntington's patients often suffer from uncontrollable movement and cognitive deficits due to degeneration of striatum. Subramaniam's findings not only explained the cause for striatal damage in Huntington's disease, but also its unique mechanism of action, and suggested a potential new therapeutic target.

In a 2011 Nature Neuroscience study, Subramaniam found that Rhes is also involved in the uncontrollable movement, a side effect that occurs during the treatment for Parkinson's disease. Subramaniam's studies suggest that drugs targeted at Rhes could mitigate multiple symptoms and may have therapeutic value in more than one brain disease.

Ultimately, Subramaniam is working towards a better understanding of how various neurogenerative diseases, including Alzheimer's disease and spinal muscular atrophy, as well as Huntington's and Parkinson's, develop different pathologies as they progress. "We want to understand the signaling networks that mediate the selective vulnerability of brain cells to design better therapeutic strategies to prevent or slowdown these debilitating neurodegenerative disorders," he said.

Subramaniam lives with his wife, Neelam Shahani, PhD, who is also a neuroscientist, and two daughters, six-year-old Vyapti and 14-month-old Anvika, in Jupiter, Florida.

NIH Executive Selected to Head Scientific Operations for Scripps Florida

The Scripps Research Institute has named Dawn Johnson, PhD, currently with the National Institutes of Health (NIH), as senior director of scientific operations for the Scripps Florida campus.

"As the campus continues to expand as a center of scientific excellence, Dawn brings her experience as a scientist, knowledge of the federal funding process for research, and talents as a manager to Scripps Florida," said Scripps Research President Michael A. Marletta. "We want to offer her our warmest welcome."

"I'm delighted to be joining Scripps Florida," said Johnson, "and look forward to working at such a dynamic scientific institution."

Johnson, age 40, is currently the associate director for science management in the Office of the Scientific Director at the National Institutes of Mental Health (NIMH) Intramural Research Program. The program, with an annual budget of $168 million, includes 47 active clinical and basic labs and eight core facilities. Since joining the NIH in 2002, Johnson has won several NIMH and NIH Director awards for her work on planning and communications projects.

A native of Atlanta, Johnson earned an associate's degree in liberal arts from the Oxford College of Emory University in 1991, a BS from Georgia State University in biology in 1993, and a PhD in neuroscience from the University of Wisconsin, Madison, in 1999. She also received a certificate in public health policy from George Washington University in 2005. Johnson is

excited to return to Florida, having participated in postdoctoral training in two labs at the University of Miami from 1999 to 2002. She also has family in Palm Beach County.

Johnson will start her new position at Scripps Florida on May 7, 2012.

Johnson replaces Harry Orf, who headed the Jupiter campus from its inception until last month when he returned to Massachusetts General Hospital in Boston to manage scientific research operations there.

Part 2: Grant Awards and Licensing Agreements

Scripps Florida Scientists Awarded $8.4 Million Grant to Develop New Anti-Smoking Treatments

Scientists from the Florida campus of The Scripps Research Institute has been awarded an $8.4 million grant from the National Institute on Drug Abuse of the National Institutes of Health (NIH) to develop new compounds to help prevent relapse in smokers who are kicking the habit.

The new five-year NIH award is a program project grant, which is designed to support an institutionally based research program with a well-defined research focus that requires several interrelated subprojects as part of the overall study.

Paul Kenny, a Scripps Research associate professor, is the program director and principal investigator for the study.

"This really is a broad-based, multi-disciplinary team effort," Kenny said. "We've assembled a team of first-class scientists at Scripps Florida with all the experience necessary to develop novel therapeutics for the treatment of tobacco abuse."

Others involved in the study are Michael Cameron, Theodore Kamenecka, and Patricia McDonald of The Translational Research Institute on the Scripps Florida campus.

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.

To combat these dismal statistics, the study is focused on an entirely new mechanism to help smokers break the habit.

That mechanism is a receptor for a specific neuropeptide (short chain of amino acids found in nerve tissue) that, when blocked, significantly decreases the desire for nicotine in animal models.

The neuropeptide, known as hypocretin-1 or orexin A, initiates a key signaling cascade that maintains tobacco addiction in human smokers. In a 2008 study in the *Proceedings of the National Academy of Sciences*, Kenny and colleagues showed that blocking hypocretin-1 receptors not only decreased nicotine use in animal models, but also abolished the stimulatory effects of nicotine on brain reward circuitries. These results demonstrated that hypocretin-1 plays a major role in driving the desire for more nicotine.

These findings also highlighted the importance of hypocretin-1 receptors in a region of the brain called the insula, a walnut size part of the frontal lobe. While all mammals have insula regions that sense the body's internal physiological state and direct responses to maintain homeostasis, this region has also been implicated in cravings. In one study, it was reported that smokers who sustained damage to the insula lost the desire to smoke, an insight that revealed the insula as key for sustaining the tobacco habit in smokers.

Scripps Florida Scientist Awarded $4.2 Million for Type 1 Diabetes Research

Grant Will Fund Research into Early Diagnoses and New Treatment Options

A scientist at The Scripps Research Institute has been awarded $4.2 million from the National Institutes of Health in a program to advance what the agency calls "bold and creative research" into Type I diabetes.

Thomas Kodadek, a professor in the Department of Chemistry on the Scripps Florida campus, is the principal investigator on the study. The award will be shared with researchers at the University of Miami and Opko, a Florida-based biotechnology company.

The new four-year grant from the NIH National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is a special Type I Diabetes Impact Award (DP3). Type I diabetes is an autoimmune disease, in which the immune system attacks the body's own tissues. In Type 1 diabetes, the immune system attacks cells in the pancreas that produce insulin, which leads to insulin deficiency; the condition is treated with regular insulin injections.

The new grant to Kodadek and his colleagues will fund research to determine early autoimmune reactions that drive the development of Type I diabetes, as well as to look for ways to selectively block such autoimmune diseases without shutting down or damaging the entire immune response.

"Once the earliest autoimmune reactions have been identified," Kodadek said, "we can develop compounds that specifically target the autoimmune cells to see if we can block the disease in mice without affecting the normal function of the 'good' parts of the immune system. This would set the stage for similar studies in human diabetic patients. Obviously, if we succeed in

developing a therapy for humans, it would have a radical impact on the detection and treatment of diabetes—and other autoimmune conditions as well."

The research funded by the new grant may also lead to new ways to detect Type 1 diabetes. Currently, immunoassays, a technique that detects auto-antibodies for human insulin, are used as early diagnostic markers for Type I diabetes, and for screening and risk assessment in clinical trials. Because progression of diabetes is often haphazard, additional markers are needed to improve overall risk assessment.

The novel approach Kodadek uses in his research involves peptoids, synthetic molecules similar to peptides that make up proteins when joined together. His lab uses these peptoids to screen or search for molecules that bind to and affect the action of a type of immune system molecule called an antibody.

Like the handmade flies used by fishermen, the synthetic peptoids are a lure to capture disease-specific antibodies—in this case, for diabetes—well enough to pull them from blood samples. It's a novel way to short-circuit the discovery process that has been used successfully in the lab for Alzheimer's disease. In the new project, once novel autoimmune cells for diabetes have been identified, Kodadek said, the scientists will begin to determine whether they can be turned off selectively, proof-of-principle for what could be a powerful therapeutic strategy.

Scientists Share $3.85 Million NIH Grant to Develop New Class of Cancer Therapies

Study Will Focus on Inhibiting a Hallmark of Cancer Cell Metabolism

A pair of Scripps Research Institute scientists, one a cancer biologist and the other a chemist, has been awarded $3.85 million from the National Institutes of Health (NIH) to develop a new generation of broad spectrum anti-cancer therapeutics, including breast cancer and lymphoma.

John Cleveland, chair of Scripps Florida's Department of Cancer Biology, and William Roush, chemistry professor, executive director of Medicinal Chemistry, and associate dean of graduate studies at Scripps Florida, are co-principal investigators for the new five-year project.

The focus of the research is on two proteins considered high priority targets for cancer therapeutics, Mct1 and Mct4. These "transmembrane transporters," which specifically transport lactic acid, a byproduct of cancer cell metabolism, out of cancer cells, are expressed at low levels in normal tissues but at high levels in most malignancies.

"This project represents the culmination of three years of collaboration between our two laboratories to design, develop, and validate novel anti-cancer therapeutics targeting these transporters," Cleveland said. "They are a new and unexploited avenue for cancer therapy, a potential Achilles' heel to attack a broad spectrum of tumor types. A lot of malignancies express Mct1 and we think we can tailor these inhibitors to treat afflicted patients."

Mct1 and Mct4 come into play during a process called "aerobic glycolysis," a pathway used by cancer cells to generate energy from glucose and to produce essential building blocks. In cancer

cells, this process produces an excess of lactate or lactic acid, which is a predictor of malignancy and even metastasis—the spread of cancer. Cleveland and Roush have shown that targeting Mct1 and Mct4 not only disrupts lactate homeostasis in certain types of lymphoma, but also disables tumor cell metabolism and proliferation.

So far, Cleveland and Roush have developed more than 190 small molecules to inhibit Mct1. With the new grant, the scientists plan to optimize these Mct1 inhibitors, synthesize new small molecule inhibitors of Mct4, and to devise new approaches to selectively deliver these agents to cancer cells.

"This is an example of the very best kind of collaboration at Scripps Research," Roush said, "leading from discoveries in cancer biology to the development of novel compounds through the work of the Medicinal Chemistry and the Pharmacokinetics groups to produce an entirely new generation of cancer therapeutics."

In the new project, the scientists will also explore the roles played by Mct1 and Mct4 in lymphomas and breast cancer driven by the Myc oncoprotein, which is activated in approximately 70 percent of all human cancers.

Scripps Florida Scientist Awarded $3.4 Million for HIV/AIDS Research

Grant Will Fund Study of New Drug Target and Treatment Options

A scientist at The Scripps Research Institute has been awarded $3.4 million from the National Institutes of Health to study the mode of action and the therapeutic potential of a new compound that blocks a step of HIV replication not targeted by current therapies.

Susana Valente, an assistant professor at Scripps Florida, is the principal investigator of the five-year grant. Valente will lead research into the viral protein known as Tat, a potent activator of HIV gene expression, and a Tat inhibitor that is extremely effective at reducing viral output from acutely and chronically infected cells in culture. Most antiretroviral compounds only block new infections; a Tat inhibitor can reduce viral replication from cells already infected.

"Our main goal with this grant is to fully understand the underlying mechanism of this new compound's inhibitory strength against Tat," Valente said, "and then to evaluate its therapeutic potential in animal models. If that's successful, the next obvious step would be to optimize it for use in human clinical trials."

Despite recent advances, HIV/AIDS continues its deadly global march, affecting more than 35 million individuals worldwide. The virus stubbornly persists in infected subjects despite Highly Active Antiretroviral Therapy (HAART). This residual viremia is the major hurdle for HIV eradication. Valente's newly identified Tat inhibitor defines a novel class of anti-viral drugs that could potentially inhibit viral production from stable reservoirs and reduce viral persistency during HAART.

"Initially, we though this compound was targeting another protein, but the data suggested that it was actually an inhibitor of Tat," Valente said. "We soon discovered we had a powerful inhibitor of HIV-1 transcription in our hands—and that's where we are today. This work was made possible by the great ongoing collaboration with Professor Phil Baran of Scripps California."

Scientists Awarded $3 Million to Develop New, More Effective Pain Treatments

Scripps Florida scientists have been awarded $3.1 million by the National Institute on Drug Abuse, part of the National Institutes of Health, to study and develop several new compounds that could prove to be effective in controlling pain without the unwanted side effects common with opiate drugs, such as morphine, *Oxycontin*®, and *Vicoden*®.

Laura Bohn, an associate professor in the Department of Molecular Therapeutics and Neuroscience at Scripps Research, and Thomas Bannister, an assistant professor in the Department of Chemistry and associate scientific director in the Translational Research Institute at Scripps Research, will serve as joint principal investigators for the new five-year study.

Their study will focus on four new classes of compounds that appear to differ fundamentally from opiates in the side effects that they can produce. "Once we more fully understand how these compounds work, we expect to optimize and develop them as novel drugs," said Bohn. "We hope to produce potent pain relievers without the problems associated with current treatments." The adverse side effects of morphine and other opiate drugs can range from the uncomfortable (constipation) to the dangerous (addiction, respiratory suppression, and death by overdose).

While the new compounds bind and activate the same receptor as morphine—the mu opioid receptor or MOR—they do so in a way that avoids recruiting the protein beta arrestin 2. Genetic studies have shown that animal models lacking beta-arrestins experience robust pain relief with diminished side effects.

In an encouraging sign for further development, compounds in the four chemical classes have already been synthesized by Bannister's medicinal chemistry group. "We designed compounds intended to have biological activity in the brain," said Bannister. "While we expected to find pain relievers, we were thrilled to see that some compounds also had the chemical and biological properties necessary for showing reduced side effects. The added financial support should help us build upon these exciting results and identify safer pain medications."

Scientist Awarded $2.2 Million Grant to Study Hepatitis C

Funding Could Help Identify Underlying Mechanisms of Virally Induced Liver Cancer

The Scripps Research Institute has been awarded a $2.2 million grant by the National Institutes of Health (NIH) to determine how the hepatitis C virus (HCV) induces liver cancer. The research could lead to potentially new therapeutic targets for treating those chronically infected with the virus. Timothy Tellinghuisen, an assistant professor on the Florida campus of Scripps Research, is the principal investigator for the project.

Hepatitis C virus infection is a major public health problem worldwide. Estimates place the number of HCV infected individuals at approximately 170 to 200 million, representing nearly three percent of the world's population, according to the World Health Organization. HCV infection and its assorted pathologies are responsible for an estimated 250,000 deaths a year worldwide.

A majority of patients remain chronically infected, which can lead to progressive liver damage, cirrhosis, and often the development of hepatocellular carcinoma—liver cancer. An estimated 60 to 70 percent of all those infected develop chronic infections and most progress to major liver damage. Each year, as many as five percent of these chronically infected patients will develop liver cancer.

While the mechanisms by which HCV induces liver cancer are largely unknown, Tellinghuisen's ongoing research points to host cell signaling pathways that are likely altered by the virus, creating a replication niche for the virus that avoids the body's innate immune system. "We have identified a host protein—called CARD14—as an important factor for HCV RNA replication," he said. "We believe that a pathway regulated by this protein gets manipulated by the virus to maintain chronic infections and that this contributes, in part, to liver cancer development. The new grant will help us explore the extensive role of CARD14 in HCV replication and, quite possibly, identify new ways to attack chronic HCV infection."

Overall, the new grant will enable Tellinghuisen and his colleagues to characterize how the virus manipulates this host cell pathway, identify the genes regulated by this pathway and determine their effect on viral infection and persistence, and define the function of this protein in normal liver physiology.

Scientists Win $2 Million to Study New Pathway Important in the Development and Maintenance of Lymphoma

The Researchers Hope the Project Will Reveal Suitable Drug Targets

The National Institutes of Health has awarded The Scripps Research Institute $2 million to study the role of a pathway in the development and maintenance of B-cell lymphoma, a type of cancer that begins in immune system and turns normal disease fighting cells into cancers. The disease affects immune cells known as lymphocytes, which are part of our white blood cells.

John Cleveland, PhD, chair of the Department of Cancer Biology on the Scripps Florida campus, will be the principal investigator for the new five-year study.

B-cell lymphomas tend to occur in older patients and in those people whose immune system has been compromised. It is one of the most common blood cancers in the United States and kills about 20,000 Americans each year.

The new project will focus on the role of Myc oncoproteins—the products of Myc oncogenes—which are activated in over half of all human tumor types. Myc oncoproteins accelerate the rate of cell growth, which increases the risk of acquiring additional mutations that allow a

premalignant cell to develop into a full-blown tumor. In this project, the Cleveland lab will investigate the role of a pathway that controls the destruction of a class of messenger RNAs (mRNAs) that encode proteins that regulate the development and maintenance of tumors.

"This grant allows us to focus on a new pathway that is controlled by Myc that we think is suitable to target for the development of new anti-cancer drugs," said Cleveland, who has led numerous studies shedding light on this oncogene. "We are very hopeful that learning more about this process will open the door for the development of new treatments."

Specifically, the new project aims to define the mechanisms by which Myc controls the expression and function of Tristetraprolin or TTP, a mRNA-binding protein that normally controls the destruction of a subset of important mRNAs. Importantly, Research Associate Robert Rounbehler, PhD, and other colleagues in the Cleveland lab have shown that TTP functions as a tumor suppressor that impairs the development and maintenance of B lymphoma. Their findings indicating that agents that regulate TTP or affect its key mRNA targets hold great promise as anti-cancer agents.

Esther B. O'Keeffe Foundation Gives $2 Million to The Scripps Research Institute

The Esther B. O'Keeffe Charitable Foundation has made a $2 million donation to The Scripps Research Institute to fund biomedical research and education on the Florida campus. In recognition of the gift, the Founders Room and the adjoining board room at Scripps Florida have been named the Esther B. O'Keeffe Founders Suite.

"I know I speak for the entire Scripps community when I wholeheartedly thank the Esther B. O'Keeffe Charitable Foundation," said Scripps Research President and CEO Michael A. Marletta. "Gifts of this magnitude are transformative and will go directly towards the next generation of discoveries to understand, cure, and treat human disease."

"We are delighted to contribute to The Scripps Research Institute's important scientific and educational work," said Clare O'Keeffe, executive trustee of the foundation. "These efforts are tremendously exciting and we are proud to be part of them."

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 broad spectrum of arts and cultural programs.

Over the years, the foundation has supported innovative non-embryonic stem cell research at Scripps Research, helping to advance breakthroughs in the development of new treatments for conditions such as diabetes, Alzheimer's, Parkinson's, hearing loss, and spinal cord damage.

The new unrestricted gift will be used to fund special initiatives on the Florida campus. In the past, unrestricted funds have provided state-of-the-art scientific infrastructure, funded "out of the

box" research projects, provided crucial "bridge funding" for scientists between grants, and enabled graduate students to study in the institute's top-ranked PhD program. With this gift, the foundation and its trustees become Scripps Florida Founders, a designation that honors donors who have made lifetime contributions of $2 million or more to the Jupiter campus.

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.

Scripps Florida Team Awarded Nearly $1.5 Million to Develop Potent New HIV Inhibitors

A Scripps Florida team has been awarded nearly $1.5 million by the National Institutes of Health to identify and develop novel potent inhibitors of the human immunodeficiency virus (HIV), the cause of AIDS.

A. Donny Strosberg, a professor on the Florida campus of The Scripps Research Institute, is the principal investigator for the new three-year study.

Current treatments of HIV-infected patients are based on combinations of drugs—called cocktails—that target several critical key steps in the early and late stages of the viral replication cycle. While these combinations have proven effective in controlling the infection in many patients, the continuous emergence of new multi-resistant viral strains requires the development of new classes of drugs that can be aimed at different targets on HIV.

Strosberg's target is the capsid protein or CA, the primary component of the HIV virion—the infectious particle responsible for transporting the viral genome to host cells. This viral protein forms a cone-shaped shell around the HIV genome, and plays a critical role in the lifecycle of the virus by packaging and organizing the viral genome so that HIV can replicate efficiently.

"Because of the growing resistance of HIV against current treatments, a new, differently targeted approach to treating the disease is urgently needed," Strosberg said. "We expect to use the HIV capsid protein as a new high-throughput screening target for the discovery of novel anti-HIV/AIDS agents."

Identifying new compounds that could target the CA protein might make it possible to prevent the protein's assembly into capsid shells in the first place, blocking the virus's infectivity, and adding a potent complement to existing treatments, he said. This strategy has worked well for Strosberg's group, which has in the past years discovered several potent inhibitors of the hepatitis C virus.

Strosberg and his colleagues, who include Susana Valente, PhD, an assistant professor at Scripps Florida, and Massimo Caputi, PhD, an associate professor of biomedical science at the Florida

Atlantic University Charles E. Schmidt College of Medicine, plan to perform an initial screening of some 350,000 compounds in the Molecular Libraries Probe Centers Network at Scripps Research; Scripps Research is one of only four such large probe centers nationwide.

Two Scripps Research Scientists Win Prestigious NIH Innovator Awards

Michael Petrascheck and Brian Paegel Each Will Receive $1.5 Million

Two Scripps Research Institute scientists have won prestigious National Institutes of Health (NIH) Director's New Innovator Awards. The recipients are Assistant Professor Michael Petrascheck of the institute's La Jolla, California campus, and Assistant Professor Brian Paegel of the Jupiter, Florida campus.

The awards, which were announced by NIH Director Francis S. Collins at the Seventh Annual NIH Director's Pioneer Award Symposium September 20, will provide each recipient with $1.5 million in research funding over five years.

"The NIH Director's Award programs reinvigorate the biomedical work force by providing unique opportunities to conduct research that is neither incremental nor conventional," said James M. Anderson, director of the Division of Program Coordination, Planning and Strategic Initiatives, who guides the NIH Common Fund's High-Risk Research program. "The awards are intended to catalyze giant leaps forward for any area of biomedical research, allowing investigators to go in entirely new directions."

Petrascheck, who is a member of the Department of Chemical Physiology, the Department of Molecular and Experimental Medicine, and the Dorris Neuroscience Center at Scripps Research, will use the award to conduct research on aging and lifespan in C. elegans, a flatworm widely used in aging research. The project will test strategies that might be used in human therapies. "The innovator award will allow me to focus more of my attention on science," said Petrascheck. "We now have the means necessary to develop the tools that will allow us to determine how sensory perception influences aging and how sensory perception could be targeted by small molecules to treat age-related disease."

Paegel, an assistant professor in the Department of Chemistry, will use his award to evolve new molecular tools for protein sequencing. "Imagine being asked to take apart a sophisticated race car with a single Phillips-head screwdriver," said Paegel. "This is basically where we are today with protein sequencing technology. We will evolve a suite of custom-tailored molecular tools that will allow us to identify all sites of protein modification, and to correlate those changes with normal cellular function and disease. Our approach integrates the institute's strengths in chemistry and high-throughput screening with my laboratory's expertise in microfluidic technology development and evolution."

Winners of the NIH Director's New Innovator Award are selected on the basis of individual creativity, the innovativeness of his or her research approaches, and the potential of the proposed project, if successful, to have a significant impact on an important biomedical or behavioral

research problem. More information on the New Innovator Award is at http://commonfund.nih.gov/newinnovator, including information on this year's awardees.

Scripps Research Scientist Receives $1 Million Research Grant from Novo Nordisk

Andrew Butler, an associate professor in The Scripps Research Institute's Department of Metabolism and Aging, has been awarded $1 million in funding over the next two years to further his research into a novel protein with the potential to improve the understanding and future treatment of diabetes.

The award is notable in that it comes not from the US National Institutes of Health but from Novo Nordisk, an international healthcare company based in Denmark recognized as a world-leader in diabetes treatment. The Novo Nordisk Diabetes Innovation Award Program was launched in 2011 to help scientists substantiate early research efforts that could result in new treatment options for diabetes and obesity.

Butler's two-year research project, entitled the "Investigation of a Novel Peptide Hormone in Diabetes Treatment," was selected from more than 80 submitted proposals from US and Canadian research institutions. The research involves a peptide hormone secreted by the liver called adropin. Animal models have shown that peptide hormones play an important role in regulating glucose levels and fatty acid metabolism and that irregular function of these hormones can have a direct effect on an individual's risk of developing obesity and/or diabetes.

"We were studying animal models of insulin resistance as precursor to type 2 diabetes, when we came across adropin," Butler said. "We found it provocative that this particular peptide hormone was distributed in the brain, liver, and pancreas—three tissues that are of great interest to those of us in the diabetes research field." Butler noted that adropin seems to play a role in maintaining normal insulin sensitivity—whereby only a relatively small amount of insulin is needed to maintain regular blood glucose levels. In type 2 diabetes, insulin sensitivity is often blunted, which means that the normal amounts of insulin produced by the body are no longer as effective in lowering blood glucose levels.

"What has not been established are the mechanisms and sites of action that effect glucose homeostasis [equilibrium]," he said. "So that's what we're going to spend the next two years finding out with the help of this research grant from Novo Nordisk."

The research will also explore adropin's potential role as a protein-based therapy for treating type 2 diabetes, a chronic disease that affects over 300 million people worldwide, according to the World Health Organization. "Clearly, there is an urgent need to identify new and more effective drugs for treating diabetes," Butler said. "Studying how adropin works in this regard could eventually contribute to this effort."

Scientist Awarded $1 Million Grant to Develop New Tools for Hepatitis C Treatment Discovery

Scientists from the Florida campus of The Scripps Research Institute have been awarded just over $1 million from the National Institutes of Health for a three-year study to develop new high-throughput screening tests to find compounds that disable a protein essential to hepatitis C virus (HCV) replication.

Timothy Tellinghuisen, a Scripps Florida associate professor, is the principal investigator for the study.

Hepatitis C is a slow-progressing disease that causes inflammation of the liver and affects some 170 million people worldwide, according to the Hepatitis Foundation International. Like the current approach to HIV/AIDS, a cocktail-based therapeutic approach, which uses multiple inhibitors targeting distinct aspects of the HCV life cycle, has emerged as one of the most promising.

In the search for new treatments against HCV, it has become critical to develop novel targets to attack. Tellinghuisen's new research is focused on a potentially potent, but somewhat neglected, enzyme. This protease—an enzyme that breaks down proteins—is known as NS2, which is necessary for productive infections that produce new viruses and spread the infection among cells.

"The NS2 protein is needed for hepatitis C infections, but is poorly understood," Tellinghuisen said. "The new grant will help us develop potential chemical tools to look at the role of NS2 in HCV biology because we really don't know how the protein works."

Some recent studies suggest that the NS2 protease may be involved in altering gene expression in the host cell and in helping the virus defend against apoptosis or programmed cell death, in addition to the more direct roles for the protein in viral replication and particle assembly.

Tellinghuisen and his colleagues have already developed a small-scale screen to identify compounds that disrupt viral replication through NS2 protease activity. "Our overall goal is to turn our small-scale NS2 assay into an assay appropriate for high-throughput small-molecule screening," he said, noting that would give the team access to the more expansive Molecular Libraries Probe Production Centers Network (MLPCN) screening center program at Scripps Florida. MLPCN is a collaborative research network that uses use high-tech screening methods to identify small molecules to investigate the diverse functions of cells; Scripps Research is one of four large national centers.

Scientist Awarded $1 Million for Stress-Associated Disease and Aging Research

A scientist from the Florida campus of The Scripps Research Institute has been awarded just over $1 million from the National Institutes of Health to develop a range of new tests that could

lead to new treatments for a number of stress-associated and degenerative disorders of advancing age.

Shuji Kishi, an assistant professor at Scripps Research, is the principal investigator for the three-year study.

The new tests will focus on diseases linked to oxidative stress (and the stress-induced inflammation that often accompanies it), closely associated with aging. Those diseases include atherosclerosis, Alzheimer's and Parkinson's disease, diabetes, heart attack, sarcopenia, liver and kidney disease, and stroke. Despite the widespread damage caused by oxidative stress, the number of therapeutic remedies for it remains virtually non-existent.

During periods of cellular stress, such as exposure to UV radiation or chronic diseases like cancer, the level of highly reactive oxygen-containing molecules in cells can increase, resulting in misfolded proteins and cell damage. Cells can protect themselves from this damage by activating certain antioxidant genes, but age and extended periods of stress can impair that response.

In the new study, Kishi plans to develop a series of tests to identify drug leads that will prevent oxidative damage in a novel vertebrate model. His approach will involve high-content screens in zebrafish. "The cell-based assays can be pursued using the ultra-high-throughput screening resources available at Scripps Florida, including a chemical library comprised of approximately 1 million compounds with structures that we know have properties suitable for drug development," Kishi said.

Beyond the cell-based tests, Kishi plans to use newly developed transgenic zebrafish as a model organism for testing any drug candidates uncovered during cell-based screening. Those with potential after this round of testing will then be further evaluated to determine organ specificity and developmental toxicity, and for overall efficacy in preventing oxidative damage. "We want to understand how these selected small molecules work in the zebrafish so that additional drugs can be designed based on the in vivo antioxidant response," Kishi said.

Kishi's laboratory is broadly focused on developing experimental models of aging and geriatric diseases, including neurodegenerative diseases.

Scripps Florida Scientist Awarded $700,000 to Develop New Treatments for Cocaine Addiction

A scientist on the Florida campus of The Scripps Research Institute has been awarded more than $700,000 by the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health (NIH), to study and optimize newly discovered compounds to combat cocaine addiction.

Thomas Bannister, an assistant professor in the Department of Chemistry and associate scientific director in the Translational Research Institute at Scripps Florida, is the principal investigator for

the five-year study. Chemists in the Bannister group discovered the compounds as part of an effort to find new classes of molecules capable of treating brain disorders.

"Long-term drug addiction can cause biochemical changes in the brain of the drug user," said Bannister. "Unfortunately the changes can reinforce the addiction, making it much more difficult to resist the urge to relapse. Animal studies suggest that there may be ways to normalize the brain chemistry of long-term drug users and raise the odds for a successful recovery."

The Bannister lab's hypothesis is that drugs capable of selective interactions with a brain protein called the NOP receptor will be beneficial in addiction therapy. The main hurdle in testing this hypothesis has been that drugs known to interact with the NOP receptor also interact with opioid receptors, where drugs such as morphine, Oxycontin®, and Vicoden® act to provide both pain relief and unwanted addictive effects. Thus if these drugs were used for treating cocaine addiction, they could simply cause a different addiction, a trade-off that wouldn't be particularly useful.

The key finding prompting the grant application was new chemistry that gave molecules increased selectivity for the NOP receptor over the opioid receptors. "We found molecules that were biologically specific, acting only at the NOP receptor and having no opiate effects," said Bannister. "We made these advances while receiving funding from a NIH/NIDA one-year "economic stimulus" grant, in collaboration with Claes Wahlestedt and co-workers at the University of Miami. Claes's group used studies with mice to show that our selective new compounds were not addictive. They also found that drug-adapted mice, after taking one of our best lead molecules, consumed less cocaine than untreated mice."

While many more studies are needed to see if such therapy can work in humans, the new grant represents a major step toward that objective. "This grant will allow us to optimize the chemical and biological properties of these molecules and to extensively study their effects in the brain," said Bannister. "The long-term goal is to develop an entirely new and effective method for treating cocaine addiction."

Scripps Research Scientist Awarded $500,000 Grant from Michael J. Fox Foundation to Study Parkinson's Disease

Funding Could Help Uncover Novel Therapeutic Target for Neurodegenerative Disorder

The Scripps Research Institute has been awarded a $500,000 grant by the Michael J. Fox Foundation to study a pair of genetic mutations that could lead to a new and potentially vital therapeutic target for Parkinson's disease, a progressive and fatal neurodegenerative disorder.

Philip LoGrasso, PhD, a professor in molecular therapeutics and senior director for drug discovery at Scripps Florida, is the principal investigator for the project.

The study will focus on two genes, the leucine-rich repeat kinase 2 (LRRK2) and the serum glucocorticoid-regulated kinase 1 (SGK1). Genetic testing of several thousand Parkinson's patients has shown that the risk of Parkinson's disease associated with mutations in the LRRK2

gene are substantially reduced by mutations in the SGK1 genes, bringing the risk back in line with that of the general population.

"As a kinase, LRRK2 is the kind of molecule that drugmakers have a great deal of experience targeting. And as a significant genetic contributor to Parkinson's disease, it provides important therapeutic avenues for understanding the biological mechanisms and clinical aspects of PD," said Todd Sherer, PhD, CEO of The Michael J. Fox Foundation. "Dr. LoGrasso's expertise in kinases and his well known work in developing novel treatments for Parkinson's disease will be a particularly valuable addition to the promising research already being carried out with funding from the Foundation."

SGK1 was discovered by 23andMe, Inc., a leading personal genetics company. The company currently has 125,000 genotyped customers, and nearly 90 percent have opted-in to participate in the company's Institutional Review Board-approved research. 23andMe has amassed the single largest Parkinson's research cohort in the world, which now comprises approximately 6,000 participants and includes one of the largest cohorts of individuals carrying the pathogenic mutations in the LRRK2 gene.

With this award Dr. LoGrasso joins the LKRR2 Consortium, established last year by the Michael J. Fox Foundation. The consortium is an international group of academic and industry partners dedicated to accelerating LRRK2 therapeutic development.

"I want to thank the Fox Foundation for their generous grant," LoGrasso said, "and for giving me the opportunity to study the links between these intriguing genetic mutations. The question our laboratory will explore is how SGK1 works and how it impacts the LRRK2 mutation. We're all hoping that ultimately this produces a new target for treatment intervention – because there are no viable long-term treatments available today."

Since the 1960s the mainstay for the treatment of Parkinson's disease has been levodopa (L-DOPA), a drug that provides only symptomatic relief. Unfortunately, L-DOPA loses efficacy over time and has numerous side effects that limit its effectiveness.

Patients with Parkinson's disease suffer from a loss of dopaminergic neurons in a specific area of the brain. An estimated one million Americans are believed to suffer from the disease, according to the Parkinson's Disease Foundation; approximately 40,000 new cases are reported annually.

The LRRK2 gene was first linked to Parkinson's disease in 2004, and many believe it to be the most common genetic contributing factor to the disease. While hereditary forms of the disease are relatively rare – an estimated five to 10 percent – unlocking the mechanisms involved in both LRRK2 and SGK1 could eventually benefit all patients.

Mutations in the LRRK2 gene have been linked with an increased risk not only of Parkinson's disease, but also of Crohn's disease. SGK1 is involved in a number of biomolecular processes including inflammation, cell proliferation, and apoptosis or programmed cell death. It is believed that the gene also plays a role in brain disorders other than Parkinson's disease, such as schizophrenia, depression, and Alzheimer's disease.

Scientist Wins Pair of Grants to Study Critical Component of Memory

Sathyanaryanan Puthanveettil, an assistant professor on the Florida campus of The Scripps Research Institute, has been awarded a pair of notable grants to study a critical component of long-term memory formation.

Puthanveettil will receive $225,000 over three years from the prestigious Whitehall Foundation to study the role in long-term memory of a motor protein called kinesin. In this study, he will use the marine snail, Aplysia, a favorite of memory researchers because of its exceptionally large neurons and simple nervous system.

In addition to the Whitehall award, Puthanveettil has received a one-year, $100,000 grant from the Alzheimer's Drug Discovery Foundation. Puthanveettil also plans to use the award to study kinesin, in this case to develop molecular screens to identify small molecules that can modulate kinesin function in the mammalian brain. This work will be conducted in collaboration with Scripps Research colleagues Peter Hodder, senior scientific director of lead identification, and William Roush, chemistry professor, executive director of Medicinal Chemistry, and associate dean of graduate studies at Scripps Florida.

"To be selected for an award by the Whitehall Foundation is a great honor," Puthanveettil said. "I'm also delighted with the grant from the Alzheimer's Drug Discovery Foundation, another important institution that supports the search for new therapeutics. Both awards will help advance my research substantially."

Puthanveettil has long been interested in axonal transport and its role in the molecular mechanisms underlying long-term memory storage, in particular the cellular transport of various gene products such as proteins and RNAs in the brain.

In a 2008 study published in the journal *Cell*, Puthanveettil showed for the first time that the induction of long-term facilitation—the cellular basis of memory and learning involving enhancement of communication between neurons—requires upregulation of specific isoform of kinesin.

Ultimately, he hopes his research will lead to an understanding of the basic pathology of various neurological disorders.

"For example, in the case of Huntington's disease, kinesin is responsible for transport of molecules that play a role in the disease," he said. "We want to know how the transport of these molecules is modified during the disease's development. Likewise for Alzheimer's disease—if you can find a way to manipulate the transport system, you may be able to overcome some of the defects involved in the disease's pathology."

Scripps Florida is Awarded Grant to Create National Anti-Addiction Network

Initiative Will Focus on Finding Cures for Tobacco Abuse, Nicotine Addiction

The Florida campus of The Scripps Research Institute has received a multistage cooperative grant to create a national public-private network that will work to combat the nation's lingering addiction to tobacco.

The new National Institutes of Health (NIH) program will eventually become a broad collaborative effort between academia, the pharmaceutical industry, and charitable organizations to deliver new anti-smoking medicines—in essence the first large-scale federally sponsored tobacco addiction research and drug development center in the United States.

Scripps Florida was awarded $125,000 to complete the first stage of the multistage cooperative NIH grant. The first stage is a planning stage, which kicks off this month. The leadership team is well into developing several projects that could influence its chances of next year being chosen as the national center's managing partner.

"We have a number of important objectives for the coming year, including a major international scientific symposium with tobacco addiction experts from academia, the Food and Drug Administration, the NIH, and the pharmaceutical industry," said Patrick R. Griffin, chairman of the Department of Molecular Therapeutics and director of the Translational Research Institute at Scripps Florida, and program director of the new project.

Griffin will collaborate with Scripps Florida Associate Professor Paul J. Kenny, a noted addiction expert and the grant's principal investigator, to host this symposium and to create a Web portal that will include a vast range of tobacco addiction data—basically, everything there is to know scientifically about the issue will be available on the site. This all-encompassing resource will be available to public, providing information about the addiction, which kills approximately 440,000 Americans each year, according to the National Institute on Drug Abuse, and costs the nation $160 billion annually. One in every five American deaths is the direct result of smoking.

Griffin and Kenny will also conduct an extensive review of the science of tobacco addiction, which will summarize the data from the new website, outcomes from the symposium, and other findings by the close of the planning year.

"We intend this review to be the most focused and comprehensive on tobacco addiction to date," Griffin said.

Currently, there are six active drug discovery research programs at Scripps Florida, all supported by the NIH, aimed at developing novel compounds with the potential to help smokers quit.

In January of this year, for example, Kenny identified a novel pathway in the brain that regulates an individual's vulnerability to the addictive properties of nicotine. Kenny's laboratory is already

working on research in collaboration with scientists at the University of Pennsylvania to develop new drugs that could decrease the addictive properties of nicotine.

The Griffin lab has recently developed novel modulators of the nuclear receptor PPARG, a target currently being investigated in clinical trials for smoking cessation. "Our compounds may offer a significant advantage in terms exposure to the target in the brain, as well as a much-improved side effect profile compared with the drug currently being evaluated in the clinic," noted Griffin.

Scripps Research Licenses New Instrumentation Platform That Dramatically Improves Compound Management

Scientists from the Florida campus of The Scripps Research Institute have designed and licensed a major new technology that dramatically improves the quality control and management of compounds used for high-throughput screening, a process that can be used to search for potential new drugs.

The technology, which consists of an automated instrumentation platform called the Plate AuditorTM, has been licensed for manufacture and sale to the Brooks Life Science Systems division of Brooks Automation, a leading worldwide provider of automation, vacuum, and instrumentation solutions for multiple markets including semiconductor manufacturing, life sciences, and clean energy.

The Plate AuditorTM was designed by Peter Hodder, senior scientific director, and his laboratory staff, Louis Scampavia and Pierre Baillargeon. It combines advanced spectroscopy and image analysis techniques to perform rapid, automated, and nondestructive quality assessment of compounds in high-throughput screening collections. It also monitors the quality of all samples through their lifecycle, a practice not currently possible with existing technologies. "This is the first instrument of its kind and first in its class," Hodder said. "As a detection platform, it provides a wealth of information about a compound sample that you simply couldn't get from one instrument." Scripps Research uses the instrument routinely for quality control of more than 1 million compounds in its drug-discovery screening operation.

John Lillig, senior vice president and managing director of Brooks Life Science Systems, commented, "As the leader in providing automated compound and biological sample management systems to pharmaceutical and biotech companies around the world, Brooks is very excited to be working together with the Scripps Research Institute's Compound Management Group on the development and the commercialization of this innovative and very useful Compound/HTS Quality Assurance technology. With over 350 million samples stored in Brooks Sample Management Systems around the world, the new Scripps Research/Brooks Plate AuditorTM will be a very nice complement to our Brooks Tube AuditorTM product offering and a valuable new quality enhancement tool for our many Compound Management colleagues around the world."

The new instrument will debut at the First Annual Society for Laboratory Automation and Screening (SLAS) in February in San Diego, CA. Hodder himself will be presenting the new HIAPI-CM at a European Lab Automation Conference this May.

Hodder hopes the new technology gets people thinking about Scripps Florida in a brand new way. "We want people to know that in addition to discovering therapeutic molecules, we can also design and build novel instrumentation for screening operations," said Hodder, who founded and has directed the high-throughput screening laboratory at Scripps Florida since 2005.

More information on the technology can be found in a recent publication, "Monitoring of HTS compound library quality via a high-resolution image acquisition and processing instrument, by Baillargeon P., Scampavia L., Einsteder R., and Hodder P. in the *Journal of Laboratory Automation* 2011 Jun;16(3):197-203) or the technology patent (http://www.wipo.int/patentscope/search/en/WO2010057081)

Scripps Research Institute and OPKO Health Announce Global License Agreement for a Novel Compound That Blocks Brain Cell Destruction in Parkinson's Disease

The Scripps Research Institute and OPKO Health, Inc. (NYSE: OPK) today announced a global agreement for the development and commercialization of SR 3306, a novel compound discovered by scientists from the Florida campus of The Scripps Research Institute that blocks the destruction of brains cells in animal models of Parkinson's disease.

"This licensing agreement will help insure that the development of this promising compound keeps moving forward," said Scripps Research Professor Philip LoGrasso, Ph.D., whose laboratory has led the research on the compound to date. "This is one of the best opportunities we have for the development of an effective neuroprotective treatment for Parkinson's patients."

Under the terms of the agreement, Scripps Research has granted to OPKO Health exclusive worldwide rights to develop, manufacture, and commercialize SR 3306 and related compounds that inhibit a class of enzymes called jun-N-terminal kinsases (JNK) that play an important role in neuron survival. The new compound would potentially be the first to protect the brain from the ravages of Parkinson's disease.

"We are excited to be working with Dr. LoGrasso and The Scripps Research Institute to develop this important compound which could prevent the progression of Parkinson's disease and not just treat the symptoms of the disease," said Phillip Frost, M.D., Chairman and Chief Executive Officer of OPKO.

Parkinson's disease, a degenerative neurological disorder that reduces the brain's ability to produce dopamine, affects about 1 million Americans. Currently prescribed drugs for Parkinson's disease—including levodopa and so-called MAO-B inhibitors—can counteract symptoms of the disease but not stop its progression.

The LoGrasso lab described SR-3306 in a pair of studies published in February 2011 in the journal *ACS Chemical Neuroscience*.

Part 3: Scientific Accomplishments

Scripps Research Scientist Identifies Critical Role for Night Blindness Gene

New Findings Explain Rapid Signal Transmission in Eye's Initial Response to Light

A scientist from the Florida campus of The Scripps Research Institute has determined how a particular gene makes night vision possible.

The study, which was published in the August 10, 2011 edition of *The Journal of Neuroscience*, focuses on a gene called nyctalopin. Mutations in the gene result in inherited "night blindness," a loss of vision in low-light environments.

"Until now, our understanding of the role of this gene in the visual signaling pathway has been very limited," said Kirill Martemyanov, an associate professor on the Florida campus of The Scripps Research Institute. "This is the first time we have uncovered a functional role for it—and we linked that function to a much larger molecular complex that's needed for low-light vision."

Quick as a Flash

Our vision begins when photons hit light-sensitive photoreceptor cells in the retina. When excited by light, photoreceptors generate a response that needs to be rapidly transmitted to the downstream neurons (nerve cells) for the signal to be processed and sent to the brain, which then interprets the visual picture. The hand off of the information occurs at the specialized contact points called synapses.

"The proper function of a particular type of synapse between rod photoreceptors and bipolar cells is absolutely critical for the transduction of the visual signal," Martemyanov explained. "Even if rods generate response to light but are unable to properly transmit the signal, this results in an inability to see in the dark. Without this signaling, we'd have a tough time surviving in the world where it is dark half of the time."

In addition, the transmission across the synapse must occur rapidly. "The quickness of our signaling response to light creates a clear temporal resolution of what we see," he said. "For example, when you turn your head suddenly, you see different objects clearly, not just a blur. We couldn't drive a car without it."

In the new research, the scientists searched for proteins associated with nyctalopin in the mouse retina. Scientists had known for a decade that the gene encoding nyctalopin is one of the most frequent culprits of night blindness, but its function had remained a mystery. The results showed that the protein expressed by the gene serves as a kind of molecular glue that holds together key

elements of the signal transduction machinery at the synapse, allowing for the rapid and intact transmission of these sensory signals.

In molecular terms, the study strongly suggests that nyctalopin coordinates the assembly and precise delivery to the synapse of the macromolecular complex consisting of mGluR6, a neurotransmitter receptor protein, which directly communicates with rod photoreceptors and TRPM1, a protein channel that generates the response, making vision possible.

While the new findings are relevant to the processing of low-light vision, Martemyanov said, the role of nyctalopin might go far beyond the eye. Proteins similar to nyctalopin exist in the central nervous system, and it is possible that they coordinate synaptic signaling in a manner similar to the retina. Indeed, communication between neurons across synapses is fundamental to the nervous system function and disruption of this process is thought to be the main factor contributing to a range of the neuropsychiatric diseases.

The first author of the study, "TRPM1 Forms Complexes with Nyctalopin In Vivo and Accumulates in Postsynaptic Compartment of ON-Bipolar Neurons in mGluR6-dependent Manner," is Yan Cao. In addition to Martemyanov and Cao, Ekaterina Posokhova is an author of the paper. All of the authors work at Scripps Research.

The study was supported by the National Institutes of Health.

Scripps Research Scientists Expand Knowledge of Cell Process Involved in Many Diseases

As part of a joint research effort with the University of Michigan, scientists from the Florida campus of The Scripps Research Institute have for the first time defined the structure of one of the cell's most basic engines, which is required for cell growth, as it assembles from its components.

The study reveals a series of redundant mechanisms that assure production of these critical structures while avoiding any missteps that could lead to their destruction or to the production of incorrect cellular building blocks. These findings throw new light on a process that is integrally involved in a number of disease states, including cancer and Alzheimer's disease.

The study, published on August 11, 2011, in the advance online edition of the prestigious journal *Science*, reveals the structure of an assembly intermediate of the small ribosomal subunit.

Ribosomes, which are large macromolecular machines required for cell growth in all organisms, catalyze the production of proteins in all cells. They read the genetic code carried by messenger RNA, and then catalyze or translate that code into proteins within cells, assembling them from amino acids.

Understanding the process of ribosome assembly—which involves almost 200 essential proteins known as "assembly factors" in addition to the four RNA molecules and 78 ribosomal proteins that are part of the mature ribosome—is a potentially fruitful area of research because of the

importance of ribosome assembly for cell growth. The link between defects in ribosome assembly and cancer clearly points to this pathway as a new target for anti-cancer drugs.

In the current study, the scientists used cryo-electron microscopy (where samples are studied at temperatures of -150°C) to image the 40S ribosome structure.

"This is the best-defined ribosomal assembly intermediate we have ever had with true structural information on the location of each assembly factor," said Katrin Karbstein, an associate professor at Scripps Florida and one of the senior authors of the study. "It will be helpful in determining what's going on in what is still a relatively unknown process."

While most ribosome assembly takes place in the nucleolus, a protein-nucleic acid structure inside the nucleus, the final maturation process occurs in the cytoplasm, the "general" cellular compartment where protein translation occurs. In the cytoplasm, these pre-mature ribosomal subunits encounter large pools of mature subunits, messenger RNA, and various translation factors.

This cellular stew presents a unique challenge, especially keeping 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.

The new study shows that that the bound assembly factors cooperate with one another in a highly redundant and multi-pronged approach to prevent such occurrences, chaperoning the pre-40S subunits to keep them from falling victim to the translational apparatus.

"We had thought the role of assembly factors was to help mature this intermediate form of the ribosome," said Karbstein. "But our new research has shown that these assembly factors also prevent a number of unwanted things from happening. If one of these intermediate forms were to bind prematurely to a messenger RNA, there could be no protein produced, or worse, a wrong protein might be produced and that could lead to early cell death."

It's important to note that this is a single snapshot of the late-stage assembly process, Karbstein added. "We know better how the process works but this is by no means a final statement," she said.

The first authors of the study, "Ribosome Assembly Factors Prevent Premature Translation Initiation by 40S Assembly Intermediates," are Bethany S. Strunk of Scripps Research, and Cherisse R. Loucks and Min Su of The University of Michigan. Other authors include Harish Vashisth, Shanshan Cheng, Justin Schilling, Charles L. Brooks III, and Georgios Skiniotis of The University of Michigan. For more information, see http://www.sciencemag.org/content/early/2011/08/10/science.1208245.abstract?sid=adbd44ad-f124-492f-8d73-ebb6dc4761aa

The study was supported by the National Institutes of Health and the National Science Foundation.

Scripps Research Scientists Help Pinpoint Cause of Stress-Related DNA Damage

Findings Suggest New Model for Developing Novel Therapeutic Approaches

Working closely with a team of researchers from Duke University, scientists from the Florida campus of The Scripps Research Institute have helped identify a molecular pathway that plays a key role in stress-related damage to the genome, the entirety of an organism's hereditary information.

The new findings, published in the journal *Nature* on August 21, 2011, could not only explain the development of certain human disorders, they could also offer a potential model for prevention and therapy.

While the human mind and body are built to respond to stress—the well-known "fight or flight" response, which lasts only a few minutes and raises heart rate and blood glucose levels—the response itself can cause significant damage if maintained over long periods of time.

When stress becomes chronic, this natural response can lead to a number of disease-related symptoms including peptic ulcers and cardiovascular disorders. To make matters worse, evidence indicates that chronic stress eventually leads to DNA damage, which in turn can result in various neuropsychiatric conditions, miscarriages, cancer, and even aging itself.

Until the new study, however, exactly how chronic stress wreaks havoc on DNA was basically unknown.

"Precisely how chronic stress leads to DNA damage is not fully understood," said Derek Duckett, associate scientific director of the Translational Research Institute at Scripps Florida. "Our research now outlines a novel mechanism highlighting β-arrestin-1 as an important player."

The long-term effects of these stress hormones on DNA damage identified in the study represent a conceptual as well as a tangible advance, according to Robert J. Lefkowitz, a Duke University professor of medicine who led the study.

Since stress is not time-limited and can be sustained over months or even years, it is well appreciated that persistent stress may have adverse effects for the individual. These new findings not only uncover a novel pathway, but also have important practical implications.

"Our results provide a possible mechanistic basis for several recent reports suggesting that significant risk reductions for diseases such as prostate cancer, lung adenocarcinoma, and Alzheimer's disease may be associated with blockade of this particular stress-response pathway by beta blockers," Leftkowitz said. "Although there are most likely numerous pathways involved in the onset of stress-related diseases, our results raise the possibility that such therapies might reduce some of the deleterious DNA-damaging consequences of long-term stress in humans."

A Newly Discovered Mechanism

The newly uncovered mechanism involves β-arrestin-1proteins, β2-adrenoreceptors (β2ARs), and the catecholamines, the classic fight-or-flight hormones released during times of stress—adrenaline, noradrenaline, and dopamine. Arrestin proteins are involved in modifying the cell's response to neurotransmitters, hormones, and sensory signals; adrenoceptors respond to the catecholamines noradrenaline and adrenaline.

Under stress, the hormone adrenaline stimulates β2ARs expressed throughout the body, including sex cells and embryos. Through a series of complex chemical reactions, the activated receptors recruit β-arrestin-1, creating a signaling pathway that leads to catecholamine-induced degradation of the tumor suppressor protein p53, sometimes described as "the guardian of the genome."

The new findings also suggest that this degradation of p53 leads to chromosome rearrangement and a build-up of DNA damage both in normal and sex cells. These types of abnormalities are the primary cause of miscarriages, congenital defects, and mental retardation, the study noted.

The first author of the study, "Stress Response Pathway Regulates DNA Damage through β2-Adrenoreceptors and β-Arrestin-1," is Makoto R. Hara of Duke University. In addition to Duckett and Hara, other authors include Jeffrey J. Kovacs, Erin J. Whalen, Sudarshan Rajagopal, Ryan T. Strachan, Aaron J. Towers, Barbara Williams, Christopher M. Lam, Kunhong Xiao, Sudha K. Shenoy, Simon G. Gregory, Seungkirl Ahn, and Robert J. Lefkowitz of Duke University; and Wayne Grant of Scripps Research.

The study was supported by the National Institutes of Health.

Scripps Research Scientists Define Cellular Pathway Essential to Removing Damaged Mitochondria

New Findings Could Have Important Implications for Current Cancer Treatments

In a joint research effort with researchers at St. Jude Children's Research Hospital, and with help from scientists at The University of Pennsylvania, The University of Minnesota, and the National Institutes of Health, investigators from the Florida campus of The Scripps Research Institute have defined a specific protein complex that allows cells to rid themselves of damaged mitochondria, which are the energy producing machines of the cell.

"This protein complex is already being targeted in cancer therapeutics," said John Cleveland, chair of the Department of Cancer Biology at Scripps Florida, "but now we understand why some of the therapies that target this complex work and this new knowledge will have tremendous impact on both current and potential cancer therapies."

In particular, the study, which appears in the current issue of the journal *Molecular Cell*, focuses on how the cell uses a process known as autophagy—the major recycling center of the cell—to

remove damaged mitochondria. The autophagy pathway is exploited by many tumors to survive stressful conditions and to remove damaged components.

The Cell under Stress

On a molecular level, the new study focuses on the role of the molecular complex known as "Hsp90-Cdc37 chaperone complex," which orchestrates various aspects of the cellular stress response. Although scientists had known that both the Hsp90-Cdc37 complex and autophagy help maintain the integrity of mitochondria, the exact relationship between Hsp90-Cdc37 and autophagy has not been well understood until the new study.

Hsp90, is a heat-shock protein, one of the cell's most abundant proteins, and assists in everything from protein folding and tumor repression to cell signaling. Cdc37, also a protein, is a co-chaperone to Hsp90 and is involved in cell signal transduction and connecting Hsp90 to the right kinases (kinases add a phosphate group to various molecules and can modify protein activity).

The study highlights the interaction between Hsp90-Cdc37 and Ulk1, a kinase that the authors show is required for the degradation and elimination of damaged mitochondria. Hsp90-Cdc37 stabilizes and activates Ulk1, which in turn phosphorylates its substrate Atg13, which is then released from the complex. Atg13 then eliminates damaged mitochondria via the autophagy pathway. Thus, the study links Hsp90-Cdc37-Ulk1-Atg13 in a direct pathway that is essential for efficient mitochondrial clearance.

"The new study shows that the key regulatory mechanism of this process is the Hsp90-Cdc37 chaperone, which functions as an on-off switch that is critical for the correct functioning of the Ulk1 kinase," Cleveland said. "Thus, if we can control this switch, we can significantly improve the therapeutic window."

The first authors of the study, "Hsp90-Cdc37 Chaperone Complex RegulatesUlk1- and Atg13-mediated Mitophagy," are Frank C. Dorsey of Scripps Research and Joung Hyuck Joo, Aashish Joshi, and Kristin M. Hennessy-Walters of St. Jude Children's Research Hospital. Other authors include Kristie L. Rose, Stephanie M. Prater, Meredith A. Steeves, and John L. Cleveland of Scripps Research; Chang-Hwa Jung, and Do-Hyung Kim of the University of Minnesota; Der-Fen Suen, Chia-Ying Yang, Craig B. Thompson of the University of Pennsylvania School of Medicine; and Richard Youle of the National Institutes of Health; and Kelly McCastlain, Rekha Iyengar, Paul A. Ney and Mondira Kundu of St. Jude Children's Research Hospital. For more information, see http://www.cell.com/molecular-cell/abstract/S1097-2765%2811%2900464-3.

The study was supported by the National Institutes of Health, the Burroughs Welcome Fund, the American Society of Hematology, the Scripps Florida Funding Corporation, and the American Lebanese Syrian Associated Charities.

Scripps Research Scientists Establish New Class of Anti-Diabetic Compound

Research Offers Hope for Better Treatments for Diabetes Patients

In a joint study, scientists from The Scripps Research Institute and Harvard University's Dana-Farber Cancer Institute have established a new class of anti-diabetic compound that targets a unique molecular switch.

The finding paves the way for the development of anti-diabetic therapeutics with minimal adverse side effects plaguing currently available drugs such as Avandia (rosiglitazone), scheduled to be removed from pharmacy shelves this fall due to concerns about increased risk of heart attack.

The new study, led by Patrick R. Griffin, professor and chair of the Department of Molecular Therapeutics at Scripps Florida, Bruce Spiegelman, professor of cell biology at the Dana-Farber Cancer Institute, and Theodore Kamenecka, associate scientific director of medicinal chemistry at Scripps Florida, was published September 4, 2011, in the journal *Nature*. The study describes a new compound known as SR1664.

"In this study, we demonstrate that we have discovered novel compounds that work effectively through a unique mechanism of action on a well-validated clinical target for diabetes," said Griffin. "This unique mechanism of action appears to significantly limit side effects associated with marketed drugs. This study is a great example of interdisciplinary, inter-institutional collaboration with chemistry, biochemistry, structural biology, and pharmacology."

"It appears that we may have an opportunity to develop entire new classes of drugs for diabetes and perhaps other metabolic disorders," said Spiegelman.

Diabetes affects nearly 24 million children and adults in the United States, according to the America Diabetes Association.

A Viable Therapeutic Target

The study follows previous research by the authors published last year in Nature (Volume 466, Issue 7305, 451-456) that suggested an obesity-linked mechanism that may be involved in the development of insulin-resistance. In that research, the team found disruptions in various genes when a protein known as PPARγ undergoes phosphorylation (when a phosphate group is added to a protein) by the kinase Cdk5, an enzyme involved in a number of important sensory pathways.

The new study confirms that blockage of Cdk5's action on PPARG is a viable therapeutic approach for development of anti-diabetic agents. The new SR1664 compound is a potent binder to the nuclear receptor PPARG, but does not activate gene transcription via the receptor's normal mechanism.

While Griffin stressed the difficulty of fully assessing side effects of new compounds such as

SR1664, the new research is extremely positive in that it clearly demonstrated fewer of the major well-documented side effects, such as weight gain or increased plasma volume, from SR1664 as compared to Avandia in diabetic mice.

While both the mice treated with Avandia and those treated with SR1664 demonstrated improved blood sugar levels, those treated with Avandia showed weight gain and increased fluid retention within a few days of beginning treatment; those being treated with SR1664 showed none of these side effects. In cell culture studies, SR1664 also appeared to have little effect on bone formation, nor did it increase fat generation in bone cells, another side effect of current therapies such as Avandia.

While S1664 likely will not be developed as a drug, it now serves as a molecular scaffolding for the creation of similar compounds with potential to treat diabetes. "With data in hand showing that our compounds are as efficacious as the currently marketed PPARG modulators, while demonstrating a significant improvement of side effects in limited studies, we are now advancing newer compounds with improved pharmaceutical properties into additional studies," Griffin said.

The first authors, denoted as equal contributors to this study, "Anti-Diabetic Actions of a Non-Agonist PPARG Ligand Blocking Cdk5-Mediated Phosphorylation," are Jang Hyun Choi and Alexander S. Banks of Dana-Farber Cancer Institute and Theodore M. Kamenecka and Scott A. Busby of The Scripps Research Institute. Other authors include Michael J. Chalmers, Naresh Kumar, Dana S. Kuruvilla, Youseung Shin, Yuanjun He, David Marciano, and Michael D. Cameron of Scripps Research; Dina Laznik of the Dana-Farber Cancer Institute; Michael J. Jurczak and Gerald I. Shulman of the Howard Hughes Medical Institute; Stephan C. Schürer and Dušica Vidović of the University of Miami; and John B. Bruning of Texas A&M University.

The study was supported by The National Institutes of Health.

Scripps Research Scientists Pinpoint Shape-Shifting Mechanism Critical to Protein Signaling

Findings Show How Form Controls Function in Sought-After Therapeutic Target

In a joint study, scientists from the California and Florida campuses of The Scripps Research Institute have shown that changes in a protein's structure can change its signaling function and they have pinpointed the precise regions where those changes take place.

The new findings could help provide a much clearer picture of potential drugs that would be both effective and highly specific in their biological actions.

The study, led by Patrick Griffin of Scripps Florida and Raymond Stevens of Scripps California, was published in a recent edition of the journal *Structure*.

The new study focuses on the β2-adrenergic receptor, a member of the G protein-coupled receptor family. G protein-coupled receptors convert extracellular stimuli into intracellular

signals through various pathways. Approximately one third of currently marketed drugs (including for diabetes and heart disease) target these receptors.

Scientists have known that when specific regions of the receptor are activated by neurotransmitters or hormones, the structural arrangement (conformation) of the receptor is changed along with its function.

"While it's accepted that these receptors adopt multiple conformations and that each conformation triggers a specific type of signaling, the molecular mechanism behind that flexibility has been something of a black box," said Griffin, who is chair of the Scripps Research Department of Molecular Therapeutics and director of the Scripps Florida Translational Research Institute. "Our findings shed significant light to it."

The study describes in structural detail the various regions of the receptor that are involved in the changes brought about by selective ligands (ligands are molecules that bind to proteins to form an active complex), which, like a rheostat, run the gamut among activating the receptor, shutting it down, and reversing its function, as well as producing various states in between.

To achieve the results described in the study, the team used hydrogen-deuterium (HDX) mass spectrometry to measure the impact of interaction of various functionally selective ligands with the β2-adrenergic receptor. A mass spectrometer determines the mass of fragments from the receptor by measuring the mass-to-charge ratio of their ions. HDX has been used to examine changes in the shape of proteins and how these shape changes relate to protein function. The approach is often used to characterize protein-protein interactions that are critical for signal transduction in cells and to study protein-folding pathways that are critical to cell survival.

"At this early stage in understanding GPCR structure and function, it is important to view the entire receptor in combination with probing very specific regions," said Stevens, who is a professor in the Scripps Research Department of Molecular Biology. "Hydrogen-deuterium exchange mass spectrometry has the right timescale and resolution to asked important questions about complete receptor conformations in regards to different pharmacological ligand binding. The HDX data combined with the structural data emerging will really help everyone more fully understand how these receptors work."

"Using the HDX technology we can study the intact receptor upon interaction with ligands and pinpoint regions of the receptor that have undergone change in position or flexibility," Griffin said. "By studying a set of ligands one can start to develop patterns that are tied to activation of the receptor or shutting it down. Once we get a picture of what a functional ligand looks like, it might be possible to develop a drug to produce a highly selective therapeutic effect."

The lead author of the study, "Ligand-Dependent Perturbation of the Conformational Ensemble for the GPCR b2 Adrenergic Receptor Revealed by HDX," is Graham M. West of Scripps Research. Other authors include Ellen Y.T. Chien, Jovylyn Gatchalian, and Michael J. Chalmers of Scripps Research, and Vsevolod Katritch of the University of California, San Diego.

The study was supported by the National Institutes of Health.

Scripps Research Scientists Develop Brand New Class of Small Molecules through Innovative Chemistry

Novel Approach Could Greatly Expand, Accelerate Drug Discovery Process

Inspired by natural products, scientists on the Florida campus of The Scripps Research Institute have created a new class of small molecules with the potential to serve as a rich foundation for drug discovery.

Combining the power of synthetic chemistry with some advanced screening technologies, the new approach could eventually expand by millions the number of provocative synthetic compounds available to explore as potential drug candidates. This approach overcomes substantial molecular limitations associated with state-of-the-art approaches in small molecule synthesis and screening, which often serve as the foundation of current drug discovery efforts.

The study, led by Scripps Research Associate Professor Glenn Micalizio, was published November 20, 2011, in an advanced online edition of the journal *Nature Chemistry*.

To frame the significance of this advance, Micalizio explains that high-throughput screening is an important component of modern drug discovery. In high-throughput screening, diverse collections of molecules are evaluated en masse for potential function in a biological area of interest. In this process, success is critically dependent on the composition of the molecular collections under evaluation. Modern screening centers maintain a relatively static collection of molecules, the majority of which are commercially available materials that have structures unrelated to natural products—molecules that are appreciated as validated leads for drug development.

"This divergence in structure between natural products and commercially available synthetics lies at the heart of our inquiry," said Micalizio. "Why should we limit discovery of therapeutic leads to compound collections that are influenced by concerns relating to commercial availability and compatibility with an artificial set of constraints associated with the structure of modern screening centers?"

To expand the compounds available for investigation, the scientists embraced an approach to structural diversity that mimics nature's engine for the discovery of molecules with biological function. This process, termed "oligomerization," is a modular means of assembling structures (akin to the way that letters are used in a sequence to provide words with meaning) where a small collection of monomeric units can deliver a vast collection of oligomeric products of varying length, structure, and function (like the diversity of words presented in a dictionary).

Coupling this technique with a synthetic design aimed at generating molecules that boast molecular features inspired by the structures of bioactive natural products (specifically, polyketide-derived natural products, which include erythromycin, FK-506, and epothilone), the scientists established a new chemical platform for the discovery of potential therapeutics.

Micalizio points out: "The importance of oligomerization to drive discovery is well appreciated in chemistry and biology, yet a means to realize this process as an entry to small molecule natural product-inspired structures has remained elusive. The crux of the problem is related to challenges associated with the control of shape for each member of a complex oligomer collection—the central molecular feature that defines biological function."

"It is the stability associated with the shape of these new compounds that lies at the heart of the practical advance," he continued. "The unique features of this science now make possible the ability to synthesize large collections of diverse natural product-inspired structures that have predictable and stable three-dimensional shapes."

Micalizio said that the science described represents a first step toward revolutionizing discovery at the interface of chemistry, biology, and medicine by embracing nature's strategy for molecular discovery. Coupling this type of advance with modern screening technology that can handle the evaluation of large compound collections at low cost (such as work by Scripps Florida Professor Thomas Kodadek, a co-author of the new study), can dramatically enhance the future of pharmaceutically relevant science.

The potential of this vision was highlighted in the new study, in which a 160,000-member compound collection was employed to discover the first non-covalent small molecule ligand to the DNA binding domain of p53—an important transcription factor that regulates a variety of genes involved in cell cycle control and cell death.

The first author of the study, "A Biomimetic Polyketide-Inspired Approach to Small-Molecule Ligand Discovery," is Claudio Aquino of Scripps Research. In addition to Micalizio and Kodadek, other authors include Mohosin Sarkar, Michael J. Chalmers, and Kimberly Mendes.

The study was supported by the Fidelity Biosciences Research Initiative, The State of Florida (The Florida Funding Corporation), and the National Institutes of Health.

Scripps Research Scientists Uncover New Role for Gene in Maintaining Steady Weight

The Findings May Help Scientists Combat Obesity and Diabetes

Against the backdrop of the growing epidemic of obesity in the United States, scientists from the Florida campus of The Scripps Research Institute have made an important new discovery regarding a specific gene that plays an important role in keeping a steady balance between our food intake and energy expenditure. The study may help scientists better understand the keys to fighting obesity and related disorders such as diabetes.

The study, which was published in the November 25, 2011 print edition of *The Journal of Biological Chemistry*, focused on the melanocortin-3 receptor (MC3R), which normally responds to signals of nutrient intake.

"What we discovered was quite a surprise," said Scripps Research Associate Professor Andrew Butler, who led the study. "We thought that the actions of the receptor expressed in the brain would be critical for metabolic homeostasis. However, what we found is that actions of the receptor expressed outside the brain appear to be equally important."

The existence of drug targets in areas outside of the central nervous system (the body's "periphery") might help in the effort to develop drugs that influence metabolism without major side effects, Butler said.

The findings were made possible by the team's development of a new transgenic animal model, where expression of the MC3R gene can be selectively "switched on" in different cell types.

In the study, the suppression of MC3R expression in the brain and peripheral tissues had a marked impact on metabolic homeostasis (equilibrium). Interestingly, mice expressing the MC3R gene in the brain only displayed an obese phenotype (physical appearance) similar to those where all types of expression was suppressed, indicating that actions of this receptor in the brain are not sufficient to protect against weight gain. The finding that loss of MC3R activity in the periphery impairs metabolic homeostasis is startling, Butler said, and point to a distinct role for MC3R signaling in the peripheral tissues. However, how the actions of these receptors impacts on obesity remains to be determined.

"It's clear that these peripheral receptors are important and the new mouse model will let us explore that potential," Butler said.

The first author of the study, "Genetic dissection of melanocortin-3 receptor function suggests roles for central and peripheral receptors in energy homeostasis," is Karima Begriche of Scripps Research. In addition to Butler and Begriche, other authors include Jari Rossi, Danielle Skorupa, Laura A. Solt, Brandon Young, and Thomas P. Burris from The Scripps Research Institute in Florida; Randall L. Mynatt and Jingying Zhang at the Pennington Biomedical Research Center, which is part of the Louisiana State University System; and Peter R. Levasseur and Daniel L. Marks at the Oregon Health & Science University. See http://www.jbc.org/content/early/2011/10/07/jbc.M111.278374.abstract?sid=8a17ce75-de95-45d1-b688-a039da52b5f1

The study was supported by National Institutes of Health and the Pennington Biomedical Research Foundation.

Scripps Research Scientists Elevate Little-Studied Cellular Mechanism to Potential Drug Target

For years, science has generally considered the phosphorylation of proteins—the insertion of a phosphorous group into a protein that turns it on or off—as perhaps the factor regulating a range of cellular processes from cell metabolism to programmed cell death. Now, scientists from the Florida campus of The Scripps Research Institute have identified the importance of a novel

protein-regulating mechanism—called sulfenylation—that is similar to phosphorylation and may, in fact, open up opportunities to develop new types of drugs for diseases such as cancer.

The study was published December 11, 2011, in an advance online edition of the journal *Nature Chemical Biology*.

"With this paper, we've elevated protein sulfenylation from a marker of oxidative stress to a bona fide reversible post translational modification that plays a key regulatory role during cell signaling," said Kate Carroll, a Scripps Research associate professor who led the study. "The sulfenyl modification is the new kid on the block."

During periods of cellular stress, caused by factors such as exposure to UV radiation or chronic disease states like cancer, the level of highly reactive oxygen-containing molecules can increase, resulting in inappropriate modification of proteins and cell damage. In sulfenylation, one oxidant, hydrogen peroxide, functions as a messenger that can activate cell proliferation through oxidation of cysteine residues in signaling proteins, producing sulfenic acid. Cysteine, an amino acid (natural protein building block), is highly oxidant sensitive.

Conventional wisdom has long held that if hydrogen peroxide does exist in the cell at any appreciable level, it represents a disease state, not a regulatory event. The new study shows that sulfenylation is actually a positive protein modification, and that it's required for signaling through the pathway, a validation of a long-held belief in some scientific circles that hydrogen peroxide functions as a general signaling molecule, not an oxidative "bad boy" to be eliminated at all costs.

A New Chemical Probe

To explore the process, Carroll and her colleagues developed a highly selective chemical probe—known as DYn-2—with the ability to detect minute differences in sulfenylation rates within the cell.

With the new probe, the team was able to show that a key signaling protein, epidermal growth factor receptor (EGFR), is directly modified by hydrogen peroxide at a critical active site cysteine, stimulating its tyrosine kinase activity.

The technology described in the new paper is unique, Carroll said, because it allows scientists to trap and detect these modifications in situ, without interfering with the redox balance of the cell. "Probing cysteine oxidation in a cell lysate is like looking for a needle in a haystack," she said, "our new approach preserves labile sulfenyl modifications and avoids protein oxidation artifacts that arise during cell homogenization."

As with phosphorylation, future studies on sulfenylation will delve into the exciting discovery of new enzymes, new signaling processes, and new mechanisms of regulation.

Another broad impact of these findings, Carroll said, is to open up an entirely new mechanism to exploit for the development of therapeutics, particularly in cancer. "It should influence the design of inhibitors that target oxidant-sensitive cysteine residues in the future," she said.

The first author of the study, "Peroxide-dependent Sulfenylation of the EGFR Catalytic Site Enhances Kinase Activity," is Candice E. Paulsen of the University of Michigan. Other authors include Thu H. Truong and Stephen E. Leonard of the University of Michigan; and Francisco J. Garcia, Arne Homann and Vinayak Gupta of Scripps Research.

The study was supported by the Camille Henry Dreyfus Teacher Scholar Award and the American Heart Association.

Scripps Research Scientists Paint New Picture of Dance Between Protein and Binding Partners

New Findings Could Influence Design of Future Diabetes Treatments

Using a blend of technologies, scientists from the Florida campus of The Scripps Research Institute have painted a new picture of how biochemical information can be transmitted through the modification of a protein.

Previously, scientists believed that during the pairing of proteins and their binding partners ("ligands"), proteins modified their shape while ligands remained stable. The new study shows this one-size-fits-all solution is not entirely accurate.

Instead, the situation resembles a kind of complex but carefully organized dance routine, where the ligand samples a variety of binding modes while the protein also modifies its shape, a process that results in their pairing and changes in the protein critical for its function.

These new findings, published in the January 11, 2012 edition of the journal *Structure*, could affect future drug design.

"Using a multidisciplinary approach, we gleaned something from our data that no one else has," said Douglas Kojetin, an assistant professor on the Scripps Florida campus who led the study. "The conventional wisdom is that ligands bind in one orientation but our study shows that they can bind in multiple modes. That means if we can optimize a ligand to bind in mode B rather than mode A, we might be able to select the therapeutic results we want."

The new study—which used a number of complementary technologies including NMR spectroscopy and hydrogen/deuterium exchange (HDX) coupled to mass spectrometery, combined with previous x-ray crystallography analyses—provides detailed insights into the real-time actions of molecules that could never be determined with a single technology.

Specifically, the researchers revealed insights into ligand and receptor dynamics in the nuclear receptor known as PPARγ (peroxisome-proliferator-activated receptor). PPARγ has been implicated in metabolic diseases including obesity, diabetes, and atherosclerosis.

The study also found that various gradations in these ligands influence the dynamics of this exchange, adding another layer of complexity. "One of the compounds, MRL24, binds to the receptor and has anti-diabetic efficacy, but doesn't activate it very well," Kojetin said. "This is what you want because when the receptor is activated you get side effects such as weight gain and brittle bones."

"This study in particular highlights the importance of multidisciplinary collaborative efforts to truly understand the molecular details of drug-receptor interactions", says Kojetin. "This work is an excellent example of the strong campus collaborations we have with the laboratories of Patrick Griffin, Thomas Burris, and Theodore Kamenecka."

The first author of the study, "Ligand and Receptor Dynamics Contribute to the Mechanism of Graded PPAR γ Agonism," is Travis S. Hughes of Scripps Research. Other authors include Michael J. Chalmers, Scott Novick, Dana S. Kuruvilla, Mi Ra Chang, Theodore M. Kamenecka ,Thomas P. Burris, and Patrick R. Griffin of Scripps Research; Mark Rance of the University of Cincinnati; and Bruce A. Johnson of One Moon Scientific Inc.

The study was supported by the James and Esther King Biomedical Research Program, Florida Department of Health start up funds for Scripps Research, the National Institutes of Health, and the National Center for Research Resources.

Scripps Research Scientists Create Novel RNA Repair Technology

Discovery Could Aid Search for Huntington's, Spinocerebellar Ataxia, and Kennedy Disease Treatments

Scientists from the Florida campus of The Scripps Research Institute have identified a compound that can help repair a specific type of defect in RNA, a type of genetic material. The methods in the new study could accelerate the development of therapeutics to treat a variety of incurable diseases such as Huntington's disease, Spinocerebellar ataxia, and Kennedy disease.

The new study, published January 17, 2012 in an advance, online edition of the journal *ACS Chemical Biology*, describes a method to find compounds that target defective RNAs, specifically RNA that carries a structural motif known as an "expanded triplet repeat." The triplet repeat, a series of three nucleotides repeated many more times than normal in the genetic code of affected individuals, has been associated with a variety of neurological and neuromuscular disorders.

"For a long time it was thought that only the protein translated from this type of RNA was toxic," said Matthew Disney, an associate professor at Scripps Florida who led the new study. "But it has been shown recently that both the protein and the RNA are toxic. Our discovery of a

small molecule that binds to RNA and shuts off its toxicity not only further demonstrates that the RNA is toxic but also opens up new avenues for therapeutic development because we have clearly demonstrated that small molecules can reverse this type of defect."

In the new research, the scientists used a query molecule called 4', 6-diamidino-2-phenylindole (DAPI) as a chemical and structural template to find similar but more active compounds to inhibit a toxic CAG triplet repeat. One of these compounds was then found effective in inhibiting the RNS toxicity of the repeat in patient-derived cells, which demonstrated an improvement in early-stage abnormalities.

"The toxic RNA defect actually sucks up other proteins that play critical roles in RNA processing, and that is what contributes to these various diseases," Disney said. "Our new compound targets the toxic RNA and inhibits protein binding, shutting off the toxicity. Since the development of drugs that target RNA is extremely challenging, these studies can open up new avenues to exploit RNA drug targets that cause a host of other RNA-mediated diseases." Disney and his colleagues are already hard at work to extend the lab's findings.

The lead author of the study, "Chemical Correction of Pre-mRNA Splicing Defects Associated with Sequestration of Muscleblind-Like 1 Protein by Expanded r(CAG)-containing Transcripts," is Amit Kumar of Scripps Research. Other authors include Raman Parkesh and Jessica Childs-Disney of Scripps Research, and Lukasz J. Sznajder and Krzysztof Sobczak of Adam Mickiewicz University, Poland. For more information, see http://pubs.acs.org/doi/abs/10.1021/cb200413a

The study was supported by the National Institutes of Health and the Polish Ministry of Science and Higher Education, Camille & Henry Dreyfus Foundation, and the Research Corporation for Science Advancement.

An Intriguing Combination in the Brain May Modify Our Appetites, Alter Other Key Processes

Finding Paves the Way for New Therapies

The interaction between a disparate pair of brain proteins may have a profound effect on the regulation of appetite, according to a new study by scientists from the Florida campus of The Scripps Research Institute. The complex partnership may also have an impact on other signaling pathways linked to neuropsychiatric disorders as wide-ranging as Parkinson's disease, schizophrenia, and addiction.

"Our findings provide new insights into the way the body regulates appetite and other processes," said Roy G. Smith, chair of the Scripps Research Department of Metabolism and Aging, who authored the new study with Staff Scientist Andras Kern and other Scripps Research colleagues. "The work provides exciting opportunities for designing next generation therapeutics with fewer side effects for both obesity and psychiatric disorders associated with abnormal dopamine signaling."

The study, published in the most recent issue of the journal *Neuron*, reveals a fascinating partnership within the brain neurons that regulate appetite, a unique complex of hormone and neurotransmitter receptors that no one suspected existed before the new research.

One of these is the receptor for ghrelin (GHSR1a), a small peptide hormone that is produced mainly in the stomach. As an evolutionary warning signal that promotes weight gain and fat during periods of weight loss, ghrelin can be blamed for the failure of most modern diets. The other key player is the dopamine receptor known as subtype-2 (DRD2), part of the dopamine signaling pathway. Dopamine is a neurotransmitter that plays a key role in the brain's reward centers, and can lead to pleasure producing behavior, such as drug abuse and overeating.

The study identifies this twin receptor complex, which is naturally present in the brain's neurons that regulate appetite, and sheds light on its role in modifying dopamine signaling. "We were able to show there are subsets of brain neurons that express both the ghrelin receptor and the dopamine receptor subtype-2," Smith said.

The study went on to show that when these two receptors are co-expressed, the receptors physically interact with each other, which leads to an alteration of dopamine signaling. And when mice were treated with a molecule (cabergoline) that selectively activates the dopamine receptor, they lost weight. Interestingly, cabergoline-stimulated weight loss did not require ghrelin, but was dependent on the receptor for ghrelin and its interaction with the dopamine receptor.

In addition, cabergoline blocked dopamine signaling only for the complex—a fact that Smith finds promising. "This allows for neuronal selective fine-tuning of dopamine signaling because neurons expressing only the dopamine receptor will be unaffected," he said.

In addition to Smith and Kern, authors of the paper, "Apo-Ghrelin Receptor forms Heteromers with DRD2 in Hypothalamic Neurons and is Essential for Anorexigenic Effects of DRD2 Agonism," are Rosie Albarran-Zeckler and Heidi E. Walsh of Scripps Research. For more information, see http://www.cell.com/neuron/fulltext/S0896-6273(11)01087-7

The study was supported by The National Institutes of Health.

Scripps Research Scientists Identify Most Lethal Known Species of Prion Protein

Findings Suggest New View of "Mad Cow" and Other Neurodegenerative Diseases

Scientists from the Florida campus of The Scripps Research Institute have identified a single prion protein that causes neuronal death similar to that seen in "mad cow" disease, but is at least 10 times more lethal than larger prion species.

This toxic single molecule or "monomer" challenges the prevailing concept that neuronal damage is linked to the toxicity of prion protein aggregates called "oligomers."

The study was published this week in an advance, online edition of the journal *Proceedings of the National Academy of Sciences*.

"By identifying a single molecule as the most toxic species of prion proteins, we've opened a new chapter in understanding how prion-induced neurodegeneration occurs," said Scripps Florida Professor Corinne Lasmézas, who led the new study. "We didn't think we would find neuronal death from this toxic monomer so close to what normally happens in the disease state. Now we have a powerful tool to explore the mechanisms of neurodegeneration."

In the study, the newly identified toxic form of abnormal prion protein, known as TPrP, caused several forms of neuronal damage ranging from apoptosis (programmed cell death) to autophagy, the self-eating of cellular components, as well as molecular signatures remarkably similar to that observed in the brains of prion-infected animals. The study found the most toxic form of prion protein was a specific structure known as alpha-helical.

New Paths to Explore

In addition to the insights it offers into prion diseases such as "mad cow" and a rare human form Creutzfeldt-Jakob disease, the study opens the possibility that similar neurotoxic proteins might be involved in neurodegenerative disorders such as Alzheimer's and Parkinson diseases.

In prion disease, infectious prions (short for proteinaceous infectious particles), thought to be composed solely of protein, have the ability to reproduce, despite the fact that they lack DNA and RNA. Mammalian cells normally produce what is known as cellular prion protein or PrP; during infection with a prion disease, the abnormal or misfolded protein converts the normal host prion protein into its disease form.

Lasmézas explains that prion diseases are similar to Alzheimer's and other protein misfolding diseases in that they are caused by the toxicity of a misfolded host protein. Recent work, as reported in The New York Times, also found that diseases such as Alzheimer's resemble prion diseases by spreading from cell to cell.

The new study adds another twist. "Until now, it was thought that oligomers of proteins are toxic in all these diseases," Lasmézas said. "Since we found for the first time that an abnormally folded monomer is highly toxic, it opens up the possibility that this might be true also for some other protein misfolding diseases as well."

The first author of the study, "Highly Neurotoxic Monomeric α-Helical Prion Protein," is Minghai Zhou of Scripps Research. Other authors include Gregory Ottenberg and Gian Franco Sferrazza also of Scripps Research. For more information on the study, see http://www.pnas.org/content/early/2012/02/07/1118090109.abstract

The study was supported by the State of Florida.

Scripps Research Scientists Create Potent Molecules Aimed at Treating Muscular Dystrophy

The new approach could have implications for many genetic diseases

While RNA is an appealing drug target, small molecules that can actually affect its function have rarely been found. But now scientists from the Florida campus of The Scripps Research Institute have for the first time designed a series of small molecules that act against an RNA defect directly responsible for the most common form of adult-onset muscular dystrophy.

In two related studies published recently in online-before-print editions of *Journal of the American Chemical Society* and *ACS Chemical Biology*, the scientists show that these novel compounds significantly improve a number of biological defects associated with myotonic dystrophy type 1 in both cell culture and animal models.

"Our compounds attack the root cause of the disease and they improve defects in animal models," said Scripps Research Associate Professor Matthew Disney, PhD. "This represents a significant advance in rational design of compounds targeting RNA. The work not only opens up potential therapies for this type of muscular dystrophy, but also paves the way for RNA-targeted therapeutics in general."

Myotonic dystrophy type 1 involves a type of RNA defect known as a "triplet repeat," a series of three nucleotides repeated more times than normal in an individual's genetic code. In this case, the repetition of the cytosine-uracil-guanine (CUG) in RNA sequence leads to disease by binding to a particular protein, MBNL1, rendering it inactive. This results in a number of protein splicing abnormalities. Symptoms of this variable disease can include wasting of the muscles and other muscle problems, cataracts, heart defects, and hormone changes.

To find compounds that acted against the problematic RNA in the disease, Disney and his colleagues used information contained in an RNA motif-small molecule database that the group has been developing. By querying the database against the secondary structure of the triplet repeat that causes myotonic dystrophy type 1, a lead compound targeting this RNA was quickly identified. The lead compounds were then custom-assembled to target the expanded repeat or further optimized using computational chemistry. In animal models, one of these compounds improved protein-splicing defects by more than 40 percent.

"There are limitless RNA targets involved in disease; the question is how to find small molecules that bind to them," Disney said. "We've answered that question by rationally designing these compounds that target this RNA. There's no reason that other bioactive small molecules targeting other RNAs couldn't be developed using a similar approach."

The first authors of the JACS study, "Design of a Bioactive Small Molecule that Targets the Myotonic Dystrophy Type 1 RNA via an RNA Motif-Ligand Database & Chemical Similarity Searching" (http://pubs.acs.org/doi/abs/10.1021/ja210088v), are Raman Parkesh and Jessica Childs-Disney of Scripps Research. Other authors include Amit Kumar and Tuan Tran also of Scripps Research; Masayuki Nakamori, Jason Hoskins and Charles A. Thornton of the

University of Rochester; and Eric Wang, Thomas Wang and David Housman of the Massachusetts Institute of Technology. This study was supported by the National Institutes of Health, Scripps Research, the Camille & Henry Dreyfus Foundation, and the Research Corporation for Science Advancement.

The first author of the ACS Chemical Biology study, "Rationally Designed Small Molecules Targeting the RNA That Causes Myotonic Dystrophy Type 1 Are Potently Bioactive" (http://pubs.acs.org/doi/abs/10.1021/cb200408a) is Jessica L. Childs-Disney of Scripps Research. Other authors include Suzanne G. Rzuczek of Scripps Research and Jason Hoskins and Charles A. Thornton of the University of Rochester. This study was supported by the National Institutes of Health, the Muscular Dystrophy Association, Scripps Research, the Camille & Henry Dreyfus Foundation, and the Research Corporation for Science Advancement.

Scripps Florida Scientists Uncover Inflammatory Circuit That Triggers Breast Cancer

Findings Point to Potentially Effective New Therapeutic Target for Cancer Treatment and Prevention

Although it's widely accepted that inflammation is a critical underlying factor in a range of diseases, including the progression of cancer, little is known about its role when normal cells become tumor cells. Now, scientists from the Florida campus of The Scripps Research Institute have shed new light on exactly how the activation of a pair of inflammatory signaling pathways leads to the transformation of normal breast cells to cancer cells.

The study, led by Jun-Li Luo, an assistant professor at Scripps Florida, was published online before print by the journal *Molecular Cell* on February 23, 2012.

The scientists' discovery points to the activation of a self-sustaining signaling circuit that inhibits a specific RNA, a well-known tumor suppressor that helps limit the spread of cancer (metastasis). Therapies that disable this circuit and halt this miRNA repression could have the potential to treat cancer.

The Spark that Ignites Trouble

In the new study, scientists identified the specific pathways that transform breast epithelial cells into active cancer cells.

The researchers found immune/inflammatory cells ignite the transient activation of MEK/ERK and IKK/NF-kB pathways; the MEK/ERK pathway then directs a consistent activation of a signaling circuit in transformed cells. This consistent signaling circuit maintains the malignant state of the tumor cells.

Luo compares this process to starting a car—a car battery starts the engine much like the transient signal activation turns on the consistent signal circuit. Once the engine is started, it no longer needs the battery.

The scientists go on to show that the initial activation of these pathways also activates IL6, a cytokine involved in a number of inflammatory and autoimmune diseases, including cancer. IL6 acts as a tumor initiator, sparking the self-sustaining circuit in normal breast cells necessary for the initiation and maintenance of their transformed malignant state.

In establishing that self-sustaining signal circuit, IL6 represses the action of microRNA-200c, which is responsible for holding down inflammation and cell transformation. Since enhanced microRNA-200c expression impairs the growth of existing cancer cells and increases their sensitivity to anti-tumor drugs, compounds that disable microRNA-200c repression have the potential to act as a broad-spectrum therapeutic.

Interestingly, the new findings dovetail with the "multiple-hits theory" of tumor formation, which posits that once normal cells in the human body accumulate enough pre-cancerous mutations, they are at high-risk for transformation into tumor cells. While the newly described initial pathway activation is momentary and not enough to cause any lasting changes in cell behavior, it may be just enough to tip the cell's transformation to cancer, especially if it comes on top of an accumulation of other cellular changes.

The first author of the study, "IL6-Mediated Suppression of Mir-200c Directs Constitutive Activation of an Inflammatory Signaling Circuit That Drives Transformation and Tumorigenesis," is Matjaz Rokavec of Scripps Research. Other authors include Weilin Wu, also of Scripps Research.

The study was supported by the National Institute of Health, the United States Department of Defense, the Florida Department of Health, and Frenchman's Creek Women for Cancer Research.

Scripps Research Institute Scientists Create Compounds that Dramatically Alter Biological Clock and Lead to Weight Loss

The New Molecules Could Lead to Unique Treatments for Obesity, Diabetes, High Cholesterol, and Sleep Disorders

Scientists from the Florida campus of The Scripps Research Institute have synthesized a pair of small molecules that dramatically alter the core biological clock in animal models, highlighting the compounds' potential effectiveness in treating a remarkable range of disorders—including obesity, diabetes, high cholesterol, and serious sleep disorders.

The study was published on March 29, 2012, in an advance, online edition of the journal *Nature*.

The study showed that when administered in animal models the synthetic small molecules altered circadian rhythm and the pattern of core clock gene expression in the brain's hypothalamus, the site of the master cellular clock that synchronizes daily rhythms in mammals; circadian rhythms are the physiological processes that respond to a 24-hour cycle of light and dark and are present in most living things.

When given to diet-induced obese mice, these same small molecules decreased obesity by reducing fat mass and markedly improving cholesterol levels and hyperglycemia—chronically high blood sugar levels that frequently lead to diabetes.

"The idea behind this research is that our circadian rhythms are coupled with metabolic processes and that you can modulate them pharmacologically," said Thomas Burris, a professor at Scripps Florida who led the study. "As it turns out, the effect of that modulation is surprisingly positive—everything has been beneficial so far."

Burris stressed that these compounds were first generation—the first to hit their targets in vivo with room for improvement as potential treatments. "In terms of therapeutics, this is really the first step," he said.

In the new study, the team identified and tested a pair of potent synthetic compounds that activate proteins called REV-ERBα and REV-ERBβ, which play an integral role in regulating the expression of core clock proteins that drive biological rhythms in activity and metabolism.

In the study, the scientists observed clear metabolic effects when the synthetic compounds were administered twice a day for 12 days. Animals displayed weight loss due to decreased fat mass with no changes in the amount of food they ate. The animals followed the human model of obesity closely, eating a standard Western diet of high fat, high sugar foods, yet still lost weight when given the compounds.

In one of the study's more striking findings, both synthetic compounds were shown to reduce cholesterol production. Cholesterol in the blood of treated animal models decreased 47 percent; triglycerides in the blood decreased 12 percent.

The circadian pattern of expression of a number of metabolic genes in the liver, skeletal muscle, and in fat tissue was also altered, resulting in increased energy expenditure, something of a surprise. In the study, the scientists observed a five percent increase in oxygen consumption, suggesting increased energy expenditure during the day and at night. However, these increases were not due to increased activity—the animals displayed an overall 15 percent decrease in movement during those same time periods.

In addition to its impact on metabolism, the two compounds also affected the animals' activity during periods of light and darkness, suggesting that this class of compound may be useful for the treatment of sleep disorders, including the common problem of jet lag.

The first authors of the study, "Regulation of Circadian Behavior and Metabolism by Synthetic REV-ERB Agonists," are Laura A. Solt and Yongjun Wang of Scripps Research. Other authors include Subhashis Banerjee, Travis Hughes, Douglas J. Kojetin, Thomas Lundasen, Youseung Shin, Jin Liu, Michael D. Cameron, Romain Noel, Andrew A. Butler, and Theodore M. Kamenecka of Scripps Research; and Seung-Hee Yoo and Joseph S. Takahashi of the Howard Hughes Medical Institute and University of Texas Southwestern Medical Center.

The study was supported by the National Institutes of Health and the Howard Hughes Medical Institute.

Scripps Florida Scientists Shed Light on Age-Related Memory Loss and Possible Treatments

Fruit Flies Offer Insights on Aging

Scientists from the Florida campus of The Scripps Research Institute have shown in animal models that the loss of memory that comes with aging is not necessarily a permanent thing.

In a new study published this week in an advance, online edition of the journal *Proceedings of the National Academy of Science*, Ron Davis, chair of the Department of Neuroscience at Scripps Florida, and Ayako Tonoki-Yamaguchi, a research associate in Davis's lab, took a close look at memory and memory traces in the brains of both young and old fruit flies.

What they found is that like other organisms—from mice to humans—there is a defect that occurs in memory with aging. In the case of the fruit fly, the ability to form memories lasting a few hours (intermediate-term memory) is lost due to age-related impairment of the function of certain neurons. Intriguingly, the scientists found that stimulating those same neurons can reverse these age-related memory defects.

"This study shows that once the appropriate neurons are identified in people, in principle at least, one could potentially develop drugs to hit those neurons and rescue those memories affected by the aging process," Davis said. "In addition, the biochemistry underlying memory formation in fruit flies is remarkably conserved with that in humans so that everything we learn about memory formation in flies is likely applicable to human memory and the disorders of human memory."

While no one really understands what is altered in the brain during the aging process, in the current study the scientists were able to use functional cellular imaging to monitor the changes in the fly's neuron activity before and after learning.

"We are able to peer down into the fly brain and see changes in the brain," Davis said. "We found changes that appear to reflect how intermediate-term memory is encoded in these neurons."

Olfactory memory, which was used by the scientists, is the most widely studied form of memory in fruit flies—basically pairing an odor with a mild electric shock. These tactics produce short-term memories that persist for around a half-hour, intermediate-term memory that lasts a few hours, and long-term memory that persists for days.

The team found that in aged animals, the signs of encoded memory were absent after a few hours. In that way, the scientists also learned exactly which neurons in the fly are altered by

aging to produce intermediate-term memory impairment. This advance, Davis notes, should greatly help scientists understand how aging alters neuronal function.

Intriguingly, the scientists took the work a step further and stimulated these neurons to see if the memory could be rescued. To do this, the scientists placed either cold-activated or heat-activated ion channels in the neurons known to become defective with aging and then used cold or heat to stimulate them. In both cases, the intermediate-term memory was successfully rescued.

The study, "Aging Impairs Intermediate-Term Behavioral Memory by Disrupting the Neuron Memory Trace," was supported by the Ellison Medical Foundation and the Japan Society for the Promotion of Science.

Scripps Florida Scientists Identify Neurotransmitters that Lead to Forgetting

While we often think of memory as a way of preserving the essential idea of who we are, little thought is given to the importance of forgetting to our wellbeing, whether what we forget belongs in the "horrible memories department" or just reflects the minutia of day-to-day living.

Despite the fact that forgetting is normal, exactly how we forget—the molecular, cellular, and brain circuit mechanisms underlying the process—is poorly understood.

Now, in a study that appears in the May 10, 2012 issue of the journal *Neuron*, scientists from the Florida campus of The Scripps Research Institute have pinpointed a mechanism that is essential for forming memories in the first place and, as it turns out, is equally essential for eliminating them after memories have formed.

"This study focuses on the molecular biology of active forgetting," said Ron Davis, chair of the Scripps Research Department of Neuroscience who led the project. "Until now, the basic thought has been that forgetting is mostly a passive process. Our findings make clear that forgetting is an active process that is probably regulated."

The Two Faces of Dopamine

To better understand the mechanisms for forgetting, Davis and his colleagues studied Drosophila or fruit flies, a key model for studying memory that has been found to be highly applicable to humans. The flies were put in situations where they learned that certain smells were associated with either a positive reinforcement like food or a negative one, such as a mild electric shock. The scientists then observed changes in the flies' brains as they remembered or forgot the new information.

The results showed that a small subset of dopamine neurons actively regulate the acquisition of memories and the forgetting of these memories after learning, using a pair of dopamine receptors in the brain. Dopamine is a neurotransmitter that plays an important role in a number of processes including punishment and reward, memory, learning and cognition.

But how can a single neurotransmitter, dopamine, have two seemingly opposite roles in both forming and eliminating memories? And how can these two dopamine receptors serve acquiring memory on the one hand, and forgetting on the other?

The study suggests that when a new memory is first formed, there also exists an active, dopamine-based forgetting mechanism—ongoing dopamine neuron activity—that begins to erase those memories unless some importance is attached to them, a process known as consolidation that may shield important memories from the dopamine-driven forgetting process.

The study shows that specific neurons in the brain release dopamine to two different receptors known as dDA1 and DAMB, located on what are called mushroom bodies because of their shape; these densely packed networks of neurons are vital for memory and learning in insects. The study found the dDA1 receptor is responsible for memory acquisition, while DAMB is required for forgetting.

When dopamine neurons begin the signaling process, the dDA1 receptor becomes overstimulated and begins to form memories, an essential part of memory acquisition. Once that memory is acquired, however, these same dopamine neurons continue signaling. Except this time, the signal goes through the DAMB receptor, which triggers forgetting of those recently acquired, but not yet consolidated, memories.

Jacob Berry, a graduate student in the Davis lab who led the experimentation, showed that inhibiting the dopamine signaling after learning enhanced the flies' memory.

Hyperactivating those same neurons after learning erased memory. And, a mutation in one of the receptors, dDA1, produced flies unable to learn, while a mutation in the other, DAMB, blocked forgetting.

Intriguing Issues

While Davis was surprised by the mechanisms the study uncovered, he was not surprised that forgetting is an active process. "Biology isn't designed to do things in a passive way," he said. "There are active pathways for constructing things, and active ones for degrading things. Why should forgetting be any different?"

The study also brings into a focus a lot of intriguing issues, Davis said—savant syndrome, for example.

"Savants have a high capacity for memory in some specialized areas," he said. "But maybe it isn't memory that gives them this capacity, maybe they have a bad forgetting mechanism. This also might be a strategy for developing drugs to promote cognition and memory—what about drugs that inhibit forgetting as cognitive enhancers?"

In addition to Davis and Berry, authors of the paper "Dopamine is required for Learning and Forgetting in Drosophila" include Isaac Cervantes-Sandoval and Eric P. Nicholas, also of Scripps Research. See http://www.cell.com/neuron/abstract/S0896-6273(12)00338-8

The study was supported by the National Institutes of Health.

Scripps Florida Scientists Identify New Molecules Important for Vision and Brain Function

In a pair of related studies, scientists from the Florida campus of The Scripps Research Institute have identified several proteins that help regulate cells' response to light—and the development of night blindness, a rare disease that abolishes the ability to see in dim light.

In the new studies, published recently in the journals *Proceedings of the National Academy of Sciences* (*PNAS*) and *The Journal of Cell Biology*, Scripps Florida scientists were able to show that a family of proteins known as Regulator of G protein Signaling (RGS) proteins plays an essential role in vision in a dim-light environment.

"We were looking at the fundamental mechanisms that shape our light sensation," said Kirill Martemyanov, a Scripps Research associate professor who led the studies. "In the process, we discovered a pair of molecules that are indispensible for our vision and possibly play critical roles in the brain."

In the *PNAS* study, Martemyanov and his colleagues identified a pair of regulator proteins known as RGS7 and RGS11 that are present specifically in the main relay neurons of the retina called the ON-bipolar cells.

"The ON-bipolar cells provide an essential link between the retinal light detectors—photoreceptors and the neurons that send visual information to the brain," explained Martemyanov. "Stimulation with light excites these neurons by opening the channel that is normally kept shut by the G proteins in the dark. RGS7 and RGS11 facilitate the G protein inactivation, thus promoting the opening of the channel and allowing the ON-bipolar cells to transmit the light signal. It really takes a combined effort of two RGS proteins to help the light overcome the barrier for propagating the excitation that makes our dim vision possible."

In the *Journal of Cell Biology* study, Martemyanov and his colleagues unraveled another key aspect of the RGS7/RGS11 regulatory response—they identified a previously unknown pair of orphan G protein-coupled receptors (GPCRs) that interact with these RGS proteins and dictate their biological function.

GPCRs are a large family of more than 700 proteins, which sit in the cell membrane and sense various molecules outside the cell, including odors, hormones, neurotransmitters, and light. After binding these molecules, GPCRs trigger the appropriate response inside the cell. However, for many GPCRs the activating molecules have not yet been identified and these are called "orphan" receptors.

The Martemyanov group has found that two orphan GPCRs—GPR158 and GPR179—recruit RGS proteins and thus help serve as brakes for the conventional GPCR signaling rather than play an active signaling role.

In the case of retinal ON-bipolar cells, GPR179 is required for the correct localization of RGS7 and RGS11. Their mistargeting in animal models lacking GPR179 or human patients with mutations in the GPR179 gene may account for their night blindness, according to the new study. Intriguingly, in the brain GPR158 appears to play a similar role in localizing RGS proteins, but instead of contributing to vision, it helps RGS proteins regulate the m-opioid receptor, a GPCRs that mediates pleasurable and pain-killing effects of opioids.

"We are really in the very beginning of unraveling this new biology and understanding the role of discovered orphan GPR158/179 in regulation of neurotransmitter signaling in the brain and retina," Martemyanov said. "The hope is that better understanding of these new molecules will lead to the design of better treatments for addictive disorders, pain, and blindness."

The first author of the May 15, 2012 *PNAS* study, "Regulators of G Protein Signaling RGS7 and RGS11 Determine the Onset of the Light Response in ON Bipolar Neurons" is Yan Cao of The Scripps Research Institute. Other authors include Johan Pahlberg and Alapakkam P. Sampath of the University of Southern California; Ignacio Sarria of The Scripps Research Institute; and Naomi Kamasawa of the Max Planck Florida Institute. See
http://www.pnas.org/content/109/20/7905.long

The first author of the June 11, 2012 *Journal of Cell Biology* study, "GPR158/179 Regulate G Protein Signaling by Controlling Localization and Activity of the RGS7 Complexes" is Cesare Orlandi of The Scripps Research Institute. Other authors include Ekaterina Posokhova and Ikuo Masuho of The Scripps Research Institute and Thomas A. Ray, Nazarul Hasan, and Ronald G. Gregg of the University of Louisville, Kentucky. See
http://jcb.rupress.org/content/197/6/711.abstract

Both studies were supported by the National Institutes of Health. The *PNAS* study was also supported by the McKnight Endowment Fund for Neurosciences.

SCRIPPS FLORIDA ANNUAL REPORT
FOR THE YEAR ENDING JUNE 30, 2012

PART II – MILESTONES AND UPDATES FROM AGREEMENT SECTIONS

Part II of the annual report addresses the milestones and provides updates to specific components of the formal agreement, listed by agreement section.

Section 9.3 **Annual Report. Scripps (The Scripps Research Institute) shall prepare the Annual Report for Scripps Florida each year and deliver such Annual Report to Funding by August 31st of each year. The Annual Report shall include, but not be limited to, the following information:**

Section 9.3(a) **An accounting of the expenditures of Grant Funds for the twelve months ended June 30th of each year (the "Report Year" [as amended]) and financial commitments made by Scripps during the Report Year.**

Report of SFFC Grant Fund Cash Disbursements from October 1, 2011 to June 30, 2012.

Salaries & Benefits	$ 5,780,459
Supplies	$ 878,150
Scientific equipment	$ 2,173,226
External affairs & other program support	$ 1,443,561
Project commencement, facilities, administration and other capital expenditures	$ 3,700,140
Total	$ 13,975,536

The schedule reflects cash expenditures charged to the grant from the State of Florida from October 1, 2011 to June 30, 2012. The expense categories set forth above reflect those used by Scripps to report grant activity to grantors. This schedule includes: unpaid commitments; unspent grant funds received of $121,842,049; and expenditures funded by other sources.

Section 9.3(b) **Data regarding the activities and performance of Scripps Florida during such Report Year and detailing the progress of Scripps in meeting its Business Plan, including but not limited to:**

Section 9.3(b)i **Information on the number and salary level of jobs created by Scripps within Scripps Florida, including the number and salary level of jobs created for residents of Florida;**

On June 30, 2012, Scripps Florida employed 440 people. The breakdown of those employees is shown below.

Faculty – 41
Research Faculty – 9
Staff Scientists – 28
Research Associates – 160
Scientific Support – 96
Administrative Support – 106

Of the 440 employees hired, 181 were residents of Florida and 108 were residents of Palm Beach County. The average salary/range for those employees was:

Faculty – $89,315 - $412,547
Research Faculty – $108,867 - $215,363
Staff Scientists – $59,530 - $126,838
Research Associates – $38,496 - $78,042
Administrative Support – $53,490 average

Section 9.3(b)ii **A description of the status of the performance expectations set forth in Section 9.5 of this Agreement and the disbursement conditions set forth in Schedule 4.4(c) of this Agreement;**

See responses to Sections 9.5 and 4.4(c), below.

Section 9.3(b)iii **Information on positions and funds to be required to be committed for equipment for such positions by means of the next annual disbursement of Grant Funds;**

The budgets for Scripps Florida for the year ending September 30, 2013, and for the Grant Year Ended March 14, 2014, will be submitted to SFFC after approval by The Scripps Research Institute Board of Trustees. These budgets set forth all anticipated revenue and expenses for Scripps Florida for the stated fiscal periods. The equipment requirements for new positions will be incorporated into these budgets.

Fiscal year equipment reporting:

Approximately $2,173,226 of equipment – acquired with State grant funds – was purchased from October 1, 2011 through June 30, 2012. $590,715 of this amount was acquired between October 1, 2011 and January 31, 2012. In addition, $1,260,941 of equipment was purchased using non-state funds during the period from October 1, 2011 through June 30, 2012.

Equipment purchases acquired from Florida State grant funds from February 1, 2012 to June 30, 2012 totaled $1,582,511—of which $1,357,033 was acquired since the start of the ninth grant year March 15, 2012.

Section 9.3(b)iv **Commencing with the Annual Report for 2006 Report Year and ending with the Report Year after which Scripps has moved the Scripps Florida operations to its permanent facility and such facility is fully operational, a description of the status of Scripps' relocation to its second planned temporary facility and the progress of construction activities for its permanent facility, as described in the Business Plan, including a projected date for and status of Scripps' occupancy of its permanent facility.**

Scripps Florida officially opened its Permanent Facilities in February of 2009.

Section 9.3(b)v **And commencing with the Annual Report for the Report Year during which Scripps commences activities at its permanent facility, a description of the status of Scripps' activities in its permanent facility, including its educational and outreach programs.**

Over the past eight years (since 2004) Scripps Florida has placed considerable effort in community and education outreach programs. Palm Beach County K-12 students and teachers have participated in science education lessons and events designed and presented by Scripps Florida education outreach, graduate students, post doctoral fellows, faculty and staff researchers. The programs described in Sections 4.4(c)6 and 4.4(c)7 define the goals of Scripps Florida's K-12 education programs: to work directly with students and teachers, to help develop instructional materials, and to contribute to science literacy in Palm Beach County and the State of Florida. Scripps Florida has taken a leadership role in science education since its inception; presenting at state and national meetings such as National Science Teacher's Association, Florida State Department of Education, Florida Council of 100, State University System of Florida Board of Governors, STEM Florida and the Sunshine State Scholars. To date, more than twelve thousand students, teachers, and community members of Palm Beach County have participated in the Scripps Florida Education Outreach programs.

Scripps Florida community outreach has offered opportunities for the public to gain insight into cutting edge biomedical research while providing opportunities for Scripps Florida faculty and staff to respond to the social needs of Palm Beach County. Since 2004, Scripps Florida has hosted and/or participated in Community Outreach events that include

symposia on Alzheimer's disease, breakthroughs in cancer research, and current discoveries in drug development, just to name a few.

Following is a list of Scripps Florida Education and Community outreach activities from the past year:

Community Outreach	Date	Participants	Recipients/Event
Community Outreach	14-Jul-11	Roy Smith	Dr. Ivan Krisko, Jupiter Medical Center
Community Outreach	21-Jul-11	Alex Bruner	Loxahatchee Groves Landowners' Association Virtual Exploration
Community Outreach	28-Jul-11	Ron Davis, Gavin Rumbaugh, Damon Page, Kirill Martemyanov and Sathya Puthanveettil	JFK Medical Center, tour and dinner, Scripps
Community Outreach	16-Aug-11	Roy Smith	Jupiter Medical Center / NuVista Living Reception
Community Outreach	18-Aug-11	Paul Kenny	Interview with Norine Dworkin-McDaniel for article to appear in Lifescript.com
Community Outreach	18-Aug-11	Barbara Noble, Dr. Paul Kenny	Behavioral Health of the Palm Beaches site visit and meetings
Community Outreach	25-Aug-11	Dr. Phil LoGrasso, Barbara Noble	National Parkinson's Foundation, PBC Chapter - Overview of Scripps Florida and Scientific Presentation
Community Outreach	25-Aug-11	Ben Starling	Forum Club of the Palm Beaches
Community Outreach	25-Aug-11	Barbara Noble	Women's Cancer Awareness Days (WCAD) Executive Committee: Presentation of Cancer Research
Community Outreach	2-Sep-11	Paul Kenny	Interview with Charles Kim of Korean Television re: addiction article
Community Outreach	13-Sep-11	Harry Orf, Barbara Noble	Nova Southeastern University Biotechnology campus grand opening
Community Outreach	15-Sep-11	Barbara Noble	South Florida Business Journal 2011 Most Influential Women luncheon, Ft. Lauderdale
Community Outreach	17-Sep-11	Barbara Noble	PBC Business Development Board Annual Dinner
Community Outreach	19-Sep-11	Alicia F. Brantley	Literacy Coalition of PB County Great Grown-up Spelling Bee.
Community Outreach	21-Sep-11	Dr. John Cleveland, Barbara Noble	ThinkPINKkids of Wellington for Cancer Research
Community Outreach	22-Sep-11	Roy Smith	Dr. Ivan Krisko, Jupiter Medical Center
Community Outreach	23-Sep-11	Barbara Noble	Community Partnership Meeting; FPL Juno Beach
Community Outreach	1-Oct-11	Barbara Noble, Susan Rode	Fraternal Order of Eagles, Jupiter - charity night presentation
Community Outreach	3-Oct-11	Ben Starling, Barbara Noble, Lisa Huertas	Forum Club of the Palm Beaches
Community Outreach	12-Oct-11	Lisa Huertas	Kiwanis Club of the North Palm Beaches Virtual Exploration

Community Outreach	15-Oct-11	Susan Rode, Lisa Huertas, Barbara Noble, Deborah Leach-Scampavia	Scripps Florida booth at Jupiter Inlet Colony's inaugural KidFest at Roger Dean Stadium
Community Outreach	17-Oct-11	Ben Starling and Damon Page	Pundits of Palm Beach
Community Outreach	18-Oct-11	Alex Bruner	Palm Beach Gardens Library Virtual Exploration
Community Outreach	19-Oct-11	Roy Smith	Harris Bank Lecture, PGA National
Community Outreach	19-Oct-11	Dr. Roy Smith, Alex Bruner	Discussion on Wellness and Aging at PGA National
Community Outreach	27-Oct-11	Dr. Roy Smith, Dr. Paul Kenny	Future of Medicine Summit
Community Outreach	26-Oct-11	Donald Phinney	Meet with Dr. Michael Ellis, et al.
Community Outreach	27-Oct-11	Roy Smith	Palm Beach County Medical Conference
Community Outreach	27-Oct-11	Dr. John Cleveland	Science of Health, Community Outreach Event
Community Outreach	4-Nov-11	Alex Bruner	Urban Land Institute Virtual Exploration
Community Outreach	8-Nov-11	Dr. Derek Duckett	Accelerate Brain Cancer Cure Foundation and Rendina Family Presentation of Brain Cancer Research
Community Outreach	10-Nov-11	Ben Starling	Community Leaders Gathering
Community Outreach	13-Nov-11	Alex Bruner	Lakeridge Falls Community Virtual Exploration
Community Outreach	13-Nov-11	Richard A. Gephardt / Scripps Wide	The Scripps Research Institute 50th Anniversary Gathering
Community Outreach	14-Nov-11	Paul Kenny	Invited speaker Scripps Florida Council, Jupiter, FL
Community Outreach	15-Nov-11	Donald Phinney	Lunch with Scripps Florida Council
Community Outreach	16-Nov-11	Donald Phinney	Meet with Dr. Michael Ellis, George Cadwagan, et al.
Community Outreach	18-Nov-11	Alex Bruner	Loxahatchee Club Virtual Exploration
Community Outreach	28-Nov-11	Alex Bruner, Barbara Noble, Ben Starling	Forum Club of the Palm Beaches
Community Outreach	1-Dec-11	Dr. Katrin Karbstein, Dr. Antonio Amelio, Barbara Noble, Susan Rode	Women's Cancer Awareness Days (WCAD) Presentation of Cancer Research and Campus Tour
Community Outreach	1-Dec-11	Dr. Susana Valente	Front Lines of Hope Community Outreach Event
Community Outreach	8-Dec-11	Dr. Kirill Martemyanov	Mental Health Association of Palm Beach County Presentation of Addiction Research
Community Outreach	9-Dec-11	Alex Bruner	Community Virtual Exploration of Scripps Florida
Community Outreach	12-Dec-11	Ben Starling	Forum Club of the Palm Beaches
Community Outreach	12-Dec-11	Dr. Phil LoGrasso, Barbara Noble	National Parkinson's Foundation, South Palm Beach County Presentation of Parkinson's Research
Community Outreach	13-Dec-11	Barbara Noble	Palm Beach County Estate Planning Council annual meeting, Scripps FL overview and campus tour
Community Outreach	14-Dec-11	Charles Weissmann	Taras Lecture - Jupiter High School

Community Outreach	26-Dec-11	Roy Smith	Ira & Ronnie Levine and Mr. & Mrs. Harold Wilkinson, Prader Willi Syndrome
Community Outreach	4-Jan-12	John Cleveland	PGA's Women's Cancer Awareness Days fundraiser for Cancer Biology, kick-off presentation
Community Outreach	4-Jan-12	Dr. John Cleveland, Barbara Noble, Susan Rode	Scripps FL kick-off presentation for Womens Cancer Awareness Days Event
Community Outreach	6-Jan-12	Cristin Gavin, Lisa Huertas	Hatikvah North County Chapter of Hadassah, Memory Research
Community Outreach	8-Jan-12	Paul Kenny	Interview with Nasfim Haque of Outline Productions Co (UK) re: obesity
Community Outreach	10-Jan-12	Alex Bruner	Planned Giving Council of Palm Beach County, Meeting
Community Outreach	11-Jan-12	Dr. Brian Paegel, Dr. Harry Orf, Barbara Noble	Admiral's Cove Virtual Exploration, Overview of Scripps FL and Microfluidics in Research
Community Outreach	13-Jan-12	Dr. Roy Smith, Barbara Noble, Susan Rode	Prader Willi Syndrome research annual dinner
Community Outreach	13-Jan-12	Lisa Huertas	Community Virtual Exploration of Scripps Florida
Community Outreach	15-Jan-12	Barbara Noble	Frenchman's Creek Women for Cancer Research (FCWFCR) for Scripps FL - house tours
Community Outreach	16-Jan-12	Barbara Noble	Frenchman's Creek Women for Cancer Research (FCWFCR) for Scripps FL - tennis tourn
Community Outreach	17-Jan-12	Dr. Kendall Nettles, Barbara Noble	Frenchman's Creek Women for Cancer Research (FCWFCR) for Scripps FL - golf/luncheon
Community Outreach	19-Jan-12	Courtney Miller	Philanthropy Presentation
Community Outreach	19-Jan-12	Ron Davis, Courtney Miller, Alex Bruner	Morgan Stanley, Learning and Memory Research
Community Outreach	22-Jan-12	Alex Bruner	Temple Beth El Virtual Exploration
Community Outreach	23-Jan-12	Dr. Roy Smith, Alex Bruner	Ibis Golf and Country Club Virtual Exploration and Anti-Aging Research
Community Outreach	27-Jan-12	Barbara Noble, Dr. Patrick Griffin, Dr. Damon Page	Fraternal Order of Eagles FL Statewide leadership - meeting, overview and campus tour
Community Outreach	29-Jan-12	Paul Thompson	Fit for Scripps Women's Cancer Awareness Day 5K
Community Outreach	29-Jan-12	Dr. John Cleveland, Susan Rode	WCAD Fit for Scripps
Community Outreach	31-Jan-12	Lisa Huertas	Rotary Club of Jupiter/Palm Beach Gardens Virtual Exploration
Community Outreach	31-Jan-12	Barbara Noble, Susan Rode	WCAD Reception for Cancer Research
Community Outreach	2-Feb-12	Ronald L. Davis, Trina Kemp, Bindu Raveendra, Gavin Rumbaugh, Sathya Puthanveettil,	Front Lines of Hope - Moderator, Royal Poinciana Chapel, Palm Beach
Community Outreach	2-Feb-12	Barbara Noble, Susan Rode	WCAD Golf and Tennis Tournament for Cancer Research
Community Outreach	3-Feb-12	Donald Phinney	Meet with McCubbin family

Community Outreach	3-Feb-12	Paul Kenny	Invited speaker - Institute for Brain Potential Seminar, West Palm Beach, FL
Community Outreach	5-Feb-12	Barbara Noble, Dr. Laura Bohn	American Psychological Association, Florida meeting
Community Outreach	8-Feb-12	Lisa Huertas	Community Virtual Exploration of Scripps Florida
Community Outreach	8-Feb-12	Cristin Gavin, Alex Bruner	Devonshire at PGA National, Virtual Exploration and Memory Research
Community Outreach	11-Feb-12	John Cleveland, Howard Petrie, Jun-Li Luo and other people from the Cancer Biology Department	Audubon Society Volunteer Day
Community Outreach	15-Feb-12	Patricia McDonald	Frontlines of Hope - Presenter on Diabetes, Scripps, FL
Community Outreach	20-Feb-12	Paul Kenny	Invited speaker - Institute for Brain Potential Seminar, Ft. Lauderdale, FL
Community Outreach	22-Feb-12	Paul Kenny	Invited speaker - Institute for Brain Potential Seminar, Vero Beach, FL
Community Outreach	23-Feb-12	Paul Kenny	Interview with Johnny Holden of Irish Times Science Section
Community Outreach	24-Feb-12	Alex Bruner, Ben Starling	Forum Club of the Palm Beaches
Community Outreach	25-Feb-12	Barbara Noble, Dr. Laura Bohn	Caron Institute Annual dinner and meeting
Community Outreach	27-Feb-12	Barbara Noble	Frenchman's Creek External Affairs Committee - North County Annual Luncheon
Community Outreach	28-Feb-12	Gavin Rumbaugh, Courtney Miller	Philanthropy Event - Presentation at PNC Wealth Management, Vero Beach
Community Outreach	28-Feb-12	Dr. Gavin Rumbaugh, Barbara Noble	PNC Wealth Management Learning and Memory Research, Vero Beach
Community Outreach	28-Feb-12	Dr. Courtney Miller, Alex Bruner	Morgan Stanley, Learning and Memory Research
Community Outreach	29-Feb-12	Ron Davis, Gavin Rumbaugh, Sathya Puthanveettil	Rare Disease Day, Scripps
Community Outreach	3-Mar-12	Dr. Kendall Nettles, Alex Bruner	5th Annual W.B. Ingalls Prostate Cancer Seminar
Community Outreach	6-Mar-12	Dr. Ron Davis, Alex Bruner	BallenIsles Country Club Community Virtual Exploration and Learning and Memory Research
Community Outreach	7-Mar-12	Alex Bruner	Jones, Foster, Johnston & Stubbs Virtual Exploration
Community Outreach	8-Mar-12	Ron Davis	George Tokesky, Gilbert Brown and Paula Alderson from Hospice by the Sea, Scripps
Community Outreach	9-Mar-12	Alex Bruner	Community Virtual Exploration of Scripps Florida
Community Outreach	15-Mar-12	Ron Davis, Gavin Rumbaugh, Sathya Puthanveettil	Front Lines of Hope - Long Term Memory Presentation
Community Outreach	19-Mar-12	Paul Kenny	Invited speaker - Institute for Brain Potential Seminar, Coral Gables, FL

Community Outreach	20-Mar-12	Paul Kenny	Interview with Kathriona Devereaux and Philip Boucher Hayes re: documentary titled "What's Ireland Eating" for Ireland's Public Broadcaster RTE
Community Outreach	22-Mar-12	Dr. Michael Marletta	The Night of Science
Community Outreach	23-Mar-12	Alex Bruner, Barbara Noble, Ben Starling	Forum Club of the Palm Beaches
Community Outreach	25-Mar-12	Derek Duckett, Paul Thompson	Florida Brain Cancer 5K Accelerating the Cure
Community Outreach	28-Mar-12	Patricia McDonald	PNC Wealth Management/Presenter at the Science of Health Event, Royal Poinciana Chapel, Palm Beach, FL
Community Outreach	30-Mar-12	Paul Thompson	American Cancer Society Relay for Life
Community Outreach	30-Mar-12	Dr. Phil LoGrasso, Barbara Noble	National Parkinson's Foundation Conference for Patients and Caregivers, Palm Beach/Broward Counties, Keynote Speech
Community Outreach	10-Apr-12	Donald Phinney	Meet with Jeanne Loring and Barbara Noble
Community Outreach	10-Apr-12	Lisa Huertas	National Active and Retired Federal Employees Assoc., North Palm Beach Chapter Virtual Exploration
Community Outreach	11-Apr-12	Dr. Jeanne Loring, Barbara Noble	Women in Power Luncheon, PNC Wealth Management, Stem Cell Research, Vero Beach
Community Outreach	16-Apr-12	Dr. Roy Periana	Front Lines of Hope Community Outreach Event
Community Outreach	19-Apr-12	Alex Bruner	Planned Giving Council of Palm Beach County and East Coast Estate Planning Council, Joint Meeting
Community Outreach	20-Apr-12	Alex Bruner	Martin County Taxpayers Association Annual Dinner Virtual Exploration
Community Outreach	23-Apr-12	Briana Weiser, Lisa Huertas	P.E.O. International Virtual Exploration and Hepatitis C Research
Community Outreach	24-Apr-12	Paul Kenny	Interview with MORE Magazine
Community Outreach	24-Apr-12	Dr. Ron Davis, Ben Starling	Coleman Hogan Fund for Memory Research Event
Community Outreach	26-Apr-12	Dr. Patricia McDonald, Barbara Noble	PNC Wealth Management Diabetes and Obesity Research, Vero Beach
Community Outreach	26-Apr-12	Dr. Ron Davis	Friends of Neuroscience and Palm Beach County Medical Society Reception
Business Outreach	30-Apr-12	Barbara Noble, Ben Starling	Forum Club of the Palm Beaches
Community Outreach	5-May-12	Dr. William Roush, Dr. Glenn Micalizio	Scripps Chemistry Symposium
Community Outreach	10-May-12	Donald Phinney	Invited speaker Columbia Alum Stem Cell Event, West Palm Beach, FL
Community Outreach	11-May-12	John Cleveland, Jun-Li Luo, Barbara Noble	ThinkPINKkids of Wellington for Cancer Research Walk
Community Outreach	14-May-12	Damon Page	Pundits, Guest Speaker, City Place Marriott, West Palm Beach, FL

Community Outreach	17-May-12	Alex Bruner, Lisa Huertas	AFP and Planned Giving Council of Palm Beach County, Joint Meeting
Community Outreach	21-May-12	Alex Bruner, Ben Starling, Lisa Huertas	Forum Club of the Palm Beaches
Community Outreach	22-May-12	Lisa Huertas	Professional Resource Network Virtual Exploration
Community Outreach	22-May-12	Dr. Kendall Nettles	Diane's Voice, Gilda's Club of South Florida Ovarian Cancer Symposium
Community Outreach	23-May-12	Barbara Noble	Realtor's Association of Palm Beach County Virtual Exploration
Community Outreach	24-May-12	Barbara Noble, Paul Thompson, Matt Gill	FAU Science Journalism Workshop - Neil Santaniello
Community Outreach	25-May-12	Paul Kenny	Interview with Mary Jane Fine of Florida Weekly Magazine
Community Outreach	30-May-12	Dr. Patricia McDonald, Barbara Noble	Quantum Foundation/BCBS Foundation - HBO's *Weight of the Nation* Screening and Community Conversation about Obesity and Diabetes
Community Outreach	4-Jun-12	Peter Hodder	Families of Spinal Muscular Atrophy (FMSA), Translational Advisory Council Member, 2012
Community Outreach	15-Jun-12	Deborah Leach-Scampavia	Scripps Tour - Arsha Vuppuluri
Community Outreach	15-Jun-12	Alex Bruner, Barbara Noble, Ben Starling, Lisa Huertas	Forum Club of the Palm Beaches

Education Outreach	**Date**	**Participants**	**Recipients/Event**
Education Outreach	20-Jul-11	Roy Smith	Lecture for Professor Juan Acuna, University of Miami
Education Outreach	1-Jul-11	Susana Valente	Lincoln Park Academy Student Internship-Rohan Reddy
Education Outreach	1-Jul-11	Susana Valente	Florida Atlantic University Student Internship-Sarah Hoxha
Education Outreach	01-Jul-11	Peter Hodder	Intern mentor
Education Outreach	1-Jul-11	Scripps wide	Summer Internship program - high school and undergraduate
Education Outreach	7-Jul-11	Deborah Leach-Scampavia	PBSC Summer Math Camp
Education Outreach	22-Jul-11	Scripps wide & High School Interns	Scripps Florida Summer High School Intern Research Presentations
Education Outreach	1-Aug-11	Matt Gill	Mentor Darrin Zahornacky, FAU Undergraduate Intern, Harriet Wilkes Honors College, Outstanding thesis award at graduation. Now in Graduate School at Johns Hopkins University, Baltimore
Education Outreach	1-Aug-11	Matt Gill	Mentor Tiffany Kaul, FAU Undergraduate Intern, Harriet Wilkes Honors College
Education Outreach	12-Aug-11	Scripps wide & Undergraduate Interns	Scripps Florida Undergraduate Intern Poster Competition

Education Outreach	17-Aug-11	Deborah Leach-Scampavia, Jeremy Pyle	Palm Beach Co. School Dist Science Symposium
Education Outreach	22-Aug-11	Donald Phinney	Intern for credit (Megha Mahabole) - Florida Institute of Technology, Melbourne, FL
Education Outreach	24-Aug-11	Katrin Karbstein	University of Michigan, Defense of Bethany Strunk for receipt of Ph.D.
Education Outreach	31-Aug-11	Donald Phinney	Intern for credit (Nibal Eid) - Florida Atlantic University, Wilkes Honors College, Jupiter, FL
Education Outreach	1-Sep-11	Brian Paegel	Lecture at University of California, Berkeley, CA
Education Outreach	16-Sep-11	Paul Kenny	Invited speaker Washington State University, Pullman, WA - Alcohol and Drug Abuse Research Program/Graduate Neuroscience Program
Education Outreach	25-Sep-11	Roy Periana	FESC Summit in Gainesville- talk titled: "Chemistry: The Key to Sustainability and Energy Independence"
Education Outreach	4-Oct-11	Douglas Kojetin	Florida A&M University/
Education Outreach	5-Oct-11	Thomas Creson	Mentored HS intern Kelsey Kruse
Education Outreach	20-Oct-11	Paul Kenny	Invited speaker University of North Carolina, Chapel Hill, NC
Education Outreach	25-Oct-11	Deborah Leach-Scampavia, Jeremy Pyle, Briana Weiser, Ryan Stowe, Christine Crumbley, Rosie Albatram	Career Panel - grad students for visiting high school
Education Outreach	1-Nov-11	Paul Kenny	Invited speaker University of Washington, Seattle, WA
Education Outreach	2-Nov-11	Deborah Leach-Scampavia, Louis Scampavia, Tim Spicer, Cathy Trivigno	St. Marks Science Fair
Education Outreach	4-Nov-11	Deborah Leach-Scampavia, Jeremy Pyle, High School Interns	Middle School Genomics Lesson - Royal Poinciana
Education Outreach	8-Nov-11	Derek Duckett	The Rendina Family Foundation/Speaker - Brain Cancer: Novel Therapies Fighting Back, Jupiter, FL
Education Outreach	10-Nov-11	Patrick Griffin	Speaker and Q&A; Nova Southeastern University Chemistry Club; Davie, FL
Education Outreach	16-Nov-11	Donald Phinney, Christopher Haga, Siddaraju Boregowda, Veena Krishnappa	Phinney lab participation LST HUB and BASFlorida event, Palm Beach State College Bioscience and Technology Complex, Palm Beach Gardens, FL
Education Outreach	17-Nov-11	Paul Kenny	Invited speaker Emory University, Atlanta, GA
Education Outreach	23-Nov-11	Damon Page	Thesis Committee, Graduate Student MIT, Boston, MA
Education Outreach	29-Nov-11	Deborah Leach Scampavia	Quantum Foundation Neuroscience Meeting with Max Planck

Education Outreach	1-Dec-11	Deborah Leach-Scampavia, Rosie Albarran	Introduction to Science - Spanish
Education Outreach	2-Dec-11	Deborah Leach-Scampavia	Roosevelt Middle School Advisory Board
Education Outreach	7-Dec-11	Katrin Karbstein	Jupiter Academy Middle School, "What do scientists do?" Career presentation on invitation from the science teacher
Education Outreach	7-Dec-11	Deborah Leach-Scampavia, Jeremy Pyle, Barbara Noble	The Gardens Mall - Cellebrate Science Advisory Meeting
Education Outreach	13-Dec-11	Deborah Leach Scampavia	U.S. Imaging / United Way Meeting on STEM Education
Education Outreach	1-Jan-12	Brian Paegel	Lecture at Florida Atlantic University, Boca Raton, FL
Education Outreach	1-Jan-12	Deborah Leach-Scampavia, Jeremy Pyle	Summer Intern application, selection and placement - High School and Undergrad
Education Outreach	1-Jan-12	Deborah Leach - Scampavia, Jeremy Pyle, Society of Research Fellows	InSPIRE - Secondary Science Teachers Professional Development Workshop
Education Outreach	3-Jan-12	Sathya Puthanveettil	FIT Intern training
Education Outreach	3-Jan-12	Donald Phinney	Intern for credit (Jacqueline Strivelli) - Palm Beach State College, Palm Beach Gardens, FL
Education Outreach	6-Jan-12	Deborah Leach-Scampavia, Tim Spicer	Curriculum Meeting with P.B. Co. Sch Dist Kristen Perez
Education Outreach	9-Jan-12	Alicia F. Brantley	Mentored intern, Rachael Tocco, from Palm Beach State College Biotechnology Program
Education Outreach	10-Jan-12	Deborah Leach Scampavia	Education Outreach Discussion with Florida Atlantic University
Education Outreach	18-Jan-12	Douglas Kojetin	Allamanda Elementary School/Science Fair Judge, Palm Beach Gardens, FL
Education Outreach	30-Jan-12	Paul Kenny	Invited speaker University of Alabama @ Birmingham - Nutrition Obesity Research Center Seminar Series
Education Outreach	31-Jan-12	Deborah Leach Scampavia	I-TEACH Steering Committee Meeting with Palm Beach County Schools
Education Outreach	4-Feb-12	Scripps wide	Scripps Florida Cellebrate Science Day
Education Outreach	12-Feb-12	Jeremy Pyle	Florida - Sunshine State Scholars
Education Outreach	13-Feb-12	Briana Weiser	Meeting with Dr. and Mrs. Jeff Abrams
Education Outreach	15-Feb-12	Andrew Butler	FAU Medical School, Boca Raton Campus
Education Outreach	22-Feb-12	William Roush	Presentation at Florida International University on career opportunities in Chemistry, Miami, FL
Education Outreach	4-Mar-12	Paul Kenny	Invited speaker University of Colorado
Education Outreach	9-Mar-12	Paul Kenny	Invited speaker Vanderbilt University, Nashville, TN - Vanderbilt Institute for Obesity and Metabolism
Education Outreach	12-Mar-12	Patricia McDonald	GE Healthcare/Presenter: Introducing the IN Cell 6000 Confocal Imaging System, Jupiter, FL

Education Outreach	13-Mar-12	Paul Kenny	Provide interview to Kyle Jardim (HS student from South Carolina) re: research paper on addictiveness of fast food and its similarity to drugs and alcohol
Education Outreach	18-Mar-12	Timothy Tellinghuisen	Western Academy Science Fair Judge
Education Outreach	20-Mar-12	Paul Kenny	Provide interview to Alison Watson (HS student from Maryland) re: research paper on fatty diets and how they relate to food addictions.
Education Outreach	22-Mar-12	Timothy Tellinghuisen	Career Day at Western Academy
Education Outreach	25-Mar-12	William Roush	NOBCChE Lecturer, San Diego, CA
Education Outreach	4-Apr-12	Deborah Leach-Scampavia, Jeremy Pyle, Society of Research Fellows	InSPIRE - Secondary Science Teachers Professional Development Review Lesson
Education Outreach	16-Apr-12	Donald Phinney	Intern for credit (Amira Barghouthy) - Florida Atlantic University, Wilkes Honors College, Jupiter, FL
Education Outreach	14-May-12	Kirill Martemyanov	Mentored FAU intern Chris Holmquist
Education Outreach	14-May-12	Massimiliano Aceti	Mentored FAU intern Megan McGuire
Education Outreach	16-May-12	Deborah Leach Scampavia	U.S. Imaging / United Way Meeting on STEM Education
Education Outreach	24-May-12	Katrin Karbstein	University of Michigan, Defense of Crystal Young for receipt of Ph.D.
Education Outreach	4-Jun-12	Susana Valente	University of Texas at San Antonio Student Internship-Gwendolyn Quintana
Education Outreach	4-Jun-12	Scripps wide	Undergraduate Summer Interns
Education Outreach	5-Jun-12	Brian Paegel, Deborah Leach-Scampavia, Jeremy Pyle	Research Seminar for Undergraduate Summer Interns
Education Outreach	11-Jun-12	Scripps wide	High School Summer Interns
Education Outreach	12-Jun-12	Pat Griffin, Deborah Leach-Scampavia, Jeremy Pyle	Research Seminar for Undergraduate Summer Interns
Education Outreach	18-Jun-12	Roy Periana	Summer Intern from University of Rochester, Michael Robo
Education Outreach	19-Jun-12	Tim Tellinghuisen, Deborah Leach-Scampavai, Jeremy Pyle	Research Seminar for Undergraduate Summer Interns
Education Outreach	21-Jun-12	Deborah Leach-Scampavia, Cheryl Marra, Jeremy Pyle	Undergrad and Grad Social Presentation
Education Outreach	21-Jun-12	Louis Scampavia, Pierre Baillargeon, Deborah Leach-Scampavia	Lego MindStorm Lesson - Beta Test Middle School
Education Outreach	25-Jun-12	Camilo Rojas	Mentored HS intern Erika Gesner
Education Outreach	30-Jun-12	Peter Hodder	Intern mentor

Section 9.3(c) **A schedule of the shares of stock (or other securities) held by Scripps as payment of the royalty referred to in Section 10.2(a) and a report on any trades or activity concerning such stock (or other securities);**

As partial consideration for previous license agreements with Ember Therapeutics, Xcovery and Curna, TSRI received 150,000, 263 and 107 shares, respectively, of the companies' common stock as a "License Issue Equity" royalty. TSRI is still holding its Ember and Xcovery stock, but has liquidated its Curna stock as a result of Curna's acquisition by Miami, FL-based Opko Health, generating proceeds of $314,000.

Section 9.4 **Annual Scientific Report. Scripps shall prepare the Annual Scientific Report that describes its scientific activities for Scripps Florida each year and deliver such annual report to Funding within one hundred twenty (120) days after the end of each fiscal year of Scripps. The form of the annual report will be substantially similar to the form Scripps uses at such time with respect to its California operations.**

The Annual Scientific Report is not due until January of 2013.

Section 9.5 **Performance Expectations. Scripps, in cooperation with OTTED, shall report to Funding not less than annually on its progress in meeting certain performance expectations that reflect the aspirations of the Florida Governor and Legislature for the benefits accruing to Florida as a result of the Grant Funds. These reports shall include, but are not limited to, performance expectations addressing the following with respect to Scripps Florida;**

Section 9.5(a) **(Also see Section 9.5(h).) The number and dollar value of research grants obtained by Scripps with respect to Scripps Florida from the Federal Government or sources other than Florida;**

Scripps Florida scientists were awarded 54 research grants from non-Florida sources between July 1, 2011 and June 30, 2012. The total dollar amount of those grants was $55,748,269. To date, Scripps Florida scientists have been awarded over 240 research grants totaling over $275,000,000.

Section 9.5(b) **The percentage of total research dollars received by Scripps from sources other than Florida, which is used to conduct research activities by Scripps in Florida;**

Between July 1, 2011 and June 30, 2012, scientists at Scripps Florida expended about $51.3 Million in research grant support. During that same time, about $13.4 Million of SFFC funds were expended at

Scripps Florida. Thus, about 79% of total research dollars came from sources other than Florida.

Section 9.5(c) **The number or value of patents obtained by Scripps with respect to Scripps Florida;**

Between July 1, 2011 and June 30, 2012, 22 foreign and domestic patent applications were filed. Since inception, 58 "families" of patent applications have been filed covering Scripps Florida technology, with each family containing 1-6 patent applications. No value has been assigned to these patents.

Section 9.5(d) **The number or value of licensing agreements executed by Scripps with respect to Scripps Florida;**

Three license agreements were executed between July 1, 2011 and July 1, 2012 with respect to Scripps Florida technologies.

Section 9.5(e) **The extent to which research conducted by Scripps Florida results in commercial applications;**

Because of the early stage of the technology being developed at Scripps Florida and the time delay attendant to further development, no commercial applications have emerged to date.

Section 9.5(f) **The number of collaborative agreements reached and maintained with colleges and universities in Florida and with research institutions in Florida, including agreements that foster participation in research opportunities by public and private colleges and universities and research institutions in Florida with significant minority populations, including historically black colleges and universities;**

The Scripps Research Institute has developed a template entitled the Joint Cooperation Agreement (JCA) to encourage and support research collaborations with Florida institutions. Provisions are included to make it easier to collaborate on filing patents for jointly developed technologies and to share revenues from commercialized innovations. By executing these agreements in advance, we expect to streamline the scientific collaboration process between Florida organizations and Scripps Florida as they work together on biomedical research. Nine Florida institutions have currently executed this formal agreement with TSRI:

Florida International University;
University of Florida;
Florida Atlantic University;
University of Central Florida;

University of Miami;
Florida State University;
Nova Southeastern University;
University of South Florida;
Max Planck Florida Institute

Scripps scientists have also participated in formal scientific meetings with colleagues at **Florida** foundations, colleges and universities (See Table, below).

Science Outreach	Date	Participants	Recipients/Event
Science Outreach	14-Jul-11	Paul Kenny	Invited speaker SSIB (Society for the Study of Ingestive Behavior) Presidential Symposium, Clearwater, FL
Science Outreach	27-Jul-11	Sathya Puthanveettil	University of Florida, Seminar Presentation
Science Outreach	18-Aug-11	Paul Kenny	Behavioral Health of the Palm Beaches
Science Outreach	25-Aug-11	Peter Hodder	Daiqing Liao, University of Florida, Gainesville, FL, USA
Science Outreach	1-Sep-11	Paul Kenny	Behavioral Health of the Palm Beaches
Science Outreach	7-Sep-11	Philip LoGrasso	Invited Speaker at Torrey Pines - Port St. Lucie, FL
Science Outreach	12-Sep-11	Tim Spicer	University of South Florida, Center for Biological Defense - 10th Consortium of Biodefense Researchers
Science Outreach	23-Sep-11	Philip LoGrasso	Invited Speaker at FAU Seminar Research Series - Boca Raton, FL
Science Outreach	28-Sep-11	Christopher Haga	Invited speaker Jupiter Medical Center, Jupiter, FL
Science Outreach	29-Sep-11	Andrew Butler	Novo Nordisk Symposium (Orlando)
Science Outreach	1-Oct-11	Matt Gill	Presented "Regulation of development and lifespan by small molecules in the nematode C. elegans" Seminar at FAU, Boca Raton, FL
Science Outreach	2-Oct-11	Paul Kenny	Session Chair - Brain Activity and Reward - Obesity Society Annual Meeting 2011, Orlando, FL
Science Outreach	3-Oct-11	Jonathan Hollander	Research Trainee Seminar Series - Dept. of Neuroscience, TSRI ("Putting Addiction to Bed: Sleep-related Neuropeptide may be Key for Treatment of Nicotine Dependence")
Science Outreach	4-Oct-11	Katrin Karbstein	Visit by FAMU faculty
Science Outreach	4-Oct-11	Paul Kenny	Symposium speaker (Orexin Action in Ingestion and Reward) Obesity Society Annual Meeting 2011, Orlando, FL
Science Outreach	6-Oct-11	Paul Kenny	Invited speaker - Institute for Brain Potential Seminar, Gainesville, FL
Science Outreach	12-Oct-11	Ron Davis	University of Florida Chemical Senses Seminar Series, Gainesville, FL
Science Outreach	13-Oct-11	Gavin Rumbaugh	Alzheimer's Presentation at the Mental Health Association of Palm Beach County
Science Outreach	13-Oct-11	Paul Kenny	Invited speaker - Institute for Brain Potential Seminar, St. Augustine, FL

Science Outreach	25-Oct-11	Timothy Tellinghuisen	BioFlorida Panelist on Vector Borne Diseases in Florida
Science Outreach	1-Nov-11	Alicia F. Brantley	Invited Chair – Society for Neuroscience Satellite Symposium "Standardization of Behavioral Tests in Mouse Phenotyping" Sponsored by Noldus Information Technology"
Science Outreach	7-Nov-11	Roy Smith	Global Discovery & Development: Innovation Leaders Summit (Orlando)
Science Outreach	9-Dec-11	Roy Smith	American Federation for Aging Research Board Meeting (Miami)
Science Outreach	12-Dec-11	Philip LoGrasso	Presentation - National Parkinson's Southern Palm Beach County Chapter - Boca Raton, FL
Science Outreach	15-Dec-11	Donald Phinney	Invited speaker - press conference announcing 2012 World Stem Cell Summit scheduled for December 2012
Science Outreach	29-Feb-12	Sathya Puthanveettil	Florida Rare Disease Day
Science Outreach	1-Mar-12	Thomas Kodadek	Florida Atlantic University, Boca Raton
Science Outreach	2-Mar-12	Timothy Tellinghuisen	Florida Vector Borne Disease Alliance meeting presentation on Scripps Technology
Science Outreach	6-Mar-12	Ron Davis, Seth Tomchik, Ayako Tonoki-Yamaguchi, Isaac Cervantes-Sandoval, Damon Page, Youjun Chen, Amy Clipperton-Allen and Danielle Llaneza	Max Planck Florida Institute's Neural Circuit Symposium, Jupiter, FL
Science Outreach	8-Mar-12	Roy Smith	Seminar/Meetings with Judith Altarejos, Sanford Burnham Research Institute
Science Outreach	12-Mar-12	Kate Carroll	Florida Atlantic University, Boca Raton
Science Outreach	16-Mar-12	Sathya Puthanveettil	International Molluscan Neuroscience Conference
Science Outreach	30-Mar-12	Philip LoGrasso	Keynote Speaker - Parkinson's Disease Conference - Royal Palm Beach, FL
Science Outreach	11-Apr-12	Paul Kenny	Invited speaker Torrey Pines Distinguished Lecture Seminar, Port St. Lucie, FL
Science Outreach	12-Apr-12	Min Guo	Invited Speaker - Florida Atlantic University, Boca Raton, FL

Science Outreach	21-Apr-12	Davis Lab: Ron Davis, Isaac Cervantes-Sandoval, Germain Busto, Sonal Harbaran, Ayako Tonoki-Yamaguchi, Erica Walkinshaw, Daniel Richter, Yunchao Gai, Caitlin DeStefanis, and Jennifer Verriotto, Bill Ja	Flies on the Beach Meeting - Boca Raton, FL
Science Outreach	27-Apr-12	Timothy Tellinghuisen	Lecture to Florida Department of Health on Hepatitis C Virus
Science Outreach	1-May-12	Roy Periana	Solar Cell Talk at Florida Atlantic University
Science Outreach	4-May-12	Jun-Li Luo	Invited Speaker - 2012 Florida Prostate Cancer Research Symposium, Lake Buena Vista, FL
Science Outreach	5-May-12	Kirill Martemyanov, Ignacio Sarria	ARVO Conference in Ft. Lauderdale
Science Outreach	16-May-12	Ron Davis, Damon Page, Ayako Tonoki Yamaguchi, Isaac Cervantes-Sandoval	Molluscan Neuroscience in the Genomic Era: from Gastropods to Cephalopods", Scripps
Science Outreach	18-May-12	Patrick Griffin	Invited Speaker at the Morsani College of Medicine, USF in Tampa FL
Science Outreach	23-May-12	Kirill Martemyanov	Future of Medicine Summit VI Speaker/Presentation
Science Outreach	30-May-12	Roy Smith	David Bjorkman, Dean, FAU Medical School
Science Outreach	31-May-12	William Roush	Meeting with Dean, FAU Medical School regarding FAU/Kellogg M.D., Ph.D. program
Science Outreach	22-Jun-12	Paul Kenny	ACNP (American College of Neuropsychopharmacology) Program Committee Meeting, Hollywood, FL

Section 9.5(g) **The number of collaborative partnerships established and maintained with businesses in Florida, including small businesses;**

Scripps Florida continues to maintain collaborative relationships with four Florida based biotechnology companies: Envoy Therapeutics, Opko Health, Dyadic and Protix.

Envoy Therapeutics

Envoy Therapeutics is a drug discovery company located in Jupiter, FL. Envoy founded by scientists from Rockefeller University (NY, NY) and investors from 5AM Ventures (Menlo Park, CA) and located in Jupiter to access the high-throughput drug screening capabilities of Scripps Florida.

Envoy and Scripps Florida are currently collaborating to develop screens and find drug candidates for four novel targets identified using Envoy's proprietary technology.

Opko Health

Opko Health, Inc. is a publicly traded healthcare company involved in the discovery, development, and commercialization of pharmaceutical products, vaccines and diagnostic products. Opko and Scripps are currently collaborating to develop novel diagnostic products to detect Alzheimer's and other diseases and on the development of novel drug candidates to treat Parkinson's Disease.

Dyadic

A collaborative effort between scientists at Scripps Florida and Dyadic was established to provide a complete annotation of the genome of Dyadic's proprietary fungal organism, Chrysosporium lucknowense ("C1"). The knowledge gained from this effort is expected to facilitate further development of the C1 Host Technology as a robust platform for the discovery, development and production of various materials for medical and industrial applications. Furthermore, this collaboration promotes the development of a successful biotechnology cluster in South Florida.

Dr. Richard Lerner, past President of The Scripps Research Institute, said, "In addition to its potential contributions to Dyadic's success, this partnership for our new Palm Beach County-based research group also will benefit Scripps Florida and the broader scientific community. Because relatively few fungal genomes have been sequenced and annotated to date, our work on Dyadic's C1 host strain will increase the body of knowledge on this important class of lower eukaryotes. We expect that the information gained through the comparative genomics of fungi will provide insights into eukaryotic cellular processes, and provide important clues for the treatment of genetic, metabolic and infectious diseases."

Protix

Protix is a start-up company located in Palm Beach County that has platform technology for the identification of amino-acids sites on protein targets that are required for their degradation within the cell to facilitate certain cellular regulatory processes such as mitosis. The company is utilizing this technology to identify sites on proteins that play a role in cellular processes, such as mitotic entry, which can be further exploited as targets for therapeutic and diagnostic applications in a broad range of diseases including cancer and neurodegenerative disorders. The company

was founded by Scripps Florida professors Nagi Ayad and Donny Strosberg and is based on an invention made in the laboratory of professor Ayad at Scripps Florida.

A-1 MOVING & STORAGE
AAA APPLIANCE
AFFORDABLE DRY ICE
AIR COMPRESSOR WORKS INC
AIR EZE
AIRCOMO
AKRON BIOTECH
AL PACKER FORD
AMERICAN BEVERAGE DEPOT
ARCHIVES MANAGEMENT CENTERS INC
BEST MAINTENANCE & JANITORIAL SERVICES INC
BILL ANDERSON & SONS INC
BOCA BUSINESS EQUIPMENT
BOCA SCIENTIFIC
BRAAS COMPANY
BRANDON TRANSFER
CAPO CONSULTING
CERTIFIED BACKFLOW PROTECTION INC
CHEMPEP INC
CITATION COMMUNICATIONS
CLARUS GLASSBOARDS LLC
CLEAN FUELS OF FLORIDA
CMH SOLUTIONS INC
COMMERCIAL DOOR & ACCESS INC
COMPLETE ACCESS CONTROL INC
CUSTOM SIGNS TODAY
DISKOVERY EDUCATIONAL SYSTEMS CORP
EARL STEWART TOYOTA
ENVIROLIGHT & DISPOSAL INC
FLORIDA FLUID SYSTEM TECH INC
FLORIDA PIPETTE CALIBRATIONS
GOLD COAST ENVIRONMENTAL SOLUTIONS INC
GRAPHICS PLUS INC
HILL YORK
HOOVER PUMPING SYSTEMS CORPORATION
HPE AUTOMATION
IMPERIAL FASTENER COMPANY INC
INNOVATIVE RESEARCH OF AMERICA
J.R. MANNO UNIFORM AND POLICE EQUIPMENT
JUPITER PRINTING INC
KMI INTERNATIONAL INC
LASER SUPPLY

LJB EQUIPMENT SALES CO INC
LOTSPEICH CO. OF FLORIDA INC.
MC2 INC
MEDREP TECHNOLOGIES INC
MERCEDES MEDICAL INC
MICRO OPTICS OF FLORIDA INC
MILLER TOOL AND DIE
MOLECULAR DIMENSIONS
MORROW ENTERPRISES
NEWTON SEATING CO
OFFICE ELEMENTS INC
PACE MACHINE & TOOL INC
PENINSULAR ELECTRIC DISTRIBUTORS
PHOENIX LANDSCAPE MAINTENANCE, INC
PINNACLE SCIENTIFIC INC
PROSHRED SECURITY
PROTEC SYSTEMS INTERNATIONAL INC.
RAPID ROOTER
RELIABLE POWER SOLUTIONS
SMITHCO SERVICES
SOUTHERN LOCK & SUPPLY CO
SOUTHERN MAINTENANCE HIGH RISE SERVICES INC
SPEEDY ROOTER INC
SULLIVAN ELECTRIC & PUMP INC
SUNCHASER SYSTEMS INC
SYNQUEST LABORATORIES INC
TOTAL DYNAMIC BALANCE INC
TOWN & COUNTRY FEED AND SUPPLY INC
TRUE LINES INC
TURBOVACUUM
UNIVERSAL MEDICAL SYSTEMS INC
URBAN DESIGN KILDAY STUDIOS
VACTEK INC
VILA & SON LANDSCAPING CORP
VISION DATABASE SYSTEMS
WELLINGTON GOLF CARS
WEST PALM BEACH PLASTICS
WILDLIFE REMOVAL SERVICES
WORKSCAPES SOUTH LLC
WORLD PRECISION INSTRUMENT INC

Section 9.5(h) **The total amount of funding received by Scripps with respect to Scripps Florida from sources other than Funding, including a breakdown of amounts received from Grants and other sources.**

Since inception through June 30, 2012, Scripps Florida has been awarded **$283,513,391** million in grants and sponsored research funding from state and federal agencies (including the NIH), foundations, pharmaceutical companies and other grantors.

Other Revenue sources	$7,963,874	9 mos. ended 6/30/12
Grant Awards	$41,910,584	9 mos. ending 6/30/12
Contributions at net present value	$2,931,126*	9 mos. ended 6/30/12
Palm Beach County	$210,069,431**	since inception

*The amount reported above was determined in accordance with generally accepted accounting principles. Therefore, certain non-cash items, such as promises to give, are reflected at their estimated net realizable value.

**The value of construction paid directly by the County of Palm Beach to contractors and other vendors for either the permanent facility or the temporary facility at FAU - Jupiter has not been included.

Section 9.5(i) **The number or value of spin off businesses created in Florida as a result of commercialization of the research of Scripps.**

The three Florida companies that spun off from Scripps Florida, and the additional Florida company located in Jupiter to access Scripps Florida (Envoy Therapeutics), are described above. No attempt has been made by Scripps to assign a value to these spin offs, with the exception of Curna, which was purchased by Miami-based Opko Health for $10,000,000.

Section 9.5(j) **The number or value of businesses that locate in Florida as a result of Scripps Florida.**

Scripps cannot determine what businesses located in Florida as a result of Scripps Florida.

Section 9.5(k) **The establishment and implementation of policies to promote supplier diversity using the guidelines developed by the Office of Supplier Diversity under Section 287.09451, Florida Statutes, and to comply with the ordinances, including any small business ordinances, enacted by applicable local governments and which are applicable to Scripps Florida.**

The TSRI Procurement Department & Mrs. Darci Garbacz, Procurement Manager/ Supplier Diversity Coordinator, continue to pursue opportunities to partner with the diverse business community. Scripps Florida continues to participate in county, state and national diverse supplier shows. These shows help Scripps Florida to identify diverse businesses that can provide goods and services to the institute at a competitive price. Participation in these shows has resulted in partnerships with local companies that provide furniture, pipette calibrations, refrigeration services, relocation services, dry ice services, landscaping and irrigation services, building maintenance services, printing services, shredding services and more.

Section 9.5(l) **The designation by Scripps of a representative to coordinate with the Office of Supplier Diversity.**

Mrs. Darci Garbacz serves in this position as the Scripps Supplier Diversity Coordinator. Mrs. Garbacz represents Scripps in working with small and minority business enterprises in the State of Florida, and is actively involved in many state and local supplier diversity outreach programs.

Supplier Diversity Mission and Vision Statements

Mission

Our Supplier Relations and Diversity Program will integrate small and diverse businesses into the procurement process - creating awareness, ownership, and an understanding of the principals of a competitive supply base. These partnerships will maximize cost savings and efficiencies within our internal processes and our supply chain.

Vision

We recognize the importance of a diverse supply chain and strive to develop relationships with small and diverse life science and service suppliers who can assist us in achieving our biomedical research goals. Also, we expect our strategic suppliers to establish business opportunities for small and diverse suppliers.

Section 9.5(m) **The establishment and implementation of a program to conduct workforce recruitment activities at public and private colleges and universities and community colleges in Florida, regardless of their size, which request the participation of Scripps Florida.**

Scripps Florida has extended workforce recruitment efforts to Florida's higher education institutions throughout the state. A list of

Institution Career Fair and Expositions attended by Scripps Florida Human Resources Analyst, Recruiter is shown below.

Event	Location/Institution	Date	Lead/Rep
Career Fair	BioFlorida, Tampa FL	10/22/2011	Vanessa Paulman
Career Fair	FMU, Miami FL	03/22/2012	Hollie Alkema
Career Fair	Statewide, Orlando FL	05/09/2012	Hollie Alkema

Section 4.4(c)1 **Scripps shall create new jobs at Scripps Florida, the number of which shall be measured at the end of each calendar year. In any given year, SFFC may allow Scripps to deviate downward from the job creations goal to achieve flexibility.**

On June 30, 2012, Scripps Florida employed full-time 440 people. The job creation target for 12/31/2012 is 500 jobs.

Section 4.4(c)2 **Beginning 18 months after Scripps' occupancy of it permanent facility, Scripps shall obtain $100,000 of non-state funding for each full-time equivalent tenured track faculty member employed at Scripps Florida.**

On June 30, 2012, Scripps Florida employed 41 tenured track Faculty. By that same date, over $275 Million in non-state funding had been obtained. Thus, for each tenure track Faculty, about $6.7 Million of non-state funding had been obtained.

Section 4.4(c)3 **No later than 3 years after occupancy of its permanent facility, Scripps shall apply to the relevant accrediting agency for accreditation of its Florida graduate program.**

The re-accreditation of the Scripps Ph.D. program was successfully completed in early 2011. The Kellogg School of Science in Technology is a bi-coastal Ph.D. program, reflecting the "one institution/two campus" makeup of The Scripps Research Institute. Owing to the larger size and earlier date of establishment of the Ph.D. program on the La Jolla campus, the reaccreditation process was handled by WASC (the Western Association of Schools and Colleges Accrediting Commission for Senior Colleges and Universities). The re-accreditation process included a specific site visit and assessment of the Scripps Florida graduate program in October, 2010, by Dr. Karen Holbrook, Senior Vice President for Research, Innovation & Global Affairs, University of South Florida, and President, University of South Florida Research Foundation. As a result of the overall review and re-accreditation process, the Kellogg School of Science and Technology—including the graduate program at Scripps Florida—received re-accreditation for a 10-year period, effective March 7, 2011.

Thus, the requirement of Section 4.4(c)3 has been satisfied, within the requirement of "no later 3 years after occupancy of its permanent facility".

Section 4.4(c)4 **Scripps shall purchase equipment for Scripps Florida [using State grant funds] according to an agreed upon schedule. Equipment purchases [acquired with State grant funds] are to be measured as of January 31st of each year.**

Report due in February 2013.

Section 4.4(c)5 **Doctoral Research. No later than 18 months after occupying its permanent facility, Scripps shall establish a program for qualified graduate students from Florida universities permitting them access to the facility for doctoral, thesis-related research.**

Scripps Florida has established a Ph.D. program in 2005 as part of Scripps' Kellogg School of Science and Technology, well ahead of the September 2010 deadline, 18 months after the anticipated occupancy of the permanent facility.

Thirty (30) graduate students were enrolled in the Scripps Florida graduate program in 2011-12, five of whom completed Ph.D. theses during the 2011-12 academic year. Two students left the program for personal (non-academic) reasons. A total of twelve students have now completed Ph.D. degrees at Scripps Florida since the establishment of the Ph.D. program in 2005. We had another successful recruiting year for new graduate students; 9 new graduate students will enter the program August 1, 2012. Efforts are made to identify and recruit highly qualified students from Florida colleges and universities to join the Scripps Florida graduate program. This past year, the Scripps Florida Graduate Admissions Committee sent representatives to on-campus recruiting events at four Florida Institutions (University of Florida; Florida State University; Florida Atlantic University; and Florida International University). The Scripps Florida Graduate Admissions Committee also reviews all completed applications submitted by Florida residents, or students from Florida colleges and universities, who submit applications to TSRI's graduate program. As the faculty ranks continue to expand at Scripps Florida over the next several years, additional efforts will be made to recruit highly qualified Florida students to the Scripps Florida Ph.D. program. Of the nine new students entering the Scripps Florida Ph.D. program in August, 2012, one has an undergraduate degree from the University of South Florida in Tampa, and a second has an undergraduate degree from New College of Florida. Of the 32 graduate students in the Scripps Florida graduate program as of September, 2012, at least eight will have a Florida connection (undergraduate degrees from Florida

colleges and universities, or is a native Floridian who took her/his undergraduate degree out of state). Thus, the graduate program is off to a flying start, and continues to be well ahead of schedule in meeting state requirements.

In addition, Scripps Florida has entered into a Joint Education Agreement with Florida Atlantic University. In March of 2006, FAU and Scripps Florida signed a "joint education agreement" that provided a framework for planning and implementing a variety of programs to promote education and research in areas involving biomedical science and related fields. The programs envisioned include collaborations in the areas of graduate and professional education, including post-doctoral training; undergraduate education and training, including laboratory and administrative internships and, community outreach activities, including continuing education for credit and service activities. This agreement also provides a blueprint for partnerships with other educational institutions throughout the region and state to facilitate similar cooperative activities.

From July 1, 2011 through June 30, 2012, nineteen (19) FAU undergraduates performed research at Scripps Florida as research interns.

In June 2010, Scripps finalized an agreement with FAU to establish an innovative MD-PhD program. The first applications for admission into this program were received in early 2011; three students were offered joint admission, and two accepted the offers and matriculated into the FAU Medical School in August, 2011. One of the two students completed his undergraduate degree at University of Florida. The MD-PhD students will spend their first three years as MD students at FAU, then will begin the Scripps Ph.D. program in the fourth year of MD program. During the first three years, the MD students will take 2-3 special topics courses with Scripps Florida faculty members to enable the students to identify research mentors and to make a smooth transition into the Ph.D. program. After successful completion of the first year at Scripps Florida, the students will then be awarded their MD degrees. The Ph.D. component of this degree program will proceed according to the Kellogg School policies and procedures, but provision will be made to avoid duplication of coursework so as to minimize the time that the students spend in the Ph.D. program.

Section 4.4(c)6 **Summer Internships. No later than 18 months after occupancy of the permanent facility, Scripps shall establish a summer internship for high school students.**

Scripps Florida High School Student Summer Internship Program and Sponsored Undergraduate Summer Internship Program

Since 2005, high school students and secondary science teachers (Section 4.4(c)7) in Palm Beach County have participated in the six-week summer research internship program. In 2009, ten-week undergraduate internships were added to the summer program. Interaction between the students has added a positive dynamic to the summer experience. University undergraduates have acted as role models and mentors for college bound high school students.

In the summer of 2012, fifteen high school students, two secondary science teachers and ten undergraduates participated in the internship program. Students and teachers were placed in the Departments of: Neuroscience, Infectious Diseases, Cancer Biology, Metabolism and Aging, Molecular Therapeutics, Chemistry and The Translational Research Institute. Support for the internship program has been provided by the William R. Kenan, Jr. Charitable Trust, The Kellogg School of Science and Technology, and the BallenIsles Charities Foundation, Inc.

The duration of the high school program continues to be six-weeks where students are placed at the "research bench" with the faculty, post-docs, and Ph.D. students working at the cutting edge of basic biomedical research. In 2012 the program culminated in a public presentation at the Scripps Florida campus where each student presented their research findings to Scripps researcher mentors, parents, teachers, and Palm Beach County students. The Kenan Fellows Facebook page continues to allow us to maintain contact and track alumni from the high school program. To date 100% of the college age alumni are pursuing post-secondary degrees, 95% within STEM fields. Following is a list of some of the academic institutions Kenan Fellows now attend: UF, UCF, USF, FAU, MIT, Harvard, Princeton, U Penn, Yale, Cal Tech., Columbia, Brown, Berkeley, Stanford, Rice, Emory, U Rochester, Swarthmore, Duke and Washington Univ. (St Louis).

The ten-week undergraduate program continues to elevate the intensity and independence of the research experience. Working with faculty and post-doc mentors, students are provided the research and laboratory experience needed to successfully compete in graduate school admissions and gain valuable experience outside the context of basic undergraduate laboratory instruction. The program culminates in a Scripps-wide research poster competition. Students return to their academic institutions able; to participate in campus undergraduate poster sessions; act as ambassadors for the research and graduate programs offered at Scripps Florida; and enjoy an enhanced knowledge base as they continue their classroom instruction. The Undergraduate Facebook page allows us to continue our mentorship with this talented group of students and promote an ongoing interest in the research and graduate efforts at Scripps Florida. This past year, three of the undergraduate summer interns

were accepted to present their research posters at national scientific conferences.

A list of the faculty seminars for the high school and undergraduate programs can be found in Section 4.4(c)11 Seminar Series.

Scripps Florida Education Outreach Director, Ms. Deborah Leach-Scampavia, continues to work in collaboration with the Palm Beach County School District, to insure that all county high schools, principals, science teachers, science supervisors, and parents are aware of the annual high school program. Faculty presentations, undergraduate "ambassadors" from the high school program, and correspondence with department Chairs at targeted academic institutions provide information about the sponsored undergraduate program. Detailed descriptions and on-line applications can be found on the Scripps Florida Education Outreach web pages.

Special emphasis is placed on providing opportunities for students from underrepresented populations (i.e., female, minority). Since its inception in 2005 the seven year average for underrepresented participation in the Scripps Florida summer internship programs is ~ 67%.

Eligibility / Compensation

Research Internships are awarded on a competitive basis to United States citizens or permanent residents. High school students must be beginning their junior or senior year in a Palm Beach County high school in the Fall preceding their summer internship. All applicants must have a minimum grade point average of 3.0 and be 16 years of age or older. Undergraduates must be a rising sophomore, junior, or senior and pursuing a post-secondary degree in a STEM subject.

High school students are awarded a gross compensation of $8.00 per hour for the six-week summer program. Undergraduates are awarded a gross compensation of $10.00 per hour for the ten-week summer program.

Application Procedures

The application time period for the internship programs runs from January 1st to the last Friday in February. The following is required for application to each program:

- A completed application form, including the Statement of Goals (high school) or 1,000 word Essay (undergraduate);
- A current academic transcript;
- A resume/CV;

- Two letters of recommendation

Selection Process for 2012 Scripps Summer Intern Program

Applications are reviewed at the close of the application period by a committee composed of education outreach staff and research faculty. A rubric is used to award points for:

- completed application
- effective statement/essay (what is your interest in the summer internship program, what do you hope to learn, is there a particular faculty member you wish to work with (and why))
- strength of recommendation letters (are they from STEM faculty)
- STEM classes completed
- GPA (from transcript)

The highest scoring applicants are matched with Scripps Florida faculty. The final selection is made by the individual faculty members (average pool of applicants from which faculty choose is 4.)

Travel Award (Undergraduate)

The undergraduate poster competition awards the top three students an opportunity to submit their winning research poster to a national conference of the intern and faculty mentor's choice. Expenses are paid for registration, travel, and housing for the intern and their faculty advisor to present their poster.

2012 SUMMER HIGH SCHOOL INTERNS

Name	Ethnicity	School	Student
Sofiya Andreyeva	Caucasian	Palm Beach Gardens HS	Senior
Lorena Benitez	Hispanic	Atlantic HS	Senior
Ricardo Canelo	Hispanic	John I Leonard HS	Senior
Randell Doane	Caucasian	The Benjamin School	Senior
Claire Dykas	Caucasian	Spanish River HS	Senior
Lauren Fremont	Caucasian	Jupiter HS	Senior
Kristina Garcia	Hispanic	Boca Raton HS	Senior
Alexandra Kaye	Caucasian	The Benjamin School	Senior
Angela Liang	Asian	Suncoast HS	Junior
Hashna Manoharan	East Indian	FAU HS	Senior
Courtney McEwen	Caucasian	Jupiter H.S.	Senior
Ryan Meingasner	Caucasian	Seminole Ridge HS	Senior
Adrienne Propp	Caucasian	The Benjamin School	Senior
Julia Rothschild	Caucasian	Suncoast HS	Senior
Jordan Zeldin	Middle Eastern	Spanish River HS	Senior

2012 SUMMER UNDERGRADUATE *SPONSORED* INTERNS

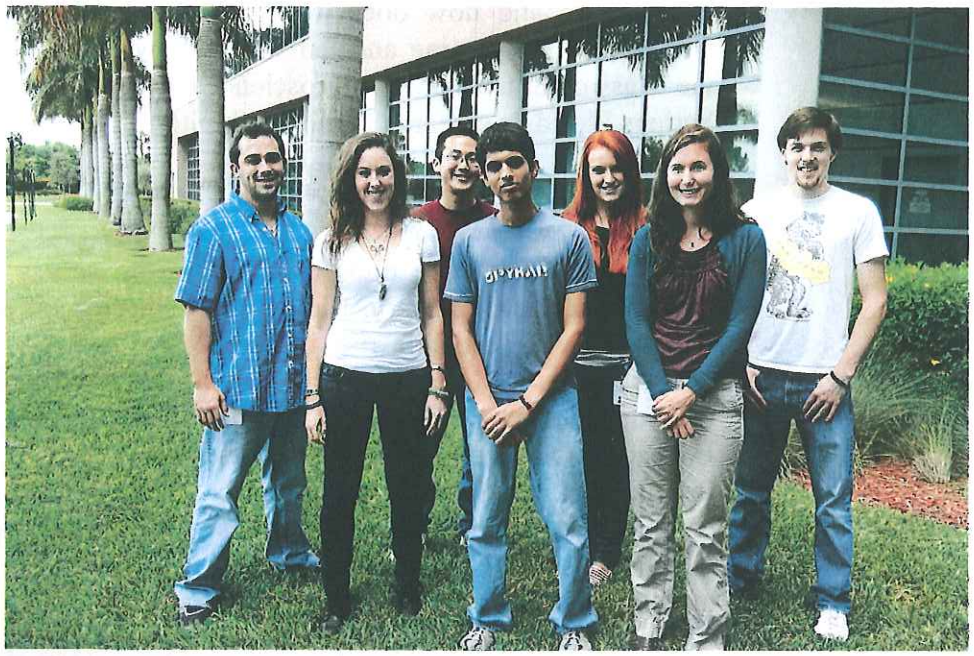
Name	Ethnicity	School	Student
James Alburger	Caucasian	Grove City College	Junior
Jacqueline Cox	Hispanic	U.C. Berkeley	Senior
Matthew Feldman	Asian	Univ. Miami	Junior
Ankit Kaushik	Asian	Georgia Tech	Junior
Alexandra Morgan	Caucasian	Florida State Univ	Senior
Angela Phillips	Caucasian	Univ. Florida	Senior
Tate Storey	Caucasian	Univ. Florida	Senior
Sergine Brutus	African American	Emory	Sophomore
Yimin Chen	Asian	MIT	Senior
Kasey Haugen	Caucasian	Univ. Central Florida	Senior

The July 2012 photograph below (taken in front of the Scripps Florida research facility in Jupiter, FL) includes all of the 2012 Kenan Fellow High School Summer Interns.

2012 Kenan Fellows- High School Interns

The pictures below show the 2012 Scripps Florida undergraduate summer interns grouped by funding source

2012 Kenan Fellows- Undergraduate Interns
Yimin Chen, Sergine Brutus, Kasey Haugen



2012 SURF Undergraduate Interns
Tate Storey, Alexandra Morgan, Matthew Feldman, Ankit Kaushik
Jacqueline Cox, Angela Phillips, James Alburger

The William R. Kenan, Jr. Charitable Trust, The Quantum Foundation, The Robert and Mary Pew Public Education Fund, The Berlin Family Foundation, the BallenIsles Charitable Foundation and The Gardens Mall (Forbes Company) supply funding for the following K-12 education programs developed through the efforts of Scripps Florida education outreach staff, faculty and research staff.

Scripps Florida Neuroscience Saturday Program

A new program for freshmen and sophomores attending Title I high schools in Palm Beach County is to be offered during the school district's academic year. Neuroscience Saturday is designed to immerse students in cutting-edge brain research, while introducing them to modern science in a way that is accessible, fun, and inspirational. The program follows the success of Scripps Florida's Title I "Science Saturday" high school lesson (initiated in 2005). Expanding the theme to highlight basic neuroscience and neuroimaging, Scripps Florida is inviting colleagues from The Max Planck Florida Institute (MPFI) to join their researchers in this Saturday program that brings together world-class scientists and Palm Beach County high school students.

This all-day workshop will explore brain function and dysfunction. How do we learn and form memories? How is the brain structured? What

is a neuron and how does it work? The curriculum is designed for students in grades nine and ten with follow-on resource information for the classroom teacher. Neuroscience Saturday will take place at the Scripps Florida's research facility in Jupiter.

Scripps Florida Introduction to Science Program

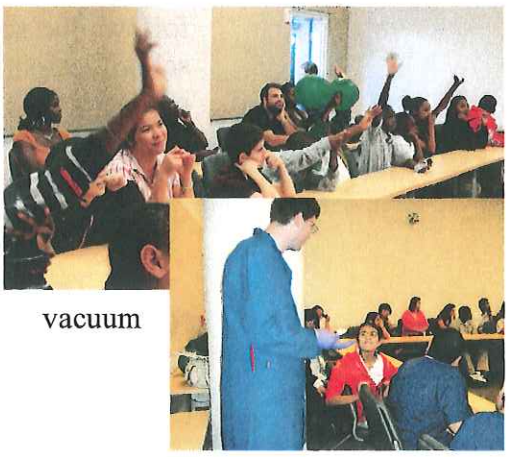
This interactive middle school lesson serves to tie together the basics of Math, Chemistry, Biology, and Physics for a student age group found to be at academic risk in math and science. Using inexpensive, everyday objects, Scripps Florida Education Outreach has leveraged its Introduction to Science program to community education partners allowing a significant expansion of the middle school lesson in Palm Beach County. A Spanish language version of the lesson has been completed and will be presented at the 2012 Palm Beach County School District Science Symposium for middle school teachers. The September 2011 picture of education director Deborah Leach-Scampavia was taken at Watson B Duncan Middle School.

The Scripps Florida Biotechnology Tour

An up-close view of the biomedical technologies used in the battle against human diseases at Scripps Florida continues to be presented to Neuroscience Saturday high school students. The "Biotechnology Tour" provides students an opportunity to see basic biology and chemistry research laboratories. As students move through the laboratories, they gain an understanding of how genomics based research and the processes of organic synthesis lead contemporary efforts in the therapeutic drug discovery process.

The Scripps Florida – Middle School Wow Chemistry

An after-school activity that allows middle school classes to visit Scripps Florida for demonstrations in chemistry. Presented by Ph.D. graduate students and post docs, a series of chemistry experiments are demonstrated to the students (i.e. chemical clock reactions, vacuum



experiments with eggs, freezing and shattering objects with liquid nitrogen, and exploding hydrogen balloons!). Student interaction is encouraged.

Ph.D. graduate student Ryan Stowe working with fifth and sixth grade students from Roosevelt Middle School in West Palm Beach, Florida.

The Scripps Florida High School Career Panel

An after-school interactive panel with Scripps Florida Ph.D. graduate students and post-doc fellows. Scripps scientists share experiences about their undergraduate and graduate careers and the type of research they are conducting at Scripps. The intent is to demystify the higher education/science process, encourage relationships, and answer student questions. The panel concludes with a tour of the Scripps Florida research laboratories.

TSRI graduate students Steven Bischof, Ryan Stowe, Christine crumbly, and William Hudson meet with a group of high school students from Jupiter High School in Jupiter, Florida.

Scripps Florida Middle School Genomics with Kenan High School Fellows

A new program was beta tested during the 2011/2012 academic year that allowed high school students from the summer intern program to visit Palm Beach County middle schools. Students shared their love of science, their experience as a summer researcher at Scripps and a lesson in genomics (geared for the middle school classroom). The high school students were enthusiastic role models for the younger students and well received by the classroom teachers.

Cellebrate Science Day with Scripps Florida

Since 2009, Scripps Florida researchers host an annual public science day, sponsored by and held at The Gardens Mall in Palm Beach Gardens, Florida. More than 100 Scripps Florida research faculty, post doctoral fellows, graduate students and staff interact with thousands of Palm Beach County students, parents, teachers and interested community members - all excited to learn about the science of Scripps and to have an opportunity to meet research scientists. Five fun, interactive science booths dot the mall grand court, each themed around Scripps Florida's research and technology:

- "Chemistry" – interactive chemistry demonstrations, including an electronic periodic table
- "Technology" – engineering and robotics
- "Science of Safety" – try on a lab coat, goggles and respirator and see how safe science is done in the lab
- "Model Organisms" – what do zebra fish, fruit flies, worms and slugs tell us about human biology and disease
- "Disease Biology" – what is the difference between a viral and bacterial infection and how do Scripps scientists study and use each to understand disease

Scripps Florida also uses their *Cellebrate* day to provide a public opportunity for Palm Beach County School District middle and high school Science Fair winners to display their winning posters before moving on to the Florida state competition.

Below: thousands gather each year at The Gardens Mall to "Cellebrate Science" with Scripps Florida researchers.

Scripps Florida Undergraduate Internships

In addition to the new, sponsored summer undergraduate initiative on the Scripps Florida campus, we attempt to accommodate as many students as possible who contact us for research opportunities during the summer months. Numerous undergraduate students from Florida colleges and universities, and students from Florida who are attending college out of state, seek opportunities/incentives to return to Florida to further their research experience.

Last Name	First Name	Start Date	Term Date	Scripps FL P.I.	School
KESNER	JORDAN	7/6/11	8/5/11	Dr. Thomas Kodadek	Emory
DATSKO	JOSEPH	7/18/11		Dr. Peter Hodder	PB Atlantic
ROBO	MICHAEL	6/18/12		Dr. Roy Periana	U Rochester
ABOVICH	ARIELLE	6/27/12		Dr. Peter Hodder	U Penn
PETERSON	JULIE	6/25/12		Dr. Thomas Kodadek	UCF
MOAWAD	AMANDA	5/21/12		Dr. Min Guo	UF
QUINTANA	GWENDOLYN	6/4/12	7/19/12	Dr. Susana Valente	U Texas
FISHER	EMILY	6/11/12		Dr. Jun-Li Luo	U Penn
MORGENSTERN	MAX	5/30/12	7/20/12	Dr. Brian Paegel	U Penn
JAIN	RITESH	1/3/12	4/30/12	Dr. Sathya Puthanveettil	FIT
MAHABOLE	MEGHA	8/22/11	11/18/11	Dr. Donald Phinney	FIT
LLANEZA	DANIELLE	2/1/12		Dr. Damon Page	SUNY
YONEZAWA	ALINE	7/18/11	8/5/11	Dr. Patricia McDonald	UF

FAU Wilkes Honors College Program

In 2005-06 Scripps Florida established an intern program for FAU Honors College students to perform research in the laboratories of Scripps Florida faculty members. The students can receive FAU academic credit or a stipend (if research funds are available from the Scripps Florida faculty member) for research performed during the school term or summer months. During the period of July 1, 2011 – June 30, 2012, seventeen FAU undergraduate students participated in research internships at the Scripps Florida research facility.

Last Name	First Name	Start Date	Term Date	Scripps FL P.I.	School
ZAHORNACKY	DARRIN	8/3/11	6/22/12	Dr. Matthew Gill	FAU
AITKEN	MARIA	10/26/11		Dr. Patricia McDonald	FAU
AL-SAID	SUZANNE	1/18/12	5/2/12	Dr. William Ja	FAU
BALUTA	KRISTIANN	1/16/12	5/7/12	Dr. Kirill Martemyanov	FAU
BARGHOUTHY	AMIRA	4/16/12		Dr. Donald Phinney	FAU
BLONZINSKI	JOHN	2/8/12		Dr. Katrin Karbstein	FAU
EID	NIBAL ARDULNASSER	8/31/11		Dr.Phillip LoGrasso	FAU
HOLMQUIST	CHRISTOPHER	5/14/12		Dr. Kirill Martemyanov	FAU
KAUL	CHRISTOPHER	9/30/11	12/9/11	Dr. Andrew Butler	FAU
KAUL	TIFFANY	6/11/12		Dr. Matthew Gill	FAU
MCGUIRE	MEGAN	5/16/12		Dr. Gavin Rumbaugh	FAU
RICHMAN	JEFFREY	5/21/12		Dr. Sathy Puthanveettil	FAU
RICHMOND	MICHAEL	11/7/12	5/4/12	Dr. Brian Paegel	FAU
RODRIGUEZ	CRISTINA	9/26/11	12/9/11	Dr. Andrew Butler	FAU
STUBBS	HARRISON	5/9/12		Dr. Courtney Miller	FAU
TRACY	DANIEL	6/11/12		Dr. Matthew Gill	FAU
WILLIAMS	JOSEPH	5/29/12		Dr. William Ja	FAU

Palm Beach State College (PBSC)

PBSC offers two degree programs in biotechnology in response to the community need for research technicians and associates. Students enrolled in the PBSC program can receive academic credit for additional experience in the laboratory. To help students gain this experience, internships have been made available at the Scripps Florida facility as space has been available. Following is a list of students who participated as Scripps Florida interns during the July 1, 2011 – June 30, 2012 time period.

Last Name	First Name	Start Date	Term Date	Scripps FL P.I.	School
STRIVELLI	JACQUELINE	1/4/12		Dr. Donald Phinney	PBSC
TOCCO	RACHAEL	1/9/12	5/4/12	Dr. Alicia Brantley	PBSC
SHEHATA	SAMAH	10/10/11	2/3/12	Dr. Brian Paegel	PBSC

Section 4.4(c)7 **Research Program. No later than three years after occupancy of the permanent facility, Scripps shall establish a research program for middle and high school teachers.**

No response is due until March/April of 2012. However, Scripps has established a research program for teachers.

Scripps has established a professional development science workshop for secondary science teachers, as well as, a workshop for middle school teachers. In addition, Scripps Florida offers summer internships to secondary science teachers.

Scripps Florida High School Teacher Summer Internship Program

Continued support from the William R. Kenan, Jr. Charitable Trust, has allowed Scripps Florida Education Outreach to continue to expose teachers to current laboratory techniques and procedures, provide information on a variety of contemporary issues in basic biomedical research, create ties and linkages to working scientists who can assist them in curriculum development, and create opportunities for teachers to share information and knowledge with their peers.

High school science teachers in the Palm Beach County School District conduct basic biomedical research in a laboratory under the supervision of a Scripps Florida scientist. The program emphasizes the scientific process, research planning, bench experience, experimental design, data analysis and interaction with laboratory personnel. As an adjunct to their day-to-day responsibilities, participants required to attend specially designed seminars throughout the course of the summer. In addition to the intensive, hands-on six-week summer program, teachers are expected to use the laboratory experience as a springboard to create opportunities in discovery-based learning for their students, effect change in their classrooms and serve as a resource for other educators. Each participant gives a presentation and writes a scientific abstract on his/her project at the end of the summer.

To extend information about the summer program to all PBC eligible high school teachers, the Scripps Florida Education Outreach Director, Ms. Leach-Scampavia, supplied program information flyers to each of the PBC high schools' Principals for display at the schools and gave an information presentation about the summer intern program to a meeting of the high school science supervisors. In addition, working through the PBC school district's science coordinator, flyers were e-mailed to each of the science teachers in the district.

Eligibility

Research internships are awarded on a competitive basis to United States citizens or permanent residents teaching science at the secondary level in Palm Beach County.

An on-line application is available at the Scripps Florida education web page:
http://www.scripps.edu/florida/edprograms/flteacher.html.

The application time period for the internship program is from January until March.

Compensation

Teachers are awarded a gross compensation of $20.00 per hour for the six-week program (not to exceed 240 hours).

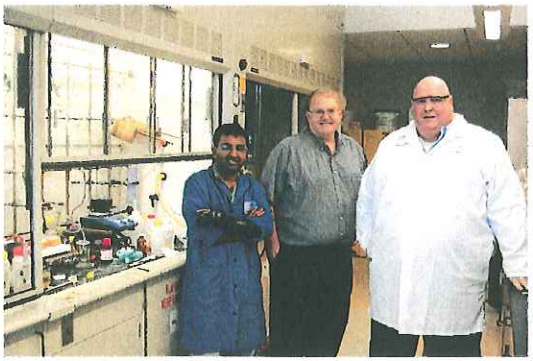
Selection Process for 2012 Scripps Summer Intern Program

After receipt of completed packages and due date expiration, the PBC science coordinator, the Scripps Florida education Administrator and several scientists reviewed each application package. Scripps Florida faculty mentors then reviewed and selected from the pool of interns a "best candidate" for the summer teacher internship.

2012 SUMMER HIGH SCHOOL TEACHER INTERNS

Name	Ethnicity	School	Subject
Lucas Basso Samuel Jackson	Caucasian Caucasian	Palm Beach Central HS Glades HS	Biology Chemistry

Lucas Basso (left) with Dr. Christopher Warner



Samuel Jackson (right) with Dr. Reji Nair (left) and Dr. Tom Bannister

Scripps Florida Secondary and Middle School Teacher Workshops:

Scripps Florida is directing greater efforts to address the needs of the classroom science teacher by establishing Teacher Workshops in basic science, math and laboratory skills. The programs offer direct interaction with the bioscience researchers at Scripps Florida and provide greater professional development opportunities for pre-service and in-service middle and high school science teachers in a supportive engaging

environment. Institutes are designed around curriculum units that integrate lessons, activities and laboratory-based biological and chemical experiments designed by research scientists at Scripps Florida. Portability of the lessons allows teachers to leverage the institute curriculum to their own classrooms during the course of the school year.

The programs provide opportunities for teachers from all of the secondary and middle schools within the Palm Beach County school district to attend the Teacher Workshops. Through its partnership with the school district, Scripps Florida emphasizes teacher recruitment from schools with limited resources in rural and urban Palm Beach County, particularly in areas with large underrepresented and disadvantaged student populations.

Palm Beach County science teachers with Dr. Heidi Walsh

Palm Beach County science teachers with Dr. Cindy Qi (right)

Section 4.4(c)8 **Adjunct Professors. No later than 18 months after occupancy of the permanent facility, Scripps shall establish a program for adjunct professors.**

Many current Scripps Florida Faculty have received adjunct Faculty appointments with the University of Florida, University of Miami and/or Florida Atlantic University. Such adjunct appointments are intended to provide a mechanism for graduate students enrolled in Florida research universities to collaborate with, to be co-mentored by, and to perform research in the laboratories of a Scripps Florida faculty member.

A mechanism has been established for faculty members at Florida institutions who have established collaborative research programs with Scripps Florida faculty to be appointed to an Adjunct Professor position.

The process is initiated by a Scripps Florida faculty member who submits a nomination to his/her department chair. If the chair concurs, the chair submits the nomination to the Office of the President for review and approval.

Current adjunct faculty:

Dr. Chris Liang of Xcovery in West Palm Beach, FL – Adjunct Associate Professor, Molecular Therapeutics

Dr. Andrew Hodge of BioMotion Institute in Jupiter, FL – Adjunct Professor, Metabolism and Aging

Dr. Samuel Young of Max Planck Florida Institute in Jupiter, FL – Adjunct Assistant Professor, Neuroscience

Dr. Jason Christie of Max Planck Florida Institute in Jupiter, FL – Adjunct Assistant Professor, Neuroscience

Dr. James Schummers of Max Planck Florida Institute in Jupiter, FL – Adjunct Assistant Professor, Neuroscience

Dr. Richard Flavell of Yale University in New Haven, CT – Adjunct Professor, Infectology

Dr. Stephen Hitchcock of Envoy Therapeutics in Jupiter, FL – Adjunct Professor, Molecular Therapeutics

Dr. Reddy Moola of Opko Health in Miami, FL – Adjunct Associate Professor, Chemistry

Dr. Michele A Miller (Chief Veterinary Officer) of the Palm Beach Zoo in West Palm Beach, FL – Adjunct Professor, Infectology

Section 4.4(c)9 **Access for Science Projects. No later than 6 months after commissioning its high throughput technology, Scripps shall establish a program to allow open access for qualified science projects.**

Scripps Florida initiated the "Access to Technologies" program in January of 2006 to invite scientists from Florida universities and other academic research institutions to use state-of-the-art screening technologies at Scripps Florida's facilities in Jupiter for qualifying projects. A seventh "Core" platform is now available at the Scripps Florida facility that combines basic research with advanced technology.

Access to Technologies

Scripps Florida was created to interface cutting-edge high throughput technologies with pioneering research programs relevant to current medical needs in human diseases. One of our key goals is to develop dynamic relationships with Florida institutions to foster a knowledge-based economy that will transcend traditional barriers to moving scientific discoveries into the clinic. Florida scientists who may not have these technologies available at their respective institutions are encouraged to open the links to learn more about these Core Technologies and opportunities to access them

(http://www.scripps.edu/florida/technologies/). A list of collaborative Florida researchers can be found in Section 4.4(c)10 (Collaboration with Florida Colleges and Universities).

Macromolecular X-ray Crystallography Facility

Macromolecular X-ray crystallography core facility of Scripps Florida offers state-of-the-art equipment and resources to scientists inside and outside of the Scripps FL campus by providing crystallographic analysis of their chosen biological macromolecules.

The core facility offers and operates as a full service core by performing protein crystallization, X-ray diffraction data collection (both in-house and at various synchrotron sources) and processing, phasing, crystallographic refinement, model building, and visualization. The structural data obtained by the core provide scientists with a wealth of information including but not limited to biological functions, 3D-folding, ligand binding (small molecule or protein), or mutational effect of target macromolecules of their interests.

Crystallization Screening: For macromolecular crystallization experiments, the core facility uses commercially available 960 crystallization conditions plus various optimization reagents whose combination can make millions of different crystallization conditions. The equipment available for crystallization is:

(1) a Minstrel III, an automatic plate handling and imaging system,
(2) two RoboIncubators, which can store crystallization plates in a temperature and humidity controlled environment,
(3) a Leica stereomicroscope and a high powered stereoscope for manual crystal photography, crystal screening, and crystal manipulation.
(4) The TTP LabTech mosquito crystallization robot, Innovadyne 96+8 crystallization robot, and Emerald's Matrix Maker are used to perform automated protein crystallization and optimization experiments.

Data Collection Service: Diffraction experiments are performed at in-house x-ray facility as well as synchrotron beamlines (APS and SSRL). The equipment setup for in-house X-ray diffraction data collection consist of:

(1) a Rigaku MicroMax-007 HFM X-ray generator with a VariMax HR optics and an X-Stream 2000 crystal cryo-freezing system,
(2) a Proteros Free Mounting System (FMS) for handling and manipulating room temperature grown crystals for diffraction optimization,
(3) Mar345dtb image plate detector for recording X-ray diffraction patterns,

(4) two dedicated computers in the facility for data collection and processing.

Structure Determination and Analysis: A complete data set collected at home or synchrotron are processed for macromolecular structure determination, model building, and crystallographic refinement.

This past year, the core facility has produced 7 publications in major research journals and acquired data for additional 3 manuscripts. The core facility supported 6 intramural laboratories for their on-going grant researches. The core facility was also actively involved in preliminary studies for grant applications of these laboratories. During this period, the core facility produced and deposited multiple macromolecular structures.

Genomics Core

The Scripps Florida Genomics Core was established to enable access by Scripps Florida and external investigators to the latest technologies for gene expression analysis and high-throughput genotyping. These technologies allow for interrogation and subsequent comparison of the role genetics play in disease state at the global level, or at specified locations in the genome. Gene expression analysis provides a profile of active and inactive genes in a given tissue sample or cell type. The technologies used in the Genomics Core allow for a wide range of cost effective options for discovery on multiple platforms.

Listed below are the available services provided by the Cell Based Screening facility:

Affymetrix GeneChip Arrays:
Gene Expression Mouse 430 2.0 and Human U133
Gene ST 1.0 arrays (Human and Mouse)
Genotyping Human (1MM)
Parallele custom arrays (5K, 10K, 20K)

Illlumina arrays:
Human ref-8 and HT12
Mouse ref-8
WG DASL Human FFPE

Illumina Next Generation Sequencing:
mRNA Seq single sample or multiplexing up to 12 samples
miRNA Seq multiplexing up to 48 samples
DNA/ChIP Seq multiplexing up to 12 samples

Florida researchers can apply for access to Scripps expertise through the Scripps "Access to Technologies" program.

The Cell Based Screening Core

Researchers in the Cell-Based Screening Core leverage high-throughput technologies towards a systematic description of the function of genes encoded by the human genome, and a more comprehensive understanding of the genetic basis for human disease. The CBS group provides Scripps investigators, as well as select outside collaborators, with access to genome-wide collections of cDNAs and siRNAs that can be used to interrogate cellular models of signal transduction pathways and phenotypes.

Listed below are the available services provided by the Cell Based Screening facility:

1. Qiagen Druggable Genome siRNA Library (v.2): 28,000 siRNAs generated against 7,000 target genes plated in 384 well format as a single siRNA per well at a concentration of 20 nM (1x 20 nM) or 4 pooled siRNA per well at a final concentration of 50 nM (12.5 nM for each siRNA) or 20 nM (5 nM for each siRNA).

2. Mammalian Genome Collection (MGC) cDNA Library: 16,953 human (6609 clones; 5537 unique sequences) and mouse (10,344 clones; 7718 unique sequences) cDNA sequences in an expressible vector are plated in 384 well format as 1 clone per well at a concentration of 40 ng.

3. MGC focus set generation and screening: focus sets from the MGC cDNA library can be picked, prepped and plated in 96 or 384 well format then screened in a functional assay.

4. Gal4-Transcription Factor Library: 837 human or 721 mouse transcription factors fused to the Gal4. DNA binding domain plated in 384 well format as 1 clone per well at a concentration of 40 ng.

5. Sigma Lopac: Library of Pharmacologically Active Compounds (1280 cmpds)

6. Mutagenesis Screening: To identify residues important for gene function, the gene cDNA is chemically mutagenized. Clones are plated in 384 well format and screened in a functional assay. Hits can then be picked and counter-screened.

Screening:

The CBS core can run the screen for the investigator after the investigator has optimized the functional assay on a fee for service basis. We can also provide lipid reagents for transfection and read-out reagents such as BriteLite and AlphaScreen beads for screens.

Screening Parameters:

Cell line:	transfectability of cell line is paramount and requires optimization of lipid reagent used.
Controls:	Positive and negative controls are highly encouraged. Plate sets have space for 4 controls with an n=4 each (16 wells). Need minimal %CV.
Read-out:	Fluorescence Luminescence Absorbance Alphascreen (homogenous bead based ELISA assay-PE) Acceptable dynamic range (signal to noise)

Florida researchers can apply for access to Scripps expertise through the Scripps "Access to Technologies" program.

The Proteomics Core

The Proteomics Core at Scripps Florida conducts research in the field that examines the expression and action of proteins and other gene products. Its faculty and staff focus on such questions as how proteins are modified by cells in certain diseases. In particular, the scientists concentrate on developing and applying the techniques of mass spectrometry for discovery and quantitative proteomic experiments. The core also supports the small molecule mass spectrometry needs of the institute and collaborators.

Listed below are the available services provided by the proteomics facility:

1. Proteomics: HPLC MS/MS characterization of gel bands and complex protein mixtures such as whole cell lysates. Posttranslational modifications can also be mapped. Database searches are performed with multiple search engines and data are presented with Scaffold (Proteome Software, Portland, OR).

2. Mass Spectrometry: High resolution mass spectrometry analysis of small molecules for confirmation of structure.

3. HPLC Purification: Peptides or small proteins can be purified using reverse phase separation. Detection systems include UV, multi wavelength and fluorescence.

Florida researchers can apply for access to Scripps expertise through the Scripps "Access to Technologies" program.

The Flow Cytometry Core

Flow cytometry measures and analyzes the characteristics of single particles, normally cells, as they move in a stream and are passed through a laser. Thousands of cells can be analyzed by a flow cytometer in a single second. Among the measurements derived from flow cytometry are the size, relative fluorescence and complexity of the particle.

The Flow Cytometry group utilizes one cell sorter, two analyzers, one laser capture micro-dissection microscope and an animal blood cell counter/differential analyzer to aid investigators with their studies.

The FACSAriaII is a three-laser cell sorter. The FACSAriaII uses a 488nm (blue), 633nm (red), and a 407nm (violet) laser system. Sorting using up to thirteen fluorescence parameters as well as light scatter discrimination (cell size, organelle composition and density, and doublet discrimination). Applications include high speed, four-way cell sorting, cell purification, slide sorting, cell cloning (by automated deposition into 6, 12, 24, 48, 96 well plates), and sorting of potentially hazardous materials (human samples, retro-virally transduced cells) at the BSL2 level.

The BD LSRII is a five-laser analyzer. The LSRII uses a 488nm (blue), 561nm (yellow green), 640nm (red), 407 nm (violet), and a 355nm (UV) laser system. Analyses of up to fourteen fluorescence parameters as well as light scatter discrimination (cell size, organelle composition and density, and doublet discrimination). Applications include but are not limited to immunophenotyping, cell cycle analysis (DNA content), and calcium flux (ratiometric imaging).

The Beckman Coulter Gallios is a three-laser analyzer. The Gallios uses a 488nm (blue), 638nm (red), and a 405 nm (violet). Analyses of up to ten fluorescence parameters as well as light scatter discrimination (cell size, organelle composition and density, and doublet discrimination). Applications include but are not limited to immunophenotyping, and cell cycle analysis (DNA content), The Gallios also features a 32-tube multi carousel loader that allows for faster tube sampling.

The Leica LMD laser capture microdissection microscope has 4X, 6.3X, 10X, 20X, 40X, and 63x objectives, automated motorized scanning and positioning, and remote stylus operated input. Laser capture

microdissection allows for the precise and contamination-free isolation of specific areas of tissue (e.g. tumor material) from single cells or cell groups according to morphological criteria. The dissected material is then directly accessible for further analysis.

The Hemavet 950 FS is an animal blood cell counter/differential analyzer. The Hemavet allows for a fast and complete five-part WBC differential. It includes 20 parameters including platelets. The Hemavet is fully automated and simple to operate. Whole blood analysis is available for mouse and rat blood specimens with as little as 30ul. Tissue culture counting is also available.

Florida researchers can apply for access to Scripps expertise through the Scripps "Access to Technologies" program.

The Nuclear Magnetic Resonance Core

Nuclear magnetic resonance, known as NMR, uses the magnetic properties of certain nuclei to study molecular structure. A wide variety of information can be gathered using NMR including protein and nuclei acid structure and function. In early 2011, Scripps Florida added a new state-of-the-art 700 MHz instrument to the NMR core, complementing the two 400 MHz instruments already on site. While the two 400 MHz instruments are used primarily for small molecule (chemistry) studies, the new 700 MHz instrument will be used primarily by biologists for studying structure and interactions among biomolecular components (proteins, RNA, etc.). The three machines run 24 hours a day, 365 days of the year. By connecting these highly sensitive instruments to the Internet via a proprietary Scripps Florida server, scientists can access the data produced from their office or the laboratory.

Florida researchers can apply for access to the NMR Core and Scripps expertise through the Scripps "Access to Technologies" program.

High Throughput Screening Core Description Background

High Throughput Screening (HTS) is a drug-discovery process widely used in the pharmaceutical industry. It leverages automation to quickly assay the biological or biochemical activity of a large number of drug-like compounds. It is a useful for discovering ligands for receptors, enzymes, ion-channels or other pharmacological targets, or pharmacologically profiling a cellular or biochemical pathway of interest. Typically, HTS assays are performed in "automation-friendly" microtiter plates with a 96, 384 or 1536 well format.

Capabilities

The Lead Identification group at Scripps Florida has set-up a state-of-the art HTS operation to support Scripps' intramural HTS efforts. This Core has both HTS and compound management automation, and expertise in adapting biological and biochemical bench-top assays into high-throughput screens.

Listed below are the available services provided by Lead Identification Core:

1. Assay Implementation: If an assay is accepted into the Access to Technologies Program, Scripps will use its expertise to execute an HTS assay to 384-well or 1536-well plate format as necessary.

2. Access to Technologies Compound Library: Scripps has designated a subset of its HTS compound collection (~1280 pharmacological entities) to be used for Access to Technologies screening efforts. This collection contains known inhibitors/activators of the most common HTS target classes (GPCRs, ion channels, etc.).

3. HTS Screening & Follow-up: Once the submitted assay has been optimized for HTS, the "Access to Technologies" Compound Library will be screened (n=3 per compound) at a single concentration. [Compounds will be assayed in triplicate to confirm activity.] Upon completion of the follow-up assay, a table of data listing the compound id#, screening concentration, and %activity (or %inhibition) for each hit compound will be provided to the researcher.

Although there are a variety of biochemical and biological assays, only a subset is amenable to HTS. Only a limited number of HTS campaigns/year is available through the Access to Technologies program. The Scripps selection process includes a review of various criteria, such as assays that are amenable to automation and research programs that may have significant impact on the scientific community.

Florida researchers can apply for access to Scripps expertise through the Scripps "Access to Technologies" program.

HTS users:

Hitchcock, S., Ph.D.	Envoy Therapeutics
Leissring, M., Ph.D.	Mayo Clinic, Jacksonville, FL
Fields, G., Ph.D.	TPIMS
Minond, M., Ph.D.	TPIMS

Cudic, P., Ph.D.	TPIMS
Weissbach, H., Ph.D.	FAU
Zervos, A., Ph.D.	UCF
Liao, D., Ph.D.	UF
Potter, J., Ph.D.	U Miami
Ayad, N., Ph.D.	U Miami

Section 4.4(c)10 **Collaboration with Florida Colleges and Universities. Beginning June 2004, Scripps shall commence collaborative efforts with Florida public and private colleges and universities, and shall continue cooperative collaboration through the term of the Agreement.**

On-going and new scientific collaborations between Scripps Florida scientists and colleagues from Florida colleges, universities, and local companies are described in the table below.

Scripps Florida Collaborator	Institutional Collaborator(s)	Institution	Description of Collaboration
Peter Hodder	Zervos, Anthony	UCF	High Throughput Screening
Peter Hodder	Fields, Gregg B	TPIMS	High Throughput Screening
Peter Hodder	Dmitriy Minond	TPIMS	High Throughput Screening
Peter Hodder	Malcolm Leissring	Mayo Clinic	High Throughput Screening
Peter Hodder	Nagi Ayad	U Miami	High Throughput Screening
Peter Hodder	James Potter	U Miami	High Throughput Screening
Michael Chalmers	Neil Glynn	USDA-ARS Canal Point, FL	Proteomics
Michael Chalmers	Sanjoy Bhattacharya Gaofeng Wang Mary Lou King	U Miami	Proteomics
Michael Chalmers	Gregg Fields	TPIMS	Proteomics
Timothy Tellinghuisen	Eugene Schiff	U Miami	HCV induced hepatocellular Carcinoma
John Cleveland	Paul Okunieff	U Florida	The Florida Collaborative Cancer Research Initiative
	Herbert Weissbach	FAU	
Paul Kenny	Barbara Krantz	Hanley Center	Human studies on addiction

Paul Kenny	Karen Dodge	Hanley Center	Human studies on addiction
Michael Conkright	A. Massimo Caputi	FAU	Post-translational gene regulation
Michael Conkright	B. Glen Barber	U Miami	Identification of molecules involved in innate immunity
William Roush	Gregg Fields	TPIMS	Design and synthesis of inhibitors of metallomatrix proteinases
William Roush	Arthur Edison	U Florida	Structure determination, synthesis, and biological evaluation of natural products from insects
William Roush	Stephan Schurer	U Miami	1) Modeling of ligand binding to orphan nuclear receptors 2) Modeling inhibitors targeting kinases involved in regulation of cell cycle
William Roush	Dimitriy Minond	TPIMS	Design and synthesis of inhibitors of metallomatrix proteinases (MMP's and ADAM's)
William Roush	Nagi Ayad	U Miami	Design, synthesis and biological characterization of inhibitors of Wee1degradation
Philip LoGrasso	Sam Young	Max Planck Florida	SGK-1 viral expression for Protection in Parkinson's Disease
Philip LoGrasso	Dennis Steindler	U Florida	JNK inhibition in glioblastoma stem cells and adult neural precursor cells
Philip LoGrasso	Stephan Schurer	U Miami	Modeling of bidentate JNK inhibitors
Patricia McDonald	Dr. Robert Speth	Nova Southwestern	Investigating ligand Bias at the Angiotensin II Receptor
Patricia McDonald	Dr. Xin Qi	U Florida	Characterizing novel Peptoids targeting GLP1R and OX1R
Brandon Young	Joe Doyle	Envoy Therapeutics	Array and NGS experiments
Brandon Young	Nagi Ayad	U Miami	Cell Based Screening
Brandon Young	Claes Wahlestedt	U of Miami	Gene Expression studies
Brandon Young	Joseph Benito	Ocean Ridge Biosciences	Gene Expression profiling

Brandon Young	Kumaravel Chidamparam	Ocean Ridge Biosciences	Array & Gene Expression profiling
Brandon Young	David Willoughby	Ocean Ridge Biosciences	Cell Based Screening
Alicia F. Brantley	Jahansha Amin	University of South Florida	Biosciences Behavioral testing of novel compound
Donald Phinney	Dr. Singla	UCF	Collaborative Agreement with University of Central Florida – Dr. Phinney (Scripps) to provide recombinant retroviral expression vectors and Dr. Singla (UCF) to transfect or infect the constructs and virus containing the constructs into human ES and iPS cells maintained in his lab.
Donald Phinney		Jupiter Medical Center	Collaboration with Jupiter Medical Center (JMC provides cancer cells to Phinney lab per MTA June 21, 2011
Katrin Karbstein	Bethany Stroupe	FSU	Electron microscopic analysis of pre-ribosomal complexes and ribosome assembly factors.
Sathya Puthanveettil	Tom Capo	U Miami	Aplysia Aging
Sathya Puthanveettil	Lynne Fieber	U Miami	Aplysia Aging
Sathya Puthanveettil	Leonid Moroz	U Miami	Aplysia Genome

Section 4.4(c)11 **Seminar Series. Beginning 18 months after Scripps occupies the permanent facility, Scripps shall establish an annual seminar series featuring a review of the science work done by Scripps and its collaborators.**

The establishment of a seminar series is not scheduled to begin until September of 2010. However, 2005 saw the start of the Scripps Florida Collaborative seminar series and in 2006 the Scripps Florida External seminar series was established.

Collaborative seminars feature prominent Florida-based speakers from the academic, biotechnology or pharmaceutical communities and focus on topics within the broad fields of biomedical science, advanced technologies applied to biomedical research, drug discovery, and energy. External seminars are part of the institute series, inviting prominent researchers from national and international institutions. Both serve as a major foundation for creating knowledge- and technology-sharing opportunities, team building, and collaborations among biomedical

researchers between Scripps Florida, Florida, and other research and academic institutions and companies. The sessions are open to interested professionals within the Scripps Florida and Florida scientific communities.

The weekly summer intern series, an adjunct to summer intern day-to-day responsibilities, features faculty members from Scripps Florida. High school and college undergraduate interns attend specially-designed seminars throughout the course of the summer. Each seminar highlights basic science principles and the research focus/application efforts of the Scripps Florida biology, chemistry, and Core laboratories.

External Seminars

September 22, 2011	Speaker: Dr. Alan Hall Memorial Sloan Kettering Cancer Center Lecture - "Rho GTPases controlling epithelial morphogenesis and migration"
October 6, 2011	Speaker: Dr. Marc Reitman National Institutes of Health (NIH) Lecture - "BRS-3 Agonists for the Treatment of Obesity"
October 13, 2011	Speaker: Dr. Ron Emerson Vanderbilt University Lecture - "Prader-Willi Syndrome, RNA Editing and the Tyranny of Evidence"
October 20, 2011	Speaker: Dr. David Lawrence University of North Carolina Lecture - "Organic Chemistry at the Edge of Biology: Taming Cell Behavior with Light Responsive Molecules"
October 27, 2011	Speaker: Dr. Jiyong Hong Duke University Lecture – "Natural Product Synthesis at the Interface of Chemistry and Biology
November 3, 2011	Speaker: Dr. Olke Unlenbeck Northwestern University Lecture - "tRNA Tuning in Translation"
November 10, 2011	Speaker: Dr. Sandy Schmid The Scripps Research Institute, California Lecture - "Dynamin: The Brains and Brawn of Clathrin-Mediated Endocytosis"
November 17, 2011	Speaker: Dr. Richard Flavell Yale University School of Medicine Lecture - "Inflammasomes and homeostasis in the intestine and beyond"

November 29, 2011	Speaker: Dr. M.G. Finn Professor The Scripps Research Institute, California Lecture - "Engineered Virus-Like Particles for Medicine and Catalysis"
December 1, 2011	Speaker: Dr. Christine Keating The Pennsylvania State University Lecture - "Polymer solutions as a model cytoplasm in primitive artificial cells based on lipid vesicles"
December 8, 2011	Speaker: Dr. Donna Blackmond The Scripps Research Institute, California Lecture - "Mechanistic Studies in Asymmetric Organocatalysis: A New Paradigm for Stereocontrol"
December 15, 2011	Speaker: Dr. Stuart Schreiber Broad Institute of Harvard & MIT Lecture - "Relating genetic features of cancers to cancer dependencies using small-molecule probes"
January 12, 2012	Speaker: Dr. Paul Fox Cleveland Clinic Lecture - "The GAIT system: A gatekeeper of inflammatory gene expression"
January 16, 2012	Speaker: Dr. Victor Garcia-Martinez University of North Carolina, Chapel Hill Lecture – "In vivo Evaluation of Novel Approaches to Prevent, Treat, and …Cure?? HIV/AIDS"
January 19, 2012	Speaker: Dr. Alcino Silva University of California Los Angeles (UCLA) Lecture - "Light activated memories: Molecular, cellular and systems mechanisms of memory allocation"
February 2, 2012	Speaker: Dr. John Clardy Harvard Medical School Lecture - "Bacterial Communications and the Discovery of New Molecules"
February 9, 2012	Speaker: Dr. P. Jeffrey Conn Vanderbilt University Medical Center Lecture - "Allosteric Modulators of GPCRS as a Novel Approach to Treatment of CNS Disorders"
February 23, 2012	Speaker: Dr. William Carlezon Harvard University Lecture - "Roles of CREB and dynorphin in dysregulation of motivation"
February 29, 2012	Speaker: Dr. Seth Grant University of Edinburgh School of Molecular & Clinical Medicine Lecture - "Postsynaptic MAGUK Associated Signaling Complexes underlie the organization and evolution of behavior"

March 8, 2012	Speaker: Dr. Nevin Lambert Georgia Health Sciences University Lecture - "Organization of G protein signaling proteins in live cells"
March 15, 2012	Speaker: Dr. Amy Herr University of California, Berkeley Lecture - "Talking about a Revolution: Microfluidic Integration for Next-Generation Protein Analysis"
March 22, 2012	Speaker: Dr. Kristin Baldwin The Scripps Research Institute, California Lecture - "Stochastic diversity among induced pluripotent stem cells and neurons"
March 29, 2012	Speaker: Dr. Jeremy Nicholson Imperial College, London Lecture - "Host-microbiome metabolic and signaling interactions in human health and disease"
April 5, 2012	Speaker: Dr. Akira Sawa Johns Hopkins University School of Medicine Lecture - "Is schizophrenia a systemic disorder?: a multifaceted translational approach"
April 19, 2012	Speaker: Dr. Shu-ou Shan California Institute of Technology Lecture – "Molecular mechanism of co-translational protein targeting"
April 27, 2012	Speaker: Dr. Peter Vogt The Scripps Research Institute, California Lecture: "Oncogenic signaling in the PI3K pathway"
May 3, 2012	Speaker: Dr. Ailong Ke Cornell University Lecture – "Conformation dynamics in SAM-III translational riboswitch and RNA interference in Type I-C CRISPR-Cas system"
May 10, 2012	Speaker: Dr. Robert Batey University of Colorado Boulder Lecture – "Structural insights into biological riboswitches and their application to synthetic biology"
May 24, 2012	Speaker: Dr. Leslie Vosshall Howard Hughes Medical Institute Lecture – "The Genetics of Innate Behavior: Smell, Sex, and Eating"

Collaborative Seminars

July 27, 2011	Speaker: Leonid L. Moroz, PhD Professor of Neuroscience, Biology & Chemistry Department of Neuroscience & The Whitney Laboratory for Marine Bioscience, University of Florida Lecture - "Genomic Organization of Neural Circuits at Single-cell Resolution: Insights into Memory Mechanisms and Neuronal Origins"
November 28, 2011	Speaker: Mario Stevenson, PhD Chief, Division of Infectious Diseases Professor of Medicine, University of Miami Lecture - "Strategies for HIV Eradication"
December 6, 2011	Speaker: Jay P. McLaughlin, PhD Associate Member, Torrey Pines Institute for Molecular Studies Lecture - "Functional consequences of opioid receptor ligand-directed signaling"
January 20, 2012	Speaker: Aaron Aponick, Ph.D. Professor, Department of Chemistry, University of Florida Lecture - "Catalytic Dehydrative SN2' Reactions: Mechanistic and Synthetic Implications"
March 30, 2012	Speaker: Kailiang Jia, PhD Assistant Professor, Department of Biological Sciences, Florida Atlantic University Lecture - "ATP production: the key to understand the role of autophagy in apoptosis and aging"
April 13, 2012	Speaker: Robert C. Speth, PhD Department of Pharmaceutical Sciences School of Pharmacy Nova Southeastern University Lecture - "New developments in the renin-angiotensin system: Holding two ACEs and a Wild Card"

Summer Intern Seminars

July 4, 2011	William Ja, Ph.D. Assistant Professor, Department of Metabolism and Aging TSRI- Florida Lecture - "Drosophila as a Model Organism"
July 12, 2011	Roy Smith, Ph.D. Professor and Chair Department of Metabolism and Aging TSRI- Florida Lecture - "Understanding Alterations in Whole-body Metabolism"
July 19, 2011	Paul Kenny, Ph.D. Associate Professor, Molecular Therapeutics TSRI- Florida Lecture - "Neurobiological Mechanisms of Drug Addiction"
June 5, 2012	Brian Paegel, Ph.D. Assistant Professor, Department of Chemistry TSRI-Florida Lecture – "Discovering Drug Discovery"
June 12, 2012	Patrick Griffin, Ph.D. Professor and Chair, Department of Molecular Therapeutics TSRI-Florida Lecture – "Nuclear Receptors"
June 19, 2012	Tim Tellinghuisen, Ph.D. Associate Professor, Department of Infectology TSRI-Florida Lecture – "Weird Biology: Host/Virus Coevolution"
June 26, 2012	Matthew Gill, Ph.D. Associate Professor, Department of Metabolism and Aging TSRI-Florida Lecture – "C elegans as a Model Organism"

Section 4.4(c)12 **Collaboration with OTTED. Beginning June 2004, Scripps shall commence collaboration efforts with the Office of Tourism, Trade and Economic Development by complying with reasonable requests for cooperation in economic development efforts in the biomed/biotech industry, and no later than July 2004, Scripps shall designate a person who shall be charged with assisting in these collaborative efforts.**

Business outreach efforts include participation in meetings facilitated by local business and government agencies such as the Office of Tourism, Trade and Economic Development, Palm Beach County Business Development Board, and the technology Entrepreneurship & Capital Committee meeting. Similarly, community efforts involve presentations to local residential groups, various cultural organizations,

and specialty groups. Numerous educational programs such as the Summer Research Internship, Science Saturday, and Introduction to Science series have been ongoing including presentation to elementary, secondary, and high schools, selecting high school students as interns, and hands-on workshops. Scientific outreach spans a variety of regional, state and international interactions from conferences, seminars and workshops; to peer-to-peer discussions. A list of such outreach programs is shown below.

Business Outreach	Date	Participants	Recipients/Event
Business Outreach	27-Jul-11	Roy Periana, M.G. Finn, Nicolas J. Schork, Ali Torkamani, Peter Hodder, Louis Scampavia	July 28th SABIC meeting and presentation in La Jolla, CA
Business Outreach	26-Jul-11	Douglas Kojetin	BioTools, Inc./Instrument assistance, Jupiter, Florida
Business Outreach	27-Jul-11	Barbara Noble	Economic Forum of Palm Beach County
Business Outreach	4-Aug-11	Peter Hodder	Agios Pharmaceuticals, Cambridge, MA, USA
Business Outreach	22-Aug-11	Peter Hodder	SANOFI, Tucson, AZ, USA
Business Outreach	13-Sep-11	Paul Kenny	Interview with Bob Langreth of Bloomberg Business
Business Outreach	20-Sep-11	John Cleveland	American Cancer Society, North Palm Beach Unit Board Meeting at Scripps
Business Outreach	6-Oct-11	Donny Strosberg	U.C.F. presentation: "Biotechnology: What it means to Florida's Community"
Business Outreach	12-Oct-11	Roy Periana	AirProducts meetings and presentation
Business Outreach	14-Oct-11	Donald Phinney	Meet with Richard Shaw of IntelliCell, Boynton Beach, FL
Business Outreach	17-Oct-11	Louis Scampavia	SABIC, La Jolla, CA, USA
Business Outreach	19-Oct-11	Peter Hodder	Nexus Biosystems/Brooks Automation, Poway, CA, USA
Business Outreach	2-Nov-11	Roy Periana	Argonne National Laboratories meeting/talk
Business Outreach	7-Nov-11	Paul Thompson	Seminar at Constellation Pharmaceuticals, Inc. Cambridge, MA
Business Outreach	8-Nov-11	Paul Thompson	Seminar speaker at Epizyme. Cambridge, MA
Business Outreach	15-Nov-11	John Cleveland	Scripps/Pfizer Meeting at Scripps
Business Outreach	22-Dec-11	Peter Hodder	Envoy Therapeutics, Jupiter, FL, USA
Business Outreach	9-Jan-12	Ron Davis	Palm Beach Round Table, Palm Beach, FL
Business Outreach	9-Jan-12	Donny Strosberg	JP Morgan - California
Business Outreach	16-Jan-12	Paul Kenny	Meet with new CEO The Hanley Center, West Palm Beach, FL
Business Outreach	17-Jan-12	Alex Bruner, Ben Starling, Lisa Huertas	Forum Club of the Palm Beaches
Business Outreach	31-Jan-12	Barbara Noble, Ben Starling, Lisa Huertas	Forum Club of the Palm Beaches
Business Outreach	1-Feb-12	Donny Strosberg	Florida Venture Forum - Naples, Florida

Business Outreach	14-Feb-12	Alex Bruner	Planned Giving Council of Palm Beach County, Meeting
Business Outreach	28-Feb-12	Peter Hodder	Ironwood Pharmaceuticals, Boston, MA, USA
Business Outreach	28-Feb-12	Roy Periana	Mainstream Engineering meeting in Rockledge, Florida
Business Outreach	29-Feb-12	Peter Hodder	Lilly, Indianapolis, IN, USA
Business Outreach	8-Mar-12	Barbara Noble	Palm Beach Chamber of Commerce meeting
Business Outreach	13-Mar-12	Peter Hodder	NoNO, Inc., Toronto, Canada
Business Outreach	6-Apr-12	Ron Davis	Drs. Kini, Perdoma and Jayakar from Miami Children's Hospital, Scripps
Business Outreach	9-Apr-12	Peter Hodder	Energesis Pharmaceuticals, Cambridge, MA, USA
Business Outreach	12-Apr-12	Barbara Noble	Palm Beach Chamber of Commerce meeting
Business Outreach	24-Apr-12	Peter Hodder	Ember Therapeutics, Boston, MA, USA
Business Outreach	3-May-12	Barbara Noble	Executive Women of the Palm Beaches
Business Outreach	11-May-12	Peter Hodder	DavosPharma, Upper Saddle River, New Jersey, USA
Business Outreach	14-May-12	Dr. Damon Page, Ben Starling	Pundits of Palm Beach
Business Outreach	21-May-12	Ron Davis	Future of Medicine Summit Leadership Committee Meeting, West Palm Beach, FL
Business Outreach	30-May-12	Corinne Lasmexas	Meeting about technology commercialization
Business Outreach	6-Jun-12	Christoph Rader	Meeting between The Scripps Research Institute (La Jolla, CA and Jupiter, FL) and Vanderbilt University (Nashville, TN) in Dallas, TX
Business Outreach	7-Jun-12	Ron Davis	Steering Committee Meeting, Dallas TX
Business Outreach	13-Jun-12	Alex Bruner	Palm Beach Planning Council
Business Outreach	15-Jun-12	Paul Kenny	Conference with Michael DeVivo of Pfizer re: potential collaboration
Business Outreach	18-Jun-12	Ron Davis	Future of Medicine Committee Meeting, West Palm Beach, FL
Business Outreach	19-Jun-12	Ron Davis and Damon Page	Dick Busto, Autism Project Meeting, West Palm Beach, FL
Business Outreach	20-Jun-12	Ron Davis	Palm Beach County Medical Society BOD Meeting, West Palm Beach, FL
Business Outreach	21-Jun-12	Susana Valente	Sirenas consulting in La Jolla, CA
Business Outreach	22-Jun-12	Paul Kenny	Meet with Dawn Johnson, Alex Bruner and Rob Baird from Woodrow Wilson Drug Development Fellowship
Business Outreach	25-Jun-12	Paul Kenny	Meet with Drs. Patrick Griffin and Phillip Frost (The Frost Group) at The Frost Group offices in Miami, FL
Business Outreach	28-Jun-12	Paul Kenny	Telephone conference with Rob Baird of Woodrow Wilson Drug Development Fellowship
Business Outreach	10-Jul-12	Ron Davis	Palm Beach County Medical Society Kickoff Meeting, West Palm Beach, FL
Business Outreach	Monthly 2011-2012	Christopher Haga	Life Science Technology Hub meetings (Bio Florida)

Science Outreach below is outside FL. See Section 9.5(f) for Florida Science Outreach

Science Outreach	Date	Participants	Recipients/Event
Science Outreach	1-Jun-12	Shuji Kishi	Presented at International Conference on Zebrafish Development and Genetics; University of Wisconsin-Madison, Madison, WI
Science Outreach	1-Jul-11	Brian Paegel	Lecturer at National Institute of Standards & Technology, Gaithersburg, MD
Science Outreach	1-Jul-11	Ben Shen	Presentation at SIOC, CAS, Shanghai, China, hosted by Prof. Wen Liu Title: Natural Products Drug Discovery: Challenges and Opportunities
Science Outreach	4-Jul-11	Ben Shen	Presentation at Wuhan University, Wuhan, China, hosted by Prof. Zixin Deng Title: Natural Products Drug Discovery: Challenges and Opportunities
Science Outreach	4-Jul-11	Ron Davis	Kemali IBRO Mediterranean School of Neuroscience, Naples, Italy
Science Outreach	6-Jul-11	Peter Hodder	Ruslan Dorfman & Dave Garman, Neuroscience and Mental Health Program, Sickkids Hospital, Toronto, ON, CANADA
Science Outreach	8-Jul-11	Ben Shen	Presentation at the 5th Sino-US Round-Table Conference on Chemical Biology and Drug Discovery, Changsha, China (US organizer) Title: Natural Products Drug Discovery: Challenges and Opportunities
Science Outreach	10-Jul-11	William Roush	MLPCN Annual Steering Committee Meeting, Washington, DC
Science Outreach	12-Jul-11	Patrick Griffin	Centre for Drug Research and Development; Annual General Meeting of the Board; Vancouver CANADA (Board Director and Bi-monthly meetings for review of scientific grants)
Science Outreach	20-Jul-11	Peter Hodder	Irina Petrache, IUPUI, Indianapolis, IN, USA
Science Outreach	25-Jul-11	Donald Phinney	Invited speaker 2011 Stem Cell Therapies in Lung Biology and Lung Diseases Conference, University of Vermont, Burlington, VT
Science Outreach	27-Jul-11	Glenn Micalizio	Meeting at Amgen, Thousand Oaks, CA
Science Outreach	27-Jul-11	Sathya Puthanveettil	Hosted Dr. Leonid Moroz, University of Florida, Seminar Presentation
Science Outreach	28-Jul-11	Glenn Micalizio	Lecture at UCSB, Santa Barbara, CA
Science Outreach	30-Jul-11	Katrin Karbstein	Invited Speaker - FASEB Conference, Steamboat Springs, CO
Science Outreach	1-Aug-11	Bill Ja	Attended The Ellison Medical Foundation Colloquium on the Biology of Aging; Marine Biological Laboratory, Woods Hole, MA

Science Outreach	1-Aug-11	Patrick Griffin	Speaker for the Gordon Research Conference in Andover, NH; Biological Molecules in the Gas Phase & in Solution
Science Outreach	7-Aug-11	Courtney Miller	Gordon Research Conference: Epigenetics (Easton, MA)
Science Outreach	8-Aug-11	Ron Davis	Ellison Medical Colloquium, Woods Hole, MA
Science Outreach	9-Aug-11	Paul Kenny	Invited speaker Gordon Research Conference, Bates College, Lewiston, ME ("MicroRNAs in dopaminoceptive neurons regulate cocaine intake")
Science Outreach	10-Aug-11	Courtney Miller	Gordon Research Conference: Catecholamines (Bates College, ME)
Science Outreach	10-Aug-11	Paul Kenny	Invited speaker Cold Spring Harbour Summer Course re: cell biology of addiction, Cold Spring Harbour, NY
Science Outreach	25-Aug-11	Peter Hodder	Aimee Shen, University of Vermont, Burlington, VT, USA
Science Outreach	26-Aug-11	Peter Hodder	Scott Pegan, University of Denver, Denver, CO, USA
Science Outreach	27-Aug-11	Andrew Butler	Queenstown Molecular Biology Conference (New Zealand)
Science Outreach	27-Aug-11	Roy Periana	242nd ACS National Meeting-talk titled: "Modulating catalyst reactivity with acidic and basic solvents"
Science Outreach	29-Aug-11	Peter Hodder	David Mangelsdorf, University of Texas, Southwestern Medical Center, TX, USA
Science Outreach	30-Aug-11	Roy Smith	Helsinn Therapeutics
Science Outreach	1-Sep-11	Matt Gill	Presented "Regulation of Development & Lifespan by Small Molecules in C. elegans", to the Department of Cell Biology at the University of Georgia, Athens
Science Outreach	1-Sep-11	Bill Ja	Attended Dr. Rich Mathies' 65th Birthday Symposium "Eyes to the sky, feet on the ground - from rhodopsin and DNA to Mars: at 65 years looking back on a Rich career in biophysical and bioanalytical chemistry"; University of California, Berkeley; Berkeley, CA
Science Outreach	3-Sep-11	Roy Smith	European College of Neuropsychopharmacology (ECNP) Paris, France
Science Outreach	3-Sep-11	Kate Carroll	Seminar Speaker ESF-EMBO Symposium-Barcelona, Spain
Science Outreach	6-Sep-11	Peter Hodder	Kosta Petrukhin, Columbia University, New York, NY, USA
Science Outreach	7-Sep-11	Susana Valente	FLAD Conference on HIV/AIDS Research in Lisbon, Portugal
Science Outreach	7-Sep-11	Ron Davis	Virginia Tech Carillion Research Institute, Roanoke, Virginia
Science Outreach	8-Sep-11	William Roush	Eli Lilly Lectures on Organic Chemistry, Peking University, China

Science Outreach	8-Sep-11	Paul Kenny	Invited speaker Mini-Convention on Genetics of Substance Abuse - NIDA/NIAAA Satellite Symposium at the WCPG (World Congress of Psychiatric Genetics), Washington, DC
Science Outreach	10-Sep-11	Kate Carroll	Seminar Speaker Karolinska Institute & University of Stockholm, Stockholm, Sweden
Science Outreach	10-Sep-11	Roy Periana	ISHHC XV in Berlin, Germany-talk titled: "Design and Study of new Homogeneous Catalysts for Small Molecule Activation and Conversion."
Science Outreach	11-Sep-11	Paul Kenny	Invited speaker Symposium at WCPG (World Congress of Psychiatric Genetics), Washington, DC
Science Outreach	14-Sep-11	Paul Kenny	Invited reviewer - The Neurobiology of Addiction Research Center Review @ Medical University of South Carolina
Science Outreach	19-Sep-11	Thomas Kodadek	Pioneer Award Symposium, Washington, DC
Science Outreach	22-Sep-11	Ron Davis	Pavlovian Society Meeting, Milwaukee, WI
Science Outreach	23-Sep-11	Peter Hodder	Mark Yeager, University of Virginia School of Medicine, Charlottesville, VA, USA
Science Outreach	27-Sep-11	Paul Kenny	Reviewer MNG Study Section Review Panel, Washington, DC
Science Outreach	3-Oct-11	John Cleveland	2011 BloodCenter of WI Scientific Advisory Board review meeting
Science Outreach	3-Oct-11	Courtney Miller	Harvard Medical School, McClean Hospital Psychiatry Seminar
Science Outreach	3-Oct-11	Matthew Disney	The RNA Institute, University of Albany, Albany, NY Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	3-Oct-11	Tugba Guven Ozkan	Neurobiology of Drosophila Meeting, Cold Spring Harbor, NY
Science Outreach	4-Oct-11	Thomas Kodadek	NIDDK Review, Washington, DC
Science Outreach	5-Oct-11	Courtney Miller	Harvard Medical School, MassGeneral Hospital Neurology Seminar
Science Outreach	5-Oct-11	Thomas Kodadek	TSRI 50th Anniversary, La Jolla, CA
Science Outreach	5-Oct-11	Kirill Martemyanov	Seminar Presentation at the University of Brescia in Italy
Science Outreach	5-Oct-11	Gavin Rumbaugh	Seminar Presentation at MassGeneral Institute for Neurodegenerative Disease
Science Outreach	5-Oct-11	Katrin Karbstein	Grant Review Panel - Molecular Genetics A Study Section, Bethesda, MD
Science Outreach	6-Oct-11	Ben Shen	Molecular Discovery Program, NCI, Frederick, MD; hosted by Jeff Gildersleeve. Title: Natural Products Drug Discovery: Challenges and Opportunities

Science Outreach	7-Oct-11	Ben Shen	Ian Scott Symposium, Texas A&M University; hosted by Prof. Tadhg Begley Title: Natural Products Drug Discovery: Challenges and Opportunities
Science Outreach	10-Oct-11	Patrick Griffin	NIH Scientific Review DMP Study Section; San Francisco CA
Science Outreach	12-Oct-11	Thomas Kodadek	Seminar Speaker University of Texas at Austin Seminar, Austin, TX
Science Outreach	12-Oct-11	Ben Shen	Vanderbilt Institute of Chemical Biology Seminar, Vanderbilt University; hosted by Prof. Brian Bachmann Title: New Opportunities for Natural Product Biosynthesis, Engineering, and Drug Discovery
Science Outreach	18-Oct-11	Kate Carroll	Seminar Speaker University of California, Irvine and San Diego
Science Outreach	20-Oct-11	Ben Shen	College of Pharmacy and Department of Chemistry, Oregon State University, Corvallis, Oregon Hosted by Prof. Taiho Mahmud Title: Natural Products Biosynthesis - Opportunities for New Chemistry and Drug Discovery
Science Outreach	21-Oct-11	Ben Shen	Department of Chemistry, Portland State University, Portland, Oregon; hosted by Erik Johansson Title: Synthesis of Sorbicillactone A and 9-epi-Sorbicillactone A
Science Outreach	24-Oct-11	Katrin Karbstein	Invited Speaker - Yale School of Medicine, New Haven, CT
Science Outreach	26-Oct-11	Philip LoGrasso	Parkinson's Disease Therapeutics Conference - New York, NY
Science Outreach	27-Oct-11	Patrick Griffin	Biochemistry Seminar Speaker at Emory University, Decatur GA
Science Outreach	27-Oct-11	Damon Page	Developmental Biology Symposium, Cambridge, United Kingdom
Science Outreach	27-Oct-11	Roy Periana	C3Bio Annual Meeting at Purdue University
Science Outreach	31-Oct-11	Ben Shen	Cornell University; hosted by Prof. Shu-Bing Qian Title: Natural Products Drug Discovery: Challenges and Opportunities
Science Outreach	3-Nov-11	Roy Periana	Northwestern University talk
Science Outreach	6-Nov-11	William Roush	MLPCN Meeting, Nashville, TN
Science Outreach	7-Nov-11	Thomas Kodadek	Seminar Speaker Duke University, Durham, NC
Science Outreach	8-Nov-11	Paul Kenny	Reviewer National Institute on Drug Abuse (NIDA) Board of Scientific Counselors meeting
Science Outreach	9-Nov-11	Thomas Kodadek	Seminar Speaker-University of North Carolina, Chapel Hill, NC
Science Outreach	9-Nov-11	Gavin Rumbaugh	Autism Meeting, Washington, DC
Science Outreach	9-Nov-11	Susana Valente	Cold Springs Harbor Laboratories, NY-Viruses and Oncogenes: Stephen Goff Symposium

Science Outreach	9-Nov-11	Matthew Disney	CHDI Foundation, New York, NY Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	9-Nov-11	Pierre Baillargeon	IQPC Compound Management & Integrity Online 2011 - "Addressing Quality Control Issues in Day-to-Day HTS Compound Management Operations"
Science Outreach	9-Nov-11	Peter Hodder	David N. Frick, University of Wisconsin, Milwaukee, WI, USA
Science Outreach	10-Nov-11	Courtney Miller	NIH/National Institute of Drug Addiction Conference
Science Outreach	10-Nov-11	Courtney Miller	Molecular and Cellular Cognition Society Annual Meeting
Science Outreach	10-Nov-11	Ben Shen	UCLA Organic Colloquium special seminar, UCLA; hosted by Prof. Yi Tang. Title: Natural Products Drug Discovery: Challenges and Opportunities
Science Outreach	11-Nov-11	Paul Kenny	Invited attendee (as past award recipient) Waletzky Award dinner, Cosmos Club, Washington, DC
Science Outreach	12-Nov-11	Courtney Miller	Society for Neuroscience Annual Meeting
Science Outreach	12-Nov-11	Paul Kenny	Invited participant Neuropharmacology Editorial Board Meeting, Washington, DC
Science Outreach	12-Nov-11	Gavin Rumbaugh	SFN Annual Meeting in Washington, DC
Science Outreach	12-Nov-11	James Chelliah	SFN Annual Meeting in Washington, DC
Science Outreach	12-Nov-11	Massimiliano Aceti	SFN Annual Meeting in Washington, DC
Science Outreach	12-Nov-11	Ron Davis	Society for Neuroscience 2011, Washington DC
Science Outreach	14-Nov-11	Paul Kenny	Program Committee Meeting SfN (Society for Neuroscience), Washington, DC
Science Outreach	16-Nov-11	Andrew Butler	Neuroscience Center, University of Helsinki (Finland)
Science Outreach	16-Nov-11	Roy Periana	ERFC meetings/presentations
Science Outreach	16-Nov-11	Donny Strosberg	Life Science Summit 2011 - New York
Science Outreach	16-Nov-11	Jacob Berry, Germain Busto, and Seth Tomchik	Society for Neuroscience 2011, Washington DC
Science Outreach	18-Nov-11	Peter Hodder	Frederick Miao, AfaSci, Inc. University of California, San Francisco, CA, USA
Science Outreach	18-Nov-11	Jun-Li Luo	Invited Speaker - Michael karin Symposium, La Jolla, CA
Science Outreach	21-Nov-11	William Roush	Research Seminar at Dow AgroSciences, Indianapolis, IN
Science Outreach	23-Nov-11	Roy Smith	Helsinn Therapeutics
Science Outreach	25-Nov-11	Ben Shen	Meet with collaborators on Natural Products from Underexplored Microorganisms P41 grant. Beijing and Changsha, China.
Science Outreach	29-Nov-11	Gavin Rumbaugh	Invited Speaker - American College of Neuropsychopharmacology 50th Annual Meeting In Hawaii
Science Outreach	29-Nov-11	Katrin Karbstein	Grant Review Panel - Gene Express Fall 2011 Panel, National Science Foundation, Arlington, VA

Science Outreach	30-Nov-11	Matthew Disney	UF-Clearwater; IDMC-8-001 - 8th Intl. Myotonic Dystrophy Consortium Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	30-Nov-11	Donny Strosberg	CME symposium at Weill Cornell Medical College in Qatar
Science Outreach	3-Dec-11	Andrew Butler	Natural Peptide to Drugs (NP2D) International Congress (Zermatt, Switzerland)
Science Outreach	3-Dec-11	Damon Page	Autism Research Consortium "Think Tank", Boston, MA
Science Outreach	4-Dec-11	Paul Kenny	Invited speaker ACNP (American College of Neuropsychopharmacology) Annual Meeting, Waikoloa, Hawaii
Science Outreach	5-Dec-11	Jonathan Hollander	Presented "Reward mechanisms in feeding and addiction: Paradoxical roles for hypocretin (orexin) transmission" at ACNP (American College of Neuropsychopharmacology) Annual Meeting, Waikoloa, HI
Science Outreach	5-Dec-11	Susana Valente	Pathegenesis Affinity Group talk in La Jolla, CA: "Identification and characterization of HIV-1 mRNA processing regulators"
Science Outreach	5-Dec-11	Ben Shen	Department of Chemistry, Brandeis University Title: Natural Product Biosynthesis - Inspiration for Novel Chemistry and Drug Discovery
Science Outreach	6-Dec-11	Paul Kenny	Panel presentation to ACNP (American College of Neuropsychopharmacology) Member Advisory Task Force at Annual Meeting in Waikoloa, Hawaii
Science Outreach	6-Dec-11	Ben Shen	Department of Chemistry and Biochemistry, Boston University Title: Platensimycin and Platencin - Biosynthesis, Engineering, and Mechanism of Resistance
Science Outreach	7-Dec-11	Jun-Li Luo	Grant Review Panel - NCI New Grantee Workshop, Rockville, MD
Science Outreach	18-Dec-11	Kate Carroll	Seminar Speaker-Chemical Biology Conference Academia Sinica, Taipei Taiwan
Science Outreach	28-Dec-11	Peter Hodder	Jeanine D'Armiento, Columbia University, New York, NY, USA
Science Outreach	28-Dec-11	Peter Hodder	Scott Pegan, University of Denver, Denver, CO, USA
Science Outreach	2-Jan-12	Matthew Disney	SomaLogic, Boulder, CO Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	4-Jan-12	Sathya Puthanveettil	Jupiter Neuroscience Faculty Forum Monthly Meeting
Science Outreach	8-Jan-12	William Roush	UCSD Research Collaborators Meeting, San Diego, CA
Science Outreach	11-Jan-12	Andrew Butler	The Obesity Society Meeting

Science Outreach	12-Jan-12	Roy Periana	ARPA-E Workshop titled: "Natural Gas Conversion Technologies", Houston, TX
Science Outreach	16-Jan-12	Patrick Griffin	CDRD Review; Vancouver BC, CANADA
Science Outreach	18-Jan-12	Roy Smith	FDA, Rockville, MD
Science Outreach	19-Jan-12	Katrin Karbstein	Invited Speaker - Furman University, Greenville, SC
Science Outreach	23-Jan-12	Paul Kenny	Panel participant WCBR (Winter Conference on Brain Research), Snowbird, UT ("Challenges and opportunities in treatment discovery for nicotine dependence: An integrated perspective")
Science Outreach	24-Jan-12	Roy Smith , Andrew Butler, Courtney Miller	Dr. Mads-Tang Christensen, NOVO Nordisk
Science Outreach	24-Jan-12	Katrin Karbstein	Grant Review Panel - RNA Mechanisms in Cancer (RMC), American Cancer Society, Atlanta, GA
Science Outreach	25-Jan-12	William Roush	Research Seminar at UC Irvine, Irvine, CA
Science Outreach	26-Jan-12	Roy Smith	Baylor College of Medicine: Symposium Steroid Receptor & Coregulators
Science Outreach	26-Jan-12	Paul Kenny	Panel participant WCBR (Winter Conference on Brain Research), Snowbird, UT ("Sex, drugs, and rocky road: Neurobehavioral similarities and differences between drug and nondrug reinforcers")
Science Outreach	29-Jan-12	Patrick Griffin	Speaker for Genetic and Molecular Basis of Obesity and Body Weight Regulation (Keystone Symposium); Santa Fe NM
Science Outreach	1-Feb-12	Bill Ja	Presented at the Gordon Research Seminar Biology of Aging "Cell Signaling, Metabolism and Aging"; Ventura, CA
Science Outreach	1-Feb-12	Brian Paegel	SLAS Meeting, San Diego, CA
Science Outreach	3-Feb-12	Matthew Disney	University of Minnesota, Dept. of Chemistry Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	5-Feb-12	Tim Spicer	SLAS 2012 Presentation:"Biotix Tips vs. OEM: Case Scenarios for Compounds Transfers and for Ca++ Signaling Assays on the FLIPR Tetra", San Diego, CA, USA
Science Outreach	6-Feb-12	Thomas Kodadek	Adler Symposium, La Jolla, CA
Science Outreach	6-Feb-12	Pierre Baillargeon	SLAS 2012 Presentation: "Novel Platform to Improve HTS Compound Management Operations", San Diego, CA, USA
Science Outreach	8-Feb-12	Paul Kenny	Invited speaker Faculty Lecture Series, Scripps Research Institute, La Jolla, CA
Science Outreach	9-Feb-12	William Roush	Zing Conference on Natural Products, Spain
Science Outreach	9-Feb-12	Pierre Baillargeon	Brooks Life Science Systems User Meeting, "Addressing HTS Compound Quality Control", San Diego, CA, USA
Science Outreach	10-Feb-12	Andrew Butler	NOVO Nordisk

Science Outreach	10-Feb-12	Patrick Griffin	Genome Canada British Columbia TPAH Panel Meeting, Vancouver BC, CANADA
Science Outreach	10-Feb-12	Sathya Puthanveettil	Hosted Dr. Priya Rajasethupathy, Columbia University, Seminar Presentation
Science Outreach	10-Feb-12	Peter Hodder	Gerry R. Smith, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
Science Outreach	12-Feb-12	John Cleveland	Talk at Keystone Symposia in Banff Alberta
Science Outreach	13-Feb-12	Thomas Kodadek	NHLBI PI meeting, San Antonio, TX
Science Outreach	16-Feb-12	Paul Kenny	Reviewer MNG Study Section Panel, San Francisco, CA
Science Outreach	22-Feb-12	Patrick Griffin	Speaker at the Molecular Med Tri-Conference, San Francisco CA
Science Outreach	25-Feb-12	Patrick Griffin	Molecular Biophysics Subgroup 2012 Symposium Presenter; San Diego CA
Science Outreach	27-Feb-12	Paul Kenny	SfN (Society for Neuroscience) Program Committee Meeting
Science Outreach	27-Feb-12	Timothy Tellinghuisen	University of Kentucky, Lexington, KY
Science Outreach	1-Mar-12	Bill Ja	Attended 53rd Annual Drosophila Research Conference; Chicago, IL
Science Outreach	1-Mar-12	Patrick Griffin	Cornell Medical School Carl Nathan Meeting at Scripps Florida to gather information on developing their own Drug Discovery center
Science Outreach	1-Mar-12	Matthew Disney	Broad Institute, Chemical Biology Program, Cambridge, MA Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	4-Mar-12	Susana Valente	Keystone Symposia -Protein-RNA Interactions in Biology and Disease-Santa Fe, TX-poster title: "Differential regulation of HIV-1 and HIV-2 mRNA 3' end processing by eIF3f, CDK11, and splice factor 9G8 "
Science Outreach	4-Mar-12	Corinne Lasmezas	ASN meeting in Baltimore. Seminar titled: "Highly neurotoxic prion protein"
Science Outreach	5-Mar-12	Donald Phinney	Invited speaker Oklahoma State University seminar (Myron Hinsdale, PhD host)
Science Outreach	6-Mar-12	John Cleveland	Cancer Prevention Research Institute of Texas (CPRIT) Review Meeting
Science Outreach	6-Mar-12	Peter Hodder	Don Gardiner and Katharine Trenholme, Queensland Institute of Medical Research, Queensland, Australia
Science Outreach	12-Mar-12	Paul Kenny	Invited speaker SFRNT (Society for Research on Nicotine & Tobacco) pre-conference workshop, Houston, TX
Science Outreach	12-Mar-12	Patrick Griffin	Society for Research on Nicotine & Tobacco Pre-Conference Workshop; Houston TX
Science Outreach	14-Mar-12	Roy Periana	EFRC FY12 Science Review for the CCHF - Charlotte, NC

Science Outreach	16-Mar-12	Peter Hodder	SLAS2013 Program Planning Meeting, Chicago, IL, USA
Science Outreach	16-Mar-12	Min Guo	Invited Speaker - Shanghai Inst. For Biological Sciences, Shanghai, China
Science Outreach	18-Mar-12	Ron Davis	M.R. Bauer Foundation Colloquium Series
Science Outreach	18-Mar-12	Min Guo	Invited Speaker - Institute for Materia Medica, Shanghai, China
Science Outreach	19-Mar-12	Philip LoGrasso	Keystone Symposia: Cell Death Pathways: Beyond Apoptosis - Banf, Alberta CANADA
Science Outreach	21-Mar-12	Susana Valente	NIH Center for Scientific Review-ADDT
Science Outreach	21-Mar-12	Peter Hodder	Kosta Petrukhin, Columbia University, New York, NY, USA
Science Outreach	24-Mar-12	Courtney Miller	Cold Spring Harbor Laboratories Seminar
Science Outreach	24-Mar-12	Matthew Disney	243rd ACS National Meeting, San Diego, CA Title: Rational Design of Small Molecules Targeting RNA
Science Outreach	25-Mar-12	William Roush	Organic Letters Editorial Advisory Board Meeting @ ACS Meeting, San Diego, CA
Science Outreach	26-Mar-12	William Roush	Organic Syntheses Board of Directors' Meeting @ ACS Meeting, San Diego, CA
Science Outreach	26-Mar-12	William Roush	ACS National Meeting and Expo 2012, San Diego, CA
Science Outreach	26-Mar-12	Kate Carroll	FASEB 2012 Editorial Board Meeting, Bethesda, MD
Science Outreach	28-Mar-12	Courtney Miller	Johns Hopkins Pharmacology Seminar
Science Outreach	28-Mar-12	Donald Phinney	Reviewer Maryland Stem Cell Research Foundation fellowship grants
Science Outreach	30-Mar-12	Min Guo	Participant - American Association for Cancer Research, Chicago, IL
Science Outreach	1-Apr-12	Bill Ja	Attended Michelson/Found Animals Foundation Grantees Meeting in Santa Monica, CA
Science Outreach	3-Apr-12	Kirill Martemyanov	University of Massachusetts-Amherst Seminar Presentation
Science Outreach	5-Apr-12	Glenn Micalizio	Lecture at Brigham Young University, Provo, UT
Science Outreach	10-Apr-12	Timothy Tellinghuisen	Lecture at Gilead, Inc. San Mateo, CA
Science Outreach	12-Apr-12	William Roush	JACS Editorial Board Meeting & Chinese Chemical Society Meeting, China
Science Outreach	12-Apr-12	Pierre Baillargeon	Greiner Bio-One User Meeting April 2012 - "Microtiter plates from different perspectives", Charlotte, NC, USA
Science Outreach	13-Apr-12	Peter Hodder	Noa Noy, Case Western Reserve University School of Medicine, Cleveland, OH, USA
Science Outreach	15-Apr-12	Kate Carroll	Speaker-Harvard University, Boston MA
Science Outreach	15-Apr-12	Patrick Griffin	Nuclear Receptor Matrix: Reloaded; Speaker; Whistler BC CANADA
Science Outreach	16-Apr-12	William Roush	Research Seminar at Eli Lilly China

Science Outreach	17-Apr-12	William Roush	Research Seminar at Shanghai Institute of Organic Chemistry, China
Science Outreach	17-Apr-12	Gavin Rumbaugh	Fairmont Mayakoba to discuss international science meeting in 2013
Science Outreach	19-Apr-12	William Roush	Research Seminar at National University of Singapore
Science Outreach	19-Apr-12	Peter Hodder	David Smithson, Oregon Translational Research and Drug Development Institute (OTRADI), Portland, OR, USA
Science Outreach	19-Apr-12	Peter Hodder	Michael Conn, Oregon Health & Science University, Portland, OR, USA
Science Outreach	20-Apr-12	Glenn Micalizio	Lecture at Rutgers University, Piscataway, NJ
Science Outreach	20-Apr-12	Kate Carroll	Experimental Biology 2012, San Diego, CA
Science Outreach	20-Apr-12	Peter Hodder	Walter Fast, University of Texas, Austin, TX, USA
Science Outreach	24-Apr-12	Thomas Kodadek	Seminar Speaker Wayne State University, Detroit, MI
Science Outreach	24-Apr-12	Katrin Karbstein	Invited Speaker - 1st International RNA Symposium, Frankfurt, Germany
Science Outreach	25-Apr-12	Patrick Griffin	Speaker at the Novartis Institutes for BioMedical Research, Scientific Seminar Series; Cambridge MA; SAR OF Nuclear Receptor, GPCR and Kinase Modulators Revealed with Diffential HDX
Science Outreach	25-Apr-12	Patrick Griffin	Speaker at the Novartis Institutes for BioMedical Research, Scientific Seminar Series; Cambridge MA; *SAR OF NUCLEAR RECEPTOR, GPCR AND KINASE MODULATORS REVEALED WITH DIFFERENTIAL HDX*
Science Outreach	1-May-12	Bill Ja	Met with Professor Mimi Shirasu-Hiza at Columbia University; New York, NY
Science Outreach	2-May-12	Sathya Puthanveettil	Jupiter Neuroscience Faculty Forum Monthly Meeting
Science Outreach	3-May-12	Peter Hodder	Achim Schnaufer, University of Edinburgh, Edinburgh, UK
Science Outreach	4-May-12	Courtney Miller	Johns Hopkins Psychology Department Seminar
Science Outreach	5-May-12	Donald Phinney, Siddaraju Boregowda	ISCT (International Society for Cellular Therapy) Annual Meeting, Seattle, WA
Science Outreach	6-May-12	William Roush	MLPCN Steering Committee Meeting, Bethesda, MD
Science Outreach	6-May-12	Patrick Griffin	MLPCN Steering Committee Meeting; Bethesda, MD
Science Outreach	7-May-12	Paul Kenny	Reviewer MNG Study Section Review Panel, Washington, DC
Science Outreach	9-May-12	Corinne Lasmezas	Neuroprion Congress in Amsterdam, The Netherlands. Talk titled: "Strain-specific role of RNA in prion replication"
Science Outreach	14-May-12	Roy Smith	NIH/National Institute of Aging Alzheimer's Conference

Science Outreach	17-May-12	Paul Kenny	Reviewer for abstract submissions SfN (Society for Neuroscience) Annual Meeting
Science Outreach	20-May-12	William Roush	Invited Lecturer at 33rd National Medicinal Chemistry Society Symposium, Tucson, AZ
Science Outreach	20-May-12	Patrick Griffin	Vancouver BC CANADA; ASMS Conference; speaker on Genomic Mechanism
Science Outreach	21-May-12	Peter Hodder	Michael Gelb, University of Washington, Seattle, WA, USA
Science Outreach	23-May-12	Susana Valente	ISHEID Congress 2012 in Marseille, France : "Potent Suppression of HIV Viral Replication by a Novel Inhibitor of Tat"
Science Outreach	24-May-12	Matt Gill	Presented "Regulation of development & lifespan by small molecules in *C. elegans*" to 2012 Scripps Howard Institute on the Environment and Science
Science Outreach	30-May-12	Susana Valente	Pasteur Institut-seminar titled: "Pharmacological silencing of HIV transcription"
Science Outreach	30-May-12	Timothy Tellinghuisen	Lecture at Novartis, Inc. Emeryville, CA
Science Outreach	30-May-12	Peter Hodder	European Lab Automation Presentation: "The Impact of Rapid, Automated Analysis of HTS library Sample Quality" , Hamburg, Germany
Science Outreach	1-Jun-12	Patrick Griffin	NIH/NINDS-Advancing Translational Headache Meeting, Washington DC
Science Outreach	6-Jun-12	Thomas Kodadek	Vanderbilt/TSRI Steering Committee Meeting, Dallas, TX
Science Outreach	6-Jun-12	Patrick Griffin	Scripps Florida Steering Committee; Dallas TX
Science Outreach	6-Jun-12	Ben Shen	TSRI-Vanderbilt Human Chemical Sciences Institute meeting, Dallas, TX
Science Outreach	7-Jun-12	Thomas Kodadek	Gladstone Institute of Neurological Disease Exec. Committee Meeting, San Francisco, CA
Science Outreach	8-Jun-12	Matthew Disney	Mont Sainte Odile, Strasbourg, France - Unstable Microsatellites & Human Disease Conference Title: Rational Design of Small Molecules Targeting Repeating Transcripts
Science Outreach	10-Jun-12	Paul Thompson	GRC Bioorganic Chemistry Conference-Andover, NH
Science Outreach	10-Jun-12	Kirill Martemyanov, Ekaterina Posokhova, Keqiang Xie, Ikuo Masuho, Cesare Orlandi	Gordon Research Conference, Maine
Science Outreach	11-Jun-12	Thomas Kodadek	GRC Bioorganic Chemistry Conference-Andover, NH
Science Outreach	12-Jun-12	Andrew Butler	Dr. Birgitte Anderson, NOVO Nordisk
Science Outreach	14-Jun-12	Courtney Miller	Mt Sinai School of Medicine: Freidman Brain Institute Translational Neuroscience
Science Outreach	14-Jun-12	Thomas Kodadek	Alzheimer's Association International Conference, Vancouver, Canada

Science Outreach	15-Jun-12	Ben Shen	Speaker at 8th US-Japan Seminar on Natural Products Biosynthesis; Spoke at 6th Sino-US Conference. Awaji-Shima, Japan and Changsha, China.
Science Outreach	20-Jun-12	William Roush	Invited Lecturer at Victor Grignard Nobel Centennial-ACS Chemical Breakthrough Award Symposium, France
Science Outreach	23-Jun-12	Roy Smith	The Endocrine Society Annual Meeting
Science Outreach	24-Jun-12	William Roush	Invited Lecturer at Gordon Research Conference on Heterocycles, Newport, RI
Science Outreach	26-Jun-12	Katrin Karbstein	Grant Review Panel - RNA Mechanisms in Cancer (RMC), American Cancer Society, Atlanta, GA
Science Outreach	27-Jun-12	Patrick Griffin	Genome Canada Pre-Application Review Committee; Ottawa CANADA
Science Outreach	15-Jul-12	Paul Thompson	GRC Enzymes, Coenzymes and Metabolic Pathways, Waterville Valley, NH
Science Outreach	29-Aug-12	Kate Carroll	ACS 242nd National Meeting
Science Outreach	12-Sep-12	John Cleveland	Cancer Prevention Research Institute of Texas (CPRIT) Review Meeting
Science Outreach	10-Nov-12	Ben Shen	43rd ACS Western Regional meeting, hosted by the Southern California Local Section, Pasadena, CA
Science Outreach	Monthly 2011-2012	Donald Phinney	ISCT (International Society for Cellular Therapy) MSC Committee Meetings
Science Outreach	Monthly 2011 - 2012	Paul Kenny	ACNP (American College of Neuropsychopharmacology) Advisory Task Force
Science Outreach	Monthly 2011 - 2012	Paul Kenny	ACNP (American College of Neuropsychopharmacology) Public Information Cmtee
Science Outreach	Monthly 2011 - 2012	Paul Kenny	ACNP (American College of Neuropsychopharmacology) Program Committee telephone conferences