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Team Successfully Targets Hard-to-Treat Breast Cancer

Findings from a new study led by scientists from the Florida campus of The Scripps Research Institute (TSRI) suggest a potent new therapeutic approach for a number of hard-to-treat breast cancers.

The study points to an enzyme called casein kinase 1δ (CK1δ), a critical regulator of growth, as a novel and highly vulnerable therapeutic target. Increased CK1δ expression is common to breast cancer, including the difficult-to-treat subtype called “triple negative breast cancer” (those cancers not driven by estrogen, progesterone, or the HER-2/neu gene), affecting 10 to 20 percent of breast cancer patients.

The study, which was published recently in the journal Science Translational Medicine, was a collaboration among the Florida labs of Derek Duckett and William R. Roush, both of TSRI, and John Cleveland, formerly of TSRI and currently at the Moffitt Cancer Center.

“Our findings confirm that aberrant CK1δ regulation promotes tumor growth in breast cancers by activating the protein β-catenin,” said Duckett, an associate professor at Scripps Florida. “The best news, however, is that we have been able to treat CK1δ-expressing breast cancers with a highly selective and potent CK1δ inhibitor developed by Bill Roush’s lab that triggers rapid tumor cell death.”

Scientists Study Physics of Single ‘Transformer’ Proteins with Role in Cancer

A new study led by scientists at TSRI and St. Jude Children’s Research Hospital shows how a protein involved in cancer twists and morphs into different structures.

“We’re studying basic biophysics, but we believe the complexity and rules we uncover for the physics of protein disorder and folding could one day also be used for better designs of therapeutics,” said TSRI Associate Professor Ashok Deniz, senior author of the new study along with Richard Kriwacki, faculty member at St. Jude.

The study, published recently in the journal Angewandte Chemie, focuses on a protein called nucleophosmin (NPM1).
protein has many functions and, when mutated, has been shown to interfere with cells’ normal tumor suppressing ability. NPM1 has been implicated in cancers such as non-Hodgkin lymphoma and acute myelogenous leukemia.

Chemists Devise Powerful New Method for Modifying Drug Molecules

TSRI chemists have developed a versatile new technique for making modifications—especially one type of extremely difficult, but much-sought-after modification—to complex drug molecules.

The feat, reported in a recent issue of the journal Science, has already enabled pharma giant Pfizer to proceed with the evaluation of a promising cancer drug candidate that otherwise could not have been made in sufficient quantities.

“People from other pharma companies who have seen early drafts of this paper can’t get their hands on the supporting information fast enough,” said senior investigator Phil Baran, the Darlene Shiley Professor of Chemistry at TSRI and an alumnus ('01) of the TSRI graduate program. “I expect that every company in the business of making drugs will be using this chemistry soon.”

The technique, known as “strain-release amination,” also should enable the easier construction of a variety of molecules besides pharmaceuticals, including molecular probes for basic biology studies, plastics, and other materials made from organic compounds.

Team Finds Unique Anti-Diabetes Compound Using Powerful New Drug-Discovery Method

TSRI scientists have deployed a powerful new drug discovery technique to identify an anti-diabetes compound with a novel mechanism of action.

The finding, which appeared recently in Nature Communications, may lead to a new type of diabetes treatment. Just as importantly, it demonstrates the potential of the new technique, which enables researchers to quickly find drug candidates that activate cellular receptors in desired ways.

“In principle, we can apply this technique to hundreds of other receptors like the one we targeted in this study to find disease treatments that are more potent and have fewer side effects than existing therapies. It has been a very productive cross-campus collaboration, so we’re hoping to build on its success as we continue to collaborate on interrogating potential therapeutic targets,” said Patricia H. McDonald, an assistant professor at TSRI’s Jupiter, Florida campus and a senior investigator of the study.

McDonald’s laboratory collaborated on the study with the laboratory of Richard A. Lerner, the Lita Annenberg Hazen Professor of Immunochemistry at TSRI’s La Jolla campus, and with other TSRI groups. Lerner has pioneered techniques for generating and screening large libraries of antibodies or proteins to find new therapies.
Study Suggests Tumors May ‘Seed’ Cancer Metastases Earlier Than Expected

A new study from scientists at TSRI helps explain why cancer metastasis is so hard to stop. The researchers found an additional mechanism explaining how a molecule long linked to cancer progression appears to “seed” the body with metastatic cells long before doctors would typically detect a primary tumor. The molecule, known as epidermal growth factor receptor (EGFR), encourages blood vessel growth early in tumor development—not only feeding the primary tumor, but also providing vehicles for cancer to escape the primary tumor site and travel throughout the body.

“When cancer cells have high levels of EGFR, the tumor has a lot of new, angiogenic blood vessels,” said TSRI Assistant Professor Elena Deryugina, senior author of the new study. “And these vessels are very welcoming for tumor cells and facilitate their dissemination from the very early stages of tumor development.”

The study was published recently in the journal Neoplasia.

Crouching Protein, Hidden Enzyme

Meet a microscopic gymnast.

A new study led by scientists at TSRI and the University of California (UC), Berkeley shows how a crucial molecular enzyme starts in a tucked-in somersault position and flips out when it encounters the right target.

The new findings, published recently in the journal *eLife*, give scientists a clearer picture of the process through which cells eliminate proteins that promote diseases such as cancer and Alzheimer’s.

“Having an atomic-resolution structure and a better understanding of this mechanism gives us the ability to someday design therapeutics to combat cancer and neurodegeneration,” said TSRI biologist Gabriel Lander (also a TSRI alumnus ’09), who was co-senior author of the study with Andreas Martin of UC Berkeley.

Scientists Find Surprising Trait in Anti-HIV Antibodies

TSRI scientists have new weapons in the fight against HIV. Their new study, published as the cover article of the November issue of *Immunity*, describes four prototype antibodies that target a specific weak spot on the virus. Guided by these antibodies, the researchers then mimicked the molecular structure of a protein on HIV when designing their own potential HIV vaccine candidate.

“This study is an example of how we can learn from natural infection and translate that information into vaccine development,” said TSRI Research Associate Raiees Andrabi. “This is an important advance in the field of antibody-based HIV vaccine development.”

Andrabi served as first author of the study, working in the lab of senior author TSRI Professor Dennis R. Burton, who is also scientific director of the International AIDS Vaccine Initiative (IAVI) Neutralizing Antibody Center and of the National Institutes of Health’s Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID) at TSRI.
Taiwan’s Samuel Yin Provides $12.8 Million Gift for New Laboratories

Philanthropist and businessman Samuel Yin of Taiwan has given $12.8 million to The Scripps Research Institute (TSRI) to help fund construction of a new building complex on the La Jolla campus. The gift also secures additional funding from a previous challenge grant, bringing the total in private donations for the project to more than $25 million.

“I would like to express my deep appreciation to Dr. Yin for this transformative gift,” said TSRI’s CEO Peter Schultz. “Together with a generous matching grant from an anonymous donor, the support provides critical anchor funding for the construction of cutting-edge new laboratories.”

“We are extremely grateful for Dr. Yin’s gift,” said TSRI President Steve Kay, “and pleased that the donation calls on us to honor one of our most esteemed faculty members, Chi-Huey Wong, who is Professor of Chemistry at TSRI and President of Academia Sinica, the highest academic institution in Taiwan. At Dr. Yin’s request, it is our pleasure to designate one of the future new buildings the ‘Chi-Huey Wong Chemical Biology Laboratory.’”

“I am most grateful for this unexpected honor,” said Wong, whose research tackles major problems in biology and medicine—especially those associated with cancer and infectious diseases—through a focus on synthesis of glycoproteins, vaccines and other biologically active molecules. “Dr. Yin is a visionary committed to making a better world, and I am doubly appreciative of the recognition because it is at the behest of this great man.”

Yin is Chairman of the Ruentex Group and Chief Development Officer, Chief Technology Officer and Chief Engineer of Ruentex Construction & Development. He is also an Adjunct Professor in the Department of Civil Engineering at National Taiwan University and a Professor at Peking University, where he advises PhD students.

In the West, Yin is perhaps best known as the founder of the Tang Prizes. The Tang Prizes, biennial awards first given in 2014, are selected by panels of judges convened by Academia Sinica for research excellence in Sustainable Development, Biopharmaceutical Science, Sinology and Rule of Law.

Yin is also a long-time supporter of scholarships for the study of Chinese literature and history, programs in higher education, and a number of foundations he launched to serve people on both sides of the Taiwan Strait.

His latest gift to TSRI makes possible a new state-of-the-art building complex that will help consolidate research labs on the La Jolla campus, encourage collaboration among the institute’s scientists and strengthen ongoing programs at the intersection of biology and chemistry.

“It is my great honor to contribute to the building of new state-of-the-art laboratories, which will further enable major advances in biomedical research at TSRI,” said Yin.
CHARITABLE GIFT PLANNING
How to Find the Right Attorney

Sometimes people drag their feet in creating or updating their will because they don’t know where to go to get good legal help. The fact that the phone book and Internet list the names of various lawyers is little help. These are simply strangers—names and numbers with no personal connection. How to solve the problem of “lawyer leeriness”?

First, it is important to locate an attorney who specializes in estate planning. If you have a cavity, you wouldn’t go to a foot doctor; you would go to a dentist. Similarly, for a will and other estate planning documents, you should consult with someone who is skilled in this area, knows the right questions to ask and is current with tax laws and document requirements.

TSRI can help you find an attorney you can feel good about for estate-planning matters. Instead of recommending only one individual, we can provide you with a variety of dedicated professionals to call and questions to ask regarding services and rates. We can serve as a guide and facilitator to help you find an attorney you like.

You may also want to speak with your closest friends about their connections. Perhaps they could steer you to an attorney you would like. Or, if you have a long-term relationship with a professional advisor such as a CPA or a financial planner, they, too, might be able to provide a recommendation.

In any case, it is a good idea to have a short visit with any attorney you don’t know before you engage him or her as your legal advisor so you can have confidence in his or her professional expertise. Take the opportunity to learn about his or her services and to see whether you feel comfortable with the person. There should be no charge for this initial visit.

Finding the right attorney may take a little extra effort, but you will be glad you spent the time—especially when you sit down and share confidential information about your assets and your distribution wishes.

If you are just getting started with your estate planning or need planned giving information, our office offers confidential assistance. Please contact Geoff Graham, director, planned giving and estates, at (858) 784-9365 or gcgraham@scripps.edu. Or visit our website at www.plannedgiving.scripps.edu.

Finally, if you have already planned your estate and made arrangements for The Scripps Research Institute, please let us know. We would like to acknowledge you for your commitment to accelerating scientific discoveries and saving lives.

High School Student Philanthropy Group Selects TSRI for Donation

TSRI has received an “investment” award from a group of Clairemont High School students in San Diego who participated in Main Street Philanthropy, a nationwide project to impact the lives of teenagers and young adults through meaningful, hands-on involvement in charitable giving and community service.

The students, members of the school’s Academy of Business, called themselves the “Trauma Troopers” and spent 10 weeks identifying nonprofit organizations aligned with their personal values. Through quantitative and qualitative evaluations of each group, the students determined TSRI would be the best steward of their $370.44 philanthropic donation, earned from fundraising efforts and Main Street Philanthropy donors.

“Of those we considered, you rose to the top as one that would do a good job in ensuring that our investment would truly impact the causes we care about,” the students wrote.
Remicade® Developer Funds New Super-Resolution Microscope at Scripps Florida

The co-developer of Remicade®, one of the three top-selling drugs in the world, has donated more than $500,000 to fund what will be known as the Iris and Junming Le Foundation Super-Resolution Microscopy Facility on TSRI’s Florida campus.

“We are grateful to Junming and Iris for their generous contribution,” said Chair of the TSRI Department of Neuroscience Ronald Davis, who will oversee the new facility. “The gift will have a dramatic and highly positive effect on the brain science pursued by our department. This is the perfect opening to what will be a genuinely state-of-the-art facility right here in Jupiter.”

The new donation will support the purchase of a powerful microscope that will give Scripps Florida neuroscientists an extraordinarily detailed view of the brain.

“Our foundation gives money to the best institutions and hospitals to support basic medical research and patient care through those projects we think will be successful,” said Junming Le, chairman and director of The Iris and Junming Le Foundation and adjunct associate professor of microbiology at New York University School of Medicine. “This is certainly one of them. When I learned that this microscope could advance the understanding of the brain and its function, I realized this would be an important investment for us. That kind of information could lead to breakthroughs in diseases like Alzheimer’s.”

The new microscope will be one of the most advanced available. Known as a structured illumination microscope, the technology uses a super-imposed pattern (grate), taking multiple images at various angles. These images are then merged—effectively doubling the resolution of a traditional light microscope.

“With this super-resolution microscopy,” Davis said, “we will be able to see synapses between neurons and to actually count them—to determine, for example, if the number of neurons in a brain affected by Alzheimer’s or Parkinson’s disease is different than a normal brain. This is a nearly unimaginable leap forward.”

Funding for The Iris and Junming Le Foundation, based in New York and Boca Raton, is the legacy of Junming Le’s invention of Remicade®, a drug used to treat autoimmune diseases, such as rheumatoid arthritis, psoriasis, Crohn’s disease and ulcerative colitis. Remicade®, which is currently manufactured and marketed by Johnson & Johnson and Merck, has been prescribed to more than two million people worldwide.
AWARDS and HONORS

TSRI researchers have harnessed advanced structural biology techniques to shed light on HIV and advance the development of an AIDS vaccine. Scientists have also introduced a powerful new anti-HIV drug candidate.

TSRI Ranks Number One in HIV/AIDS ‘Hot Papers’
TSRI is listed as the top institution for producing “hot papers” in HIV/AIDS research over the last two years, according to a recent report by Thomson Reuters. Eight of the top 20 highly cited papers in the field were affiliated with the institute. TSRI also achieved top status in 2013, the last time Thomson Reuters published such an analysis.

Four TSRI faculty members—Andrew Ward, Ian Wilson, Dennis Burton and Pascal Poignard—were listed among 10 “authors of the hottest HIV/AIDS research.”

In addition, Discover Magazine, Genetic Engineering & Biotechnology News and the National Institute of Allergy and Infectious Diseases all highlighted TSRI’s HIV work as a “top story of 2015”—specifically Professor Michael Farzan and colleagues’ development of a powerful and broadly effective anti-HIV drug candidate. The San Diego Union-Tribune’s “Top 10 Local Stories in 2015” also cited work by Professors Dennis Burton, David Nemazee and William Schief demonstrating that the immune system can be primed to block HIV infection.

Sandra Encalada and Michael Petrascheck Win Glenn Award
TSRI’s Sandra Encalada, the Arlene and Arnold Goldstein Assistant Professor, and Michael Petrascheck, assistant professor, have received the Glenn Award for Research in Biological Mechanisms of Aging, merit awards from the Glenn Foundation for Medical Research that provide unsolicited funds to researchers investigating the biology of aging.

Using a variety of approaches, Encalada studies the mechanisms of intracellular transport in aging neurons, as well as how defective intracellular transport leads to neurodegeneration in models of aging diseases such as Alzheimer’s, amyotrophic lateral sclerosis (ALS), prion diseases and transthyretin amyloidosis.

The Petrascheck lab uses a diverse toolbox of genetics, drug screening, imaging and study of the Caenorhabditis elegans (C. elegans) nematode to determine the mechanisms underlying the aging process, focusing on how the nervous system modulates aging and how the nervous system itself is affected by aging.

Tina Izard, Priya R. Banerjee, Bernard Kok Receive 2015 AHA Awards
Tina Izard, associate professor at the Florida campus of TSRI, and Research Associates Priya R. Banerjee and Bernard Kok of TSRI’s California campus each has received 2015 American Heart Association (AHA) awards.
Izard won a two-year grant-in-aid for her project “Structure and function of cardiomyopathy-associated metavinculin mutant.” A crystallographer and cell biologist, Izard studies the structural dynamics of signaling mediators of adhesion junctions.

Banerjee, a member of the Deniz lab, and Kok, a member of the Saez lab, received AHA postdoctoral fellowships. Banerjee’s project is “Mechanism of amyloid and apoptosis regulation as a potential cardioprotective role of Hsp27 at the single-molecule level.” Kok’s project is titled “An integrated approach to establish the role of LYPLAL1 in diabetes and cardiovascular disease.”

Three TSRI Graduate Students Named ARCS Scholars

TSRI graduate students Rigo Citron-Colon, Danielle Grotjahn and Daisy Johnson have received Scholar Awards from the San Diego chapter of the Achievement Rewards for College Scientists (ARCS) Foundation, a national nonprofit organization advancing science and American competitiveness through grants to academically outstanding students pursuing degrees in science, engineering or medical research.

Citron-Colon, a second-year graduate student in the Conti lab, is working on a physiology research project titled “Nutrient and Temperature Homeostasis.”

Grotjahn, a third-year graduate student in the Lander and Encalada labs, focuses her research at the intersection of cell biology and structural biology; her project is titled “Ultrastructural analysis of motor protein conformations and regulation.”

Johnson, a second-year graduate student in the Havran lab, is pursuing a research project in immunology titled “Enhancing wound healing through the activation of γδ T cells.”

ARCS Scholars are selected annually by qualifying departments of science, engineering and medical research within the ARCS Foundation’s 54 academic partner universities.

Salome Murinello Awarded American Diabetes Association Fellowship

Salome Murinello, research associate in the Friedlander lab, has won a highly competitive, three-year American Diabetes Association Postdoctoral Fellowship Award, designed to support high-quality training for early-career researchers in disciplines and topics relevant to diabetes.

Murinello’s research focuses on diabetic retinopathy, a complication of both type I and type II diabetes and the leading cause of blindness in working-age American adults. Specifically, her project, “FAAH and NAAA regulation of erucamide-mediated retinal neuroprotection and angiogenesis in diabetic retinopathy,” seeks to elucidate the regulation of retinal levels of a molecule—erucamide—important for proper blood vessel health in the retina.
TSRI Alumni Association Launched

The TSRI Alumni Association officially launched its activities at an inaugural event held at the Beckman Center for Chemical Sciences on February 11. The event centered around the association’s motto: “Connect and benefit.” Attendees included TSRI postdoctoral and graduate student alumni, as well as current faculty, graduate students and postdocs.

The program featured presentations from:

- Phil Baran, the Darlene Shiley Professor of Chemistry and an alumnus of TSRI’s graduate program, who narrated an entertaining story about the significant role that TSRI has played in building his highly successful career.
- John Hood, former TSRI postdoc and current chief scientific officer at Samumed, who described how his scientific discoveries and connections helped him successfully transition to the pharmaceutical industry.
- Alan Ezekowitz, CEO of Abide Therapeutics, a company he co-founded with TSRI Professors Dale Boger and Ben Cravatt, delivered an inspirational talk that emphasized “make your connections before you need them.”

The TSRI alumni association is currently accepting membership requests on its LinkedIn page and will soon be launching its official website.

New Public Lecture Series Highlights TSRI Women in Biomedical Research

TSRI’s Female Faculty Group is hosting a new public lecture series, titled ResearchHERS, to give the institute’s donors and friends a behind-the-scenes look at biomedical research and the work of women in the field.

The series kicked off in October with a presentation by TSRI Professor and Trustee Linda Sherman, whose research focuses on the body’s immune system. In particular, Sherman explained how some of her lab’s insights into the immune system’s overreaction in type 1 diabetes might be harnessed to boost the body’s defenses against cancer.

Chris Lee, Scripps California director of philanthropy who introduced the lecture series, emphasized the importance of female scientists and supporters at TSRI. “Since Ellen Browning Scripps’ founding vision to create Scripps many decades ago, women’s leadership in science has been at the core of our organization,” he said. ❖
ELLEN BROWNING SCRIPPS CIRCLE HONORS DONORS PROVIDING SIGNIFICANT ONGOING SUPPORT

TSRI is pleased to honor the legacy of Ellen Browning Scripps by introducing the Ellen Browning Scripps Circle. In 1924, “Miss Ellen,” as she was affectionately known, generously gave a foundational gift that served as the catalyst for what we today know as TSRI. Thanks to the many innovators, collaborators and philanthropists who have followed her lead, TSRI has become a world leader in medical research.

The Ellen Browning Scripps Circle is comprised of donors whose significant and sustained support profoundly impacts the institute. It was established to recognize donors who give $1,000 or more annually to benefit the life-saving research at TSRI. Members include individual donors, foundations and corporations who invest in the promise that medical research has to transform health and save lives. Thank you to the 500+ members from 2015!

To learn more about giving to TSRI, visit www.scripps.edu/philanthropy.

To learn more about supporting TSRI's cutting-edge research, please contact:

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