INSTITUTE UPDATE

WASC Extends Kellogg School’s Accreditation 10 Years

> The Scripps Research Institute’s Kellogg School of Science and Technology has been reaccredited by the Western Association of Schools and Colleges (WASC) for 10 years—the maximum period possible.

“This is great news and a vote of confidence in our program,” said Jamie Williamson, dean of graduate and postgraduate studies. “Thank you to everyone who participated in the process. We have invested a lot of time in self-improvement, we have benefited in many ways, and we should continue to strive to improve our program to make it the best that it can be.”

The three-year WASC review process included site visits from the WASC committee and input from faculty, administration, students, postdoctoral fellows, and staff to clarify the program’s direction and identify areas for improvement.

According to the March 7, 2011 letter from the WASC Accrediting Commission for Senior Colleges and Universities, “Early indications are that the new teaching and learning practices are becoming part of Scripps Research’s growing ‘culture of assessment’ and may become a model for similar research institutions across the nation.”

The Scripps Research graduate program was launched in 1989. Since then, it has grown in both size and reputation, now consisting of more than 200 students on the institute’s La Jolla, California and Jupiter, Florida campuses. The program is consistently ranked among the top ten graduate programs in the country for biology and chemistry in publications such as U.S. News & World Report.

RESEARCH UPDATE

Scripps Research Study Points to Liver, Not Brain, as Origin of Alzheimer’s Plaques

> Results Could Lead to New Strategies for Prevention and Therapy

Unexpected results from a Scripps Research Institute and ModGene, LLC study could completely alter scientists’ ideas about Alzheimer’s disease – pointing to the liver instead of the brain as the source of the “amyloid” that deposits as brain plaques associated with this devastating condition. The findings could offer a relatively simple approach for Alzheimer’s prevention and treatment.

In the study, the scientists used a mouse model for Alzheimer’s disease to identify genes that influence the amount of amyloid that accumulates in the brain. They found three genes that protected mice from brain amyloid accumulation and deposition. For each gene, lower expression in the liver protected the mouse brain. One of the genes encodes

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presenilin – a cell membrane protein believed to contribute to the development of human Alzheimer’s.

“This unexpected finding holds promise for the development of new therapies to fight Alzheimer’s,” said Scripps Research Professor Greg Sutcliffe, who led the study. “This could greatly simplify the challenge of developing therapies and prevention.”

An estimated 5.1 million Americans have Alzheimer’s disease, including nearly half of people age 85 and older. By 2050, the number of people age 65 and over with this disease will range from 11 million to 16 million unless science finds a way to prevent or effectively treat it. In addition to the human misery caused by the disease, there is the unfathomable cost. A new report from the Alzheimer’s Association shows that in misery caused by the disease, there is the unfathomable cost. An estimated 5.1 million Americans have Alzheimer’s disease, including nearly half of people age 85 and older. By 2050, the number of people age 65 and over with this disease will range from 11 million to 16 million unless science finds a way to prevent or effectively treat it. In addition to the human misery caused by the disease, there is the unfathomable cost. A new report from the Alzheimer’s Association shows that in misery caused by the disease, there is the unfathomable cost.

In trying to help solve the Alzheimer’s puzzle, in the past few years Sutcliffe and his collaborators have focused their research on naturally occurring, inherited differences in neurological disease susceptibility among different mouse strains, creating extensive databases cataloging gene activity in different tissues, as measured by mRNA accumulation. These data offer up maps of trait expression that can be superimposed on maps of disease modifier genes.

As is the case with nearly all scientific discovery, Sutcliffe’s research builds on previous findings. Several years ago, researchers at Case Western Reserve mapped three genes that modify the accumulation of pathological beta amyloid in the brains of a transgenic mouse model of Alzheimer’s disease to large chromosomal regions, each containing hundreds of genes. The Case Western scientists used crosses between the B6 and D2 strains of mice, studying more than 500 progeny. The findings: the drug dramatically reduced beta amyloid not only in the blood, but also in the brain where the drug cannot penetrate. Thus, an appreciable portion of brain amyloid must originate in the liver, circulate in the blood, and enter the brain. If true, blocking production of beta amyloid in the liver should protect the brain.

To test this hypothesis, Sutcliffe’s team set up an in vivo experiment using wild-type mice since they would most closely replicate the natural beta amyloid-producing environment. “We reasoned that if brain amyloid was being born in the liver and transported to the brain by the blood, then that should be the case in all mice,” Sutcliffe said, “and one would predict in humans, too.”

The mice were administered imatinib (trade name Gleevec, an FDA-approved cancer drug), a relatively new drug currently approved for treatment of chronic myelogenous leukemia and gastrointestinal tumors. The drug potently reduces the production of beta amyloid in neuroblastoma cells transfected by amyloid precursor protein (APP) and also in cell-free extracts prepared from the transfected cells. Importantly, Gleevec has poor penetration of the blood-brain barrier in both mice and humans.

“This characteristic of the drug is precisely why we chose to use it,” Sutcliffe explained. “Because it doesn’t penetrate the blood-brain barrier, we were able to focus on the production of amyloid outside of the brain and how that production might contribute to amyloid that accumulates in the brain, where it is associated with disease.”

The mice were injected with Gleevec twice a day for seven days; then plasma and brain tissue were collected, and the amount of beta amyloid in the blood and brain was measured. The findings: the drug dramatically reduced beta amyloid not only in the blood, but also in the brain where the drug cannot penetrate. Thus, an appreciable portion of brain amyloid must originate outside of the brain, and imatinib represents a candidate for preventing and treating Alzheimer’s.

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DONOR PROFILE

Hector Leon:
For the Love of Caesar

Caesar Fernando Leon was just 31 when he succumbed to cancer. That was twenty years ago, and Hector V. Leon still visibly grieves for his son—a big, strong, handsome man who grins from every page of the photo album balanced on Hector’s knees as he sits in his Bonsall, California home and recalls “the good boy, good son, good husband” who died years too soon.

A parent never gets over the death of a child, he explains.

In 1991, Hector Leon needed to find a way to honor his son’s life. So he looked around his environment, gathered up his resources and tremendous strength of will, and discovered a way to convert his own grief into hope for others.

Not a millionaire, nor even a wealthy man, this father of six who grew up in Mexico, moved to the U.S. in 1955 and tended bar at San Luis Rey Downs for 17 years, has become one of The Scripps Research Institute’s most dedicated donors.

Since 1992, the annual Caesar Fernando Leon Charity Golf Tournament, organized by Hector V. Leon and held at San Luis Rey Downs, has raised more than $100,000 for cancer research through the Caesar F. Leon Memorial Fund for Cancer Research at Scripps Research.

Cancer has claimed a lot from Hector. His sister died of leukemia. His wife died of colon cancer in 1965, leaving him with six children to raise alone; the youngest, Caesar, was just five years old.

“When my wife died, I embraced my children and carried on. I got up early before going to work to get them all off to school, making breakfasts, lunches, dinners, ironing shirts and pants … it was very difficult.”

Caesar was an active boy who golfed, bowled and fished, even after he was diagnosed with kidney problems at age 15 and became a patient at Scripps Memorial Hospital—La Jolla. He spent the next four years undergoing kidney dialysis and waiting for the call to come that a donor kidney had been found. The kidney finally became available and at age 19, Caesar underwent a successful organ transplantation at University Hospital. A graduate of Oceanside High School, he opened his own barber shop in Crown Point and married.

But in 1990, lumps appeared on his neck. He lived another year.

When Caesar was very ill, his face swollen from his condition, the end of his life inevitably approaching, Hector took him out to play golf. It was there in the warm sun and light breezes of San Luis Rey Downs that the idea of a memorial golf tournament to raise funds for cancer research began to form. After Caesar’s death, Hector shared his idea with the friends he’d made tending bar at the country club, made up flyers and took charge of the myriad details that go into organizing a fundraising event without a formal organizational structure for support.

Today, five of Hector’s children are grown and healthy: Ed teaches in Pamplona, Spain; Salvadore teaches in El Paso, Texas; Sergio owns a barbershop; and daughter Dora is a successful businesswoman. And the sixth child, Caesar—the smiling boy who lives in his father’s memory—lends his spirit to the fundraiser held on the greens of San Luis Rey Downs each summer, and to the hopeful research conducted in the laboratories of Scripps Research each day.
Ray Stevens: Running a Dual Race for PKU

PKU is a rare, inherited metabolic disorder that is characterized by the inability of the body to utilize the essential amino acid, phenylalanine (Phe). PKU is caused by a deficiency of the liver-produced enzyme phenylalanine hydroxylase (PAH). When left untreated, PKU patients who consume too much Phe are at risk of severe neurological complications, including IQ loss, memory loss, concentration problems, mood disorders, and in some cases, severe mental retardation.

Ray’s interest in PKU began as an assistant professor at the University of California, Berkeley 20 years ago, where he had a basic scientific curiosity in making a connection between chemistry and neurobiology.

He chose to focus more directly on PKU research after receiving an invitation from renowned PKU Researcher Dr. Richard Koch at the USC Children’s Hospital, to attend an event where he met individuals and families associated with PKU. Getting to meet Dr. Koch and seeing his passion for patients with PKU personalized the disorder for Ray and he became very interested in making PKU research a major part of his career.

Ray spent the first few years in the field studying the enzyme PAH and what the enzyme looked like in a normal model, so as to better understand what happens with mutations. At Scripps Research, Ray and his colleagues made a breakthrough discovery by structurally characterizing PAH over 12 years ago. It was then that Ray became more involved on the personal side of PKU because of personal interactions and getting to know the doctors, nurses, and families of PKU patients. As a result, his level of personal commitment grew. He was very impressed by the team effort of the PKU community with the coordination of fundraising and scientific research between different groups such as the Mid-Atlantic Connection for PKU and Allied Disorders (MACPAD), the Michaux Family Foundation, and BioMarin Pharmaceuticals.

More recently, Ray and his colleagues been helping with the development of the PEG-PAL molecule now in clinical trials to treat classical PKU. PEG-PAL works by degrading Phe so the body can easily get rid of it, without ill effects. It will be used to stabilize PKU patients and cut down on the number of Phe spikes, possibly relaxing their restrictive, low-protein diet. Those individuals who don’t respond to Kuvan for PKU, another molecule Ray has been associated with, will benefit the most from PEG-PAL. However, it will be a few years before PEG-PAL is available to the PKU community. Phase II of the process was completed last year in which initial studies for efficacy were conducted. The final Phase III led by BioMarin will get underway in the near future. After this is completed and the FDA gives its approval, the product will be ready to go on the market.

On the flip side of Ray’s dual commitment to the PKU community is his fundraising through running in the Marathon des Sables, which took place in April. A story about the Marathon des Sables, or Marathon of the Sands, was featured on 60 Minutes and piqued Ray’s interest many years ago. It seemed like a great opportunity to challenge himself and raise awareness about PKU. Ray is an avid runner and has competed in many races over the last 20 years, including running in the Vermont 100 mile ultra-marathon, a trek through the mountains of Vermont. Ray likens the challenges of running a race to that of PKU drug discovery research. A major part of the work is mental and must be thought through carefully and it is grueling, requiring persistence.

The Marathon des Sables is a 6-day, 156-mile ultra marathon that begins in Morocco and goes across a section of the Sahara Desert; a distance equivalent to 6 regular marathons!

Competitors must carry all personal belongings for the entire event in their backpacks and carry their own food. Tents and water are supplied by the organizers, with a rationed amount of water handed out at each checkpoint. Daytime temperatures can exceed 120°F and the competitors travel on uneven, rocky ground for the majority of the run. Fifteen to twenty percent of the distance traveled is across the massive sand dunes seen in the movies. The exact course is not revealed until the day before the race begins.
These conditions do not deter true ultra-running enthusiasts, however. The race organizers must use a lottery system to limit the number of participants each year. There are 900 participants allowed worldwide and only 21 were from the United States this year. Ray was one of the few chosen and was notified ten months ago that he would be allowed to register. Since that time, he got ready by running long distances carrying a 20-pound backpack and exercising in a dry, 130° sauna for an hour at a time a few times a week.

When race organizers asked who he wanted to support in his run, there was no question in Ray’s mind that it would be PKU.

He says there is no other cause he would rather support. He even paid the $3,500 registration fee and additional $3,500 in travel expenses out of his own pocket so that all funds raised would go to PKU research! But it’s not just about the money. Ray believes raising awareness about PKU is just as important. Many people have never heard of PKU and Ray would like to see that changed. Everyone can help achieve that goal by spreading the word.

On the first day of the Marathon des Sables April 3, Ray felt as ready as he was going to be. With his doctor, he had tried to manage the tendinitis that had sprung up in the left ankle and the pain in the shin of his left leg from overtraining, although neither had fully healed.

In the preceding days, he had also packed and repacked his supplies, trying to minimize their weight. On the day of the race, on his back he was carrying: 2,000 calories of food per day for seven days (including oatmeal, freeze dried packages, almond peanut butter, and pop-tarts), electrolyte powders, a sleeping bag, headlamp and batteries (for running at night), as well as other required gear – an emergency space blanket, a whistle, a signal mirror, a compass, a knife, a first aid kit, a lighter, and a scorpion venom pump (because you never know when you are going to be bit by a scorpion).

The race started mid-morning April 3, when the blazing heat was beginning to emerge. The first day's course, about 21 miles, included crossing the largest sand dunes in the Sahara, where many of the runners (including Ray, whose left leg also began to swell) picked up severe blisters. The physicians in the medical tent were busy “fixing a lot of feet.”

The second day’s course consisted of about 24 miles, followed by a third day of another 24 miles. Ray struggled with increasing nausea from dehydration. He vomited twice near the third day’s final checkpoint.

The next day presented the longest stretch—51 miles and one of the hottest days of the race. After the first 18 miles, Ray was so dehydrated he was put on an IV (one IV is allowed per participant; require a second and you are forced to withdraw from the race). “I had to lay in the sand with a needle in my arm that cost me time,” Ray wrote, “but after 1 liter of saline solution and 1.5 liters of glucose solution, I felt great being fully hydrated and managed to run 32 miles straight to the long stage finish line, crossing at 3:58 AM…” He noted he was especially motivated to complete the stage before the sun came up on the fifth day; rumors had been circulating around camp that temperatures were reaching 131°F.

By the sixth day, the 26-mile marathon stage, Ray “had his head down, just putting one foot in front of another.” Finally, came day seven, 11 miles—and then the finish line!

Does Ray think the race was worth it? “Absolutely, I enjoyed it fully (which is easier to say now that the pain has gone away).” What was his favorite part? “Turning off my headlamp in the middle of the night on the 51 mile long stage . . . and running up the cold dunes in the dark looking at the stars.” Would he do it again? “No way . . . It was a once-in-a-lifetime dream.” His next challenge? “Well, there is this mountain called Everest that I have been thinking about . . .”

Many thanks go out to Ray and other researchers who work every day to find a cure for PKU.
A Gift to Scripps Research that Pays YOU!

Several of our donors are receiving checks from Scripps Research. They are receiving a payment every quarter . . . for life! They have all made charitable annuity gifts. Our gift annuity pays a fixed percentage of the initial gift amount. The more "mature" the donor, the higher the percentage. All payments are fixed and guaranteed for life by The Scripps Research Institute.

If you would like to know more about how to make a gift that pays you, please call Steve Abramson at (858) 784-9365. No obligation; no pressure.

This is not legal advice. Any prospective donor should seek the advice of a qualified estate and/or tax professional to determine the consequences of his or her gift.

The California Life Insurance Guaranty Association does not back up payments of annuities.

Las Patronas Grant Benefits Scripps Research Work in Breast Cancer Research

A grant of nearly $20,000 from the San Diego philanthropic organization Las Patronas will help advance breast cancer research at Scripps Research.

Las Patronas has a long history of giving. Since its inception in 1946, Las Patronas has donated approximately $15 million to nearly one thousand charitable institutions in San Diego.

Las Patronas is committed to providing financial assistance to nonprofit organizations in San Diego County that provide valuable community services in the areas of health, education, social services and cultural arts, and to continuing their tradition of service to enhance the quality of life in the San Diego community. The funds distributed to these organizations are generated through year-long fundraising efforts and the annual presentation of the Jewel Ball, one of San Diego’s most enduring social, cultural, and philanthropic traditions.

“This is a wonderful award,” said Associate Professor Brunhilde Felding-Habermann. “We are very grateful for Las Patronas’s support.”

The grant will fund additional specialized equipment for Felding-Habermann’s laboratory. Her group’s research focuses on uncovering the mechanisms by which breast cancer spreads to other parts of the body, particularly the brain. Specifically, the grant will enable the lab to purchase a high-resolution respirometer to investigate particular metabolic activities in tumor cells. The team recently identified these activities as critical for the metastasis (spread) of breast cancer.

Antonio Amelio Presented with Cancer Research Scholar-in-Training Award

Antonio L. Amelio, research associate in the Conkright lab, was presented a Scholar-in-Training Award by the American Association for Cancer Research (AACR) at its 102nd annual meeting in April in Orlando, Florida. Sponsored by Aflac Inc., the award recognizes outstanding papers by early-career scientists among AACR associate members.

More than 2,000 award applicants submitted recommendation letters and abstracts for which they were listed as presenters; fewer than 45 Scholars in Training were named. Amelio’s paper was titled “Emerging Roles for the cAMP Regulated Transcription Coactivators (CRTC) in Oncogenesis.”
Scripps Research Wins More than $2 Million to Study Prostate Cancer

> Scripps Florida and Moffitt Cancer Center Scientists Collaborate to Better Understand Cancer’s Progression

The Scripps Research Institute and Tampa’s Moffitt Cancer Center have been awarded more than $2 million to study the formation and progression of prostate cancer. Of the funds awarded, approximately $1.9 million will go to Scripps Research, with the remaining $138,380 supporting Moffitt Cancer Center work.

The five-year grant from the National Institutes of Health (NIH) will fund research to advance the development of novel therapeutic strategies for prostate cancer treatment and prevention.

“This new funding will help us continue our work into the origins of prostate cancer and the role that inflammation plays in its development,” said Jun-Li Luo, PhD, an assistant professor on the Florida campus of Scripps Research and principal investigator for the new study. “We are pleased that Moffitt, one of the country’s leading treatment and research centers, will be our partner in this research. Gaining a better understanding of the inflammatory process should help lay the foundation for developing novel therapeutic strategies for this disease.”

“This collaboration with Scripps Florida is a great opportunity to help uncover the underlying mechanisms of prostate cancer,” said Shohreh Dickinson, MD, an assistant professor at Moffitt, where scientists will study and interpret pathology slides of human cells as part of the new study. “It’s also a great opportunity for two Florida research centers to advance the science that, hopefully, will one day help put an end to this terrible disease.”

Prostate cancer – which, according to the American Cancer Society, will affect one in six American men in their lifetime – is the second-leading cause of death after lung cancer in American men. Prostate cancer is driven by androgen, the male sex hormone, and androgen deprivation is considered a first-line treatment of the disease once it spreads beyond the prostate gland.

Eventually, all prostate cancer becomes resistant to the treatment, and the disease grows independently of androgen. This can occur almost anytime during treatment. Currently there are no effective treatments for what is known as hormone-refractory prostate cancer.

Luo’s work has long been focused on the role of inflammation in cancer and the body’s innate inflammatory response, which encourages tumor growth. In earlier studies, he found that blocking one of the factors involved in inflammation – the nuclear factor-kappa B (NF-kB) – dramatically impaired development of the disease. In addition, Luo has identified tumor-infiltrating B cells as another critical component of the inflammatory response that enhances androgen-independent tumor growth.

The new study will further define how B cells control the spread of hormone refractory cancer.

Scripps Research Center Hosts National Cancer Institute Network Meeting

A center led by Scripps Research Professor Peter Kuhn hosted the second annual meeting for the National Cancer Institute’s (NCI) Physical Sciences-Oncology Centers (PS-OC) recently, drawing 250 scientists and a number of cancer survivors. The NCI initiative, which consists of a 12-center network, seeks to advance the understanding of the physical laws and principles that shape and govern the emergence and behavior of cancer.

“NCI is putting all the ingredients in the process and seeing what develops, not just following the same recipe with the same ingredients,” said meeting participant Carole Baas, a cancer survivor and patient advocate.

For example, Kuhn’s Four Dimensional Fluid Biopsy Center at Scripps Research aims to achieve a better understanding of the behavior of cancer cells during metastasis, the spread of cancer from a primary tumor to other sites throughout the body. This understanding is directly aimed at determining more effective methods to manage cancer.

For more information on NCI’s PC-OC, visit http://physics.cancer.gov. For more information on the Scripps Research Four Dimensional Fluid Biopsy Center, see http://physicsoncology.org/default.aspx.
Partners

1 Scripps Research hosted a special event in March to recognize San Diego area donors for their continued support and commitment to scientific discoveries at the institute. Donors were provided a behind-the-scenes update of recent discoveries at Scripps Research and a sneak peek into the breakthroughs around the corner. The High Tea was held in the galleria of the Beckman Center for Chemical Sciences. More than 30 different chemistry labs surround the galleria area; the noise of chemistry added a touch of science to the tea.

Special recognition was given to an important group of donors, the Scripps Legacy Society. Members of the Legacy Society have supported the science of Scripps Research by making a planned gift in their estate plans. Legacy Society member Kim Doren spoke briefly about her personal experience with disease and how it inspired her to support biomedical research.

Donors were moved by a presentation by Keary Engle, a third-year graduate student in the Scripps Research Kellogg School of Science and Technology. Scripps Research Chief Operating Officer Douglas Bingham also personally thanked donors for their continued support.

Pictured at the event with Scripps Research Chief Operating Officer Douglas Bingham (back row, third from left) are Scripps Legacy Society members (front, l to r) Betty Brock, Eugenia Glow, Jo Zolin (back, l to r) Kim Doren, Ron Newell, and Eleanor Mosca. (top photo)

2 Scripps Florida supporters Sydelle Meyer (left), with Norman and Simone Goldblum, were among a full-house of guests attending The Science of Health, an afternoon reception and presentation in Palm Beach featuring special guest, Dr. Ronald L. Davis, Founding Chairman and Professor, Scripps Florida's Department of Neuroscience. Dr. Davis captivated the audience by sharing the secrets of memory formation and detailing life changing research underway on the Scripps Florida campus. (left photo)

3 Susan Keenan (right), Director of Marketing and Board Member of Lydian Bank & Trust, pictured with Professor Ron Davis, Chairman of Scripps Florida’s Department of Neuroscience. Lydian recently awarded a generous gift to Scripps Florida Education Outreach to establish the Lydian Fellows Undergraduate Summer Internship program. Dr. Davis, along with four other Scripps Florida faculty members, will mentor Lydian Fellows this summer. (bottom right photo)