SCRIPPS FLORIDA FUNDING CORPORATION

ANNUAL REPORT

FOR THE YEAR ENDED SEPTEMBER 30, 2017

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Scripps Florida Funding Corporation Annual Report

For Year Ended September 30, 2017

INTRODUCTION

Florida Statute 288.955 (the "Enabling Statute") created Scripps Florida Funding Corporation ("SFFC") to facilitate the establishment and operation of a biomedical research institution for the purposes of enhancing education and research and promoting economic development and diversity. In addition, the Enabling Statute charged SFFC with the obligation to assure the compliance by The Scripps Research Institute ("TSRI") with the Enabling Statute and the agreement between SFFC and TSRI (the "Operating and Funding Agreement"). The Enabling Statute provides that SFFC shall prepare or obtain certain reports, audits, and evaluations of TSRI's compliance with the performance expectations and disbursement conditions contained in the Enabling Statute. As such, SFFC is submitting this Annual Report to the Governor, the President of the Senate, and the Speaker of the House, as required by the Enabling Statute to be submitted by December 1 of each year.

This SFFC Annual Report addresses the activities and outcomes of SFFC and Scripps Florida ("SF") for the fiscal year ended September 30, 2017 ("Fiscal 2017"). The Scripps Florida Annual Report addressed the activities and outcomes of Scripps Florida for the year ended June 30, 2017, and the information in the Scripps Florida Annual Report was informally updated for this SFFC Annual Report.

The SFFC Annual Report is presented in two parts: first, a summary that highlights the substantial events that have occurred during the year ended September 30, 2017; and second, an itemized report that corresponds with the applicable sections of the Enabling Statute.

About the Scripps Florida Funding Corporation

In November 2003, Governor Bush signed into law an historic piece of legislation that laid the framework for The Scripps Research Institute to expand its world-renowned scientific research and endeavors into Florida. The bill, passed by the Florida Legislature during special session, provided a one-time investment of $310 million from federal economic stimulus monies to create Scripps Florida and pay certain expenses for the first seven years, specifically salaries and equipment purchases. In June 2006, The Scripps Research Institute revised the Scripps Florida business plan and SFFC and TSRI revised the scheduled disbursements from the SFFC, which expanded grant funding to December 16, 2013. To oversee the investment and spending of the State's investment in Scripps Florida, the Florida Legislature created the Scripps Florida Funding Corporation, hereto referred to as SFFC, a non-profit entity comprised of a nine-member Board of Directors and one ex-officio member. The role of SFFC was enunciated by Governor Bush: "My vision for this board is that it manages the financial portion of our partnership, but lets Scripps do what it does best – conduct biomedical research."

SFFC Board of Directors

Of the nine-member Board of Directors, three Directors are appointed by each of the Governor, House Speaker and the Senate President. Mr. David Gury serves as Chair of the Board of Directors and Dr. Pamella Dana as Vice-Chair. The full Board of Directors consists of the Chair and Vice Chair and Mr. C. Gerald Goldsmith, Mr. Mark Kasten, Dr. Richard M. Luceri, and Mr. Art Wotiz.

About The Scripps Research Institute

The Scripps Research Institute (TSRI) is one of the world's largest independent, not-for-profit organizations focusing on research in the biomedical sciences. TSRI is internationally recognized for its contributions to science and health, including its role in laying the foundation for new treatments for cancer, rheumatoid arthritis, hemophilia, and other diseases. An institution that evolved from the Scripps Metabolic Clinic founded by philanthropist Ellen Browning Scripps in 1924, the institute now employs more than 2,500 people on its campuses in La Jolla, CA, and Jupiter, FL, where its renowned scientists—including two Nobel laureates and 20 members of the National Academies of Science, Engineering or Medicine—work toward their next discoveries. The institute's graduate program, which awards PhD degrees in biology and chemistry, ranks among the top ten of its kind in the nation. In October 2016, TSRI announced a strategic affiliation with the California Institute for Biomedical Research (Calibr), representing a renewed commitment to the discovery and development of new medicines to address unmet medical needs.

About Scripps Florida

Scripps Florida, in the Town of Jupiter in Palm Beach County, Florida, sits on 100 acres adjoining the Florida Atlantic University campus. Over 600 scientists, technicians, and administrative staff work in the three state-of-the-art biomedical research facilities totaling 350,000 square-feet, which opened in March 2009. In addition to the one-time grant from the State of Florida, Palm Beach County provided an economic package that included funding for land and construction of the current permanent facility.

While the faculty are organized into five academic departments – Chemistry, Immunology and Microbiology, Integrative Structural and Computational Biology, Molecular Medicine and Neuroscience - these departments have soft boundaries. Rather than defining circumscribed areas of research and isolating faculty members and laboratories into separate and distinct disciplines, the cooperative, collaborative spirit is encouraged and embraced. For more information, see www.scripps.edu.

Scripps Florida Overview and Significant Highlights for the Year Ended September 30, 2017

TSRI Ranks No. 1 in Innovation Influence

The Scripps Research Institute is the most influential research institution in the world, according to the Nature Index 2017 Innovation supplement, which sheds light on the impact of academic research on innovation. The ranking, released in August 2017 by the journal *Nature*, analyzes data about research quality and the broad influence it has on inventions.

> "This new ranking underscores the worldwide impact of TSRI scientists, who share a common goal of improving public health through scientific discovery, and, importantly, improving the way we make those discoveries," said Jamie Williamson, TSRI's Executive Vice President for Research and Academic Affairs. "We are proud to be recognized for the profound influence our science has had on other researchers and laboratories around the world."

The Normalized Lens Influence Metric used by the Nature Index measures the influence an institution's research has had on innovation by calculating the citations of its research articles in patents owned by third parties, rather than those owned by institutions themselves. According to this metric, TSRI ranks number one, above other internationally renowned research institutes such as the Rockefeller University in New York, the Massachusetts Institute of Technology and Stanford University.

A key metric in this ranking is publications. More than 40 percent of all TSRI's natural science articles appear in the Nature Index. The average across the 200 institutions listed is 21.9 percent.

TSRI scientists are also active in developing their own innovations, with more than 1,000 patents and seven FDA approved drugs to their credit. Additionally, the Institute's alliance with the California Institute for Biomedical Research (see below) adds translational research to its capabilities, enabling a new bench-to-bedside model that will accelerate the translation of basic scientific discoveries into critically-needed new medicines for unmet medical needs.

Abundance of Collaborative Agreements in 2016 - 2017

TSRI and California Institute for Biomedical Research (Calibr) Sign Strategic Affiliation to Accelerate the Development of New Medicines

These two leading non-profit research organizations signed a strategic affiliation that combines the two organizations into a new biomedical research entity with the tools and know-how to rapidly translate its scientific discoveries into life-saving medicines for the public benefit. This integration of basic scientific and translational research will reduce the costs and timelines associated with the crucial early stages of drug development, and lead to the creation of a self-sustaining model for non-profit research in which drug development successes drive the funding of new scientific discoveries and medicines many years into the future.

The union of these two non-profit organizations – both led by Peter Schultz, Ph.D. – provides the ability to rapidly move the basic scientific research carried out at TSRI into Calibr, whose expertise and infrastructure can accelerate drug development from discovery through early clinical trials,

complementing the pharmaceutical industry's increasing focus on the later stages of clinical development.

As part of the formal affiliation, the two organizations will now share a combined Board of Directors, as well as scientific and administrative resources that will be consolidated over time. Schultz, who has an outstanding track record in both basic research and drug discovery, is overseeing the integration of the two institutes' distinct cultures and operations. Both institutes will continue to collaborate with their other partners in the academic and commercial sectors.

TSRI has a strong history of success in basic science – the research that lays the groundwork for new medical advances. The Institute is internationally recognized for its scientific impact in the fields of chemistry, structural and molecular biology, immunology and neuroscience, and for its many scientific breakthroughs that have led to therapies that address infant respiratory distress, rheumatoid arthritis, lupus, hemophilia and blood cancers.

Each of the 10 regulatory agency-approved medicines emerging from TSRI took an average of more than 20 years to move from drug discovery to market availability. The new affiliation between TSRI and Calibr aspires to accelerate that timeline, as well as to increase the number of basic science discoveries that are translated into first-in-class drugs.

Founded in 2012, Calibr has leveraged its strengths in small molecule discovery, protein engineering, and translational research through collaborations with academic, foundation and industry partners. To date, Calibr has generated a pipeline of candidate medicines for a number of disease areas – including new approaches to osteoarthritis, tuberculosis, childhood diarrhea, heart disease, fibrosis, multiple sclerosis and cancer – creating opportunities to move five to 10 new molecules into the clinic within the next two years.

The two organizations have already successfully collaborated on several research programs in recent years, including the development of an antibody engineering platform that could improve treatments for chronic diseases such as diabetes and COPD, and innovative immune therapies for the treatment of cancer. These collaborations have led to several candidate therapies, two of which Calibr has partnered with major pharmaceutical companies. Moreover, these collaborations are providing a unique training environment for students and fellows at the interface of basic and translational research, resulting in high-impact publications, and preparing them to tackle some of the most important biomedical challenges in academia and industry.

Intarcia and Calibr Collaboration and In-Licensing Deal Aimed At Delivering a Next Generation Combination Product For Diabetes & Obesity

This collaboration, formally organized in January 2017, focuses on the development of a novel peptide therapeutic leveraging Calibr's Stapled-Peptide Platform Technology. Intarcia plans to develop and administer this novel therapy in combination with Exenatide (a GLP-1 receptor agonist and active agent in Intarcia's ITCA 650 product), by leveraging its proprietary Medici Drug Delivery System™.

Under the terms of the agreement, Calibr will receive an upfront grant of Intarcia equity, with additional shares vesting over key development milestones, as well as undisclosed cash payments on

achievement of predetermined regulatory and sales milestones. In addition to the milestone payments, Calibr will be eligible to receive tiered royalties on product sales.

About the Medici Drug Delivery System™
Intarcia's novel technology platform, the Medici Drug Delivery System, is a proprietary subcutaneous delivery system comprised of three unique technologies:

- A stabilization technology that allows for proteins, peptides, antibody fragments, and other highly potent small molecules to be stabilized at or above human body temperatures for up to three years or more
- A matchstick-sized osmotic mini-pump that is placed just under the dermal layer of skin to deliver a continuous and consistent flow of medication
- A placement technology including proprietary tools designed to provide an optimal user experience.

Once a drug is approved, a trained healthcare professional can place the small device in an in-office procedure. Once in place under the skin, water from the extracellular fluid enters the pump device at one end – by diffusing through a semi-permeable membrane directly into an osmotic engine – that expands to drive a piston at a controlled rate. This allows the drug within the pump to be released in a steady, consistent fashion at the other end of the device. Each osmotic mini-pump is designed to hold an appropriate volume of drug to treat a patient for up to a full year.

TSRI Collaboration Agreement with Pfizer to Advance DNA-Encoded Library Technology
In January 2017, TSRI established a research collaboration and license agreement with Pfizer Inc. (NYSE: PFE) to pioneer new DNA-encoded library (DEL) technology, including new synthetic chemistry for the creation of next-generation DELs, a potentially transformative technology for early stage drug discovery research.

Under the terms of the collaboration, Pfizer will pay a technology access fee and thereby gain access to innovative chemical synthesis technology developed at TSRI. Members of the TSRI chemistry department—Professors Phil Baran, Ph.D., Dale Boger, Ph.D., Jin-Quan Yu, Ph.D., K. Barry Sharpless, Ph.D., and others—will work alongside Pfizer scientists to adapt these chemical methods for use in creating DELs, which require stringent processes that are tolerant of the delicate DNA backbone. TSRI and Pfizer may choose to expand the scope of the joint research to include other technologies relevant for enabling DEL-based drug discovery. Financial terms of the agreement are not disclosed.

In contrast to conventional drug screening where a few million small molecules are evaluated in biological systems, DEL screening uses DNA-based "barcodes" to survey *billions* of small molecules, potentially increasing the ability of researchers to identify promising chemical leads. While this technology was originally conceived at TSRI by Richard Lerner, M.D., and Sydney Brenner, Ph.D., in the early 1990s, the reduction to practice has taken decades and required technological advances in DNA sequencing and informatics in order to be more fully realized.

TSRI / HitGen / Calibr Drug Discovery Collaboration
This collaboration is to discover and develop potential new therapies in areas of unmet clinical need, with an initial focus in oncology, regenerative medicine and virology. HitGen's technology platform, centered around the design, synthesis, and interrogation of multi□billion component libraries of DNA encoded small molecules, will be deployed to identify new small molecule leads for therapeutic targets identified by the collaboration. Leaders in basic and translational research at TSRI and Calibr will

provide target materials and relevant know-how to prosecute drug targets of interest. The parties will contribute in-kind to the discovery efforts and anticipate progressing any drug candidates that emerge to clinical proof-of-concept studies.

TSRI and ShangPharma Innovation (SPII) Translational Research Collaboration

In June 2017, TSRI and SPII announced a strategic collaboration to accelerate the development of innovative drug candidates through scientific collaboration, a services relationship with Shanghai ChemPartner Co. Ltd. (ChemPartner), and sponsored research at TSRI and its drug discovery affiliate, Calibr. The parties aim to leverage the drug discovery pipeline, expertise, and momentum emerging from the TSRI and Calibr affiliation announced late last year.

SPII facilitates and accelerates drug discovery by offering funding, incubator space, and other essential support to its collaborators. The partnership with TSRI marks a major new initiative for SPII to enable its mission to support therapeutic research at the earliest stages with the ultimate goal of getting innovative new treatments to patients. Under the terms of the collaboration, institute scientists will put forth translational research projects to a joint committee comprising drug discovery experts across TSRI, Calibr, and SPII. In turn, SPII will contribute cash and in-kind services totaling up to $15 million over an initial term of three years. TSRI and Calibr will retain control over assets resulting from the collaboration, with SPII receiving a significant share of future value.

Administrative and Faculty Modifications

Executive Team Build Out Completed

In August 2016, The Scripps Research Institute (TSRI) announced the completion of its California executive team build out, which began with the promotion of James R. Williamson to Vice President of Academic Affairs, followed by the addition of four new executive team leaders:

Richard King was named Chief Operating Officer. King was formerly president and CEO of AcelRx Pharmaceuticals, Inc.

Jennifer Crosby-Meurisse, Vice President, Human Resources joined TSRI from Oregon Health & Science University, where she served as Director, Research and Academic HR Team and the Office of International Affairs.

Cara Miller assumed the role of Vice President, Communications. Miller joined TSRI from Gilead Sciences, Inc., where she was Senior Director, Public Affairs.

Julia Ronlov has been appointed Executive Director, New Business Development, and joins TSRI on August 1. Ronlov previously served as Director, Strategic Partnerships, for Oregon Health & Science University.

Additionally, Jared Machado was promoted to Chief Financial Officer and Board Treasurer and Douglas A. Bingham was named Executive Vice President and General Counsel, and Board Secretary.

Alongside these appointments, TSRI has initiated a long-term strategic planning process that will build on the history of TSRI's academic pursuits, while also further differentiating and solidifying TSRI's position at the forefront of biomedical research.

New Board Members and Chairman of the Board

In February 2017, TSRI announced the appointment of nine new members to its Board of Directors, including John D. Diekman, who will serve as chairman of the board. Diekman replaces Richard A. Gephardt, who is retiring from the board after seven years of service.

TSRI Board of Director Appointees

Chairman John D. Diekman, Ph.D.

Diekman is a Founding Partner of 5AM Ventures, a life science venture capital firm in San Francisco. Prior to founding 5AM in 2002, Diekman was a Founder and Managing Director of Bay City Capital. Previously, he was Chairman and Chief Executive Officer of Affymetrix, and Chairman and Managing Director of Affymax. Diekman currently serves as chairman of the board of IDEAYA Biosciences and as a board member of Wildcat Discovery Technologies. He is a Charter Trustee of Princeton University and a former Trustee of The California Institute of Technology and of The Scripps Research Institute. Diekman serves on the Schaeffer Center for Health Policy and Economics Advisory Board at the University of Southern California and is an Honorary Officer of the Order of Australia. He received his doctoral degree from Stanford University and holds an honorary doctoral degree from Australia's Monash University.

Herb Boyer, Ph.D.

Boyer is internationally recognized for his pioneering discovery of recombinant DNA, which has led to numerous life-saving medicines. He co-founded Genentech in 1976 with the late venture capitalist Robert Swanson, breaking new ground for both life science technology and new business models. He is now retired and is Professor Emeritus of Biochemistry and Biophysics at the University of California, San Francisco. In 2004, *Business Week* magazine named Boyer one of the "Greatest Innovators of the Past 75 Years," and he was featured on the cover of *TIME* magazine in 1981 with a story titled, "Shaping Life in the Lab: The Boom in Genetic Engineering, Genentech's Herb Boyer." Boyer has received numerous prestigious awards for his work including the National Medal of Technology and Innovation, the National Medal of Science, the Lemelson-MIT Prize and the Albany Medical Prize. He is an elected member of the National Academy of Sciences, the American Academy of Arts and Sciences and the National Inventors Hall of Fame. He earned his doctoral degree from the University of Pittsburgh.

Gerald Chan, Ph.D.

Chan co-founded Morningside, a private equity and venture capital firm, in 1986. In life science, Morningside has been the founding or major investor in many biotechnology companies. In oncology, the investments include oncolytic viruses (Biovex, DNATrix), immuno-oncology (Aduro), modified cytotoxic agents (Nucana) and novel therapeutic targets (CellCentric, K-Gen, Vigeo). Investments in infectious diseases include antibiotics (MicuRx, Artugen), prophylactic vaccines (Matrivax) and antivirals (Atea). Investments in other therapeutic areas include metabolic diseases (CVI), autoimmune diseases (Kezar), CNS disorders (Orthogonal, Pinteon, Cognoa, Cognito) and rare orphan diseases (Stealth, Apellis). Chan received his doctoral degree from Harvard University and conducted his post-doctoral fellowship at Dana-Farber Cancer Institute.

Mark Edwards

As Founder and Managing Director of Recombinant Capital (Recap) from 1988 until its sale to Deloitte in 2008, Edwards supervised the creation and maintenance of several databases relating to the development and commercialization of pharmaceutical products, including the Recap Corporate Alliances Database. Over this period, Edwards and Recap were retained by more than 50 companies to assist in the negotiation of biopharma alliances. In 2011, Edwards founded Bioscience Advisors, Inc.

(Biosci), a consulting and database firm focused on biopharma alliances. Edwards serves on the boards of directors of AcelRx and Calibr. In 2008, Edwards was awarded a Lifetime Achievement Award by the American Liver Foundation for "two decades of leadership, thoughtful insights and detailed analysis of the biotechnology industry." He holds a Master of Business Administration from Stanford University.

Isy Goldwasser

Goldwasser is Co-Founder and Chief Executive Officer of Thync, Inc. Prior to founding Thync, Goldwasser was Chief Executive Officer of Symyx Technologies, where he was the company's first employee. In addition to his 16 years at Symyx, Goldwasser was Khosla Ventures' Entrepreneur-in-Residence in 2010. He is a named inventor on more than 30 U.S., European and Canadian patents. Goldwasser has served on Calibr's board since its inception and brings two decades of experience in managing corporate operations and business development. He holds a Master of Science degree from Stanford University.

William R. Hearst III

Hearst is Chairman of the Board of Hearst Corporation, one of the nation's largest diversified media and information companies, and he has been a Director of Hearst Corporation for more than 30 years. He is also President of the charitable William Randolph Hearst Foundation, and he has been actively engaged in the charitable activities and programs of the Hearst Foundation for the last 20 years. Hearst joined the venture capital firm of Kleiner Perkins Caufield & Byers (KPCB) in 1995 as a Managing Partner and has continued his work with KPCB as an Affiliated Partner since 2006. He currently serves on the boards of numerous organizations, including the Carnegie Institution for Science, FORA.tv, the San Francisco Film Society and The Center for Investigative Reporting. Hearst is a fellow of the American Association for the Advancement of Science and was recently appointed an associate in mathematics by the Department of Mathematics at Harvard University. He earned his bachelor's degree from Harvard University.

Ge Li, Ph.D.

Li is the Founder, Chairman and Chief Executive Officer of WuXi AppTec, a leading research and development capability and technology platform company serving the global pharmaceutical, biotechnology and medical device industries. Prior to founding WuXi in 2000, Li was a founding scientist at Pharmacopeia Inc., a leading combinatorial chemistry platform company. Li has received numerous prestigious awards and honors and was named one of Forbes 25 Notable Chinese-Americans and one of the 25 Most Influential People in Biopharma by FierceBiotech. He received his doctoral degree from Columbia University.

Christopher T. Walsh, Ph.D.

Walsh is a Consulting Professor to the Stanford University Department of Chemistry and was previously the Hamilton Kuhn Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School for 26 years when he took emeritus status. He has had extensive academic leadership experience, including Chairmanship of the Massachusetts Institute of Technology Chemistry Department and of the Harvard Medical School Department of Biological Chemistry & Molecular Pharmacology, as well as serving as President and Chief Executive Officer of the Dana-Farber Cancer Institute. Walsh has been involved in a variety of venture-based biotechnology companies since 1981 and currently serves on the boards of Ironwood Pharmaceuticals, Proteostasis Therapeutics and Calibr, and on the scientific advisory boards of Hua Medicine, Abide Therapeutics, Cidara Therapeutics and Flex Pharma, Inc. He serves as an advisor to HealthCare Ventures and is a limited investor in HealthCare Ventures, MPM Capital, Clarus Financial Technology and the Longwood Fund. Walsh is a member of the U.S. National Academy of Sciences, the U.S. National

Academy of Medicine, the American Academy of Arts and Sciences, the American Philosophical Society and is a co-recipient of the 2010 Welch Award in Chemistry. He earned a doctoral degree from Rockefeller University.

Faculty Board Appointee Paul Schimmel, Ph.D.

Schimmel is Hahn Professor in the Department of Molecular Medicine and Chemistry at TSRI. He was formerly MacArthur Professor of Biochemistry and Biophysics at the Massachusetts Institute of Technology. Author or co-author of several hundred scientific publications, he is an elected member of the American Academy of Arts and Sciences, the U.S. National Academy of Sciences, the National Academy of Medicine (Institute of Medicine), the National Academy of Inventors and the American Philosophical Society. He is the co-founder/founding director of seven biopharmaceutical corporations that went on to be NASDAQ-listed and publicly traded, and of a number of private corporations. Schimmel earned his doctoral degree from the Massachusetts Institute of Technology.

These nine new TSRI Board members joined the following current TSRI Board Members: Peter G. Schultz, Ph.D., Vice Chair of the Board and President, The Scripps Research Institute; President, Calibr; Peter C. Farrell, Ph.D., D.Sc., Founder and Chairman, ResMed; Claudia S. Luttrell, President, The Skaggs Institute for Chemical Biology; Mark Pearson, Co-Founder, Vice Chairman of the Board, Drawbridge Realty Trust; and, Bernard Saint-Donat, President, Saint-Donat & Co.

In April and May 2017, respectively, TSRI expanded its Board of Directors with the appointment of Yucaipa Companies Founder and Philanthropist Ron Burkle and Alexandria Real Estate Equities, Inc. CEO Joel Marcus.

Ron Burkle

Burkle is Founder and Chairman of the Ronald W. Burkle Foundation, whose mission is to positively influence people around the world and their communities. He also founded The Yucaipa Companies, a premier investment firm that has established a record of fostering economic value through the growth, repositioning and responsible development of individual companies. He is widely recognized as one of America's preeminent investors in the retail, distribution, technology, entertainment, sports and hospitality industries. In addition to his role as co-chairman of the Burkle Center for International Relations at the University of California, Los Angeles, Burkle is trustee of the Carter Center, the National Urban League and AIDS Project Los Angeles. He also has been an active member of the Frank Lloyd Wright Conservancy. Burkle has served as Chairman of the Board and controlling shareholder of numerous companies, including Soho House, Golden State Foods, Dominick's, Fred Meyer, Ralphs and Food4Less.

Joel Marcus

Marcus is Chairman, Chief Executive Officer and Founder of Alexandria Real Estate Equities, Inc. (NYSE: ARE), an urban office real estate investment trust (REIT) uniquely focused on collaborative life science and technology campuses in the top innovation cluster locations in the United States. Marcus co-founded Alexandria in 1994 as a startup with a business plan and $19 million in seed capital and has since led its growth into an investment-grade rated S&P 500 company. Alexandria has a total market capitalization of approximately $15 billion and a significant market presence in key locations, including Greater Boston, San Francisco, New York City, San Diego, Seattle, Maryland and Research Triangle Park. In addition to his work in life science real estate, Marcus is the founder of Alexandria Venture Investments, which focuses on investing in the biopharmaceutical, diagnostic, research tools, agtech, digital health and technology sectors. He also co-founded the Alexandria

Summit, an annual invitation-only meeting that convenes the world's foremost thought leaders from the pharmaceutical, biotechnology, agribusiness, technology, medical, academic, venture capital, philanthropic, patient advocacy and government communities to address the most critical challenges in global healthcare, agriculture and the environment. Marcus serves on the boards of directors for several biotechnology companies, including the Accelerator Corporation (which he co-founded), AgTech Accelerator Corporation, for which he serves as chairman, Atara Biotherapeutics and Intra-Cellular Therapies. He also serves on the boards of the Biotechnology Innovation Organization (BIO) and the Foundation for the National Institutes of Health (FNIH). Marcus earned his undergraduate and Juris Doctor degrees from the University of California, Los Angeles and was a recipient of the Ernst & Young Entrepreneur Of The Year Award (Los Angeles – Real Estate).

TSRI Adds New Faculty to World-Class Institute

In August 2017, TSRI announced the appointment of two new faculty members – Alexander Adibekian, Ph.D., who will join the Department of Chemistry in Jupiter, FL as associate professor, and Li Ye, Ph.D. who joins the Department of Neuroscience in La Jolla, Ca as an assistant professor.

Adibekian, a former member of Benjamin Cravatt's laboratory, joins TSRI from the Department of Organic Chemistry at the University of Geneva, Switzerland, where he was an assistant professor. His research interests include the discovery of new cysteine-reactive small molecules and the identification of their proteomic targets, as well as the development of novel chemical strategies that allow rapid access to collections of structurally diverse cysteine-reactive small molecules. Adibekian received his bachelor's and master's degrees from the Leibniz Universität in Hanover, Germany, and his Ph.D. from ETH Zürich, Switzerland, where he conducted his doctoral research fellowship in the laboratory of Professor Peter H. Seeberger.

Ye, who joins TSRI from Stanford University, is focused on the transcriptional control of peripheral metabolism through chemical biology and genetic approaches. His current research efforts aim to understand the central regulation of whole-body metabolism, especially in the context of obesity and insulin resistance. Ye received his bachelor's degree from Tsinghua University in Beijing and earned his Ph.D. at Harvard Medical School in Professor Bruce Spiegelman's laboratory. He conducted his postdoctoral training in the lab of Professor Karl Deisseroth at Stanford University.

Adibekian and Ye will officially join TSRI's ranks on November 1, 2017 and January 5, 2018, respectively.

25 Year Anniversary of TSRI's Doctoral Program

TSRI's rigorous doctoral program, which takes an average of five years to complete, consists of a year of classwork and rotation through laboratories, customizable to each student's interests and long-term goals, followed by work on individual research projects under the guidance of a faculty mentor.

U.S. News & World Report currently ranks TSRI's graduate program as second in country in the specialty of biochemistry, sixth in the specialty of organic chemistry, seventh overall in chemistry and ninth overall in the biological sciences, based on a survey of department heads, deans, directors of graduate studies, and other academics in each discipline.

In March 2017, TSRI announced the promotion of Philip Dawson, Ph.D., from Associate Dean to Dean of the TSRI Graduate Program. Dawson, who earned his Ph.D. from TSRI in 1996, replaced Jamie Williamson, Ph.D., who took on a new role as Vice President of Academic Affairs.

Dawson sees his number one responsibility as continuing the great tradition of academic and scientific excellence that has earned the program international prestige, including annual top-10 rankings in *U.S. News & World Report's Best Grad Schools*. Dawson's own research revolves around the development and utilization of methods to incorporate unnatural chemical groups into proteins. He earned his bachelor's degree in chemistry from Washington University in St. Louis, Missouri, graduating *magna cum laude***.** After earning his doctoral degree at TSRI, Dawson conducted postdoctoral work at the California Institute of Technology before returning to TSRI in 1997 as Assistant Professor in the department of Cell Biology. He was recently promoted to Professor of Chemistry and has continued to be active in the graduate program through teaching, as well as directing the graduate admissions committee under the role of Associate Dean. Dawson has authored more than 160 publications, was an Alfred P. Sloan Research Fellow and has earned such honors as the Max-Bergmann Gold Medal, the Vincent du Vigneaud Award and Leonidas Zervas Award. He explained that what makes TSRI's graduate program unique is the opportunity, from the very beginning of their education, for students to work in a variety of disciplines, with a diversity of world-renowned researchers.

During the Institute's 25th Commencement Ceremony on May 19, 2017, TSRI board members Christopher Walsh, a renowned chemist, and Gerald Chan, public health advocate, received honorary doctoral degrees and joined the graduates of the top-10 ranked program in celebrating academic achievement and individual contributions to scientific research.

Chan is the co-founder of Morningside, a private equity and venture capital firm. His investments include support for infectious disease research, vaccines, antivirals, metabolic diseases, autoimmune diseases and rare orphan diseases. Reflecting on the historic nature of this commencement, Chan addressed the legacy of science in the United States. He touched on the United States' leadership in science following World War II, a tradition he hopes this era's researchers can carry on with the support of government leaders.

Walsh is a renowned chemist and academic leader who currently serves as a consulting professor to the Stanford University department of chemistry. He has been involved in a variety of venture-based biotechnology companies since 1981 and currently serves on several boards of directors, including the TSRI affiliate, Calibr. Reflecting on his own career in chemistry, Walsh advised on the importance of intellectual curiosity.

Scripps Florida Scientific Accomplishments

Scientific Publications between October 1, 2016 and September 30, 2017

Scripps Florida Scientists Identify Potent New Anti-Obesity, Anti-Diabetes Target
In an October 2016 published series of studies led by TSRI Assistant Professor Anutosh Chakraborty, scientists have identified a new therapeutic target—a key protein that *promotes* fat accumulation in animal models by slowing the breakdown and expenditure of fat and encouraging weight gain. The studies were published in *The International Journal of Biochemistry & Cell Biology*, *Molecular Metabolism* and, most recently, *The Journal of Clinical Investigation.*

In the last few years, enhancing energy expenditure has emerged as an attractive strategy to combat obesity and diabetes, although how this might be accomplished remains something of a mystery simply because the mechanisms by which the body maintains its energy balance, is complex. The new studies point to IP6k1 (inositol hexakisphosphate kinase-1), specifically its inhibition, as a potentially rich target. Chakraborty and his colleagues found that deleting IP6K1 in fat cells enhanced energy expenditure and protected animal models from diet-induced obesity and insulin resistance.

Scripps Florida Scientists Uncover New Facets of Zika-Related Birth Defects to Help Develop Treatment
In a study that could one day help eliminate the tragic birth defects caused by Zika virus, Scripps Florida scientists from the Florida campus of The Scripps Research Institute (TSRI) have elucidated how the virus attacks the brains of newborns, information that could accelerate the development of treatments. The study, led by TSRI Associate Professors Hyeryun Choe and Damon Page, was published In October 2016 in the journal *Nature Scientific Reports*.

In the new study, the scientists observed the virus's effects in animal models at two different points—during early postnatal development, when the brain is growing rapidly, and at weaning, when the brain has largely reached adult size. The findings expand the current knowledge of cell types vulnerable to the effects of Zika infection to include not only neuron progenitor cells, but also post-mitotic neurons that have finished dividing but are still are undergoing rapid increases in cell size. These results are consistent with the theory that periods of rapid brain growth are especially susceptible to the damaging neurodevelopmental effects of Zika infection.

International Team Unveils First Atomic-Level Image of the Human 'Marijuana Receptor'
In a discovery that advances the understanding of how marijuana works in the human body, an international group of scientists, including those from Scripps Florida, have for the first time created a three-dimensional atomic-level image of the molecular structure activated by tetrahydrocannabinol (THC), the active chemical in marijuana.

The new insights into the human cannabinoid receptor 1 (CB_1) will provide an essential tool for understanding why some molecules related to THC have unexpectedly complex and sometimes harmful effects. The findings also have the potential to guide drug design for pain, inflammation, obesity, fibrosis and other indications. The new study, published in October 2016 by the journal *Cell*, was led by a quartet of scientists: TSRI's Laura Bohn, Northeastern University's Alexandros

Makriyannis, Shanghai Tech University's Zhi-Jie Liu and Shanghai Tech and University of Southern California's Raymond C. Stevens.

Scripps Florida Scientists Illuminate Key Molecular Player in Both Morphine Addiction and Rare Disease

In a remarkable "two for one" discovery, scientists from the Scripps Florida illuminated a key molecular player in the addictive effects of morphine in animal models. Interestingly, the protein - known as neurofibromin 1 (NF1) - is also known to be disrupted in an inherited disorder called neurofibromatosis type 1 (also called von Recklinghausen's disease), in which patients suffer from the growth of benign tumors beneath the skin, chronic pain, mild learning disabilities and an elevated risk of developing cancers.

The study, published online ahead of print in October 2016 in the journal *Current Biology*, described how NF1 influences opioid response through its impact on a signaling protein known as Ras in a part of the brain called the striatum, which is involved in decision making and reward. When the researchers deleted NF1 in striatal neurons of animal models, opioids failed to engage Ras and its downstream signaling reactions, dramatically diminishing the addictive effects of morphine.

What Does It Take to Make a Memory? Study Says New Proteins

TSRI researchers in Florida have for the first time identified a sub-region in the brain that works to form a particular kind of memory: fear-associated with a specific environmental cue or "contextual fear memory." The study, published in the journal *Biological Psychiatry Cognitive Neuroscience and Neuroimaging* in November 2016, was led by TSRI Associate Professor Sathyanarayanan V. Puthanveettil

In particular, the study showed new protein synthesis in a specific sub-region of the prefrontal cortex known in rodents as the prelimbic. In humans, this area corresponds to the anterior cortex, which has been linked to processing emotional responses. Initially, Puthanveettil and his colleagues ignored the medial prefrontal cortex because no one believed that it had anything to do with early encoding of long term memories. However, when they closely examined the effects on the brain of conditioning rodents with a mild foot shock, the scientists found several messenger RNAs recruited to polyribosomes in the medial prefrontal cortex—a clear indication of new protein synthesis there.

Puthanveettil and his colleagues also discovered that if they inhibited new protein synthesis in the prelimbic region right after fear conditioning took place, those memories did not form. But if the researchers waited just a few hours, inhibiting protein synthesis in prelimbic cortex had no impact and the memories took hold. There is temporal and spatial regulation of new protein synthesis in the medial prefrontal cortex.

Scripps Florida Scientists Discover Clues to Altered Brain Wiring in Autism

Autism is an agonizing puzzle, a complex mixture of genetic and environmental factors. One piece of this puzzle that has emerged in recent years is a biochemical cascade called the mTOR pathway that regulates growth in the developing brain. A mutation in one of the genes that controls this pathway, *PTEN* (also known as phosphatase and tensin homolog), can cause a particular form of autism called macrocephaly/autism syndrome. Using an animal model of this syndrome, scientists discovered that mutations in *PTEN* affect the assembly of connections between two brain areas

important for the processing of social cues: the prefrontal cortex, an area of the brain associated with complex cognitive processes such as moderating social behavior, and the amygdala, which plays a role in emotional processing.

The study was published on November 15, 2016 by the journal *Nature Communications.* The study also showed that targeting the activity of the mTOR pathway shortly after birth, a time when neurons are forming connections between these brain areas, can block the emergence of abnormal amygdala activity and social behavioral deficits. Likewise, reducing activity neurons that project between these areas in adulthood can also reverse these symptoms.

Scripps Florida Scientists Pinpoint Regulator of Amphetamine-Induced Motor Activity

In new findings that could have an impact on the development of therapies for a number of currently untreatable brain disorders such as Parkinson's and Huntington's diseases, Scripps Florida scientists found, for the first time, that a specific signaling circuit in the brain is deeply involved in motor activity. The study was led by TSRI's Associate Professor Srinivasa Subramaniam, and was published November 15, 2016 in the journal *Science Signaling*.

Despite many advances, the precise signaling mechanisms that regulate motor function in the striatum, that part of the brain responsible for motor activity, remain unknown. The new study identified for the first time a protein interaction network that helps control these functions by inhibiting the signaling of dopamine, a neurotransmitter involved in regulating movement.

In addition to Subramaniam and Shahani, other authors of the study, "RasGRP1 Promotes Amphetamine-Induced Motor Behavior through a Rhes Interaction Network ("Rhesactome") in the Striatum," are Supriya Swarnkar, Vincenzo Giovinazzo, Jenny Morgenweck, Laura M. Bohn, Catherina Scharager-Tapia, Bruce Pascal and Pablo Martinez-Acedo of TSRI; and Kshitij Khare of the University of Florida, Gainesville.

Scripps Florida Scientists Create Innovative Drug Design Strategy to Improve Breast Cancer Treatment

While there have been advances in the treatment of hormone-driven breast cancer, resistance to these therapies remains a significant problem. Side effects, including an increased risk of uterine cancer among postmenopausal women, also severely curtail their use for cancer prevention. However, a study by scientists from Florida's TSRI offered a novel structure-based drug design strategy aimed at altering the basic landscape of this type of breast cancer treatment. The findings show that the current approach is not the only, or even the best way, to block the estrogen receptor. The findings were published November 21, 2016, by the journal *Nature Chemical Biology.*

The team's new strategy, overseen by TSRI Associate Professor Kendall Nettles, taps a technique called X-ray crystallography to visualize the drug candidate as it binds to the receptor. This image is used to guide the production of estrogen receptor degraders that also lack the side chain, helping to reduce the risk of resistance and the development of other cancers.

The study was supported by the National Institutes of Health, the Breast Cancer Research Foundation, BallenIsles Men's Golf Association, Frenchman's Creek Women for Cancer Research, Susan G.

Komen for the Cure®, the National Natural Science Foundation of China and Hubei Province's Outstanding Medical Academic Leader Program.

Scripps Florida Scientists Find Surprising Answers to 'Food Coma' Conundrum

Until recently, there has been little more than anecdotal evidence to suggest that "food coma" is an actual physical condition—and the scientific evidence that does exist is unable to explain why some people fall asleep immediately after eating, some later and some not at all.

TSRI's Associate Professor William Ja, who led the study published in November 2016 in the online journal *eLife*, and his colleagues used *Drosophila*, the common fruit fly, as a model, due to the well-documented sleep-metabolism interaction in which flies suppress sleep or increase locomotion when starved. They created a system called the Activity Recording CAFE (ARC), a small plastic chamber that allowed them to record fly activity before and after feeding. Researchers found that after a meal, flies increased sleep for a short period before returning to a normal state of wakefulness. Their response varied according to food intake—flies that ate more also slept more. Further investigation of specific food components showed that while protein, salt and the amount eaten promoted sleep, sugar had no effect. The study also found some intriguing physiological reasons behind after-meal fly napping.

Scripps Florida Scientists Identify Novel Compound to Alleviate Pain and Itch While Avoiding Common Side Effects

Scientists from the Florida campus identified a possible drug candidate that suppresses pain and itch in animal models. Their new approach also reduces the potential for drug abuse and avoids the most common side effects—sedation and anxiety—of drugs designed to target the nervous system's kappa opioid receptors (KORs). The research was published in November 2016 online ahead of print in the journal *Science Signaling*.

They found that triazole 1.1 could indeed circumvent the two side effects of previously developed KOR compounds without decreasing dopamine levels, a property associated with dysphoria and sedation. TSRI Research Associate Tarsis Brust is first author of the study and the new findings clearly demonstrate that the strategy of developing biased KOR agonists offers a promising new way to treat pain and intractable itch without the potential for abuse.

SF Scientists Uncover Potential Driver of Age- and Alzheimer's-Related Memory Loss

Scripps Florida scientists made an important discovery toward the development of drugs to treat age-related memory loss in diseases like Alzheimer's. They found that reduced levels of a protein called Rheb result in spontaneous symptoms of memory loss in animal models and are linked to increased levels of another protein known to be elevated in the brains of Alzheimer's disease patients.

The study, led by TSRI Associate Professor Srinivasa Subramaniam, was published in December 2016 online ahead of print in the journal *Neurobiology of Aging*. The fact that some research shows that Rheb messenger RNA is induced during protein starvation in fruit flies, led Subramaniam and his colleagues to theorize that a high-protein diet in humans might be a risk factor for decreasing Rheb levels with age, resulting in mild-to-severe cognitive deficits, as seen in animal models.

Ancient Enzyme Morphed Shape to Carry Out New Functions in Humans

Paul Schimmel is professor at TSRI and senior author of the new study which revealed that a human enzyme has changed little from its days as a bacterial enzyme. In fact, the enzyme appears to be unique in its ability to change its shape—and its job in cells—without overhauling its basic architecture. The findings were published in the journal *Proceedings of the National Academy of Sciences* in December 2016.

The scientists in the new study took a closer look at AlaRS using two imaging techniques: X-ray crystallography and small-angle X-ray scattering. The images, combined with functional analysis, showed that a domain of AlaRS's structure, called C-Ala, had been reshaped to take on a new role in humans. The end result is the same as if AlaRS had gained a new decoration. Schimmel said the next step is to figure out the function of human C-Ala. This work may shed light on diseases linked to mutations in aminoacyl tRNA synthetases, such as the neurodegenerative disease Charcot-Marie-Tooth.

TSRI Scientists Devise New Approaches to Personalized Medicines

Scripps Florida scientists on the Florida campus of The Scripps Research Institute (TSRI) have developed broad methods to design precision medicines against currently incurable diseases caused by RNA. RNA carries out thousands of essential functions in cells, but many RNAs can act in uncontrolled ways and cause disease. For decades, scientists have tried to develop drug candidates that target human RNAs, but they have been hampered by an inability to achieve sufficient selectivity (to reduce the potential of side effects) and potency (ensuring effectiveness).

In a study published in December 2016 online ahead of press in the journal *Nature Chemical Biology*, researchers—led by TSRI Professor Matthew Disney and Research Associate Suzanne Rzuczek, with important contributions from Professor Ryohei Yasuda and Research Associate Lesley Colgan of the Max Planck Florida Institute for Neuroscience—have disclosed several approaches to overcome these hurdles.

Although these studies have broad implications for RNA diseases in general, they were demonstrated on myotonic dystrophy type 1, an incurable inherited disorder that involves progressive muscle wasting and weakness. It is caused by an 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, a cytosine-uracil-guanine (CUG) triplet. In many genetic diseases, there are two copies of the problem gene—a mutant copy that causes a disease and a normal copy that a cell needs to survive. Selective recognition of the diseased gene product has not been possible before. This study demonstrates that designer small molecules can selectively recognize larger, disease-associated repeats (alleles) over shorter, normal ones.

> Max Planck's Lesley Colgan remarked, "The combination of cutting-edge chemistry and microscopy techniques developed in Florida is a powerful approach to identify new methods to probe and manipulate (and kill) disease-causing RNA in cells."

Both Disney and Yasuda were 2015 recipients of the National Institutes of Health (NIH) Director's Pioneer Award, which supports individual scientists of exceptional creativity who propose highly innovative approaches with high-impact potential.

Scripps Florida Scientists Discover New Natural Source of Potent Anti-Cancer Drugs
Scientists from the Florida campus developed an efficient process to rapidly discover new "enediyne natural products" from soil microbes that could be further developed into extremely potent anticancer drugs. The study highlights microbial natural products as abundant sources of new drug leads. The researchers' discovery process involves prioritizing the microbes from the TSRI strain collection and focusing on the ones that are genetically predisposed to produce specific families of natural products. The scientists say this process saves time and resources in comparison to the traditional approaches used to identify these rare molecules.

The study, led by TSRI Professor Ben Shen, was published in the journal *mBio* in December 2016. Shen and his colleagues uncovered a new family of enediyne natural products, called tiancimycins, (TNMs) which kill selected cancer cells more rapidly and completely in comparison to toxic molecules used in FDA-approved antibody-drug conjugates (ADCs)— monoclonal antibodies attached to cytotoxic drugs that target only cancer cells. The scientists also discovered several new producers of C-1027, an antitumor antibiotic currently in clinical development, which can produce C-1027 at much higher levels.

It has been more than a decade since Shen first reported on the C-1027 enediyne biosynthetic machinery, and he speculated then that the knowledge obtained from studying biosynthesis of C-1027, and other enediynes, could be used for the discovery of novel enediyne natural products.

Scripps Florida Scientists Uncover Cellular Process Behind Premature Aging
Scientists from Scripps Florida have shown how two genes "balance" each other to maintain normal cell function. A disruption in one of the genes, called *spns1*, can induce degradation and premature "senescence"—or aging—while the other gene, called *atp6v0ca*, can jump in to suppress that degradation. Their experiments in zebrafish suggest that these combined genetic disruptions can counteract premature aging and extend developmental lifespan.

The findings, published in December 2016 in the journal *Autophagy*, could also guide future treatments for diseases that involve the body's inability to degrade unwanted or harmful compounds.

In the new study, the researchers took a closer look at the gene *spns1*. In vertebrates, such as zebrafish and humans, the protein encoded by *spns1* is important in a cellular process called autophagy, when the cell moves unwanted material to a cellular structure called the lysosome. Previous research had shown that defects in this gene can also cause senescence in the embryonic stage and premature aging symptoms in adulthood. The findings may also lead to the development of tools to help identify new genes that affect the aging process without the need for performing lengthy adult lifespan analyses. This approach could be applied to the high-throughput identification of pharmacological agents that control aging and lifespan through enhanced resistance to various stressors, including oxygen radicals.

Scripps Florida Scientists Develop Drug Discovery Approach to Predict Health Impact of Endocrine-Disrupting Chemicals
Breast cancer researchers from Scripps Florida developed a novel approach for identifying how chemicals in the environment—called environmental estrogens—can produce infertility, abnormal reproductive development, including "precocious puberty," and promote breast cancer. Environmental estrogens work by binding to the estrogen receptor, a protein in cells that guides sexual maturation and

reproduction. The new research shows how high-resolution imaging techniques could give scientists a window into how exposure to these chemicals may impact public health.

This research method could also be used to speed up the discovery of new drugs for breast cancer and many other diseases, added study senior author Kendall Nettles, associate professor at TSRI. The study was published in December 2016 online ahead of print in the journal *Cell Chemical Biology.*

Nettles calls the approach in the new study "super-resolution x-ray crystallography," a technique that produces a snapshot of the receptor's 3-D atomic structure. Like the images produced by photography or microscopy, x-ray crystal structures have a certain resolution, or level of detail, that can be visualized. With optical microscopy, super-resolution imaging—a discovery for which researchers were awarded the Nobel Prize in 2014—can be achieved by combining many images to produce a sharper picture. Nettles and his colleagues reasoned that they could use a similar approach with x-ray crystallography to compare molecular snapshots, or structures, and better understand how estrogenic chemicals control receptor activity.

The study was supported by the National Institutes of Health, The BallenIsles Men's Golf Association, The Frenchman's Creek Women for Cancer Research, The National Science Foundation and the University of Michigan.

Scripps Florida Scientists Uncover New Way to Defeat Therapy-Resistant Prostate Cancer

The study, led by TSRI Associate Professor Jun-Li Luo was published in December 2016 ahead of print in the journal *Molecular Cell*, and shed light on a signaling circuit in cells that drives therapy resistance in prostate cancer. The researchers found that targeting the components of this circuit suppresses advanced prostate cancer development.

Prostate cancer—which, according to the American Cancer Society, affects one in six American men—is the second-leading cause of death after lung cancer in American men. Currently, the most effective treatment for advanced prostate cancer is to deprive the cancer of what feeds it—androgen hormones, such as testosterone. Unfortunately, almost all patients eventually develop resistance to this therapy, leaving doctors with no options to counteract the inevitable.

The new study shows that a "constitutively active" signaling circuit can trigger cells to grow into tumors and drive therapy resistance in advanced prostate cancer. A cell signal pathway with constitutive activity requires no binding partner (ligand) to activate; instead, the signaling circuit continually activates itself. This signaling circuit, which is composed of the protein complex IκBα/NF-κB (p65) and several other molecules, controls the expression of stem cell transcription factors (proteins that guide the conversion of genetic information from DNA to RNA) that fuel the aggressive growth of these resistant cancer cells.

Scripps Florida Scientists Expand Toolbox to Study Cellular Function

The study, published in the journal *Proceedings of the National Academy of Sciences* in January 2017, explores how evolution can be used to discover new and useful enzyme tools, called proteases. Proteases cleave proteins into smaller peptide pieces that scientists can then analyze to determine the identity of the protein and whether a cell has made chemical changes to the protein that might alter its function.

The new protease developed in the study helps shed light on these chemical changes, called post-translational modifications. Post-translational modifications are alterations made to proteins *after* the proteins are translated from RNA. These modifications can dramatically alter a protein's stability and function, and unregulated modification can lead to disease, such as cancer. Therefore, understanding the nature and location of these modifications can be critical in the early phases of drug discovery.

The study's senior author Brian M. Paegel, TSRI associate professor, believes this new approach could be useful for mapping a wider range of post-translational modifications, and he hopes to use directed evolution to discover proteases that target many other post-translational modifications.

"I think we're on the brink of an explosion of new tools for mass spectrometry," Paegel said.

TSRI Researchers Discover Surprising Process Behind Sense of Touch

Biologists on the TSRI Florida campus discovered a new mechanism that likely underlies how we feel force or touch. Their study suggests that "rafts" of fatty lipids on the cell surface act as compartments to keep certain enzymes from mixing with their binding partners. Disrupt these rafts through touch—also called mechanosensation—and the enzymes will mix with their partners and react, triggering a signal that communicates the touch to responsive proteins in the cell.

TSRI biologist Scott Hansen supervised the study which was published in January 2017 in the journal *Nature Communications*. Hansen compared lipid rafts to compartments in a glow stick. Crack the barrier between the two sides of a glow stick and the components mix and start a chemical reaction to produce light. On the cell membrane, the mixing of enzymes and their partners produces a signaling lipid phosphatidic acid that starts the chain of events to create the sense of touch.

Hansen and his colleagues conducted this research with support from a National Institutes of Health Director's New Innovator Award, which encourages scientists to pursue high-risk, high-reward translational research. Their mission was to shed light on the complicated cellular mechanisms behind touch with the hope that this work could lead to new ways to address chronic pain and other conditions where the sense of touch goes haywire.

Scripps Florida Scientists Find Clue to Why Zika Causes Birth Defects

The most frightening aspect of Zika virus has been its ability to produce severe fetal birth defects during pregnancy, especially microcephaly—a small head. Scientists from Scripps Florida uncovered the details behind the virus's unique ability to cross the placental barrier and expose the fetus to a range of birth defects that often go beyond microcephaly to include eye and joint injury, and even other types of brain damage.

The study, led by TSRI Associate Professor Hyeryun Choe, was published online ahead of print In February 2017 in the journal *Proceedings of the National Academy of Sciences*. How Zika virus crosses the placental barrier, while other closely related viruses in the flavivirus family including dengue and West Nile viruses do not, has puzzled researchers since the crisis began some two years ago in Brazil. Obstacles to reaching the fetal brain are substantial—a virus must move from the mother's blood into fetal circulation, which is separated by placental barrier cells designed to prevent that very occurrence.

The researchers found that human umbilical endothelial cells, derived from four donors in the study, proved far more susceptible to Zika infection than to other viruses, with viral counts as much as a hundred or thousand times higher than West Nile or dengue virus. The new research also suggests that Zika virus learned to exploit something of a secret passage, a cell surface molecule known as AXL, while West Nile and dengue viruses did not.

What may help make the Zika virus particularly infectious in cells that other flaviviruses can't infect, said TSRI Research Associate Audrey Richard, a first author of the study, is that it profits from the built-in function of AXL. Zika is able to take advantage of AXL by binding to an intermediate molecule known as Gas6, which is present in blood and other bodily fluids. Gas6 acts as an active bridge between the virus and AXL by binding AXL on one end and the virus membrane on the other, helping the virus utilize AXL and gain entry to host cells. These differences may help explain why, among related viruses, only Zika can efficiently access and infect the fetal bloodstream.

Scripps Florida Scientists Take Aim at Obesity-Linked Protein

Scientists are working to understand the mechanisms that make weight loss so complicated. Exercise burns calories, of course, but scientists are also looking at how the body burns more energy to stay warm in cold temperatures.

TSRI Assistant Professor Anutosh Chakraborty's past research revealed a new therapeutic target in the battle—a protein that actually *promotes* fat accumulation in animal models by slowing stored energy (fat) breakdown and encouraging weight gain. Now, in a study published online in the journal *Molecular Metabolism* in February 2017, Chakraborty and his colleagues have shown that deleting the gene for this protein, known as IP6K1, protects animal models from both obesity and diabetes. This protective effect is seen regardless of diet, even at what's known as a thermoneutral temperature (around 86□F). This means inhibiting IP6K1 should help animals burn more energy, regardless of outside conditions.

Temperature is important in the study of obesity because an animal in lower temperatures will rapidly lose weight as it burns more energy to try to maintain core body temperature. Because humans can maintain their body temperatures in a number of ways—clothing, for example—any pathway that reduces body weight at higher temperatures is a highly encouraging target in human obesity. The new study suggests a future pharmaceutical may be able to target IP6K1 to mimic the energy burning seen at relatively lower temperatures.

Fighting Blindness: TSRI Scientists Bring a Key Protein into Focus

Scripps Florida scientists discovered how a protein called α2δ4 establishes proper vision. Their research helps explain why mutations in the gene encoding α2δ4 lead to retinal dystrophy, a disease characterized by defective color vision and night blindness. To study how this protein supports vision, the researchers modeled retinal dystrophy in mice. Like humans, mice lacking α2δ4 succumbed to the disease and their vision was compromised.

The study was published online in March 2017 in the journal *Neuron*. TSRI Professor Kirill A. Martemyanov, senior author of the new study, and his colleagues are studying the neural connections that make vision possible. In the new study, experiments spearheaded by TSRI Research Associate Yuchen Wang of the Martemyanov laboratory showed that this connectivity requires α2δ4 to join a

structure, called a higher order macromolecular complex, with ELFN1 and other proteins called calcium channels. These calcium channels trigger the release of the chemical messenger glutamate, which photoreceptors use for communicating with bipolar neurons.

Potential Drug Candidates Halt Prostate and Breast Cancer Growth

Scientists at Scripps Florida designed two new drug candidates to target prostate and triple negative breast cancers. The research, published as two separate studies in *ACS Central Science* and the *Journal of the American Chemical Society* in March 2017, demonstrated that a new class of drugs called small molecule RNA inhibitors can successfully target and kill specific types of cancer.

In their *ACS Central Science* study, Disney and his colleagues used DNA sequencing to evaluate thousands of small molecules as potential drug candidates. The researchers were on the lookout for molecules that could bind precisely with defective RNAs—like keys fitting in the right locks. Disney and his team tested their compound, called Targapremir-18a, and found that it could target microRNA-18a and trigger prostate cancer cell death.

The same screening strategy led the researchers to a drug candidate to target triple negative breast cancer, as reported in the *Journal of the American Chemical Society*. The researchers tested their drug compound, Targapremir-210, in mouse models of triple negative breast cancer. They found that the therapy significantly slowed down tumor growth. In fact, a single dose decreased tumor size by 60 percent over a three-week period. The researchers analyzed these smaller tumors and discovered that they also expressed less microRNA-210 compared with untreated tumors.

Next, the researchers plan to further develop their molecule-screening strategy into a platform to test molecules against any form of RNA defect-related disease.

Scripps Florida Scientists Develop New Drug Delivery Method for Cancer Therapy

Scientists developed a new drug delivery method that produces strong results in treating cancers in animal models, including some hard-to-treat solid and liquid tumors. The study, led by TSRI Associate Professor Christoph Rader, was published March 16, 2017, online ahead of print in the journal *Cell Chemical Biology*.

The new method involves a class of pharmaceuticals known as antibody-drug conjugates (ADCs), which include some of the most promising next-generation antibody therapeutics for cancer. ADCs can deliver a cytotoxic payload in a way that is remarkably tumor-selective. So far, three ADCs have been approved by the U.S. Food and Drug Administration (FDA), but neither attaches the drug to a defined site on the antibody.

Antibodies are large immune system proteins that recognize unique molecular markers on tumor cells called antigens. On their own, Rader noted, antibodies are usually not potent enough to eradicate cancer. However, their high specificity for antigens makes them ideal vehicles for drug delivery straight to tumor cells. Along with its potency, Rader noted, the ADC's stability is critical to its effectiveness. The researchers found that their new ADCs showed excellent stability in human blood *in vitro* and in circulating blood in animal models. Moreover, the new ADCs were highly effective against HER2 breast cancer, a particularly difficult cancer to treat, and against CD138 multiple myeloma. Importantly, the ADCs did not harm healthy cells and tissues.

The researchers plan to investigate similar ADCs going forward. Rader, along with TSRI Professor Ben Shen, was recently awarded $3.3 million from the National Cancer Institute of the National Institutes of Health to test highly cytotoxic natural products discovered in the Shen lab using selenomabs as drug delivery vehicles.

Researchers Discover Key to Drug Resistance in Common Breast Cancer Treatment

Three-quarters of all breast cancer tumors are driven by the hormone estrogen. These tumors are frequently treated with drugs to suppress estrogen receptor activity, but unfortunately, at least half of patients do not respond to these treatments, leaving them with drug-resistant tumors and few options.

Now, scientists from TSRI, the University of California, San Diego and the University of Illinois have found that two immune system molecules may be key to the development of drug resistance in estrogen-driven breast cancers. The researchers believe this finding may open the door to novel therapeutic approaches and influence treatment decisions for the tens of thousands of patients who suffer from estrogen-driven breast cancers. These molecules, which are cytokines called interleukin 1 beta (IL1β) and tumor necrosis factor alpha (TNFα), had previously been linked to the spread of drug-resistant cancer, but scientists were unsure of the exact mechanisms that led these molecules to drive drug resistance.

Their study was published March 2017 online ahead of print in the journal *Molecular Cell* and revealed that IL1β and TNFα turn on pathways that modify the actual shape of the estrogen receptor. This phenomenon appears to drive resistance to the common anti-cancer drug tamoxifen.

Scientists Discover New Class of Anti-Diabetes Compounds

Scientists may have found a new tool for studying—and maybe even treating—Type 2 diabetes, the form of diabetes considered responsible for close to 95 percent of cases in the United States. A team of scientists from TSRI, Dana-Farber Cancer Institute, Harvard Medical School and the Yale University School of Medicine, among others, have identified a new class of compounds that reduce production of glucose in the liver. One of these compounds, designed and optimized by TSRI scientists, significantly improves the health of diabetic animal models by reducing glucose levels in the blood, increasing insulin sensitivity and improving glucose balance.

The study, published in March 2017 in the journal *Cell*, was led by Pere Puigsever of Harvard Medical School and the Dana-Farber Cancer Institute and included Patrick Griffin, co-chair of the TSRI Department of Molecular Medicine, and Theodore Kamenecka, TSRI Associate Professor of Molecular Medicine.

The compound they identified, called SR-18292, modifies a protein known as PGC-1α. This protein plays a pivotal role in energy balance and helps control genes involved in energy metabolism. When cells overexpress PGC-1, during fasting or starvation, for example, glucose production in the liver soars. But when scientists modify PGC-1α function through a process called acetylation, glucose production declines. Suppressing this overproduction makes PGC-1αa target ripe for exploitation in anti-diabetes treatments.

Scientists Unravel How Protein Impacts Intellectual Disability
Your brain needs just the right balance between excitatory "on" signals and inhibitory "calm down" signals. Scientists from Scripps Florida have shown that a protein helps balance nerve cell communication. The study, published online in the journal *Cell Reports* in April 2017, could have implications for potential treatments of intellectual disability and other neurodevelopmental disorders.

Studying neuronal communication is important because the brain needs to balance excitatory neurotransmitters (to increase signal transmission) and inhibitory neurotransmitters (to calm nerve cells down). An imbalance in the excitatory/inhibitory ratio is a central feature of many neurodevelopmental disorders—which occurs through gene overexpression or a loss of gene function.

For the study, Brock Grill, a TSRI associate professor in the Department of Neuroscience, and his colleagues investigated neuronal communication balance using a simple model circuit in the nematode *C. elegans*, a small, transparent worm. Despite its small size, this worm shares half its genetic make-up with humans, which makes it an ideal model to study the genetics of neuron function.

Scientists Solve Major Cancer Protein Conundrum
Despite intense research, there's been much confusion regarding the exact role of a protein in a critical cancer-linked pathway. On one hand, the protein is described as a cell proliferation *inhibitor*, on the other, a cell proliferation *activator*, a duality that has caused a great deal of scientific head scratching.

Scripps Florida researchers found that angiomotin's activities depend on a process called phosphorylation—when a phosphate group is added to its structure at a specific location. Add a phosphate group, and the protein can inhibit cell proliferation. But remove a phosphate group from its normal makeup, and the protein promotes cell proliferation, encouraging cancer cell growth.

The study, led by Joseph Kissil, associate professor in the Department of Molecular Medicine at TSRI, was published in May 2017 in the journal *eLife*.

Firefly Gene Illuminates Ability of Optimized CRISPR-Cpf1 to Efficiently Edit Human Genome
Professor Michael Farzan, co-chair of TSRI's Department of Immunology and Microbiology, and TSRI Research Associate Guocai Zhong improved the efficiency of the CRISPR-Cpf1 gene editing system by incorporating guide RNAs with "multiplexing" capability. Guide RNAs are short nucleic acid strings that lead the CRISPR molecular scissors to their intended gene targets. The TSRI discovery means multiple genetic targets in a cell may be hit by each CRISPR-Cpf1 complex.

This study was published as an advanced online paper in the journal *Nature Chemical Biology* on June 19, 2017. Looking forward, Farzan said the Cpf1 protein needs to be more broadly understood so that its utility in delivering gene therapy vectors can be further expanded.

SF Scientists Identify Protein Deficiency Involved in Childhood Anemia and Cancers
Scientists have shown how the lack of a specific protein may be a significant contributing factor to a devastating childhood anemia that has been closely associated with a 30-to-40-fold increase in the incidence of colon cancer, osteosarcoma and leukemia in those who suffer from it. The new research, which was published in June 2017 in the journal *Nature Structural and Molecular Biology*, was led by TSRI Associate Professor Katrin Karbstein.

These new findings provide the first molecular understanding of the pathology of the disease known as Diamond-Blackfan anemia – and offer a potential target for developing new therapeutic approaches. Karbstein's research focuses on the assembly of ribosomes—large macromolecular machines that produce proteins by decoding information carried in messenger RNA (mRNA) and then turning that code into proteins, assembling them from amino acids. Problems in the assembly process or in messenger RNA (mRNA) can lead to serious problems, including birth defects like Diamond Blackfan Anemia and cancers.

The study was supported by the National Institutes of Health, the PGA National Women's Cancer Awareness Fellowship, the Richard & Helen DeVos Graduate Fellowship and the Howard Hughes Medical Institute.

A Perspective on the Biology of Forgetting

Ron Davis, Ph.D., TSRI Professor and Chair of Neuroscience in Jupiter, Florida, teamed up with Yi Zhong, Ph.D., Professor of Life Sciences at Tsinghua University in Beijing, China, to pen a call to action published June 2017 in the journal *Neuron.* The article reveals surprising new insights into how the brain manages memory storage.

Like many neuroscientists, the researchers have spent years working to understand the molecular mechanisms behind learning and memory, but about five years ago, they shifted their focus to the mechanisms behind forgetting. In the review, the pair presented evidence that our brains actively use molecular mechanisms to erode memories.

The pair asserts that active forgetting is a mechanism for maintaining homeostasis in the brain. Our bodies employ homeostatic control mechanisms to maintain healthy internal temperatures, glucose levels and more. We are bombarded with information all day long, and there may be a limit to the resources the brain can use to store memories at a given time, and active forgetting of unused and unimportant memories frees up the resources needed to encode important new memories. Davis and Zhong believe disruption of this process could be involved in a variety of neuropsychiatric disorders, such as autism spectrum disorders and post-traumatic stress disorder.

New TSRI Research Reveals Pathway for Anti-Aging Therapies

Two new studies led by scientists at TSRI could guide future therapies to improve health and lifespan. Together, the studies in animal models shed light on how reducing calorie intake directly influences lifespan by also reducing body temperature. Importantly, the researchers also identified a molecule that responds to lower body temperatures to regulate lifespan in fruit flies, giving scientists a target for future pharmaceuticals that may increase longevity. The new research was published in June 2017 in the journal *Proceedings of the National Academy of Sciences.*

TSRI Assistant Professor Manuel Sanchez-Alavez, who is a co-first author on the publication, emphasized that the research should not encourage people to try extreme diets or cool their body temperatures in the hope of living longer. "My advice is: Do not try this at home," he said. He explained that the study is significant because a better understanding of the full pathway between calorie restriction and lifespan gives scientists several points where they could attempt to intervene with a pharmaceutical.

The second study, led by Wiliam Ja, an Associate Professor in SF's Department of Neuroscience, drilled even deeper into the relationship between temperature and lifespan. Using fruit flies as a model, Ja and his colleagues found that colder ambient temperatures result in a "metabolic brake" to slow down the production of new proteins in the cell. A molecule called 4E-BP responds to cold by sparing select proteins and regulating longevity.

Although the Conti and Ja studies were conducted independently, they reveal another intriguing parallel. The biochemical pathways implicated by the two publications are related and interact extensively.

TSRI Researchers Develop Assay to Help Identify New Pain Medication Candidates

Scientists in Jupiter, Florida, have developed a test that will help scientists identify new drug candidates for treating pain that have fewer side effects, like addiction. The study conducted by scientists in Scott Hansen's lab at SF was published in *Cell Reports* in June 2017.

Neurological drugs, like painkillers, are notoriously messy. They bind to targets throughout the brain and produce myriad undesirable side effects. One reason for this is that the tests, or assays, that researchers use to identify how molecules interact with certain receptors have been difficult to apply to ion channels, a type of structure that drives brain function. The Hansen Lab has overcome this limitation by developing an assay that will allow scientists to screen an ion channel, TREK-1, that is known to be involved in pain.

Fortunately, Hansen and his team realized that like fat, once the lipid membrane could be broken up and solubilized with a little detergent, the channel could be used in a soluble assay. The team used the strategy in this study to show that a lipid called PIP2, which was thought to agonize the channel, is actually antagonizing—or blocking—it. Next, the assay will be advanced to drug discovery and used to screen for possible drug candidates that will act on the receptor and may be useful in managing pain. TSRI is known for its pharmaceutical-grade drug-screening capabilities, and the technique is likely to be applicable for screening other ion channels.

In addition to Hansen, three other researchers worked on the study: Lead Researcher Cerrone Cabanos of TSRI, as well as Miao Wang and Xianlin Han of the Sanford Burnham Prebys Medical Discovery Institute in Orlando, Florida. The work was supported by an NIH Director's New Innovator Award.

Scripps Florida Scientists Identify Compounds That Significantly Increase Healthy Aging

Scripps Florida scientists identified a class of compounds, using animal models and human cells, that significantly delays the onset of several age-related symptoms and extends healthy aging—what has come to be known as "healthspan." The study, published in June 2017 in the journal *Nature Communications*, was led by TSRI Professor Paul Robbins and Associate Professor Laura Niedernhofer.

This newly identified class of drugs targets senescent cells—cells that have stopped replicating because of chromosome damage. As we get older, senescent cells accumulate, becoming a major contributor to age-related diseases. Robbins and his colleagues developed a new screening platform to

look for drugs that specifically affect senescent cells. They identified a class of compounds that inhibits a stabilizing protein as having significant anti-senescent activity.

Although these inhibitors have anti-senescent activity in cell culture and in animal models, it is likely that they will be more effective in combination with other FDA-approved drugs that target other senescent cell pathways. More effective drug combinations, including ones with these inhibitors, could be used to extend healthspan in humans, according to the scientists. Anti-senescent drugs may also prove useful in delaying, preventing, or treating age-related chronic diseases, as well as other disorders related to increased senescent cell accumulation, such as obesity with metabolic syndrome and osteoarthritis. Cancer survivors treated with irradiation or chemotherapy could also benefit.

Scripps Florida Scientists Confirm Quality Control Mechanism to Protect Protein Production

The production of proteins is a complex process, made up of a series of smaller intricate biochemical steps that succeeds because of an equally complex number of quality controls. Without them, the process would irreparably break down and diseases like cancer would run rampant. Scientists from Scripps Florida have shown for the first time that the assembly of the cellular factories that produce proteins, the basic working units of any cell, also involves quality control steps.

The study, which was published September 7 online ahead of print in the journal *Molecular Cell,* was led by Katrin Karbstein, an associate professor in the Department of Integrative Structural and Computational Biology. 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 study was supported by the National Institutes of Health, the Howard Hughes Medical Institute and PGA National Gold Club.

Outside-In Reprogramming: Antibody Study Suggests a Better Way to Make Stem Cells

Scientists at TSRI have found a new approach to the “reprogramming” of ordinary adult cells into stem cells. In a study published in September 2017 in *Nature Biotechnology*, the TSRI scientists screened a library of 100 million antibodies and found several that can help reprogram mature skin-like cells into stem cells known as induced pluripotent stem cells (IPSCs).

The team, including graduate student Joel W. Blanchard and postdoctoral research associate Jia Xie, who were lead authors, set up a library of about 100 million distinct antibodies and used it to find any that could substitute for OSKM transcription factors. There is added value of such studies: to help scientists understand the relationship between cancer cell development and the stem cell state. The TSRI researchers now plan larger, more complex antibody-screening studies using human cells rather than mouse cells.

TSRI Researchers Explore Ways That a Drug Like Avandia Can Be Made Safer

With the heightened concerns over the dangerous side effects of the once-popular antidiabetic drug Avandia, researchers at Scripps Florida are working to understand how small molecules, like those in Avandia, can have such varied effects throughout the body. The insights could help researchers design new drugs with better efficacy and fewer side effects.

Douglas Kojetin, an associate professor at TSRI, and his team published a study in *Structure* in September 2017, showing the ways that Avandia interacts with and changes the shape of a combination of proteins, receptors and DNA — called the "complex" — resulting in the drug's effects. In addition to helping inform the design of future antidiabetic drugs, the study revealed that DNA plays an active role in determining the structure of the complex, a finding that has implications for understanding how any small molecule drug affects the body.

The study was supported in part by the James and Esther King Biomedical Research Program, Florida Department of Health, the William R. Kenan, Jr. Charitable Trust, National Institutes of Health (NIH) grants, and American Heart Association (AHA) fellowship awards.

For more details on any of this news, visit: http://www.scripps.edu/news/newsreleases.html or for the full article, visit: http://www.scripps.edu/news/inthenews.html.

Scientific Awards

Scripps Research Institute Chemist Jin-Quan Yu Wins MacArthur Fellowship

Chemist Jin-Quan Yu won a 2016 MacArthur Fellowship, sometimes called a "genius grant." Yu, who is the Frank and Bertha Hupp Professor of Chemistry at TSRI, will receive a $625,000 fellowship over five years from the John D. and Catherine T. MacArthur Foundation. The grant comes with no specific obligations or reporting requirements.

MacArthur Fellowships are awarded to individuals who have shown extraordinary originality and dedication in their creative pursuits and a marked capacity for self-direction. Individuals cannot apply for the award; they must be nominated. Typically, 20 to 30 fellows from a wide variety of fields are selected each year. Yu's work in the field of organic synthesis focuses on the development of new strategies and tools to accelerate catalytic C-H activation reactions.

> "At a time when the science and concepts were on the wish list of dream reactions not yet feasible, Jin-Quan Yu systematically and single-handedly transformed the field, developing powerful new synthetic methods for selective C–H activation," said Dale Boger, who is the Richard and Alice Cramer Professor and chair of the Department of Chemistry at TSRI. "His methods have transformed how we think about making molecules, how we conduct medicinal chemistry and how tools are created for chemical biology," Boger continued. "He is, simply, a brilliant scientist."

Yu, a graduate of East China Normal University (1987) and University of Cambridge (1999), joined the TSRI faculty in 2007 after an appointment at Brandeis University and a Royal Society fellowship at the University of Cambridge (United Kingdom). A fellow of the American Association for the Advancement of Science and the Royal Society of Chemistry, Yu is the recipient of many awards and honors. For more information, see his faculty web at http://www.scripps.edu/yu/#ad-image-1.

Grant Awards

Scientists Awarded Special Grant to Develop Memory-Altering Medication for Addiction

TSRI Associate Professor Courtney Miller is a principal investigator of a five-year grant, along with TSRI investigators Professor Patrick Griffin and Associate Professor Ted Kamenecka, given in October 2016 by the National Institutes of Health through the Blueprint Neurotherapeutics Network and the National Institute of Drug Abuse. The first year's funding is for $640,000, followed by the possibility of additional support in the millions, including outsourced studies. Each year's funding is based on reaching certain milestones, with the goal of a Phase 1a clinical trial in the fifth year.

Miller's approach has been compared to the cult film classic "Eternal Sunshine of the Spotless Mind," in which Jim Carrey's character attempts to get over a romantic breakup by erasing his memories. But for methamphetamine abusers, memories are not only painful, they can also trigger relapse. As a 2015 article highlighting Miller's research in *The Washington Post* concluded: "A spotless mind…[is] a chance for an addict to start over again."

In their research, Miller and colleagues are examining a drug candidate called blebbistatin. The compound enables scientists to take advantage of the fact that meth-related memories are more unstable than other memories. In animal models, the team was able to show that a single treatment with blebbistatin was sufficient to produce a seemingly permanent loss of meth-associated memories without affecting other types of recall. The potential of such an effect with a single treatment significantly reduces the typical safety and toxicity concerns of making a new drug.

NIH's Blueprint Neurotherapeutics Network aims to generate novel compounds and data on their activity, toward the goal of discovering and developing new drugs that will ultimately be commercialized and benefit the public.

Davis Awarded $5 Million Outstanding Investigator Grant to Study the Biology of Memory

In December 2016, Ron Davis, chair of the Department of Neuroscience on the Florida campus of The Scripps Research Institute (TSRI), was awarded a $5 million Outstanding Investigator Grant, one of the first of its kind, by the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health (NIH). The new eight-year grant will focus on the biological processes that underlie memory formation, targeting the brain mechanisms that mediate forgetting, how the brain organizes memories, and the role for genes that suppress memory formation.

The grant is fully funded for the first five years. At the end of the fifth year, an administrative review of the program's progress will decide on an additional three-year renewal. Davis, who has pioneered the study of memory formation, particularly how the brain actively forgets certain memories, will be the principal investigator for the new grant, which was launched by NINDS earlier this year. The new funding will cover virtually all the *Drosophilia* research done in the lab, Davis noted. Davis's research into how the brain actively forgets certain memories represents a breakthrough in what has been a largely unstudied area of memory formation and offers tremendous opportunities for making new discoveries in the molecular biology of the process.

According to NINDS, the Outstanding Investigator Grant is designed specifically to give scientists the freedom to "pursue longer range, innovative, high-risk research without feeling pressured to generate results quickly to renew short-term grants." The new grant also had a shorter submission process to reduce the amount of time scientists spend writing and administrating multiple grant awards.

SF Team Awarded $1.8M Grant to Develop Drugs for Heart Disease and Rheumatoid Arthritis

The co-principal investigators of the three-year project are TSRI Professor William R. Roush and Associate Professor Derek Duckett and they were awarded in January 2017 approximately $1.8 million from the National Institute of General Medical Sciences of the National Institutes of Health to develop a series of drug candidates for a number of diseases, including heart disease, rheumatoid arthritis and several neurodegenerative disorders.

The new project will focus on an enzyme known as ASK1, which is involved in mediating cell survival and programmed cell death, or apoptosis. ASK1 is part of a larger family of mitogen-activated protein kinases (MAP kinases), enzymes that help control a cell's response to stress. A number of studies have shown that animal models lacking ASK1 have decreases in the size of myocardial infarctions (heart attacks) and a marked resistance to heart cell death. Under a previous grant, Duckett and his colleagues completed a high throughput screening campaign aimed at identifying the best lead molecules to target ASK1, ultimately producing a series of small molecule inhibitor candidates from six different structural classes. The optimization strategy going forward, Duckett explained, will focus on developing inhibitor properties sufficient for use in pre-clinical testing, and ultimately, in safety assessment and clinical trials.

SF Collaboration Awarded $3.3 Million to Develop Next-Generation Breast Cancer Therapies

In February 2017, a pair of scientists from the Florida campus of TSRI were awarded up to $3.3 million from the National Cancer Institute of the NIH to create the next generation of breast cancer treatments for the thousands of patients whose current treatment options are limited. Ben Shen, TSRI professor and co-chair of the Department of Chemistry, and Christoph Rader, TSRI associate professor in the Department of Immunology and Microbiology, co-lead the new five-year study.

The researchers aim to develop a potent type of therapy known as an antibody-drug conjugate (ADC). This new class of anti-cancer drugs combines the specificity of antibodies, which attack only cells they recognize, with a highly toxic payload designed to kill specific cancer cells with far greater efficiency than most currently available treatments. So far, only three of these combination therapies have been approved by the U.S. Food and Drug Administration (FDA). The new ADC approach targets HER2-postive and ROR1-positive breast cancers, which are often aggressive and harder to treat with conventional chemotherapy and hormone drugs. Since HER2 and ROR1 expression is highly complementary, the new collaboration could provide new treatment options for at least 50 percent of breast cancer patients.

Scripps Florida Scientist Awarded $4.8 Million to Bring HIV Vaccine Closer to Human Trials

In April 2017, Professor Michael Farzan, co-chair of the Department of Immunology and Microbiology, received $4.8 million in funding through a 2017 Avant-Garde Award for HIV/AIDS research from the National Institutes of Health's National Institute on Drug Abuse (NIDA). The new funding will support a five-year project, led by Farzan, to bring a potential HIV vaccine closer to human clinical trials. This work will build on a 2015 study, published by Farzan and colleagues in the

journal *Nature*, showing that researchers can use a gene-therapy approach to prompt muscle tissue to produce HIV-fighting antibodies or antibody-like molecules. Further studies from the Farzan lab have shown that this method works as a vaccine to protect nonhuman primates from HIV.

With the new funding, Farzan and his lab will explore the development of an "off switch" that halts production of these antibodies and antibody-like molecules. Their goal is to design a way to counteract any bad reaction to the vaccine and make the vaccine safe for long-term exposure. Farzan is one of three researchers to win a 2017 NIDA Avant-Garde Award, which aims to stimulate high-impact research for the prevention and treatment of HIV/AIDS in drug users.

SF Scientist Wins $2 Million Grant to Study Childhood Disorder Linked to Behavioral Problems
Assistant Professor Seth Tomchik received $2 million in May 2017 in funding from the National Institutes of Health's National Institute of Neurological Disorders and Stroke (NINDS). The five-year grant funding will support the study of neurofibromatosis type I, an inherited disorder that results from genetic mutations affecting a protein called neurofibromin (Nf1). There is currently no FDA-approved treatment for neurofibromatosis 1. The disease begins in childhood with symptoms ranging from harmless spots to nerve tumors. It also predisposes individuals to a suite of behavioral symptoms, including attention-deficit/hyperactivity disorder (ADHD), autism-like symptoms, learning disabilities and chronic pain. The prevalence of behavioral symptoms suggests that Nf1 can affect the development or function of neurons in the brain that regulate activity levels.

Because neurofibromin is a large protein with multiple potential signaling roles in cells, Tomchik's research will focus on the functions of Nf1 at several levels, examining its molecular biology, genetic interactions and effects on signaling and development of neuronal circuits.

New Equipment at Scripps Florida Will Advance Drug Discovery
The Nuclear Magnetic Resonance (NMR) facility at Scripps Florida is becoming one of the most advanced in South Florida, thanks to a May 2017 $600,000 grant from the NIH. The grant will fund the purchase of a 600 Mhz NMR machine, which will help researchers develop drugs and understand how those drugs act in the body.

The TSRI's Florida campus currently houses three NMR machines, but as the scientists have continued to focus on translational research—studies that aim to "translate" laboratory findings into potential treatments for disease—those machines are constantly in use. "We were basically maxed out on instrument time," said TSRI Associate Professor Douglas Kojetin, project leader on the new grant. "All of our instruments were all near 100 percent usage."

The researchers use these machines throughout the drug development process. NMR applies a strong magnetic field to sample, which interacts with the individual atoms in a molecule, allowing scientists to discern that molecule's structure. Chemists at TSRI regularly use the two lower-field NMRs the institute currently owns, which apply a magnetic field around 400MHz, to confirm the structures of molecules they have either synthesized in the lab or isolated from natural sources. TSRI also has one 700mhz NMR, which Kojetin and his colleagues use to understand how small molecules interact with other molecules in the body, including proteins, receptors and RNA.

The 600mhz NMR will be able to support all types of research, with many of the capabilities of both the higher and lower field machines. Kojetin added that the new equipment will not only expedite more than 20 NIH-funded projects currently in progress at TSRI, but it will help generate new data that will lead to more grant funding and more discoveries. "The addition of this instrument will place us within the top NMR facilities in South Florida," said Kojetin.

Scripps Florida Scientist & Collaborators Win $7m Grant to Develop New ALS Treatments

In June 2017, Professor Matthew Disney of the Department of Chemistry on the Florida campus of The Scripps Research Institute (TSRI), together with scientists from Mayo Clinic's Florida campus and Johns Hopkins School of Medicine, were awarded $7.2 million from the National Institute of Neurological Disorders and Stroke of The National Institutes of Health to create new RNA-based treatments for the most common form of amyotrophic lateral sclerosis (ALS), as well as a type of frontotemporal dementia (FTD). Disney is the principal investigator on the five-year project, along with Leonard Petrucelli, chair of neuroscience at Mayo Clinic's Florida campus, and Jeffrey D. Rothstein of Johns Hopkins School of Medicine. While the scientists will initially focus on small-molecule drug candidates for ALS and FTD, the grant establishes the RNA Therapeutics Center at TSRI for the continued study of RNA-based therapies for a number of untreatable diseases.

ALS is usually fatal two to five years after diagnosis. There is no effective treatment for FTD, a neurodegenerative disease that destroys neurons in the frontal lobes of the brain. This study will focus on a lead compound that interferes with the synthesis of an abnormal protein—known as a repeat RNA expansion—that plays a key role in the development of both diseases. Disney has been a pioneer in the development of potential treatments for a number of diseases caused by defects in RNA, which affect millions worldwide. His success in identifying drug-like small molecules that bind to RNA is the result of his lab's broad, bottom-up, computational approach known as Inforna, which can deep mine information against such genome sequences and cellular RNAs.

Scripps Florida Scientists Awarded $2 Million to Develop 'Industrial Level' Screening for Treatments of Autism-Related Intellectual Disability

A team of scientists In July 2017 were awarded nearly $2 million from the National Institute of Mental Health of the National Institutes of Health to develop an 'industrial level' high throughput screening platform that could lead to new treatments for a number of childhood brain disorders. The three-year-grant is overseen by Gavin Rumbaugh, a TSRI associate professor in the Department of Neuroscience, and Associate Professor Louis Scampavia and Assistant Professor Timothy Spicer, co-directors of the campus' High Throughput Screening facility.

Over the past several years, the three scientists have worked as a collaborative group to create a cost-effective screening platform that can support medium-scale screening in neuronal networks. The new grant will allow them to optimize their current efforts to support screening campaigns of a much larger scale, which is expected to increase the chances of a successful screen. The scientists are focused on mutations in the *Syngap1* gene that can damage development of specific types of neurons in the brain and lead to intellectual disability. Problems with higher cognitive processes, such as language, reasoning and memory arise in children with these mutations. These rare genetic brain disorders offer the greatest potential for new therapeutics because the disease mechanism is generally straight forward – basically low expression of a single protein in this case.

Earlier studies done by the Rumbaugh lab demonstrated that if *Syngap1* protein expression can be fixed by a form of gene therapy in an animal model, then neuronal function and intellectual ability in the animal model were also fixed. Unfortunately, this type of gene therapy is not yet feasible in humans. However, animal studies suggest that identification of *Syngap1*-regulating compounds by ultra high-throughput screening may lead to therapies that target the disease mechanism in this genetic disorder. Damaging mutations in *Syngap1* that reduce the number of functional proteins are one of the most common causes of sporadic intellectual disability and are associated with schizophrenia and autism spectrum disorder. Some estimates suggest that these non-inherited genetic mutations account for two to eight percent of these intellectual disability cases.

New Exploratory Grant Will Help Scripps Florida Scientists Advance Treatment Development

In August 2017, Scripps Florida scientists were awarded nearly $1 million from the National Institute of Neurological Disorders and Stroke, part of the NIH, to develop a genetically engineered animal model of a debilitating inherited disease that could accelerate the development of potential treatments. Joseph Kissil, a TSRI associate professor in the Department of Molecular Medicine, is the principal investigator for the three-year grant. This is a phased award; if certain benchmarks are met, the grant is extended for a third year.

Kissil has been studying Neurofibromatosis Type 2 (NF2) for a number of years. The disease is caused by mutations in the anti-tumor gene *NF2,* which leads to tumors of the auditory nerve that connects the inner ear to the brain and causes severe hearing loss and impaired balance and walking. A majority of patients develop additional tumors throughout the nervous system, which can lead to fluid buildup in the brain and seizures.

While knowledge of the molecular mechanisms underlying the disease has improved significantly over the past two decades, there are still no effective treatments. Current options are non-curative and include surgery, radiation therapy, as well as temporary interventions for symptom control. In 2013, Kissil and his colleagues identified a new drug candidate to treat NF2. The compound —known as FRAX97—slowed the proliferation and progression of tumor cells in some preliminary animal models of the disease. Originally developed for neurodegenerative disease, the compound targets a protein family known as p21-activated kinases or PAKs. These kinases (enzymes that add a phosphate group to other proteins and change their function) play a critical role in the development of NF2.

SF Scientist Awarded $2.5 Million Collaborative Grant to Develop New Diabetes Treatment

In September 2017, Patrick R. Griffin, co-chair of the Department of Molecular Medicine, was awarded a $2.5 million collaborative grant with Brigham and Women's Hospital by the National Institute of Diabetes and Digestive and Kidney Diseases, part of the NIH. The new five-year study seeks to confirm whether the inhibition of a particular protein that plays a role in regulating the body's response to fat might be a viable target in the treatment of type 2 diabetes. Griffin and Jorge Plutzky, MD, from Brigham and Women's Hospital in Boston are co-principal investigators for the five-year multi-PI grant. TSRI's Theodore Kamenecka, an associate professor in the Department of Molecular Medicine, is a co-investigator on the study.

Griffin's work covers a wide area of diseases ranging from cancer to diabetes to age-related bone loss. But they are all characterized by their impact on human metabolism – and the galaxy of disorders that more often than not occur in clusters: obesity, abnormal cholesterol, high blood pressure and insulin

resistance. What makes the new grant significant – and something of a milestone – is that Griffin now has five similar grants running simultaneously, several in collaboration with other institutes.

The latest study with Brigham and Women's Health will focus on what is known as brown adipose tissue or brown fat, which serves as a kind of molecular furnace in humans, generating heat by burning large numbers of fat calories. Brown fat is loaded with mitochondria, the cell's energy plant, which contain iron and give the fat its red-brown tint; mitochondria use nutrients to produce energy for the cell. Brown fat is different than white adipose tissue (WAT), which stores energy and can lead to obesity. Studies have shown that brown fat characteristics can be induced in white fat through the inhibition of the protein retinaldehyde dehydrogenase 1 (ALDH1a1), which in turn protects against diet-induced obesity and diabetes.

HIVE Center Receives $27 Million in NIGMS Funding to Advance HIV Research

The HIV Interactions in Viral Evolution (HIVE) Center at TSRI was awarded nearly $27 million in October 2017 from the National Institute of General Medical Sciences (NIGMS) of the NIH. This continues the HIVE Center's crucial work for another five years studying at the atomic level the human immunodeficiency virus (HIV), which causes AIDS.

Viruses have complex interactions with the human host cells they infect, especially HIV given its capacity for utilizing human cell proteins, its ability to rapidly mutate to both immune and viral inhibitor-mediated pressures, and remain dormant in infected cells, noted HIVE Center Co-Director, Associate Professor Bruce Torbett. For the past five years, the NIGMS has funded five National Centers, of which the HIVE Center is one, dedicated to understanding how HIV functions in the body's immune cells and utilizes human cellular components to evolve, adapt and evade treatment.

The Center's highly collaborative researchers will continue to build on their past success of the initial HIVE funding period under Professor Arthur Olson. In the next five years, the goal of the Center's researchers is to obtain at the atomic level an understanding of the structural and dynamic relationships between interacting human host cell and HIV macromolecules in the HIV life cycle. These insights will shed light as to how HIV usurps human host cell proteins to move through the cell undetected and how the virus utilizes host cell proteins to insert its DNA into cellular chromatin. Genomic and structural studies on the development of HIV inhibitor resistance should provide insights for HIV inhibitor resistance prediction and novel therapies. The information obtained from all studies will help to develop computational models to visualize HIV, which should allow an unprecedented view as to how HIV is formed and functions within host cells according to Torbett.

The Center includes scientists from both the California and Florida campuses of TSRI. On the California campus, Arthur Olson, K. Barry Sharpless, James Williamson, David Millar, Stefano Forli and David Goodsell, and on the Florida campus, Patrick Griffin and Douglas Kojetin.

Other scientists from across the country and abroad also will participate as part of the Center research effort and they hail from Emory University, Ohio State University, The Salk Institute, the Dana Farber Cancer Institute, King's College, London and the National Cancer Institute-Frederick, among others.

More details on the activities and resources of the HIVE Center can be found at https://hivecenter.org.

Itemized Report for the Year Ended September 30, 2017

INTRODUCTION

Florida Statute 288.955, referred to as the Enabling Statute, sets forth certain information that is required to be included in the SFFC Annual Report. The information that follows has been organized to correspond to the sections of the Enabling Statute that address information to be included in the SFFC Annual Report. As not every section of the Enabling Statute relates to the SFFC Annual Report, only the sections of the Enabling Statute that apply are referenced herein. For convenience, the text of the Enabling Statue that describes the information to be reported in the SFFC Annual Report is set forth next to each Enabling Statute section reference.

Florida Statute 288.955

Subsection (14) **ANNUAL REPORT**
By December 1 of each year, the corporation shall prepare a report of the activities and outcomes under this section for the preceding fiscal year. The report, at a minimum, must include:

Subsection (14) (a) **A description of the activities of the corporation in managing and enforcing the contract with the grantee.**

Scripps Florida Funding Corporation Board of Directors

Purpose: To oversee the disbursement of the State's funds invested in Scripps Florida, the Florida Legislature created the Scripps Florida Funding Corporation, hereto referred to as SFFC, a non-profit entity governed by a nine-member Board of Directors and one ex-officio member.

Membership: Of the Board of Directors, three members each were appointed by the Governor, the House Speaker and the Senate President. Former Governor Bush's appointees are Mr. David Gury, former President and CEO of Nabi Pharmaceuticals, of Boca Raton, and Dr. Pamella Dana, Senior Strategic Advisor for Institute for Human & Machine Cognition, of Destin. Governor Crist re-appointed Mr. David Gury in March 2008 and Dr. Pamella Dana in February 2009. Governor Scott appointed Mr. Art Wotiz, CEO of Novabone, of Jacksonville on March 25, 2013. Former Senate President Jeff Atwater appointed Mr. Gerry Goldsmith, former Chairman of First Bank of the Palm Beaches, of Palm Beach, on November 15, 2009. Former speaker Dean Cannon appointed Dr. Richard M. Luceri, former Vice President of Healthcare Services for JM Family Enterprises, Inc., and Speaker Will Weatherford reappointed Dr. Luceri on January 24, 2013. Speaker Weatherford appointed Mr. Mark J. Kasten, CEO of Kasten Insurance, of Tequesta on August 9, 2013.

The head of the Florida Department of Economic Opportunity or his designee may serve as an ex-oficio member of the SFFC Board. Beth Walker, Karl Blischke and Eric Miller from the DEO office have periodically attended the SFFC BOD and Audit Committee meetings.

Meetings and activities: From October 1, 2016 through September 30, 2017, the SFFC Board of Directors ("BOD") met on July 11, 2017. All Board members participated as well as Project Director Ms. Sara Misselhorn, SFFC legal counsel Ms. Kathy Deutsch of Broad and Cassel, and Mr. Scott Porter,

the outside auditor from Caler, Donten, Levine, et al. At this meeting, the Board heard a presentation from Jared Machado regarding TSRI & SF Deloitte Audit Report for the year ending September 30, 2016, and Mr. Porter presented for the Board's approval the 2016 and 2017 Compliance Reports. Additionally, the Board discussed the future of the SFFC and approved a letter to the Director of DEO, reflecting the history of the SFFC and its relationship to DEO, indicating that the organization was winding down and upon dissolution of the SFFC, the SFFC contract with Scripps, among other rights and obligations of the SFFC, will be assigned to and assumed by the DEO. This letter was sent to DEO on August 1, 2017. Since the full Board and thus the audit committee was on the call the engagement letter for the SFFC's financial audit was approved.

SFFC Audit Committee

The Audit Committee reviews financial information and monitors the financial condition of TSRI and Scripps Florida. The Audit Committee also engages the SFFC auditor, provides oversight for the annual audit of SFFC and compliance monitoring of TSRI and Scripps Florida with the terms of the Operating and Funding Agreement. The Audit Committee provides direction on the scope of the audit engagements and reviews any finding or recommendations related to the audits. The Audit Committee, in turn, reports its recommendations on the reports to the full Board.

The SFFC receives and the Audit Committee reviews the following reports:

- TSRI and Scripps Florida unaudited quarterly financial statements
- TSRI and Scripps Florida audited annual financial reports
- TSRI and Scripps Florida annual budgets
- Scripps Florida Annual Report
- Scripps Florida Annual Scientific Report

There are three types of annual audit reports that are received and reviewed by the Audit Committee:

I. Scripps Florida and TSRI provide the following reports to SFFC:
    1) Audited financial statements of TSRI, including the operations of Scripps Florida.
    2) Audited financial statements of Scripps Florida as a separate division, including a report on internal control and compliance in accordance with *Government Auditing Standards*.
    3) A Federal Single Audit of TSRI in accordance with OMB Circular A-133.

    The audits are prepared by Deloitte and Touche ("D&T"), the independent auditors for TSRI. SFFC's independent auditor has been granted access to the D&T workpapers in order to assess the application of generally accepted accounting principles and the significant assumptions made by TSRI management in the preparation of its financial statements.

II. SFFC receives the following reports prepared by an independent auditor engaged by the SFFC:
    1) Audited financial statements of SFFC, including a report on internal controls and compliance in accordance with *Government Auditing Standards*.
    2) A Federal Single Audit of SFFC in accordance with OMB Circular A-133.

III. A contractual monitoring and compliance audit of the Operating and Funding Agreement between TSRI and SFFC ("contractual monitoring and compliance audit") to address the *Monitoring Checklist* (Exhibit A-1 to the Funding and Program Agreement between OTTED (now known as the Department of Economic Opportunity) and SFFC). The contractual

monitoring and compliance audit is completed by an independent auditor contracted by the SFFC who verifies many of the items covered in this Annual Report. Once the final grant from the State of Florida was distributed in 2013, the SFFC modified the compliance report to add items related to payments that SF is required to make to the Florida Biotech Fund reflecting 15% of royalty revenues and 15% of naming opportunities.

The independent auditor contracted by the SFFC also prepares the annual not-for-profit organization tax return (Form 990) for SFFC, which is reviewed by the Audit Committee prior to submission to the Internal Revenue Service.

Membership: Mr. Gury, Dr. Pamella Dana and Mr. Gerry Goldsmith serve on the Audit Committee. Other participants in the Audit Committee meetings include SFFC's auditor, Mr. Scott Porter from Caler, Donten, Levine, Porter & Veil, P.A., TSRI's Chief Financial Officer, Mr. Jared Machado.

Meetings and activities: During Fiscal 2017, the Audit Committee met on November 30, 2016 to approve the SFFC financial audit for inclusion in the SFFC Annual Report. The July BOD meeting acted as an annual meeting and TSRI and SF's audit, the compliance audit and the engagement letters were all approved as noted in the BOD section.

Subsection (14) (b) An accounting of the amount of funds disbursed during the preceding fiscal year to the grantee.

The final disbursement was made in December 2013 and consequently, the SBA and SFFC agreed to terminate their contract in early 2014. The total amount disbursed to Scripps Florida from 2003 to 2013 was $351,977,664.39, which included interest in the amount of $41,977,664.39.

Subsection (14) (c) An accounting of the expenditures by the grantee during the fiscal year of funds disbursed under this section.

Salaries & Benefits	$	4,815,510
Supplies	$	2,149,380
Scientific Equipment	$	2,589,875
External Affairs & other program support	$	4,223,502
Project commencement, facilities, administration, and other capital expenditures	$	8,684,477
Total	**$**	**22,462,744**

This schedule reflects cash expenditures charged to the grant from the State of Florida from October 1, 2016 through September 30, 2017. The expense categories set forth above reflect those used by Scripps to report grant activity to grantors. This schedule excludes unspent grant funds received of $ 40,422,655 restricted to support Scripps Florida. There were no new financial commitments made during the report year.

Subsection (14)(d) Information on the number and salary level of jobs created by the grantee, including the number and salary level of jobs created for residents of this state.

On September 30, 2017, Scripps Florida employed 607 people. Of those, 463 were full-time. The breakdown of those full-time employees is shown below.

Faculty	45
Research Faculty	5
Staff Scientists	24
Research Associates	147
Scientific Support	125
Administrative Support	117
Total	**463**

Of the 175 employees hired in this fiscal year, 84 were residents of Florida and 62 were residents of Palm Beach County.

The average salary/range for Scripps Florida employees is shown below.

Faculty	$47,486 - $340,018
Research Faculty	$131,726 - $182,042
Staff Scientists	$62,546 - $94,162
Research Associates	$9,000 - $95,502
Administrative Support	$62,201 Average

Please note that certain employees of Scripps Florida may receive additional compensation for assuming administrative responsibilities beyond their scientific duties. For example, a faculty member who also serves as an Associate Dean of the Graduate School will receive additional compensation for that service. The ranges set forth above do not incorporate such additional compensation.

Subsection (14) (e) Information on the amount and nature of economic activity generated through the activities of the grantee.

Since 2007, the Business Development Board of Palm Beach County ("BDB"), a public-private partnership established in 1982 to be the official economic development organization for Palm Beach County, has reported 48 life science expansions and relocations to the County which have created 3,674 direct jobs and retained 519 jobs. This has resulted in over $330 million in capital expenditures in the life sciences and healthcare industries. Scripps Florida remains a steadfast supporter of the many requests for tours and information for the BDS's recruitment visits.

Subsection (14) (f) An assessment of factors affecting the progress toward achieving the projected biotech industry cluster associated with the grantee's operations, as projected by economists on behalf of the Executive Office of the Governor.

According to Enterprise Florida's last life science industries report, there were 324 research & developments establishments in biotechnology, 2,760 employees with an average wage of $93,180 for a total payroll of $257,161,473. The full report may be viewed here:
http://www.enterpriseflorida.com/wp-content/uploads/LifeSciences_Wage_Datasheet.pdf

According to TEConomy Partners' report prepared for PhRMA in May 2016 entitled "The Economic Impact of the Biopharmaceutical Industry: U.S. and States Estimates", the total direct and indirect jobs supported by the biopharmaceutical sector in Florida was 148,449, and total taxes paid by workers valued at $1.6b, $57.4m of which are state taxes. By their analysis, the total output supported by the biopharmaceutical sector was $31.2b. The full report may be viewed at:
http://c.ymcdn.com/sites/www.bioflorida.com/resource/resmgr/Industry_Data/Jobs_Factsheet_FL_2016.pdf

Palm Beach County's Life Sciences Cluster is home to over 153 companies primarily engaged in R&D or manufacturing of biotechnologies, medical devices, and pharmaceuticals, and 65 companies primarily engaged in the environmental and biological sciences. Over 7,388 people are employed in the life sciences and related industries, which doesn't include all of the healthcare providers or hospitals located in the area. Since 2006, there's been 2,377 patents issued in Palm Beach County for life sciences and related industries and $40.87 million has been awarded in NIH Grants.

Last fiscal year, the BDB released a study pointing to the strengths, weaknesses, opportunities and threats in its mission to build a sustainable life science sector.
The report recommended:

- Creating a life science leadership group.
- Fostering awareness of what exists through marketing.
- Identifying industry players who have homes or other investments in South Florida to become involved.
- Enhancing the networking effort.
- Developing a regional identification and identity.
- Providing resources and support to both existing companies and startups.
- Partnering with Florida Atlantic University and other regional universities and life science institutes to catalyze entrepreneurial efforts.

The report is updated with short-term and long-term action steps and the dates they are accomplished by, and this process is overseen by a Life Science Advisory Council, of which Richard King, TSRI's Chief Operating Officer, is a member. The full report may be found at the link below:
https://www.bdb.org/clientuploads/_aaa%20-%20kb/Life%20Science%20Action%20Plan/Life%20Science%20Industry%20Action%20Plan.pdf

Subsection (14) (g) A compliance and financial audit of the accounts and records of the corporation at the end of the preceding fiscal year conducted by an independent certified public accountant in accordance with the rules of the Auditor General.

Please see the "Audited Financial Statements and Supplementary Information" at the end of this report.

Subsection (14) (h) A description of the status of performance expectations under subsection (9) and the disbursement conditions under subsection (10).

Subsection (9) PERFORMANCE EXPECTATIONS

Subsection (9) (a) The number and dollar value of research grants obtained from the Federal Government or sources other than this state.

Scripps Florida scientists were awarded 47 research grants from non-Florida sources between October 1, 2016 and September 30, 2017. The total dollar amount of those grants for the first year of funding was $54,803,867.

Subsection (9) (b) The percentage of total research dollars received by TSRI from sources other than this state which is used to conduct research activities by the grantee in this state.

For fiscal 2016, the percent of research funding from sources other than SFFC was 88%.

Subsection (9) (c) The number or value of patents obtained by the grantee.

In fiscal 2017, 50 foreign and domestic patent applications were filed and 11 U.S. patents were issued. Since inception, 107 "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 the patents at this time.

Subsection (9) (d) The number or value of licensing agreements executed by the grantee.

One license agreement was executed with respect to Scripps Florida technologies.

Subsection (9) (e) The extent to which research conducted by the grantee results in commercial applications.

Because of the early stage of the technology being developed at Scripps Florida, no commercial applications have emerged to date. Several research reagents developed at Scripps Florida continue to be available commercially through various licensing agreements.

Subsection (9)(f) **The number of collaborative agreements reached and maintained with colleges and universities in this state and with research institutions in this state, including agreements that foster participation in research opportunities by public and private colleges and universities and research institutions in this state 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, TSRI expects 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 and Max Planck Florida Institute.

Scripps Florida scientists hosted, participated and presented in a variety of forums, conferences and meetings in the local area and throughout the State of Florida from October 1, 2016 through September 30, 2017.

Subsection (9) (g) **The number of collaborative partnerships established and maintained with businesses in this state.**

Scripps Florida continues to maintain collaborative relationships with these Florida based biotechnology companies:

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 as Dyadic International, Inc. is a global biotechnology company based in Jupiter, Florida.

Florida Power and Light Scripps is collaborating with Florida Power and Light, a Juno Beach, Florida-based power utility that is the principal subsidiary of NextEra Energy Inc., to develop novel and proprietary technology which may yield cheaper and more effective ways at producing fuels and other commodities from natural gas.

Opko Health Opko Health, Inc., based in Miami, 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 in three major areas: the area of novel diagnostic products to detect Alzheimer's and other diseases, the development of novel drug candidates to treat Parkinson's Disease, and the discovery of novel antibodies.

Vova Ida Therapeutics Vova Ida Therapeutics is a Palm beach County-based company founded in 2013 to commercialize research from Corinne Lasmeza's lab at Scripps Florida. Lasmeza is a professor in the Department of Infectious Diseases and her lab researches neurodegenerative diseases.

Subsection (9) (h) The total amount of funding received by the grantee from sources other than the State of Florida.

Since inception through September 30, 2017, Scripps Florida has been awarded $556,644,495 in grants and sponsored research funding from state and federal agencies (including the NIH), foundations, pharmaceutical companies and other grantors. In addition, the County of Palm Beach provided $210 million to Scripps for construction of the permanent facility.

Funding received by Scripps Florida from sources other than the State of Florida for the period ending September 30, 2017:

Other Revenue Sources	$ 9,094,188
Grant Awards	$ 54,803,867
Contributions*	$ 1,804,664

*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.

Subsection (9) (i) The number or value of spin-off businesses created in this state as a result of commercialization of the research of the grantee.

The nine companies that spun off from Scripps Florida technology and an additional Florida company located in Jupiter to access Scripps Florida - Envoy Therapeutics - are described in Subsection (9)(g). No attempt has been made by Scripps to assign a value to these spinoffs. However, in February 2011, CuRNA, one of the first spin-offs from Scripps Florida, was purchased by Miami-based Opko Health for $10,000,000. In November 2012, Envoy Therapeutics was purchased by Japan-based Takeda for $140,000,000, and Padlock Therapeutics was purchased by New York-based Bristol-Meyers Squibb for up to $600,000,000 if all of the development milestones are achieved..

Subsection (9) (j) The number or value of businesses recruited to this state by the grantee.

To assign a numerical value to business recruitment activities is virtually impossible. Scripps Florida is extensively involved in local, state and national efforts to promote and develop the biotech industry in the State of Florida. See analyses at Subsection (14)(f).

Subsection (9)(k) The establishment and implementation of policies to promote supplier diversity using the guidelines developed by the Office of Supplier Diversity under s. 287.09451 and to comply with the ordinances, enacted by the County and which are applicable to this biomedical research institution and campus located in this state.

Scripps Florida has adopted the following Mission and Vision Statements for Supplier Diversity:

Mission: Scripps Florida's 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 Scripps Florida's internal processes and supply chain.

Vision: Scripps Florida recognizes the importance of a diverse supply chain and strives to develop relationships with small and diverse life science and service suppliers who can assist in achieving Scripps Florida's biomedical research goals. Also, Scripps Florida expects its strategic suppliers to establish business opportunities for small and diverse suppliers.

Subsection (9) (l) The designation by the grantee of a representative to coordinate with the Office of Supplier Diversity.

Mr. Adrian Orozco serves in this position as the Supplier Diversity Coordinator for Scripps which is within TSRI's Procurement Department, led by Mr. Erik Duffey, Senior Sourcing Manager. Scripps Florida continues to participate in national, state and county 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.

Subsection (9) (m) The establishment and implementation of a program to conduct workforce recruitment activities at public and private colleges and universities and community colleges in this state which request the participation of the grantee.

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

Event	Location	Date	Attendee
Career Fair	University of Central Florida	5/9/2017	Jennifer Brown
Career Fair	Florida Memorial University	3/23/2017	Jennifer Brown

Subsection (10) DISBURSEMENT CONDITIONS

Subsection (10)(a) Demonstrate creation of jobs and report on the average salaries paid.

On September 30, 2017, Scripps Florida employed 607 people (463 full-time and 144 part-time). See reply to Subsection (14) (d).

Subsection (10)(b) Beginning 18 months after the grantee's occupancy of its permanent facility, the grantee shall annually obtain $100,000 of non-state funding for each full-time equivalent tenured-track faculty member employed at the Florida facility.

There were 45 tenure track faculty employed on September 30, 2017 and the total initial (first year) award value was $15,318,327, therefore in this fiscal year each Scripps Florida faculty obtained about $325,921 in non-Florida funding.

Subsection (10) (c) No later than 3 years after the grantee's occupancy of its permanent facility, the grantee 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, which is approximately two years after Scripps Florida's occupancy of its permanent facility. 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.

Subsection (10) (d) The grantee shall purchase equipment for its Florida facility as scheduled in its contract with the corporation.

The Scripps Florida business plan requires $10 million in equipment purchases within 18 months of occupancy of the permanent facility and Scripps occupied the permanent facility on March 31, 2009, so the effective date for the $10 million required equipment purchase was September 30, 2010. The amount of equipment purchased as of September 30, 2010 was $10.7 million, thereby meeting the required amount.

Additionally, Scripps Florida was required to purchase a total of $45m of equipment over the term of the contract. The total cost of equipment purchased by Scripps Florida from inception through contract year end January 29, 2013 was $53,895,431 and thus the requirement was fully satisfied. $3,061,993 of equipment was acquired with State grant funds and $850,395 from non-State sources this fiscal year.

Subsection (10)(e) No later than 18 months after occupying its permanent facility, the grantee 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, which was 18 months after the anticipated occupancy of the permanent facility.

45 graduate students enrolled in the TSRI graduate program in 2016. A total of 34 students have now completed Ph.D. degrees at Scripps Florida since the establishment of the Ph.D. program in 2005 and 16

new graduate students entered the program on August 1, 2016. Please note the outstanding program and analysis of its admission data at the following site:
http://education.scripps.edu/accreditation/student_achievement/admissions_data.html

Subsection (10) (f) No later than 18 months after occupancy of the permanent facility, the grantee shall establish a summer internship for high school students.

Since 2005, high school students, teachers, and university undergraduates have been provided an opportunity to work with world-class scientists at Scripps Florida in a summer research internship program. Support for the internship program has been provided by the William R. Kenan, Jr. Charitable Trust, TSRI's Graduate Studies Program and a National Science Foundation Research Experience for Undergraduates (NSF-REU) grant, awarded to Cancer Biology Associate Professor, Katrin Karbstein. Special emphasis is placed on providing opportunities for students from populations underrepresented in the sciences (i.e., females, minorities).

In the summer of 2017, 12 high school students participated in the summer internship program. Participants are selected based on their interest in science, however, most come to the program without a true understanding of scientific research. This six-week program provided students with experiential learning in world-class laboratories while being mentored by faculty, post-docs, and graduate students. The program culminated in research presentations made at a public mini-symposium. To date, 100% of the college age alumni are pursuing or have completed post-secondary degrees at top-tier universities throughout the United States. Of those who have completed their baccalaureate degrees, several have continued graduate education at medical schools and doctoral graduate programs in biomedical research fields.

In the summer of 2016, 20 undergraduates participated in the ten-week undergraduate program that 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 admission and gain valuable experience outside the context of basic undergraduate laboratory instruction. The program culminated in a public research poster competition in which the top three are recognized with travel awards. As a result of the program, Students return to their academic institutions able to participate in campus undergraduate poster sessions, act as ambassadors for the research and graduate programs at Scripps Florida, and enjoy an enhanced knowledge base as they continue their classroom instruction. In addition, seven alumni of sponsored Scripps Florida undergraduate internships are now pursuing doctorate degrees in TSRI's Graduate Studies program.

K – 12 and Public Science Education Programs

The William R. Kenan, Jr. Charitable Trust and TSRI supply funding for the following K-12 and public education programs developed through the efforts of Scripps Florida Education Outreach and Community Engagement staff, faculty, and research staff.

DiVERGE: Diversity Visitation Event for Research and Graduate Education

This program is geared towards undergraduate students, particularly from underrepresented and underserved backgrounds in the sciences, who are interested in biomedical research. It allows selected students from all over the nation to learn about ongoing research projects at TSRI, internship

opportunities and the Graduate Programs, crafting successful graduate school and internship applications, writing an effective personal and research statement, constructing and giving a compelling self-introduction, and science identity and the culture of science. In the future, Scripps hopes to continue to host this program as they have found that underrepresented and underserved minorities are in need of additional training in order to become more competitive candidates for nationally ranked graduate programs.

Lending Library

This program offers teachers in Palm Beach County the opportunity to borrow scientific equipment (ex; microscopes, specimen slides, pipettes) that is sage to bring into the classrooms for science projects and hands-on activities. A few teachers have benefited from this new program thus far. In the summer of 2017, Suncoast High School teacher Brett Stubbs worked on creating curricula around the materials available and a website will be created this semester where teachers can see the inventory, request materials, and download lesson plans. In the future, Scripps will be creating a blog where teachers can post questions to which Scripps scientists can respond.

The following are some Education Outreach Events held during this Fiscal year:
(Events held at Scripps Florida unless otherwise noted)

November 3 – 5, 2016 Diversity Visitation Event for Research and Graduate Education (DiVERGE).
November 17, 2016 Palm Beach County STEM Council Meeting at Scripps Florida (~60 attendees) - Dr. Brian Paegel Spoke to group of professionals and educators about his research and outreach program.
December 8, 2016 Visit to Howell L. Watkins Middle School - this is part of Dr. Puthanveettil's CAREER award outreach program.
January 27, 2017 Campus Visit - Visit from a group of undergraduates from University of Central Florida to Scripps Florida campus.
February 25, 2017 Health and Science Career Symposium at Inlet Grove Community High School (~45 attendees).
March 14, 2017 CAREER award outreach program - Dr. Paegel's Microscopy Lesson at Royal Palm Beach Community High School.
March 16, 2017 Science Family Night at Inlet Grove High School (25 attendees).
May 20, 2017 Women's Foundation of Palm Beach County Girls Leadership Institute & STEM Academy (Palm Beach State College, Palm Beach Gardens) (100 attendees).
June 20, 2017 Campus Visit - Visit from the Math and Science Institute at PBSC to Scripps Florida (10 attendees)
July 14, 2017 Campus Visit - Operation Hope visit to Scripps Florida for tour and hands-on science activities (25 attendees)

July 24 – 26, 2017 InSPIRE Microscopy Teacher Workshop presented by Dr. Brian Paegel and his graduate students at Scripps Florida (10 attendees)
September 28, 2017 Polo Park Middle School Career Day (100 attendees)

Subsection (10) (g) No later than 3 years after occupancy of the permanent facility, the grantee shall establish a research program for middle and high school teachers.

These programs were established in 2005. The permanent facility was occupied in 2009.

Scripps Florida Secondary 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 Instructional Support Program for Innovative Research Education (InSPIRE) 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. Portability of the lessons allows teachers to leverage the institute curriculum to their own classrooms during the course of the school year.

The program, which is supported by a grant from the National Science Foundation awarded to Dr. Brian Paegel, a faculty member in the Department of Chemistry, provides opportunities for teachers in the Palm Beach County to attend the workshops at Scripps Florida. Through its partnership with the school district, Scripps Florida emphasizes recruitment from schools with limited resources in rural and urban Palm Beach County, particularly in areas with large underrepresented and disadvantaged student populations. Recently, Dr. Paegel and his graduate students developed a new curriculum based on microscopy and image analysis applications.

Subsection (10) (h) No later than 18 months after occupancy of the permanent facility, the grantee 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.

Subsection (10) (i) **No later than 6 months after commissioning its high throughput technology, the grantee 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. An additional "Core" platform is now available at the Scripps Florida facility that combines basic research with advanced technology.

Access to Technologies is available to scientists who may not have these technologies available at their respective institutions and scientists are encouraged to utilize the web platform to learn more about these core technologies, ranging from an X-Ray Crystallography Facility, the Genomics and Proteomics Cores, to the Nuclear Magnetic Resonance Core, which just received a sizable grant to increase its machinery and capacity. To access them online visit: http://www.scripps.edu/research/resources/index.html

The High Throughput Screening Core is a drug-discovery process widely used in the pharmaceutical industry. For an example of the depth of Scripps Florida's collaborations, this state-of-the art HTS operation includes users from the Torrey Pines Institute for Molecular Studies, the University of Florida, as well as a plethora of users from Scripps Florida.

Subsection (10) (j) **Beginning June 2004, the grantee 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 commenced in 2005. Also, please see the reply to Subsection (9) (f).

Subsection (10) (k) **Beginning 18 months after the grantee occupies the permanent facility, the grantee shall establish an annual seminar series featuring a review of the science work done by the grantee and its collaborators at the Florida facility.**

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 to speak. 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. Many of the CA-based seminars are live-cast to the FL campus.

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.

Time:	**Thursday, October 6, 2016** 4:00 PM - 5:00 PM
Title:	Unbiased combinational approach for targeting non-conventional biomarkers in cancer
Speaker:	Gomika Udugamasooriya, Ph.D. Associate Professor of Medicinal Chemistry Department of Pharmacological and Pharmaceutical Sciences University of Houston College of Pharmacy
Host:	Thomas Kodadek
Location:	B158
	Thursday, October 20, 2016
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Eli Gilboa, Ph.D. Department of Microbiology & Immunology University of Miami Miller School of Medicine
Host:	Brian Paegel
Location:	B158
	Thursday, October 27, 2016
Time:	4:00 PM - 5:00 PM
Title:	Chemical Tricks for Tackling Undruggable Targets
Speaker:	Kevan Shokat, PhD Professor and Chair Cellular and Molecular Pharmacology Howard Hughes Investigator University of California San Francisco
Host:	Thomas Kodadek
Location:	B158
	Thursday, November 3, 2016
Time:	4:00 PM - 5:00 PM
Title:	Regulators of brown and 'beige' adipose metabolism and energy expenditure: new twists on an old story''
Speaker:	Shiela Collins, Ph.D. Professor of Integrative Metabolism Program Sanford Burnham Prebys

	Medical Discovery Institute at Lake Nona (formerly Sanford-Burnham Medical Research Institute)
Host:	Anutosh Chakraborty
Location:	B158
	Thursday, December 1, 2016
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Gerald Joyce, MD, Ph.D. Professor Department of Chemistry The Scripps Research Institute La Jolla, California
Host:	Tom Kodadek
Location:	B158
	Tuesday, December 6, 2016
Time:	4:00 PM - 5:00 PM
Title:	Hot and spicy to cold and clammy: Thermal and chemical sensation in Drosophila
Speaker:	Paul Garrity, Ph.D. Professor of Biology Life Sciences at Bradeis University Waltham, Massachussetts
Host:	William Ja
Location:	B158
	Thursday, December 8, 2016
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Guoping Feng, PhD Investigator, McGovern Institute Professor, Department of Brain and Cognitive Sciences Massachusetts Institute of Technology
Host:	Baoji Xu
Location:	B158
	Thursday, December 15, 2016
Time:	4:00 PM - 5:00 PM
Title:	TBA

Speaker:	Ron Dror, Ph.D. Associate Professor Computer Science and Molecular and Cellular Physiology Stanford University
Host:	Laura Bohn
Location:	B158

Time:	**Thursday, January 5, 2017** 4:00 PM - 5:00 PM
Title:	Unbiased Combinatorial Approach for Targeting Non-Conventional Biomarkers in Cancer
Speaker:	Gomika Udugamasooriya, Ph.D. Associate Professor of Medicinal Chemistry Department of Pharmacological and Pharmaceutical Sciences College of Pharmacy University of Houston
Host:	Thomas Kodadek
Location:	B158
	Thursday, January 12, 2017
Time:	4:00 PM - 5:00 PM
Title:	Biology of Bedtime; Understanding Circadian Rhythms and Sleep
Speaker:	Amita Sehgal, PhD John Herr Musser Professor of Neuroscience Howard Hughes Medical Institute Perelman School of Medicine University of Pennsylvania
Host:	William Ja
Location:	B158
	Thursday, January 26, 2017
Time:	4:00 PM - 5:00 PM
Title:	Alterations in protein translation and neurological disease
Speaker:	Susan L. Ackerman, Ph.D. Howard Hughes Medical Institute Investigator The Jackson Laboratory
Host:	Katrin Karbstein
Location:	B158
	Monday, February 6, 2017
Time:	4:00 PM - 5:00 PM

Title:	A Semi-synthetic organism with an expanded genetic alphabet
Speaker:	Floyd E. Romesberg, Ph.D. Professor Department of Chemistry The Scripps Research Institute La Jolla, CA
Host:	Thomas Kodadek
Location:	B158
	Thursday, February 9, 2017
Time:	4:00 PM - 5:00 PM
Title:	Epigenetic Changes and Somatic Retrotransposition in Cellular Senescence and Aging
Speaker:	John M. Sedivy, Ph.D. Hermon C. Bumpus Chair in Biology Professor of Medical Science Department of Molecular Biology, Cell Biology and Biochemistry Brown University
Host:	Paul Robbins
Location:	B158
	Thursday, February 16, 2017
Time:	4:00 PM - 5:00 PM
Title:	Tumor Suppression by the Fbw7 Ubiquitin Ligase: Mechanisms and Opportunities
Speaker:	Bruce E. Clurman, MD, Ph.D. Associate Director Interdisciplinary and Translational Science Jose Carreras/E. Donnall Thomas Endowed Chair for Cancer Research Fred Hutchinson Cancer Research Center Seattle, Washington
Host:	Louis Scampavia & Tim Spicer
Location:	B158
	Thursday, February 23, 2017
Time:	3:00 PM - 3:50 PM
Title:	Designing ATR inhibitors for cancer: targeting a synthetic lethality in the DNA damage response
Speaker:	Novartis Chemical Science Lecture featuring: Dr. Robert Aversa Research Investigator, Global Discovery Chemistry, Novartis Institutes for BioMedical Research
Host:	Ben Shen
Sponsor:	Novartis

Location:	B158
	Thursday, February 23, 2017
Time:	4:00 PM - 5:00 PM
Title:	Cell-Penetrating Miniproteins
Speaker:	Gregory Verdine, PhD Erving Professor of Chemistry Department of Stem Cell and Regenerative Biology Harvard University and Harvard Medical School President and Chief Executive Officer Fogpharma and Lifetime Therapeutics
Host:	Ben Shen
Location:	B158
	Thursday, March 2, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Blake Wiedenheft, Ph.D. Assistant Professor Department of Microbiology and Immunology Montana State University
Host:	Katrin Karbstein
Location:	B158
	Thursday, March 9, 2017
Time:	4:00 PM - 5:00 PM
Title:	Structure-based prediction of protein-protein and protein-ligand interactions on a genome-wide scale
Speaker:	Barry Honig, PhD Professor of Biochemistry and Molecular BioPhysics, Systems Biology and Medicine Director of the Center for Computational Biology and BioInformatics Columbia University Medical Center Investigator, Howard Hughes Medical Institute
Host:	Tina Izard
Location:	TBD
	Thursday, March 16, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA

Speaker:	Liqun Luo, Ph.D. Howard Hughes Medical Institute Investigator Professor of Biology, Stanford University Professor of Neurobiology, Stanford University School of Medicine
Host:	Brock Grill
Location:	B158
	Thursday, March 30, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Casey T. Weaver, M.D. Professor Departments of Pathology, Medicine, and Microbiology University of Alabama at Birmingham
Host:	Matthew Pipkin
Location:	B158
	Thursday, April 6, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Stephen D. Nimer, Director Sylvester Comprehensive Cancer Center University of Miami Miller School of Medicine Miami, Florida
Host:	Christoph Rader
Location:	B158
	Thursday, April 13, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Drew Weissman, MD, PhD Professor of Medicine Department of Medicine, Immunology, and Cell and Molecular Biology University of Pennsylvania
Host:	Michael Farzan
Location:	B158
	Thursday, April 20, 2017
Time:	4:00 PM - 5:00 PM

Title:	TBA
Speaker:	Paul L. Modrich, Ph.D. James B. Duke Professor of Biochemistry Duke University HHMI Investigator Nobel Laureate, Nobel Prize in Chemistry, 2015
Host:	Derek Duckett
Location:	B158
	Thursday, April 27, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Gary L. Johnson, Ph.D. Kenan Distinguished Professor and Chair Department of Pharmacology University of Colorado Medical School
Host:	Joseph Kissill and Kirill Martemyanov
Location:	B158
	Thursday, May 4, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Michael Greenberg, Ph.D. Nathan Marsh Pusey Professor of Neurobiology Department of Neurobiology Harvard Medical School
Host:	Ron Davis
Location:	B158
	Thursday, May 11, 2017
Time:	4:00 PM - 5:00 PM
Title:	TBA
Speaker:	Julian Davies, Ph.D. Professor Emeritus Microbiology & Immunology Faculty of Science The University of British Columbia, Vancouver Campus
Host:	Ben Shen
Location:	B158

Subsection (10) (l) **Beginning June 2004, the grantee shall commence collaboration efforts with the Office of Tourism, Trade, and Economic Development (OTTED) by complying with reasonable requests for cooperation in economic development efforts in the biomed/biotech industry. No later than July 2004, the grantee shall designate a person who shall be charged with assisting in these collaborative efforts.**

Scripps Florida has designated Dr. Peter Policastro as its designee to assist the Department of Economic Opportunity ("DEO"), nee OTTED, regarding collaborative economic development efforts between Scripps and DEO.

Business outreach efforts include participation in meetings with local businesses, government agencies such as the Palm Beach County Business Development Board and the Technology Entrepreneurship & Capital Committee meeting in the Palm Beach County area, the region and the State of Florida.

Audited Financial Statements and Supplementary Information for the Scripps Florida Funding Corporation is presented on the next pages, as indicated in Subsection (14)(g).

Audited Financial Statements
and Supplementary Information

Scripps Florida Funding Corporation

A Component Unit of the
State of Florida

September 30, 2017

CALER, DONTEN, LEVINE,
COHEN, PORTER & VEIL, P.A.

CERTIFIED PUBLIC ACCOUNTANTS

SCRIPPS FLORIDA FUNDING CORPORATION –
A COMPONENT UNIT OF THE STATE OF FLORIDA

AUDITED FINANCIAL STATEMENTS
AND SUPPLEMENTARY INFORMATION

September 30, 2017

CALER, DONTEN, LEVINE,
COHEN, PORTER & VEIL, P.A.

CERTIFIED PUBLIC ACCOUNTANTS

WILLIAM K CALER, JR , CPA
LOUIS M COHEN, CPA
JOHN C COURTNEY, CPA, JD
DAVID S DONTEN, CPA
JAMES B HUTCHISON, CPA
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MEMBERS
AMERICAN INSTITUTE OF
CERTIFIED PUBLIC ACCOUNTANTS

FLORIDA INSTITUTE OF
CERTIFIED PUBLIC ACCOUNTANTS

Independent Auditor's Report

To the Board of Directors
Scripps Florida Funding Corporation
Jupiter, Florida

Report on the Financial Statements

We have audited the accompanying financial statements of the governmental activities and major fund of Scripps Florida Funding Corporation, a component unit of the State of Florida, as of and for the year ended September 30, 2017, and the related notes to the financial statements, which collectively comprise the basic financial statements of Scripps Florida Funding Corporation as listed in the table of contents.

Management's Responsibility for the Financial Statements

Management is responsible for the preparation and fair presentation of these financial statements in accordance with U.S. generally accepted accounting principles; this includes the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of financial statements that are free from material misstatement, whether due to fraud or error.

Auditor's Responsibility

Our responsibility is to express opinions on these financial statements based on our audit. We conducted our audit in accordance with U.S. generally accepted auditing standards and the standards applicable to financial audits contained in *Government Auditing Standards*, issued by the Comptroller General of the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the entity's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. Accordingly, we express no such opinion. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinions.

Opinions

In our opinion, the financial statements referred to above present fairly, in all material respects, the respective financial position of the governmental activities and major fund of Scripps Florida Funding Corporation, as of September 30, 2017, and the respective changes in financial position for the year then ended in accordance with U.S. generally accepted accounting principles.

Other Matters

Required Supplementary Information

U.S. generally accepted accounting principles require that *management's discussion and analysis* on pages 3 through 7 and the budgetary comparison information on pages 15 and 16 be presented to supplement the basic financial statements. Such information, although not a part of the basic financial statements, is required by the Governmental Accounting Standards Board, who considers it to be an essential part of financial reporting for placing the basic financial statements in an appropriate operational, economic, or historical context. We have applied certain limited procedures to the required supplementary information in accordance with U.S. generally accepted auditing standards, which consisted of inquiries of management about the methods of preparing the information and comparing the information for consistency with management's responses to our inquiries, the basic financial statements, and other knowledge we obtained during our audit of the basic financial statements. We do not express an opinion or provide any assurance on the information because the limited procedures do not provide us with sufficient evidence to express an opinion or provide any assurance.

Other Reporting Required by *Government Auditing Standards*

In accordance with *Government Auditing Standards*, we have also issued our report dated November 30, 2017, on our consideration of Scripps Florida Funding Corporation's internal control over financial reporting and on our tests of its compliance with certain provisions of laws, regulations, contracts, and grant agreements and other matters. The purpose of that report is to describe the scope of our testing of internal control over financial reporting and compliance and the results of that testing, and not to provide an opinion on internal control over financial reporting or on compliance. That report is an integral part of an audit performed in accordance with *Government Auditing Standards* in considering Scripps Florida Funding Corporation's internal control over financial reporting and compliance.

Caler, Donten, Levine,
Cohen, Porter & Veil, P.A.

West Palm Beach, Florida
November 30, 2017

Management's Discussion and Analysis

Acting in our capacity as the management of Scripps Florida Funding Corporation ("SFFC"), we offer readers of SFFC's financial statements this narrative overview and analysis of the financial activities of SFFC as of and for the year ended September 30, 2017. SFFC is governed by a nine member Board of Directors, three of whom are appointed by the Governor of the State of Florida, three of whom are appointed by the President of the Senate of the State of Florida, and three of whom are appointed by the Speaker of the House of Representatives of the State of Florida. Currently, there are three unfilled Board vacancies. For financial reporting purposes, management determined that SFFC should be reported as a governmental organization and a component unit of the State of Florida based on the appointment of the Board of Directors by officials of State government.

SFFC is a Florida not-for-profit public benefit corporation created by Florida Statutes, Section 288.955, and was incorporated on December 8, 2003, for the primary purpose of overseeing the establishment and operation of a state-of-the-art biomedical research institution and campus in Palm Beach County, Florida, by The Scripps Research Institute ("TSRI"). The development of the Scripps Florida project was financed by a Federal economic development grant of $310 million to the State of Florida that was passed through to SFFC to administer. SFFC was required to distribute to TSRI the $310 million grant proceeds, plus the net investment income thereon and less an annual administrative appropriation to SFFC over a ten year period ending with a final grant distribution to TSRI on December 15, 2013. Thereafter, SFFC is required to oversee the Scripps Florida project and the State's investment of public funds through the year 2024.

As part of the annual audited financial statements of SFFC, the Governmental Accounting Standards Board requires the presentation of certain comparative information for the current and prior year in this Management's Discussion and Analysis.

Financial Highlights

- The assets of SFFC exceeded its liabilities at September 30, 2017 by $149,453 (*net position)*, all of which will be utilized in future years for SFFC's oversight of the Scripps Florida project.

- SFFC's total assets were $184,286 at September 30, 2017, consisting primarily of cash attributable to the unexpended portion of the prior years' administrative appropriations for the operations of SFFC. The annual administrative appropriation ended with a final payment on December 15, 2013.

- As of September 30, 2017, the General Fund of SFFC reported ending fund balance of $149,453. Of this total amount, $8,538 is nonspendable for prepaid items and $140,915 is unrestricted and available to fund the future operations of SFFC.

Overview of the Financial Statements

This discussion and analysis is intended to serve as an introduction to SFFC's basic financial statements. The basic financial statements of SFFC include three components: (1) government-wide financial statements, (2) fund financial statements, and (3) notes to the financial statements. This report also contains other supplementary information in addition to the basic financial statements themselves.

Government-wide financial statements. The *government-wide financial statements* are designed to provide readers with a broad overview of SFFC's finances, in a manner similar to a private-sector business.

The *statement of net position* presents information on SFFC's assets and liabilities, with the difference between the two reported as *net position.* Over time, increases or decreases in net position may serve as a useful indicator of whether the financial position of SFFC is improving or deteriorating.

The *statement of activities* presents information showing how SFFC's net position changed during the most recent fiscal year. All changes in net position are reported as soon as the underlying event giving rise to the change occurs, *regardless of the timing of related cash flow.* Thus, some revenues and expenses may be reported in this statement for items that will only result in cash flows in future fiscal periods.

The government-wide financial statements present functions of SFFC that are principally supported by the unexpended portion of the prior years' administrative appropriations from the State for the operations of SFFC (*governmental activities*). The annual administrative appropriation ended with a final payment on December 15, 2013. The governmental activities of SFFC include all General Fund functions.

SFFC has no business-type activities that are intended to recover all or a significant portion of their costs through user fees and charges.

The government-wide financial statements can be found on pages 8 and 9 of this report.

Fund financial statements. A *fund* is a grouping of related accounts that is used to maintain control over resources that have been segregated for specific activities or objectives. SFFC, like other state and local governments, uses fund accounting to ensure and demonstrate compliance with finance-related legal requirements. SFFC utilizes only one fund, the *General Fund*, which is classified as a *governmental* fund and accounts for all financial resources of SFFC.

Governmental funds. Governmental funds are used to account for essentially the same functions reported as *governmental activities* in the government-wide financial statements. However, unlike the government-wide financial statements, the governmental fund financial statements focus on *near-term inflows and outflows of spendable resources*, as well as on *balances of spendable resources* available at the end of the fiscal year. Such information may be useful in evaluating a government's near-term financing requirements.

Because the focus of governmental funds is narrower than that of the government-wide financial statements, it may be useful to compare the information presented for *governmental funds* with similar information presented for *governmental activities* in the government-wide financial statements. By doing so, readers may better understand the long-term impact of SFFC's near-term financing decisions. Both the governmental fund balance sheet and the governmental fund statement of revenues, expenditures, and changes in fund balance provide a reconciliation to facilitate this comparison between the *governmental fund* and *governmental activities*. Since SFFC had no long-term assets or liabilities, there were no differences between the revenues and expenditures/expenses of the *governmental fund* and *governmental activities*.

The basic governmental fund financial statements can be found on pages 8 and 9 of this report. Explanations of the reconciling items between the governmental fund and the governmental activities can be found in Note D on page 14. SFFC adopts an annual appropriated budget for its General Fund. A budgetary comparison schedule has been provided on page 15 for the General Fund.

Notes to the financial statements. The notes provide additional information that is essential to a full understanding of the data provided in the government-wide and fund financial statements. The notes to the financial statements can be found on pages 10-14 of this report.

Other information. In addition to the basic financial statements and accompanying notes, this report also presents certain *required supplementary information* concerning SFFC's budget to actual results for the General Fund for the current fiscal year. The required supplementary information can be found on pages 15 and 16 of this report.

Government-wide Financial Analysis

As noted earlier, net position may serve over time as a useful indicator of a government's financial position. The assets, liabilities and net position of SFFC at September 30, 2017 and 2016 are summarized as follows:

Net Position

	2017	2016
Assets		
Cash and other current asset	$ 184,286	$ 243,629
Liability		
Current liability	$ 34,833	$ 2,835
Net position		
Unrestricted	$ 149,453	$ 240,794

SFFC's unrestricted net position of $149,453 represents the funds available for the future operations of SFFC that will be expensed in subsequent fiscal years. At the end of the current fiscal year, SFFC reported a positive balance of $149,453 in net position that will decrease over time as funds are expensed for future administrative operations of SFFC.

Governmental activities. Governmental activities decreased SFFC's net position by $91,341 in 2017 and by $83,364 in 2016. Key elements of this change are as follows.

Changes in Net Position

	2017	2016
Revenues	$ -	$ -
Expenses		
General government	91,341	83,364
Change in net position	(91,341)	(83,364)
Net position – beginning of year	240,794	324,158
Net position – end of year	$ 149,453	$ 240,794

The final grant payment was made by SFFC on December 15, 2013 and the expenses for 2017 and 2016 consisted solely of administrative expenses related to the oversight operations of SFFC. Those general government expenses consisted primarily of professional fees associated with the monitoring responsibilities of SFFC and administrative expenses, such as insurance.

Financial Analysis of the Government's Funds

As noted earlier, SFFC uses fund accounting to ensure and demonstrate compliance with finance-related legal requirements.

Governmental funds. The focus of the *governmental funds* is to provide information on near-term inflows, outflows and balances of *spendable* resources. Such information is useful in assessing SFFC's financing requirements. In particular, *unassigned fund balance* may serve as a useful measure of a government's net resources available for spending at the end of the fiscal year. As noted previously, SFFC has only one governmental fund, the General Fund.

As of the end of the current period, SFFC's governmental fund reported ending fund balance of $149,453. Substantially all of the ending fund balance ($140,915) constitutes *unassigned fund balance*, which is available to finance future spending by SFFC for activities related to its ongoing statutory oversight responsibility for the Scripps Florida project through the year 2024. The remaining fund balance of $8,538 relates to prepaid items and is considered *nonspendable* because it is not in spendable form.

Key factors to consider in analyzing the fund balance for the General Fund are as follows:

- SFFC is limited by Florida statutes to expenditures of $200,000 annually for administrative expenses.
- The final appropriation of $200,000 to finance the administrative expenses of SFFC was received on December 15, 2013.
- The unexpended portion of each annual administrative budget allocation was carried over from prior years and will be used to fund the future oversight functions of SFFC.

General Fund Budgetary Highlights

There were no differences between the original budget and the final amended budget for the year ended September 30, 2017.

During the year, revenues consisted solely of an allocation of $86,615 from accumulated fund balance. Expenditures were less than budgetary estimates by approximately $27,000, which was attributable primarily to lower professional fees incurred for the grant monitoring activities of SFFC.

Capital Asset and Debt Administration

Capital assets. SFFC has not purchased any capital assets.

Long-term debt. SFFC is not permitted to incur long-term debt.

Economic Factors and Next Year's Budget

SFFC's budget for the 2017-2018 fiscal year is based on the following considerations:

- The contract between SFFC and TSRI does not expire until the year 2024. During this remaining time period, SFFC has a contractual obligation to exercise continued oversight of the State's investment of public funds in the Scripps Florida project. The operations of SFFC for the fiscal year ending September 30, 2018 and for future years will include administrative expenses related to this ongoing oversight responsibility.

- There are presently no arrangements to provide further funds for SFFC to carry out its contractual oversight obligations of the Scripps Florida project through the year 2024. Accordingly, SFFC will continue to operate utilizing its remaining cash balances, until those amounts are depleted (currently estimated to be depleted in fiscal year 2019). Thereafter, management expects that SFFC will cease operations and dissolve the corporation, and all contractual responsibilities of SFFC for the Scripps Florida project will revert to the State of Florida.

Requests for Information

This financial report is designed to provide a general overview of SFFC's finances for all those with an interest in the organization's finances. Questions concerning any of the information provided in this report or requests for additional financial information should be addressed to the Scripps Project Director at 130 Scripps Way, #B41, Jupiter, Florida, 33458.

SCRIPPS FLORIDA FUNDING CORPORATION

GOVERNMENTAL FUND BALANCE SHEET/STATEMENT OF NET POSITION

September 30, 2017

	Governmental Fund		Statement of Net Position
	General Fund	Adjustments (Note D)	Governmental Activities
ASSETS			
Cash	$ 175,748	$ -	$ 175,748
Prepaid items	8,538	-	8,538
TOTAL ASSETS	$ 184,286	-	184,286
LIABILITY			
Accounts payable	$ 34,833	-	34,833
TOTAL LIABILITY	34,833	-	34,833
FUND BALANCE/NET POSITION			
Fund balance			
Nonspendable - prepaid items	8,538	(8,538)	-
Unassigned	140,915	(140,915)	-
TOTAL FUND BALANCE	149,453	(149,453)	-
TOTAL LIABILITY AND FUND BALANCE	$ 184,286		
Net Position			
Unrestricted		149,453	149,453
TOTAL NET POSITION		$ -	$ 149,453

See notes to financial statements.

SCRIPPS FLORIDA FUNDING CORPORATION

STATEMENT OF GOVERNMENTAL FUND REVENUES, EXPENDITURES,
AND CHANGES IN FUND BALANCE/STATEMENT OF ACTIVITIES

Year Ended September 30, 2017

	Governmental Fund		Statement of Activities
	General Fund	Adjustments (Note D)	Governmental Activities
Revenues	$ -	$ -	$ -
Expenditures/Expenses			
Current			
General government	91,341	-	91,341
	91,341	-	91,341
Expenditures over revenues/ Change in net position	(91,341)	-	(91,341)
Fund balance/Net position at October 1, 2016	240,794	-	240,794
Fund balance/Net position at September 30, 2017	$ 149,453	$ -	$ 149,453

See notes to financial statements.

SCRIPPS FLORIDA FUNDING CORPORATION

NOTES TO FINANCIAL STATEMENTS

September 30, 2017

NOTE A - SIGNIFICANT ACCOUNTING POLICIES

Scripps Florida Funding Corporation ("SFFC") is a Florida not-for-profit, public benefit corporation created by Florida Statutes, Section 288.955, and was incorporated on December 8, 2003, for the purpose of enhancing education and research and promoting, developing, and advancing the business prosperity and economic welfare of the State of Florida and its residents by facilitating and overseeing the establishment and operation of a state-of-the-art biomedical research institution and campus in the State by The Scripps Research Institute ("TSRI"). SFFC is exempt from income taxes under Section 501(c)(3) of the Internal Revenue Code.

SFFC is governed by a nine member Board of Directors, three of whom are appointed by the Governor of the State of Florida, three of whom are appointed by the President of the Senate of the State of Florida, and three of whom are appointed by the Speaker of the House of Representatives of the State of Florida. There were three unfilled Board vacancies at September 30, 2017.

Financial Reporting Entity: For financial reporting purposes, management determined that SFFC should be reported as a governmental organization and a component unit of the State of Florida based on the appointment of the Board of Directors by officials of State government. In considering potential component units to include in the SFFC financial reporting entity, management applied the criteria set forth in U.S. generally accepted accounting principles (GAAP). As defined by GAAP, the financial reporting entity consists of (a) the primary government, (b) organizations for which the primary government is financially accountable, and (c) other organizations for which the primary government is not accountable, but for which the nature and significance of their relationship with the primary government are such that exclusion would cause the financial reporting entity's financial statements to be misleading or incomplete. Component units are legally separate organizations for which the elected officials of the primary government are financially accountable. In addition, component units can be other organizations for which the nature and significance of their relationship with the primary government are such that exclusion would cause the financial reporting entity's financial statements to be misleading or incomplete. Based upon the application of these criteria, SFFC found that there were no entities to consider as potential component units.

Government-wide/Governmental Fund Financial Statements: SFFC is a special-purpose government engaged in one primary governmental activity, to facilitate and oversee the establishment and operation of a state-of-the-art biomedical research institution and campus in the State by The Scripps Research Institute. SFFC accounts for all financial resources in one fund, the General Fund, which includes all *governmental activities* of SFFC, which are supported primarily by accumulated net position/fund balance from prior years' administrative appropriations received from the State of Florida. Accordingly, the Government-wide and Governmental Fund financial statements of SFFC are combined using a columnar format that reconciles individual line items of General Fund financial data to Government-wide data in separate columns on the face of the financial statements. The Governmental Fund financial statements include a Balance Sheet and a Statement of Revenues, Expenditures and Changes in Fund Balance for the General Fund. The Government-wide financial statements consist of the Statement of Net Position and the Statement of Activities. Note D explains the reconciling items presented in the adjustments column of the combined Government-wide and Governmental Fund financial statements.

Measurement Focus and Basis of Accounting: Financial reporting is based upon pronouncements of the Governmental Accounting Standards Board (GASB).

NOTE A - SIGNIFICANT ACCOUNTING POLICIES (Continued)

The government-wide financial statements are reported using the *economic resources measurement* focus and the *accrual basis of accounting*. Revenue is recognized when earned and expenses are recognized when incurred, regardless of the timing of related cash flows. SFFC does not allocate indirect expenses.

Governmental fund financial statements are reported using the *current financial resources measurement* focus and the *modified accrual basis of accounting*. Under the modified accrual basis of accounting, revenues are recognized in the period in which they become both measurable and available. Revenues are considered to be available when collectible within the current period or soon enough thereafter to pay liabilities of the current period. SFFC considers revenues to be available if collected within 90 days of the end of the fiscal year to which they apply. Revenue items are considered to be measurable and available only when received in cash by SFFC. Expenditures are generally recognized in the accounting period in which the fund liability is incurred.

Cash: Cash consists of amounts on deposit in a non-interest bearing checking account with a financial institution.

Prepaid Items: Certain payments to vendors reflect costs applicable to future accounting periods and are recorded as prepaid items.

Fund Balance/ Net Position:

Fund Balance

In the fund financial statements, governmental funds report fund balance classifications that comprise a hierarchy based primarily on the extent to which SFFC is legally bound to honor the specific purposes for which amounts in fund balance may be spent. The fund balance classifications are summarized as follows:

Nonspendable - Nonspendable fund balance includes amounts that cannot be spent because they are either 1) not in spendable form; or, 2) legally or contractually required to be maintained intact.

Restricted - Restricted fund balance includes amounts that are restricted to specific purposes either by 1) constraints placed on the use of resources by creditors, grantors, contributors, or laws or regulations of other governments; or, 2) imposed by law through constitutional provisions or enabling legislation. SFFC has no restricted fund balance.

Committed - Committed fund balance includes amounts that can only be used for specific purposes pursuant to constraints imposed by SFFC's Board through a resolution. SFFC has no committed fund balance.

Assigned - Assigned fund balance includes amounts that are constrained by SFFC's intent to be used for specific purposes but are neither restricted nor committed. Assignments of fund balance are made by SFFC management based upon direction by SFFC's Board. SFFC has no assigned fund balance.

NOTE A - SIGNIFICANT ACCOUNTING POLICIES (Continued)

Unassigned - Unassigned fund balance includes amounts that have not been restricted, committed, or assigned to specific purposes within the General Fund.

SFFC considers restricted fund balance to be spent when an expenditure is incurred for the restricted purpose. SFFC considers committed, assigned or unassigned fund balance to be spent when an expenditure is incurred for purposes for which amounts in any of those fund balance classifications could be used.

The SFFC Board has not adopted a formal minimum fund balance policy because the mission of SFFC is to expend all remaining fund balance for monitoring the economic development grant to TSRI, pursuant to the terms of the Operating and Funding Agreement between SFFC and TSRI.

Net Position

The government-wide financial statements utilize a net position presentation, which is categorized as follows:

Restricted - This component of net position consists of constraints placed on the use of net position by external restrictions imposed by vendors, contributors, or laws or regulations of other governments or constraints imposed by law, constitutional provisions or enabling legislation. Restricted resources are used first to fund expenses incurred for restricted purposes. SFFC has no restricted net position.

Unrestricted - This component of net position consists of amounts that do not meet the definition of *Restricted*.

Economic Development Grant: SFFC entered into an Operating and Funding Agreement (the "Agreement") with TSRI dated January 30, 2004. Pursuant to the terms of the Agreement, SFFC provided an economic development grant to TSRI in the amount of $310 million plus the net investment income thereon and less an annual administrative appropriation to SFFC. Subject to compliance by TSRI with the terms of the Agreement and annual approval of a grant request by SFFC, the economic development grant was payable to TSRI in quarterly installments on March 15th, June 15th, September 15th and December 15th of each year through the final payment date of December 15, 2013. At September 30, 2017, all grant payments were disbursed and TSRI was in compliance with the Agreement.

Property Taxes: SFFC receives no property taxes.

Risk Management: SFFC is exposed to various risks of loss related to torts; theft of, damage to, and destruction of assets; errors and omissions; injuries to others; and natural disasters. SFFC purchases commercial insurance for the risks of losses to which it is exposed. Policy limits and deductibles are reviewed annually by management and established at amounts to provide reasonable protection from significant financial loss. Settlements have not exceeded insurance coverage since inception.

Income Taxes: SFFC is exempt from income taxes as a public charity under the provisions of Internal Revenue Code Section 501(c)(3), except for any net income derived from unrelated business activities. Management does not believe that SFFC has any unrelated business activities that could result in a tax

NOTE A - SIGNIFICANT ACCOUNTING POLICIES (Continued)

liability or any uncertain tax positions that would be material to the financial statements. SFFC's tax returns for tax years prior to 2013 are no longer subject to examination by taxing authorities.

New Accounting Pronouncements: SFFC has implemented all applicable GASB Statements effective through the fiscal year ended September 30, 2017. GASB has also issued Statements Nos. 75, 81, and 83 through 87, which will be effective in future years, although management does not believe that any of these GASB Statements will be applicable to SFFC.

Estimates: Management uses estimates and assumptions in preparing financial statements in accordance with U.S. generally accepted accounting principles. Those estimates and assumptions affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities, and the reported revenues and expenditures. Actual results could vary from the estimates that were used.

NOTE B - CASH

At September 30, 2017, SFFC had deposits with financial institutions with a carrying value and bank balance of approximately $176,000. The deposits with financial institutions were entirely covered by federal depository insurance and a collateral pool pledged to the State Treasurer of Florida by financial institutions that comply with the requirements of Florida Statutes and have been designated as a qualified public depository by the State Treasurer. Qualified public depositories are required to pledge collateral to the State Treasurer with a fair value equal to a percentage of the average daily balance of all government deposits in excess of any federal deposit insurance. In the event of a default by a qualified public depository, the amount of public funds would be covered by the proceeds of federal deposit insurance, pledged collateral of the public depository in default and, if necessary, a pro rata assessment to the other qualified public depositories in the collateral pool. Accordingly, all SFFC deposits with financial institutions are considered fully insured or collateralized in accordance with the provisions of GASB Statement No. 3, as amended.

NOTE C - COMMITMENT AND CONTINGENCY

Contract Commitment: Pursuant to the terms of the Operating and Funding Agreement, SFFC provided an economic development grant to TSRI of $310 million plus the investment income thereon and less an annual allocation to SFFC for administrative expenses of $200,000 through the contract year ended January 30, 2014, the tenth and final year of the economic development grant. The grant funds were paid to TSRI in quarterly installments over the ten year period to establish and operate a state-of-the-art biomedical research institution and campus in Florida, known as Scripps Florida. The final grant payment to TSRI was paid on December 15, 2013 and included all remaining grant funds and investment earnings thereon, less a final allocation of $200,000 to SFFC for its fiscal year administrative expense budget.

Although the final payment from SFFC to TSRI for the Scripps Florida economic development grant was made on December 15, 2013, the contract between SFFC and TSRI does not expire until the year 2024. During this remaining period, SFFC has a contractual obligation to exercise continued oversight of the

NOTE C - COMMITMENT AND CONTINGENCY (Continued)

Scripps Florida project and the State's investment of public funds. Following the final grant disbursement to TSRI and related budget allocation to SFFC on December 15, 2013, there is no further funding to SFFC to carry out its contractual obligations through the year 2024. Accordingly, SFFC presently intends to continue operations until its remaining cash balances are depleted (currently estimated to be depleted in fiscal year 2019). Thereafter, management expects that SFFC will cease operations, the corporation will be dissolved and all contractual responsibilities of SFFC for the Scripps Florida project will revert to the State of Florida.

Grants: Amounts received from grantor agencies are subject to audit and adjustment by those agencies. Any disallowed claims, including amounts already received, might constitute a liability of SFFC for the return of those funds.

NOTE D - EXPLANATION OF ADJUSTMENTS BETWEEN GOVERNMENTAL FUND AND GOVERNMENT-WIDE FINANCIAL STATEMENT AMOUNTS

The only adjustment between the Governmental Fund financial statements and the Government-wide financial statements is the reclassification of the *Fund Balance* reported for SFFC's General Fund into the *Net Position* category reported for Governmental Activities in the Statement of Net Position. There were no differences between the Governmental Fund Statement of Revenues, Expenditures and Changes in Fund Balance and the Statement of Activities.

REQUIRED SUPPLEMENTARY INFORMATION

SCRIPPS FLORIDA FUNDING CORPORATION

BUDGETARY COMPARISON SCHEDULE -
GENERAL FUND - NON-GAAP BUDGETARY BASIS

Year Ended September 30, 2017

	Budgeted Amounts		Actual	Variance with Final Budget Positive
	Original	Final	Amounts	(Negative)
Revenues				
Fund balance allocation for administrative expenses	$ 86,615	$ 86,615	$ 86,615	$ -
TOTAL REVENUES	86,615	86,615	86,615	-
General Government				
Bank charges	-	-	129	(129)
Insurance	25,000	25,000	26,789	(1,789)
Licenses and fees	65	65	60	5
Miscelaneous expenses	300	300	-	300
Office supplies	150	150	-	150
Postage	150	150	60	90
Professional fees				
Legal	25,000	25,000	6,730	18,270
Accounting and auditing	15,000	15,000	17,490	(2,490)
Consulting	15,000	15,000	7,238	7,762
Research	2,000	2,000	-	2,000
Public meeting notices	150	150	38	112
Telephone	800	800	886	(86)
Travel				
Board members	3,000	3,000	-	3,000
TOTAL EXPENDITURES	86,615	86,615	59,420	27,195
REVENUES OVER EXPENDITURES - BUDGETARY BASIS	$ -	$ -	$ 27,195	$ 27,195

See notes to budgetary comparison schedule.

SCRIPPS FLORIDA FUNDING CORPORATION

NOTES TO BUDGETARY COMPARISON SCHEDULE

September 30, 2017

NOTE A - BUDGETARY ACCOUNTING

An appropriated budget is legally required and has been legally adopted for each contract year ending December 15th for the General Fund on the cash basis of accounting. For budgetary purposes, the Board of Directors must approve all changes or amendments to the total budgeted expenditures of Scripps Florida Funding Corporation (SFFC). Total expenditures may not legally exceed total budgeted appropriations at the fund level. SFFC did not make any supplemental budget appropriations for the contract year ending December 15, 2017. Appropriations lapse at the end of each contract year.

Expenditures for general government purposes are legally limited by Florida Statutes to $300,000 for the first contract year of operations (2004) and $200,000 for each contract year thereafter. Because SFFC is legally required to adopt its budget for the contract year ended December 15th, the General Fund budgetary comparison schedule is not intended to and does not present budgetary compliance on a contract year basis. For purposes of the contract year budget and legal limitation, the budgetary basis expenditures for general government purposes were $59,420 through September 30, 2017, and were within the $200,000 statutory limitation for the contract period ending December 15, 2017. Expenditures for the contract year ended December 15, 2016 were within the statutory limitation of $200,000.

NOTE B - BUDGET TO ACTUAL COMPARISONS

The General Fund budgetary comparison schedule presents actual expenditure amounts for the fiscal year ended September 30, 2017 and budgeted amounts based on an allocation of the budget for the contract years ended December 15, 2016 and 2017. The budget amounts presented in the accompanying budgetary comparison schedule reflect the original budget and the amended budget based on legally authorized revisions to the original budget during the year, if any.

U.S. generally accepted accounting principles (GAAP) require that the General Fund budgetary comparison schedule be prepared under the cash basis of accounting used in preparing the budget. As a result, General Fund revenues and expenditures reported in the budgetary comparison schedule differ from the revenues and expenditures reported on the GAAP basis. The difference can be reconciled as follows:

	Revenues	Expenditures
Budgetary basis	$ 86,615	$ 59,420
GAAP basis adjustments:		
Fund balance allocation to revenues	(86,615)	-
Modified accrual basis adjustments	-	31,921
GAAP Basis	$ -	$ 91,341

COMPLIANCE REPORT AND MANAGEMENT LETTER

CALER, DONTEN, LEVINE,
COHEN, PORTER & VEIL, P.A.

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Independent Auditor's Report on Internal Control Over Financial Reporting and on Compliance and Other Matters Based on an Audit of Financial Statements Performed in Accordance With *Government Auditing Standards*

To the Board of Directors
Scripps Florida Funding Corporation
Jupiter, Florida

We have audited, in accordance with U.S. generally accepted auditing standards and the standards applicable to financial audits contained in *Government Auditing Standards* issued by the Comptroller General of the United States, the financial statements of the governmental activities and major fund of Scripps Florida Funding Corporation, a component unit of the State of Florida, as of and for the year ended September 30, 2017, and the related notes to the financial statements, which collectively comprise Scripps Florida Funding Corporation's basic financial statements, and have issued our report thereon dated November 30, 2017.

Internal Control over Financial Reporting

In planning and performing our audit of the financial statements, we considered Scripps Florida Funding Corporation's internal control over financial reporting (internal control) to determine the audit procedures that are appropriate in the circumstances for the purpose of expressing our opinions on the financial statements, but not for the purpose of expressing an opinion on the effectiveness of Scripps Florida Funding Corporation's internal control. Accordingly, we do not express an opinion on the effectiveness of Scripps Florida Funding Corporation's internal control.

A *deficiency in internal control* exists when the design or operation of a control does not allow management or employees, in the normal course of performing their assigned functions, to prevent, or detect and correct, misstatements on a timely basis. A *material weakness* is a deficiency, or combination of deficiencies, in internal control, such that there is a reasonable possibility that a material misstatement of the entity's financial statements will not be prevented, or detected and corrected on a timely basis. A *significant deficiency* is a deficiency, or a combination of deficiencies, in internal control that is less severe than a material weakness, yet important enough to merit attention by those charged with governance.

Our consideration of internal control was for the limited purpose described in the first paragraph of this section and was not designed to identify all deficiencies in internal control that might be material weaknesses or, significant deficiencies. Given these limitations, during our audit we did not identify any deficiencies in internal control that we consider to be material weaknesses. However, material weaknesses may exist that have not been identified.

Compliance and Other Matters

As part of obtaining reasonable assurance about whether Scripps Florida Funding Corporation's financial statements are free from material misstatement, we performed tests of its compliance with certain provisions of laws, regulations, contracts, and grant agreements, noncompliance with which could have a direct and material effect on the determination of financial statement amounts. However, providing an opinion on compliance with those provisions was not an objective of our audit, and accordingly, we do not express such an opinion. The results of our tests disclosed no instances of noncompliance or other matters that are required to be reported under *Government Auditing Standards*.

Purpose of this Report

The purpose of this report is solely to describe the scope of our testing of internal control and compliance and the results of that testing, and not to provide an opinion on the effectiveness of the entity's internal control or on compliance. This report is an integral part of an audit performed in accordance with *Government Auditing Standards* in considering the entity's internal control and compliance. Accordingly, this communication is not suitable for any other purpose.

Caler, Donten, Levine,
Cohen, Porter & Veil, P.A.

West Palm Beach, Florida
November 30, 2017

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Management Letter

To the Board of Directors
Scripps Florida Funding Corporation
Jupiter, Florida

Report on the Financial Statements

We have audited the financial statements of Scripps Florida Funding Corporation, a component unit of the State of Florida, as of and for the fiscal year ended September 30, 2017, and have issued our report thereon dated November 30, 2017.

Auditor's Responsibility

We conducted our audit in accordance with U.S. generally accepted auditing standards; the standards applicable to financial audits contained in *Government Auditing Standards*, issued by the Comptroller General of the United States; and Chapter 10.700, Rules of the Auditor General.

Other Report

We have issued our Independent Auditor's Report on Internal Control Over Financial Reporting and on Compliance and Other Matters Based on an Audit of Financial Statements Performed in Accordance with *Government Auditing Standards.* Disclosures in that report, which is dated November 30, 2017, should be considered in conjunction with this management letter.

Prior Audit Findings

Chapter 10.700, Rules of the Auditor General, requires that we determine whether or not corrective actions have been taken to address findings and recommendations made in the preceding annual financial audit report. There were no prior year findings and recommendations.

Other Matters

Chapter 10.700, Rules of the Auditor General, requires disclosure in the management letter of noncompliance with provisions of contracts or grant agreements, or abuse, that have occurred, or are likely to have occurred, that have an effect on financial statement amounts that is less than material but which warrants the attention of those charged with governance. In connection with our audit for the year ended September 30, 2017, we did not have any such findings or other recommendations to improve financial management.

Purpose of this Letter

Our management letter is intended solely for the information and use of the Legislative Auditing Committee, members of the Florida Senate and the Florida House of Representatives, the Florida Auditor General and the Board of Directors, management and others within Scripps Florida Funding Corporation, and is not intended to be and should not be used by anyone other than these specified parties.

Caler, Donten, Levine,
Cohen, Porter & Veil, P.A.

West Palm Beach, Florida
November 30, 2017