SCRIPPS DISCOVERS

Accelerating Discoveries, Saving Lives

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INSTITUTE UPDATE

Opening Ceremonies Celebrate New Scripps Florida Biomedical Research Facilities

Florida Governor Charlie Crist cuts the ribbon to officially open Scripps Florida.

> The Scripps Research Institute's leaders were recently joined by Florida Governor Charlie Crist and Palm Beach County commissioners to cut the ribbon to officially open Scripps Florida, the institute's 350,000 square-foot state-of-the-art biomedical research facility in Jupiter.

Scripps Research President Richard A. Lerner and Lead Trustee John J. Moores, Governor Charlie Crist, Palm Beach County Commission Chairman Jeff Koons and Commissioner Karen Marcus addressed some 800 Scripps Florida faculty, staff, supporters, and friends who gathered in front of the three new laboratory and administrative buildings that currently house close to 300 employees.

"This event marks a very significant milestone in the history and growth of The Scripps Research Institute," said Lerner. "The road has been long and sometimes bumpy, but today we all join together to celebrate the completion of this magnificent campus. We dedicate it to expanding biomedical research,

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Inside:

San Diego Philanthropist John Moores Gives $2.1 Million to Scripps Research Institute

Funds will support recruitment of new scientists and sustain and expand work of current researchers

John J. Moores, Chairman of the Scripps Research Board of Trustees

San Diego philanthropist, businessman, and community leader John J. Moores has contributed the first gift of $2.1 million to The Scripps Research Institute's new $50 million initiative to recruit new world-class researchers and sustain and expand the work of current scientists at the renowned La Jolla- and Florida-based biomedical organization.

Moores, majority owner of the San Diego Padres baseball team has served as a member of the Scripps Research Board of Trustees since 1997 and as Chairman of the Board since 2006.

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educating and training future scientists and, ultimately, improving human health."

The ceremonies, which also included an appearance by the Jupiter High School Warriors Band and the William T. Dwyer High School Junior ROTC, was held underneath a large white tent in an area that, until just a few months ago, was filled with construction trailers. Construction on an adjacent site has also begun for the Max Planck Society's new facilities, drawn to Jupiter by the presence of Scripps Florida.

The Scripps Florida facilities themselves are remarkable for their architectural appeal with warm tropical colors and a striking sail-shaped spire atop the center building. The spire is an interpretation of the structure of DNA, the basic building block of life.

The ribbon-cutting at the new facilities was the first of three days of celebrations. An all-day scientific symposium was also held for Scripps Research faculty from both the Jupiter and La Jolla campuses and leading scientists from other Florida biomedical research organizations and universities. A number of Nobel laureates who serve on the Scripps Research Board of Scientific Governors attended and presented papers on cellular biology, metabolism and aging, and molecular therapeutics.

Thousands attended the day devoted to science education activities for K-12 students of the Palm Beach County School District and their families. Participants visited half a dozen interactive booths dedicated to various aspects of biomedical research, including the human genome. In addition, laboratory tours and the opportunity to meet Scripps Florida scientists were available.

Scripps Research Institute President Lerner originally announced plans to establish Scripps Florida in October 2003, after months of discussions with then-Florida Governor Jeb Bush, who was looking to expand the state's economic development in biotechnology. To date, total investment in Scripps Florida from the state and from Palm Beach County has been nearly $500 million, which is going toward construction of the new campus, recruitment of top scientists from around the world, and start-up costs plus salaries, benefits, and equipment through 2013.

Initial plans called for construction on a parcel of land made available by Palm Beach County in the western part of the county, but legal and other issues caused the county, in collaboration with Florida Atlantic University (FAU), to offer instead 30 acres of the FAU campus and an adjacent 70-acre property.

In 2005, the first laboratory building to temporarily house Scripps Florida researchers opened on the FAU campus, with a second "temporary" building added in 2006. Construction of the new Scripps Florida campus, adjacent to the temporary quarters, got underway in 2006. A three-month move-in process was completed in early 2009. The total cost of construction was $187 million, with the three state-of-the-art buildings completed on time and on budget. The two laboratory buildings vacated by Scripps Florida will now be used to house Max Planck Society scientists while their facilities are constructed next to Scripps Florida. Ultimately, these buildings will revert to FAU for science education.

The economic impact of Scripps Florida has already been significant. To date, Scripps Florida has been awarded more than $50 million in outside grants and filed more than 79 patent applications.

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> The celebration included a dinner for Scripps Research philanthropists. Pictured at the dinner are trustee Gary and Carol Coburn, with trustee Tom Insley.

< Over 200 fifth and sixth grade students from throughout Palm Beach County participated in the Sir Harry Kroto lecture, and demonstrated their "Bucky Balls." All in all, over 5,000 children and their families enjoyed the Scripps Florida Science Education Day.

Opening Ceremonies, CONTINUED

According to the Governor's Office, over the next 15 years, Scripps Florida is projected to create 6,500 new jobs and generate about $1.6 billion in additional income to Floridians, while boosting the state's Gross Domestic Product by $3.2 billion.

Scripps Florida also maintains a significant education and outreach program to promote bioscience education and awareness throughout the State of Florida by advocating career opportunities in the biosciences for middle and high school students and undergraduates, assisting middle and high school teachers with bioscience education initiatives, and, for the public in general, fostering an understanding of the basic ties that exist between biomedical research and human health. Scripps Florida also trains PhD candidates in biology and chemistry.

Scripps Research Institute Board of Trustees Elects Mark Pearson as Newest Member

> The Scripps Research Institute Board of Trustees has elected philanthropist and entrepreneur Mark Pearson as its newest member.

Mark Pearson

Pearson, 43, a leader in Silicon Valley commercial real estate, is a managing partner at Cresa Partners, a national corporate real estate company with 26 offices. Pearson is also co-founder and managing partner of Drawbridge Partners, a real estate development and investment company.

He has also founded several companies with emphasis on helping people reduce the cost of health insurance along with health and wellness expenses, and Annex Ventures, a venture capital firm focused on providing early-stage financing for technology and biotechnology companies.

Pearson has been involved with the programs at Scripps Research for a number of years. In 2003, he gave $3 million to the institute to establish the Pearson Center for Alcoholism and Addiction Research. The center combines the latest biomedical research with new clinical treatments to fight the devastating, costly, and deadly disease of alcohol and drug addiction. Co-directed by Scripps Research Professors George Koob and Barbara Mason, the center's work complements and reinforces traditional treatments by focusing on the physiological changes in the brain that drive excessive drinking and drug use while creating vulnerability to relapse.

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John Moores, CONTINUED

"The Scripps Research Institute has been in the lead in establishing the scientific foundation that is essential to improve human health," Moores said. "It has the ability to accelerate discoveries that may lead to breakthroughs in HIV/AIDS, cancer, Alzheimer's disease and many more diseases. But it needs to recruit the next generation of researchers now. I hope my support will encourage the community and my fellow Institute Trustees to join me in developing and sustaining Scripps Research's most vital resource—its scientific talent."

"The Scripps Research Institute is incredibly fortunate to have John as a long-time supporter of our work and active leader in our governance," said Institute President Richard A. Lerner, M.D. "As research dollars shrink and the economy remains unsettled, biomedical research and the Institute will need the generosity of engaged philanthropists such as John to step forward. His generous gift will permit us to continue to attract the very best scientific minds to Scripps Research and San Diego and to support their work."

"Now it's time for people in San Diego, throughout California, and across the nation to help us attract and support the young researchers who will make a difference in all of our lives," Lerner added.

Moores has contributed more than $22 million to the Institute over the years, including a $4 million gift in 2005 to establish the Worm Institute for Research and Medicine (WIRM) to combat the painful, disfiguring, and debilitating diseases borne by worms that afflict hundreds of millions of people in much of the world. This contribution was an extension of his long-term interest in these conditions. He founded the River Blindness Foundation in 1989 to distribute a treatment for that disease in developing countries, principally sub-Saharan Africa. In 1997, the foundation was absorbed into The Carter Center, where Mr. Moores serves as Chairman of the Board.

Moores is also one of the founders of Scripps Research's Institute for Childhood and Neglected Diseases. His generosity continues to help make it possible for Scripps Research to access the knowledge amassed by sequencing the human genome for deeper understanding of the mechanisms underlying human disease.

Bruce Genung Joins Scripps Research as Associate Vice President of Philanthropy

> Bruce Genung recently joined Scripps Research as associate vice president of philanthropy at our La Jolla campus. Genung spent the last ten years as a senior development officer in the California Institute of Technology's office of principal and major gifts.

Bruce Genung

"We are fortunate to have attracted Bruce," said Wendy Scott Keeney, vice president of philanthropy at Scripps Research. "He brings a keen and focused approach to working with donors, and real value and professionalism to our office. I look forward to our future collaboration bringing needed funding to our incredible institution."

Genung has spent over 20 years in fundraising and management of non-profit organizations. At the California Institute of Technology, he participated in a $1.4 billion campaign completed in 2007. He received a bachelor's degree from Occidental College and an MBA from University of Redlands.

"Honestly, I feel privileged to be associated with the scientists, students, and staff who comprise this extraordinary place," said Genung. "I am looking forward to supporting and — if possible — enhancing Scripps Research's work by finding philanthropic partners in the community. With these challenging economic times, it is more important than ever that we strengthen our connections with current and past friends of the Institute and that we make more people aware of the caliber of work that goes on here, as well as the importance of research and discovery in the basic sciences."

Prior to his ten years at the California Institute of Technology, Genung served as a director of development at California State University, Northridge, where he initiated major gift programs for three colleges and the university library. Previously, he served as director of development for Pilgrim School, an urban K-12 independent school in Los Angeles. Aside from his work for research and education, Genung has also raised funds for a licensed community clinic in Los Angeles, and for an international service agency.

Mark Pearson, CONTINUED

In 2007, Pearson also funded the Pearson Family Chair, an endowed chair in alcoholism and addiction research at Scripps Research.

"The chair provides assurance that the team I assembled at Scripps Research can carry on our exciting work, which has great potential to help people in recovery," says Mason, who currently holds the chair. "As part of the Pearson Center, the chair also gives me the freedom to conduct early proof-of-concept studies and quickly build on preclinical and clinical findings, work that could be delayed for years if we had to wait for National Institutes of Health funding, or never done at all."

RESEARCH UPDATE

Scripps Florida Scientists Find Novel Use for Old Compound in Cancer Treatment

Once-Discarded Drug Proves Effective in Pediatric Neuroblastoma Models

Scientists from the Scripps Florida campus of The Scripps Research Institute have found a potentially beneficial use for a once-abandoned compound in the prevention and treatment of neuroblastoma, one of the most devastating cancers among young children.

The compound, α-difluoromethylornithine or DFMO, targets the activity of a specific enzyme and, even in very limited doses, is effective in protecting against the malignancy in animal models.

"The drug, which was developed as a cancer therapy and later shelved because of toxicity concerns, has been around since the 1970s," said John Cleveland, Ph.D., chair of the Scripps Florida Department of Cancer Biology whose laboratory conducted the study. "But over the past five years, it has undergone a rebirth as a chemoprevention agent, first showing efficacy in animal models of human cancer and more recently in human prostate and colon cancer. Our study shows that it likely works in a large cast of tumors, even those having poor prognosis, like high-risk neuroblastoma."

Neuroblastoma is a childhood malignancy of the sympathetic nervous system (part of the nervous system

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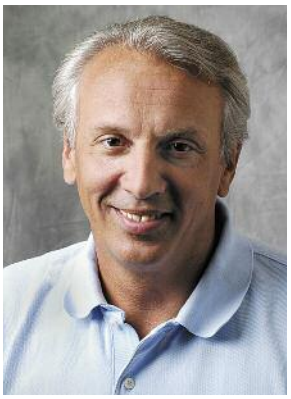
that serves to accelerate the heart rate, constrict blood vessels, and raise blood pressure) that accounts for nearly eight percent of all childhood cancers and 15 percent of pediatric cancer-related deaths. Its solid tumors arise from developing nerve cells, most commonly in the adrenal gland, but also in the abdomen, neck, and chest. Neuroblastoma usually occurs in infants and young children, appearing twice as frequently during the first year of life than in the second.

Tragically, children with stage IV, high-risk neuroblastoma have a less than a 40 percent chance of long-term survival.

The best-known genetic alteration involved in neuroblastoma is the amplification of the proto-oncogene — a molecule that when overexpressed can cause cancer — called *MYCN.* Amplification of *MYCN* occurs in about 20 percent of all neuroblastoma and is associated with the high-risk form of the disease. Targeting this and related genes directly might be therapeutically tempting, the study noted, but highly problematic because the oncoproteins they produce are also required for the growth of most normal cell types.

As a result, Cleveland and his colleagues focused on inhibiting *ornithine decarboxylase* (Odc), a protein that contributes to cancer cell growth and that is a target of the proto-oncogene *MYCN.* Increased levels of



"We were able to prevent neuroblastoma caused by *MYCN,* delaying the onset and incidence of this tumor type"

— John Cleveland, chair of the Scripps Florida Department of Cancer Biology

Odc are common in cancer, and forced Odc expression in animal models has been shown to lead to increased tumor incidence. Recent findings have shown that Odc overexpression is also an indication of poor prognosis in neuroblastoma. DFMO, the drug used by the Cleveland team, inhibits the activity of Odc.

To test the effect of DFMO on preventing neuroblastoma, the study used a transgenic mouse that faithfully models many of the hallmarks of *MYCN*-amplified neuroblastoma in humans.

"We were able to prevent neuroblastoma caused by *MYCN,* delaying the onset and incidence of this tumor type" said Cleveland. "What's even more compelling, we used low doses of the drug, and DFMO only had to be given for a moderate amount of time to prevent cancer."

While DFMO selectively impaired the proliferation of *MYCN*-amplified neuroblastoma, it had no appreciable effect on non-*MYCN*-amplified neuroblastoma cell lines, indicating that the growth of the former is "addicted" to Odc.

"Our study offers a strong suggestion to the clinical cancer community that they should keep an open mind about the Odc-polyamine pathway, and that this particular pathway might represent a novel therapeutic angle to tackle this malignancy." Cleveland said. "While there are valid safety concerns about giving DFMO to pediatric patients suffering from advanced stage *MYCN*-amplified neuroblastoma, it may be time to revisit the issue as our study showed that transient treatment with DFMO is sufficient to provide chemoprevention and may show benefit for this otherwise lethal malignancy."

DONOR PROFILE

The Need for Unrestricted Gifts — Our Donors Speak

The generosity of our donors is so important to our work. Your generosity has permitted the institute to continue to make significant progress in improving human health. All gifts from the Scripps Research donor family — whatever the amount — make our work possible.

Unrestricted gifts are the lifeblood of the institute. With unrestricted gifts, Scripps Research has been able to recruit both internationally recognized new scientists to produce groundbreaking new disease research, and to support the education of outstanding young scientists at the Kellogg School of Science and Technology.

Scripps Research depends on private philanthropists, like you, to enhance and expand its work in new, often untraditional directions.

In addition to laboratory research — the heart of the institute's work — unrestricted gifts help cover the costs of personnel and buildings which in other institutions, such as

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state universities, are subsidized by taxpayers. At Scripps Research, every unrestricted dollar supports research by insuring that scientists have well-qualified personnel, well-operated equipment, and well-maintained buildings available to them at all times.

A few of our donors relate below why they have chosen to support Scripps Research with unrestricted gifts.

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"Having served as Vice President – General Services of Scripps Clinic and Research Foundation from 1978 to 1992, I am aware first hand of the quality of the leadership and researchers of The Scripps Research Institute, the value of their biomedical research and the importance of supporting their efforts"

— **Robert Smothers** of La Jolla, a donor for the past 25 years

•••

"At the age of 31, I had breast cancer. I had one surgery, four rounds of chemotherapy, and six weeks of radiation. I kept thinking to myself, 'I wish some of these procedures were easier and less painful.' Five years later, I had a new case of breast cancer. That time, I noticed some changes in the procedures I had to go through that made my surgery and chemotherapy much easier. I will always be grateful to the people who donated to The Scripps Research Institute. Because of their contributions, my experience with my second case of breast cancer was much easier. I am 39, married and have a 12 year old son and we appreciate the dedication and hard work of those who work for Scripps Research"

— **Laurie McCormick** of Cardiff, a donor for the past six years

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"We agree wholeheartedly with your institutional mandate to take your research from 'lab bench to bedside'— it just makes good sense. Plus your outstanding outreach programs are so important with the current increased pace of scientific discoveries— the public needs to be informed so wise decisions can be made. Finally, we feel our contribution is a good investment in everyone's future"

— **Bill and Shirley Kimmich** of San Diego, donors for the past 23 years

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"We are great believers in the excellence of research at the Institute and are happy to be able to help, so that the research will continue to benefit our children and grandchildren's generations as it has ours."

— **Charles VanNote** of Oceanside, a donor for the past 20 years

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"I have spent years of my career in the research and education fields, and I have been treated a number of times by Scripps Health. With my background, I recognize that the results of the work performed at Scripps Research and its translation to the field of human health can help all patients, both at Scripps Health and other hospitals"

— **Dr. Donald Wilson** of Carlsbad, a donor for the past 14 years

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"Ten years ago, I lost my wife to cancer. In the four years prior to her death, she was hospitalized several times at Scripps Health. Since that time, I have come to appreciate the work of The Scripps Research Institute. I can only hope that my small contributions will make life easier for more cancer patients and help to eliminate this horrendous disease"

— **Victor Whitney** of Murrieta, a donor for the past nine years

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"I donate because of the vital nature of the medical research being done at the Institute. Several of my close relatives all suffered from pancreatic cancer and I believe Scripps Research contributes to the important work being done in the fight against cancer. I also worked for Edward Wyliss Scripps, the grandson of E.W. Scripps. My gifts are in memory of the important legacy left by the Scripps family"

— **Mark Hinueber** of Las Vegas, a relatively new donor of two years

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"As an alumnus of The Scripps Research Institute, I make financial contributions because I had the opportunity to experience first-hand the unique, collaborative, and extremely high caliber academic environment that fostered quality there and I want to invest in future generations of outstanding new researchers. When I see the quality and volume of research findings produced by the Scripps Research faculty in journals and conferences, I know that my donations are directly advancing science"

— **Jean Patterson** of Maynard, Massachusetts, also a donor for the past two years

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Your contributions — whatever the amount — are helping to improve the welfare of humankind. We thank you and applaud you.

Share Your Story

Invite your friends, family, and colleagues to join you in celebrating the life of a loved one, and supporting the tireless work that scientific research requires. It's now easy to create a dedicated tribute or memorial page on the Scripps Research website … just visit www.scripps.edu/philanthropy and click on "Tribute."

Jim Paulson — A Global Leader in Unraveling the Mysteries of Sugars and Their Impact on Disease

Scripps Research Professor Jim Paulson has spent about half his life studying sugars, or carbohydrates, that decorate the surface of cells to better understand their roles in cell communication and human disease… and his travails have brought him to the top of his field.

Jim has been named an industry pioneer and global leader in the field of glycomics by *Technology Review,* MIT's magazine of innovation. The magazine considers glycomics to be one of the top ten technologies that will change the future.

"By knowing what sugar binding proteins are found on specific cells, we can design synthetic sugars that will target and carry a therapeutic payload to a single type of cells."

— Professor Jim Paulson

Jim is the leader of the Consortium for Functional Glycomics, an international group of some 300 participating scientists who collaboratively study the complex dynamics of protein-carbohydrate interactions in the human body. Glycomics is important for unraveling the mysteries of the recently solved human genome because more than half of all proteins in the human body have sugar molecules attached.

"We know that sugars aid in the proper trafficking of cells in the body, and that they can modulate signaling from the outside of a cell to the inside, but what we know so far is just the tip of the iceberg," said Jim. "This consortium will help us uncover what lies beneath. While the field is still in its infancy, there has been a major upsurge — in fact, if you look at the major journals, they all typically now contain articles and reviews on glycomics."

The most popular resource established by the consortium at Scripps Research thus far has been the glycan array (glycans are relatively complex carbohydrates, sometimes called polysaccharides). It offers scientists an enormously powerful cutting-edge research tool that makes it easier and faster to determine how a diversity of glycan binding proteins interact with sugars in biological systems. From humble beginnings, there are now more than 450 structures in the array, and it has been used by over 200 investigators to investigate the biology of sugars and their roles in disease processes.

Some viruses, like influenza, use sugars on the outside of human cells to gain entry into human cells. The CFG array has been used by dozens of investigators, including recent research from Jim's lab and the lab of fellow Scripps Research scientist Ian A. Wilson, to investigate the host specificity of avian influenza virus. It was used to identify mutations that could enable adaptation of a particularly virulent form of H5N1 — the avian flu virus — to spread in the human population. A custom array is used by the Center for Disease Control to survey the avian and human influenza viruses isolated worldwide.

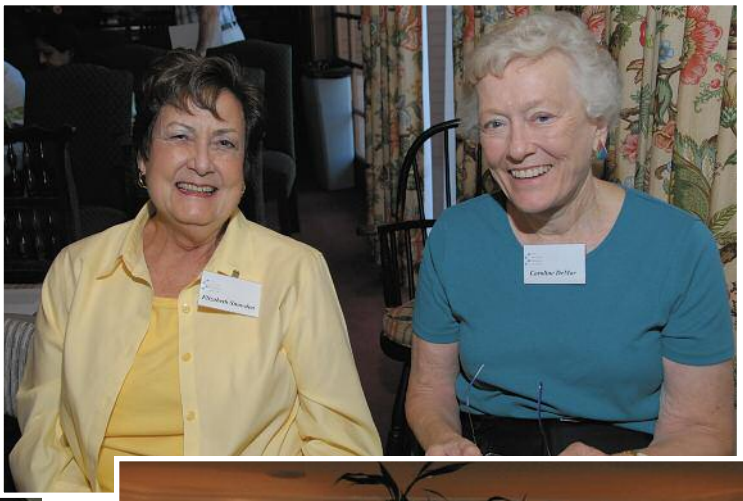
Data from the array is posted on a public web site, The Functional Glycomics Gateway, in a partnership between the consortium and Nature Publishing Group. It provides a comprehensive resource for functional glycomics research where the information generated by the consortium is rapidly disseminated to participants and the public alike, benefiting the scientific community as a whole. It highlights new and important contributions to the field, providing a one-stop overview of the latest research in glycobiology, and generates 120,000 visits per month.

Jim's own research laboratory is pursuing an approach to active targeting of sugar binding proteins on B cells for therapy of B cell leukemia and lymphoma. By targeting a single cell type, therapies can be developed with less side effects than therapies where other cells are also affected, such as through chemotherapy. Jim is one of a handful of scientists internationally attempting this approach.

"Our results are looking very good thus far. By knowing what sugar binding proteins are found on specific cells, we can design synthetic sugars that will target and carry a therapeutic payload to a single type of cells."

Jim has always had an interest in discovery. In grade school in the Midwest, he would examine protozoan life from pond water under a microscope; in high school, he was doing basement experiments on fruit flies; in college, at MacMurray College in Illinois, he had the dream to do an experiment that no one had ever done before, and by the time he reached graduate school at the University of Illinois, he was indeed doing things that no one had done before… and still is every day!

Partners



1 Scripps Research trustee Amin Khoury, with his wife Julie, (left) and Scripps Florida chair of the Department of Metabolism and Aging Dr. Roy Smith, and his wife, Jane, at Dr. Smith's recent presentation for the At the Front Lines of Hope lecture series, "Turning Back the Clock: New Anti-Aging Research." (left photo)

2 Scripps Research has launched its second year of intimate Lab Notes lectures in order to share the ground-breaking work of its scientists with its donors and friends. The lectures take place on the Institute's picturesque La Jolla campus, and are followed by a question and answer session and reception, so participants have plenty of opportunities to interact with the speakers. The free series kicked off in the fall with a lecture by Dr. Sandra Schmid on "21st Century Biology 101," in which Dr. Schmid discussed how studying what happens in a cell can lead to understanding and developing therapies for cancer, diabetes, and Alzheimer's. Pictured at the event are donors Elizabeth Snowden and Caroline DeMar. (upper right photo)

3 Mickey Berman (left), and Kathy Azeez (right), co-chairs of the Frenchman's Creek Women for Cancer Research (WFCR) stand with Dr. Harry Orf, vice president of scientific operations, Scripps Florida, at their kick-off event. The WFCR initiative raised $115,000 in support of post doctoral fellows in the Department of Cancer Biology laboratories of Dr. Kendall Nettles and Dr. Howard Petrie. (bottom right photo)

THE SCRIPPS RESEARCH INSTITUTE

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