

Researchers Identify Mechanism for Frank-Ter Haar Syndrome

An international team of investigators from the Courtneidge laboratory at Sanford-Burnham, Nijmegen Centre for Molecular Life Sciences and other organizations have discovered that TKS4, a protein implicated in cancer metastasis, also plays a significant role in Frank-Ter Haar syndrome (FTHS), a rare, fatal disorder. The research was published on February 12 in the *American Journal of Human Genetics*.

Children with FTHS suffer from skeletal, cardiovascular and eye abnormalities and usually die in infancy or early childhood. Hans von Bokhoven, Ph.D., at Nijmegen, with assistance from clinical colleagues in several countries, studied 12 families who had been affected by FTHS. The team mapped the condition in seven of these families to a mutated gene that normally contains the code to create the TKS4 protein. Dr. von Bokhoven soon discovered that Sara A. Courtneidge, Ph.D., was also studying TKS4, as it related to cancer metastasis, and had created a mouse lacking TKS4.



Dr. Sara A. Courtneidge

The Courtneidge group, together with Sanford-Burnham researchers José Luis Millán, Ph.D., Pilar Ruiz-Lozano, Ph.D., and researchers at U.C., San Diego, determined that the mice without TKS4 showed virtually identical traits to FTHS patients, confirming the results of the gene mapping.

“This research illustrates the importance of collaboration in the scientific discovery process,” says Dr. Courtneidge, “and how the study of one disease—in this case cancer—can have a profound impact on the understanding of another. In the future, we hope to use our mouse model to study the disease in more depth.”

Natural Compound Inhibits Cancer Cell Migration

Investigators in the Vuori laboratory have discovered that the natural compound sceptrin, which is found in marine sponges, reduces cancer cell motility (movement) and has very low toxicity with normal cells. Metastasis, the process in which malignant cells migrate to other parts of the body, is one of the deadliest aspects of cancer, so restricting aberrant cell movement is an important step towards advancing treatments. The research was published in *ACS Chemical Biology* in collaboration with Phil S. Baran, Ph.D., of The Scripps Research Institute.

The team tested sceptrin in multiple tumor cell types, including cervical, breast and lung cancers, and found that sceptrin restricts motility in all cell lines. Further tests showed that the compound works by limiting the cells’ ability to contract, a critical function for cell motility. The researchers also

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found that sceptrin synthesized in the laboratory was just as effective as the naturally derived compound.

“Given the recently achieved synthesis of sceptrin in multi-gram quantities by the Baran laboratory, sceptrin could prove to be an attractive lead molecule for further preclinical testing and development for therapeutic purposes,” says Kristiina Vuori, M.D., Ph.D. “It may also prove to be a useful research tool in order to elucidate the mechanisms involved in cell motility.”

Nobel Laureates Anchor Lake Nona’s Inaugural Symposium

On February 12, Sanford-Burnham at Lake Nona hosted its inaugural scientific symposium, which attracted 200 scientists from across the country. The symposium was described by one participant as the scientific equivalent of Woodstock, with a program that featured two Nobel laureates, Drs. Michael Brown and Joseph Goldstein, as well as Drs. Robert Lefkowitz, Lewis Cantley, Cynthia Kenyon, Eric Olson and Ronald Evans. Bringing high-profile scientists to Lake Nona’s Medical City helps build awareness of the region’s promise.



Drs. Michael Brown, Tim Osborne, Robert Lefkowitz and Joseph Goldstein

“This symposium helps put Orlando on the map as a destination for medical research,” said John C. Reed, M.D., Ph.D. “If we can continue to attract some of the world’s greatest scientists to meetings such as this, Orlando will become known world-wide as an area from which great research emanates.”

Age-Related Pathologies and Sestrin

Rolf Bodmer, Ph.D., and U.C., San Diego colleagues Michael Karin, Ph.D., and Ethan Bier, Ph.D., have been using the fruit fly *Drosophila* to understand the genetic mechanisms that control age-dependent deterioration of muscles and heart function. These mechanisms involve a class of conserved proteins, called Sestrins, which accumulate in cells exposed to stress and keep important protein kinases (AMPK and TOR) in check so they do not go out of control from that stress. The teams have shown that Sestrin acts as a brake upon chronic TOR activation, which would otherwise generate excessive amounts of reactive oxygen species (ROS).



Drosophila

As a result, loss of Sestrin in flies causes accelerated age-associated pathologies, including fat accumulation and mitochondrial dysfunction. These, in turn, are the likely causes of ensuing muscle degeneration, as well as cardiac malfunction and arrhythmias. Dr. Bodmer and colleagues speculate that, with age, this control of TOR and prevention of ROS-inflicted organ damage may no longer function properly, predisposing an organism to age-related diseases. The research, led by Dr. Karin, was the cover story in the March 5 issue of *Science*.

NIH Director Dr. Francis Collins Visits Sanford-Burnham

On February 20, National Institutes of Health (NIH) Director Francis Collins, M.D., Ph.D., and Congressman Brian Bilbray visited Sanford-Burnham to tour the campus, learn more about cutting-edge biomedical research and meet with Sanford-Burnham President and CEO John Reed, M.D., Ph.D., and other scientists. Later, Sanford-Burnham hosted a round table discussion with Dr. Collins, Congressman Bilbray and leaders from many of San Diego's premier academic and biotech organizations.



Dr. Ilyas Singec chats with Dr. Collins, after showing him cardiomyocytes under the microscope.

The visit began at Sanford-Burnham's stem cell facility, where Dr. Collins viewed beating cardiomyocytes (precursors to heart cells) and questioned researchers about their progress in stem cell research. Later, he toured the Conrad Prebys Center for Chemical Genomics. Sanford-Burnham has a \$98 million contract with the NIH to screen chemical compounds at the Prebys Center to gain new insights into biology and discover new medicines. Dr. Collins has high hopes for this technology and was eager to learn how the project is proceeding.



Dr. Michael Jackson, along with Dr. Steve Vasile coming live from Lake Nona, describes the Prebys Center to Dr. Collins and Congressman Bilbray.

After the tour, Dr. Collins and Congressman Bilbray met with scientists, entrepreneurs, corporate executives and community leaders from around San Diego to discuss NIH funding, the promise of biomedical research and how public/private partnerships can advance science, create jobs and lead to new cures.

Among the leaders participating in the meeting were: philanthropists Denny Sanford and Malin Burnham; Joe Panetta, CEO of Biocom; Duane Roth, CEO of CONNECT; Eric Topol, M.D., Director of the Scripps Translational Science Institute; William Brody, M.D., Ph.D., President of the Salk Institute and many others.

During this unique forum, Dr. Collins noted how important research is to growing our economy.

“Not only is medical research the way we improve the health of the nation and give people the chance to have long lives,” said Dr. Collins, “but it’s also one of the best investments in the economy. More than half of the economic growth in the United States since World War II has been the result of investments in science and technology. Every grant dollar that comes into the community results in \$2.21 in economic output. So that’s a pretty good investment.”

Rare Disease Symposium

By Claire Attwooll

On February 26, Sanford-Burnham hosted our inaugural Rare Disease Symposium, using a unique format in which patients and their families were given a voice—and the scientists were there to listen.

“What we hoped to achieve was to open the lines of communication between researchers, patients, families and advocacy groups,” said symposium organizer Hudson Freeze, Ph.D., of Sanford-Burnham. “We can learn so much from these families, and then we can give something back.”



Dr. Millán with HPP patient Morgan Fischer.

Diseases are classified as “rare” when they affect fewer than 200,000 people in the United States. But there are around 7,000 such disorders, meaning 30 million Americans are affected. Because of these diseases’ rarity, patients and their families often struggle to find information, and many have started advocacy groups to raise awareness and reach out to other families who need help. These families can be a great help to researchers, having gained personal Ph.D.s in the intricacies of an uncommon disease.

Yu Yamaguchi, M.D., Ph.D., of Sanford-Burnham, works on Multiple Hereditary Exostoses (MHE), an incurable disease where multiple bony lumps grow on bones. Dr. Yamaguchi studies mice with mutations in the genes that cause MHE. Yet, it was an MHE advocacy group that alerted him to anecdotal evidence that MHE may also be associated with autism.

“Because there is no scientific evidence, this issue is largely ignored by physicians,” said Yamaguchi. “We found that our MHE mice show clear signs of social avoidance and repetitive behavior, showing a real need for a comprehensive assessment of the link between MHE and autism.”

Sanford-Burnham researcher José Luis Millán, Ph.D., studies hypophosphatasia (HPP), which results from abnormalities in skeletal mineralization and causes bone softening. Some children with HPP are too fragile to touch. Dr. Millán described how advocacy groups brought a child from the United Arab Emirates to participate in the clinical trial for ENB-0040, the first drug developed against hypophosphatasia.

Before the trial, the girl could not walk and needed a respirator to breathe. One year after treatment, Dr. Millán watched her take unassisted steps without a respirator in sight. “These are the kinds of things we can achieve with active advocacy groups,” says Dr. Millán.

Craig Eaton, President of the MHE Research Foundation, whose 15 year-old son has MHE, agreed. “We are here to provide support for sufferers and their families, to promote research and collaboration and to appreciate and understand the problems faced by all.”

Dr. Anne Rutkowski, M.D., co-Founder and Vice Chairman of Cure CMD, an advocacy group for Congenital Muscular Dystrophy, echoed Dr. Millán’s words. “This Symposium reaffirms the belief that communication will drive research to find clinically relevant treatments,” she said. Dr. Rutkowski’s daughter has CMD, and she stresses that “as parents, we can also remind researchers that a small change can be clinically meaningful. If you’re getting up five times a night to help your child, then a treatment that allows one more hour of sleep is very relevant.”

Age-Related Retreat

The first Postdoc Retreat for the Development and Aging Program, led by Rolf Bodmer, Ph.D., was held on February 26 at the Estancia Hotel. Organized by Pam Itkin-Ansari, Ph.D., the all-day event was attended by more than 50 Sanford-Burnham investigators, who discussed a variety of topics, including retinoic acid in forebrain development, cell replacement strategies in diabetes, interventions in fly and mouse heart models, autophagy in aging and many others.



The Development and Aging Program at the Estancia.

The retreat also featured two keynote speakers:

Maike Sander, M.D., of U.C., San Diego, who discussed mechanisms of cell fate determination in the pancreas, and Andy Dillin, Ph.D., of the Salk Institute, who talked about how researching aging can inform us on fundamental principles of biology.

In addition, Anthony Cammarato, Ph.D., of the Bodmer laboratory, and Maria Cecilia Scimia, M.D., of the Ruiz-Lozano laboratory, were honored for their excellent presentations during last year's Postdoc Seminar Series.

The Zen of Caspase-8

The second Caspase-8 Symposium was recently hosted by Drs. Darren (Ben) Finlay and Stefan Riedl and brought local and national experts on this key cellular regulator to Sanford-Burnham. The symposium covered novel signaling roles for Caspase-8, as well as further characterization of its traditional role in programmed cell death. Among the high profile presentations, keynote speaker Jill Lahti, Ph.D., of St. Jude's Children's Research Hospital, presented data detailing the role of Caspase-8 in neuroblastoma and linking cutting edge research to clinical findings. The day was rounded off with a poster session and wine reception.



Drs. Ben Finlay and Stefan Riedl discuss logistics during the recent Caspase-8 Symposium.

Technician Appreciation Day

The Community Support Office held its first employee appreciation day on, February 4 for the Institute's technicians, including research assistants, research technicians, lab assistants and lab animal technicians. The technicians were invited to a free BBQ lunch and three lucky employees (Stephanie Papp, Homer Bravo and Apple Cortez) won movie tickets. The appreciation lunch was a hit with all attendees. And just so no one feels left out, the Community Support Office will be sponsoring more appreciation days throughout the year. Stay tuned.



Jo Ann Gayer works the Community Support Office table, while Luis Lopez grabs a cookie.

Call For Volunteers

On Saturday, March 27, Sanford-Burnham will be hosting a booth at the San Diego Science Festival at Petco Park, and we are looking for volunteers to help staff it. The booth will showcase the aging research in the Hansen laboratory, and will allow festivalgoers to get up close and personal with *C. elegans*. We will need people to help explain both our science and our mission. YOU DO NOT NEED TO BE A SCIENTIST TO HELP. Last year, more than 50,000 people attended the festival. This is a great opportunity to get our science and new name out in the community. If you are interested in volunteering, please drop a note to jbaxt@sanfordburnham.org. Thanks everyone.



Help Cancer.gov Evolve

The National Cancer Institute (NCI), in an effort to reach diverse audiences with the latest, evidence-based cancer information, recently announced an “evolution” of Cancer.gov. The effort is called an evolution rather than a redesign because it is part of a process rather than a one-time change. The NCI welcomes ideas from individuals and organizations on how to improve and enhance Cancer.gov through an online forum at cancergov.ideascale.com. The dialogue will be open until March 31. After that, a new section on Cancer.gov will provide updates on the site’s evolution.

Open House

The Community Support Office (CSO) held an Open House on March 4. Sanford-Burnhamites got to check out the office in Building 4, learn about the role of the CSO, chow on nachos and drink a variety of refreshing beverages. There were also games, the traditional Institute camaraderie and an iPod raffle (won by Dr. Yuan Yang, congrats). The CSO is a new resource for help resolving a work-related problem, information about policies and procedures or assistance navigating the system. If you have questions or ideas you think are a good fit for the CSO, contact Sherri Marinovich at sherrim@sanfordburnham.org.



Kevin Hall enjoys the nachos

Welcome to Sanford-Burnham

Salvatore Albani, Professor and Director of Translational Research, La Jolla

Karl Bacos, Postdoctoral Fellow, La Jolla

Jumana Bisharat, Intern, La Jolla

Stephanie Boumediene, Vice President, External Relations, Santa Barbara

Stephanie Cheng, Intern, La Jolla

Alan Chin, Research Technician, La Jolla

Sheila Collins, Professor, Lake Nona

Jessica Colomb, Executive Assistant, La Jolla

Amy Cortez, Flow Cytometry Specialist, La Jolla

Herman Davidovics, Research Technician, La Jolla

Shirin Doroudgar, Graduate Student, La Jolla

Paul Fiechtner, HRIS Specialist, La Jolla

Keith Gates, Postdoctoral Associate, La Jolla

Yushuyan Hao, Intern, La Jolla

Tae Il Jeon, Staff Scientist, Lake Nona
Xinpeng Jiang, Postdoctoral Associate, La Jolla
Nadine Keller, Postdoctoral Fellow, La Jolla
Johnny Kim, Intern, La Jolla
Ersheng Kuang, Postdoctoral Associate, La Jolla
Tanya Kuei, In Vitro Assay Development Specialist, La Jolla
Eunhye Lee, Postdoctoral Associate, Santa Barbara
Hyo Lee, Intern, La Jolla
Chang-Hun Lee, Visiting Researcher, La Jolla
Rachel Leong, Lab Assistant, La Jolla
Ricardo Leyva, Workstudy, La Jolla
Ricardo Lozano, Intern, La Jolla
Hanako Matsuo, Lab Assistant, La Jolla
Kathleen Mosure, Research Associate I, Lake Nona
Anissa Myers, Sponsored Research Administrator, La Jolla
Quy Nguyen, Lab Assistant, La Jolla
Hung Nguyen, Research Technician, La Jolla
Roger Orta, Radiation/Safety Technician, Lake Nona
Stephanie Parsons, Postdoctoral Fellow, La Jolla
Petra Pavlickova, Postdoctoral Associate, La Jolla
Joelina Peck, Senior Sponsored Research Administrator, La Jolla
Anthony Pinkerton, Associate Director, Medicinal Chemistry, La Jolla
Jasmina Racic, Intern, La Jolla
Daya Raman, Lab Assistant, La Jolla
Alan Revilas, Lab Assistant, La Jolla
Scott Shanks, Administrative Systems Developer, La Jolla
Christine Thornton, Intern, La Jolla
Theodorus Van Den Broek, Postdoctoral Associate, La Jolla
Stanley Walls, Graduate Student, La Jolla
Christian Weichenberger, Visiting Researcher, La Jolla
Grace Wood, Lab Coordinator, La Jolla
Mythili Yenjerla, Postdoctoral Associate, La Jolla
Aryan Zarrabi, Intern, La Jolla

Seen, some months ago, at Lake Nona

