Researchers at USC uncover new possibilities for sweat gland stem cells

By Marie Rippen

Sweat is important — without it, we would overheat and die. In a recent paper in the journal Public Library of Science One (PLoS ONE), USC faculty member Krzysztof Kobielak, MD, PhD, and a team of researchers explored the ultimate origin of this sticky, stinky but vital substance — sweat gland stem cells.

Kobielak and his team used a system to make all of the sweat gland cells in a mouse easy to spot: labeling them with green fluorescent protein (GFP), which is visible under ultraviolet light.

Over time, the GFP became dimmer as it was diluted among dividing sweat gland cells. After four weeks, the only cells that remained fluorescent were the ones that did not divide or divided very slowly — a known property among stem cells of certain tissues, including the hair follicle and cornea. Therefore, these slow-dividing, fluorescent cells in the sweat gland’s coiled lower region were likely to be stem cells.

Then, the first author of this paper, graduate student Yvonne Leung, tested whether these fluorescent cells could do what stem cells do — differentiate into multiple cell types.

To the researchers’ surprise, these glowing cells generated not only sweat glands, but also hair follicles when placed in the skin of a mouse without GFP.

The researchers also determined that under certain conditions, the sweat gland stem cells could heal skin wounds and regenerate all layers of the epidermis.

“That was a big surprise for us that those very quiescent sweat gland stem cells maintain multi-lineage plasticity — participating not only in their own regeneration, but also in the regeneration of hair follicles and skin after injury,” said Kobielak, assistant professor of pathology at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC.

Keck students, benefactors celebrate success at Scholarship Luncheon

By Ryan Bail

The daughter of undocumented immigrants, Maria Sandoval credits excellent mentoring for helping her become the first member of her family to graduate high school and college.

Now in her third year at the Keck School of Medicine of USC, she’s getting another boost in her quest to become a primary care physician and practice in her underserved community in the San Fernando Valley.

Sandoval is the recipient of this year’s scholarship named for Edward Zapanta, MD, the late USC neurosurgeon and first Hispanic member of the USC board of trustees. She recently had the opportunity to thank Norene Zapanta for continuing her husband’s support of Hispanic medical students.

The two shared a meal at the Keck School’s annual Scholarship Luncheon, held on Oct. 2 on the Harry and Celesta Pappas Quad.

“I get to meet the person who believed in me and thought it was important to help others to become doctors and be successful,” said Sandoval. “I’m very grateful to have the honor of accepting this scholarship.”

“It’s important for the students to know that we’re here supporting them,” said Zapanta. “And then I hope they want to give back. I think that’s the biggest thing.”

In his opening remarks, Henri Ford, MD, MHA, vice dean for medical education at the Keck School, thanked the donors for enabling the school to maintain its competitive edge.

“Scholarships, as you know, are truly vital in continuing to attract the very top students,” Ford said, “and also for Keck to continue to expand its influence locally, as well as globally, in the medical arena.”

Ford noted that the generosity of donors has allowed the Keck School to increase its number of scholarships from 19 to 42 over the past two years. Keck School Dean Carmen A. Puliafito, MD, MBA, added that it isn’t enough to attract students who are academically strong, “We’re looking to have a diverse student body with medical students from underrepresented minorities in the United States,” Puliafito said. “This is very important in the delivery of equal-access health care.”

Open enrollment an opportunity to choose Keck Medicine physicians

Open enrollment for benefits-eligible faculty and staff of the University has begun, and personnel are encouraged to choose Keck Medicine of USC providers by signing up for the USC Network Medical Plan. This plan offers choice of physicians, convenient locations and lower costs.

The USC Network Medical Plan is a PPO, allowing participants a choice of which physicians they want to see. Tier I of the plan includes nearly 600 USC physicians, as well as 1,345 doctors associated with USC Verdugo Hills Hospital, an expansion convenient to staff living in the Foothill communities. Tier II includes any doctor with a Blue Cross Anthem contract, affording a vast network of choices for where participants can receive care.

“We want our staff and faculty to keep in mind the world-class services we offer right here,” said Tom Jackiewicz, MPH, senior vice president and CEO for USC Health. “Whether you’re looking for a primary physician or a specialist, we should be your first choice.”

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See ENROLLMENT, page 3

Public Library of Science One (PLOS ONE)
Drug reduces brain damage, hemorrhaging in rodents afflicted by stroke

By Allison Trinidad

An experimental drug called 3K3A-APC appears to reduce brain damage, eliminate brain hemorrhaging and improve motor skills in older stroke-affected mice and stroke-affected rats with comorbid conditions such as hypertension, according to a new study from Keck Medicine of USC.

The study, which appears online in the journal Stroke, provides additional evidence that 3K3A-APC may be used as a therapy for stroke in humans, either alone or in combination with the FDA-approved clot-busting drug therapy tPA (tissue plasminogen activator). Clinical trials to test the drug’s efficacy in people experiencing acute ischemic stroke are expected to begin recruiting patients in the United States in 2014.

“Currently, tPA is the best treatment for stroke caused by a blocked artery, but it must be administered within three hours after stroke onset to be effective,” said Berislav Zlokovic, MD, PhD, director of the Zilkha Neurogenetic Institute (ZNI) at the Keck School of Medicine of USC and the study’s lead investigator. “Because of this limited window only a small fraction of those who suffer a stroke reach the hospital in time to be considered for tPA. Our studies show that 3K3A-APC extends tPA’s therapeutic window and counters tPA’s tendency to induce bleeding in the brains of animals having a stroke.”

Zlokovic is the scientific founder of ZZ Biotech, a Houston-based biotechnology company he co-founded with USC benefactor Selim Zilkha to develop biological treatments for stroke and other neurological ailments. ZZ Biotech's 3K3A-APC is a genetically engineered variant of the naturally occurring activated protein C (APC), which plays a role in the regulation of blood clotting and inflammation.

3K3A-APC has been shown to have a protective effect on the lining of blood vessels in rodent brains, which appears to help prevent bleeding caused by tPA.

In collaboration with Cedars-Sinai Medical Center and The Scripps Research Institute, Zlokovic and his team gave tPA — alone and in combination with 3K3A-APC — to mature female mice and male hypertensive rats four hours after stroke. They also gave 3K3A-APC in regular intervals up to seven days after stroke. They measured the amount of brain damage, bleeding and motor ability of the rodents up to four weeks after stroke.

The researchers found that, under those conditions, tPA therapy alone caused bleeding in the brain and did not reduce brain damage or improve motor ability when compared to the control. The combination of tPA and 3K3A-APC, however, reduced brain damage by more than half, eliminated tPA-induced bleeding and significantly improved motor ability.

“Scientists all around the globe are studying potential stroke therapies, but very few have the robust preclinical data package that 3K3A-APC has,” said Kent Pryor, PhD, MBA, ZZ Biotech’s chief operating officer. “The results from Dr. Zlokovic’s studies have been very promising.”

Zlokovic’s team previously reported similar results in young, healthy male rodents. A Phase 1 trial testing the safety of 3K3A-APC in healthy human volunteers, led by study co-author Patrick D. Lyden, MD, of Cedars-Sinai, concluded in February.

“We now have opened an investigational new drug application at the FDA to conduct a Phase 2 clinical trial of 3K3A-APC in patients experiencing acute ischemic stroke,” said Joe Romano, CEO and president of ZZ Biotech. “We are excited to see 3K3A-APC move from healthy volunteers to real patients suffering from this terrible disease.”

USC co-authors include Yaoming Wang, MD, PhD, senior research associate at ZNI, and Zhen Zhao, PhD, physiology and biophysics research associate. The research was supported by ZZ Biotech and grants from the National Institutes of Health (HL63290, NS075930, HL52246).

SCHOLARSHIP: Education costs "insurmountable" without help

Continued from Page 1

Fourth-year Keck student Tavis Dickerson-Young was one of the scholars invited to share his story and discuss the impact scholarships have had on his education. Brought up by a single mother with limited financial resources, he managed to work and put himself through college. However, the high cost of medical education would have been an insurmountable obstacle without help.

“It’s because of your scholarship donations that I am able to pursue my dream of becoming a physician,” said Dickerson-Young.

“While your contributions have made a substantial difference in our lives as students, what is greater is that you are also giving to all of the patients whom we will treat throughout our careers.”

Did you know?

The USC Center for Molecular Pathways and Drug Discovery opened in 2010. Led by Michael Kahn, PhD, Provost Professor of Medicine and Pharmacy, and Heinz-Josef Lenz, MD, professor of medicine and preventive medicine at the Keck School, the center’s programs aim to treat cancer and other diseases by discovering and modulating cellular communication pathways.

Most cancer research focuses on one target at a time. Cancer cells, with their voracious survival instincts, find ways to bypass single targets that have been shut down. By focusing on networks of targets, the center tries to control hubs where disease cell pathways intersect, and then correct the cells’ communication maps.
Gene variant raises colorectal cancer risk from eating processed meat

By Suzanne Wu

A common genetic variation that affects one in every three people significantly increases the risk of colorectal cancer from consuming red meat and processed meat, according to a study presented at the annual American Society of Human Genetics 2013 meeting.

In addition, the study — the first to identify the interactions of genes and diet on a genome-wide scale — reveals another specific genetic variation that appears to modify whether eating more vegetables, fruits and fiber actually lowers your colorectal cancer risk.

“Understanding who may or may not be at higher or lower risk based on their genetic profile is crucial for helping us better understand the biology of colorectal cancer and a cancer that affects one in every three people,” said lead author Jane Figueiredo, PhD, assistant professor of preventive medicine at the Keck School of Medicine of USC.

“We are not saying that if you don’t have this genetic variant that you should eat all the red meat you’d like,” Figueiredo said. “People with the genetic variant allele have an even higher increased risk of colorectal cancer if they consume levels higher of processed meat, but the baseline risk associated with meat is already pretty bad.”

The researchers searched the more than 2.7 million genetic sequences for interactions of consumption of red and processed meat. The study looked at 9,287 patients with colorectal cancer and a control group of 9,117 individuals without cancer.

The risk of colorectal cancer associated with processed meat was significantly higher among people with the genetic variant rs1269486. This variant is located on the same chromosome 10 region that includes GATA3, a transcription factor gene previously linked to several forms of cancer. The transcription factor encoded by this gene normally plays a role in the immune system, but carries this genetic variant in about 36 percent of the population.

The researchers speculate that the digestion of processed meat may promote an immunological or inflammatory response that may trigger tumor development. The GATA3 transcription factor normally would help suppress the immunological or inflammatory response. However, if the GATA3 gene region contains a genetic variant, it may result in a dysregulated transcription factor that impacts its ability to suppress the response.

But other genetic variants may be beneficial. On chromosome 8, another statistically significant diet-gene interaction was found in variant rs249866. For people with this variant, eating your fruits and vegetables may be even better for you when it comes to colorectal cancer risk, the research shows.

“Colorectal cancer is a disease that is strongly influenced by certain types of diets,” Figueiredo said. “We’re showing the biological underpinnings of these correlations, and understand whether genetic variation may make some people more or less susceptible to certain carcinogens in food, which may have future important implications for prevention and population health.”

Major funders include the National Cancer Institute of the National Institutes of Health.
Calendar of Events

Tuesday, Nov. 12


Noon - 1 p.m.: Cancer Center Grand Rounds: “Regulation of the DNA Damage Response by an Inducible Long Noncoding RNA,” Adam Schmidt. Aretsy Auditorium.


Wednesday, Nov. 13

8:30 a.m.: Department of Medicine: “Basic Lecture: Acid-Base/ABG,” Ami Oren, USC. IBD 732-734. Info: (323) 226-7923

Thursday, Nov. 14

Noon: Southern California Clinical and Translational Science Institute: “How to Apply for a Pre- and Post-Doctoral Research & Career Development Award,” Geocia Patton-Sutton, SC CTSL. Info: ece@uscctsi.org

Noon - 1 p.m.: Department of Medicine: “Biomarkers of Acetaminophen Toxicity,” Laura James, University of Arkansas for Medical Sciences. Hastings Auditorium. Info: (323) 442-1283

5:15 p.m. – 6:30 p.m.: Department of Anesthesiology Grand Rounds: “Quality in Anesthesiology – Do We Know It When We See It?” Richard P. Dutton, Anesthesia Quality Institute. Aretsy Auditorium. Info: (323) 409-6856

6 p.m.: Orthopaedic Surgery Grand Rounds: “ Tibia Fracture: How, When, What and Why of Plating of Tibia Fractures,” Raymond R. White, Tufts University. Reception at 5:30 p.m. Mayer Auditorium. RSVP: sylvia.suarez@med.usc.edu

Friday, Nov. 15

8:30 a.m.: Department of Medicine: “Basic Lecture: Interesting Radiology Cases,” A. Wilcox, USC. IBD 732-734. Info: (323) 226-7923


8:30 – 9:30 a.m.: Department of Medicine: “Biomarkers of Acetaminophen Toxicity,” Laura James, University of Arkansas for Medical Sciences. Hastings Auditorium. Info: (323) 442-1283

9:45 a.m.: Department of Medicine: “Biomarkers of Acetaminophen Toxicity,” Laura James, University of Arkansas for Medical Sciences. Hastings Auditorium. Info: (323) 442-1283

Noon - 1 p.m.: Center for Applied Molecular Medicine Monthly Seminar Series: “Tim’s as the Fourth Dimension of Cancer Complexity,” Peter Rubin, Scripps Research Institute. Harkness Auditorium. Info: kigerber@usc.edu

Sunday, Nov. 17

1 – 6 p.m.: USC Institute for Genetic Medicine Art Gallery: “Bridge to the Soul: The Art of Healing” exhibition reception, various artists. USC IGM Art Gallery, 2250 Alcazar St., 2nd floor. Info: www.usc.edu/igm

Monday, Nov. 18

Noon - 1 p.m.: KHM Research Seminar Series: “Cracking the ‘Hilstone Code’ – New Lessons Learned from UHRF1,” Brian Straath, University of North Carolina, Chapel Hill. Aretsy Auditorium. Info: (323) 442-1476, ResAdv@keck.usc.edu

Tuesday, Nov. 19

Noon - 1 p.m.: Cancer Center Grand Rounds: “Mechanistic Dissection and Therapeutic Targeting of mTOR-Regulated Translation in Cancer,” Andrew Hsieh, USC. Aretsy Auditorium.

Notice: Deadline for calendar submission is 4 p.m. Monday to be considered for that week’s issue—although three weeks’ advance notice of events is recommended. Please note that timely submission does not guarantee an item will be printed. Send calendar items to The Weekly, KAM 400 or fax to (323) 442-3823, or email to nshs@usc.edu. Entries must include day, date, time, title of talk, first and last name of speaker, affiliation of speaker, location and a phone number for information.

Halloween on the Health Sciences Campus!

Halloween celebrations for kids of all ages took place on the Health Sciences Campus last week, both for spooky fun and to raise awareness for health research initiatives.

(Top Right) THIS TOUR IS ALWAYS A TREAT As part of their annual Halloween Harvest Parade, children from the USC Child Care Center visited Keck Medicine of USC faculty and staff at the fountain outside of Keck Hospital of USC and at the lobby of the USC Norris Cancer Hospital, collecting sweets and smiles before stopping at Pappas Quad to show off their costumes. Pictured here, Adelaide Doyt (left) and Prisha Patel go trick-or-treating on the Health Sciences Campus on Oct. 31.

(Bottom Right) CARVING OUT PUBLICITY Movember, an official global charity, raises awareness and funds to make an everlasting impact on men’s health, particularly in prostate and testicular cancer initiatives. This includes grant money awarded to the USC Catherine and Joseph Aresty Departments of Urology at the Keck School of Medicine of USC to conduct critical research to end prostate and testicular cancer. The Movember team from Keck Medicine of USC needs you to help raise funds during November by growing a mo’ (moustache) or supporting those who can. To learn more, visit movember.com/men-of-keck-medicine.

In case of an emergency...

Call the Emergency Information Phone: (213) 740-3323 The emergency telephone system can handle 1,400 simultaneous calls. It also has a backup system on the East Coast.

Visit the USC Web: http://emergency.usc.edu This page will be activated in case of an emergency. Backup Web servers on the East Coast will function if the USC servers are incapacitated.

(Left) The Care and the Craftsmanship of a Mo’

(Upper Right) Under the spell of Dr. Prophet

(By Tom DeSanto)

(Left) Sydney Cuenca (left), Adalyn Morali, and Joelle Udelman stop to look at a horror-themed treat bar at the Candy Coop in the lobby of the USC Norris Cancer Hospital.

(Upper Right) Dr. Prophet visits students in the Keck School of Medicine at the University of Southern California and talks about the importance of living a healthy lifestyle.

(Lower Right) The Keck School of Medicine of the University of Southern California community celebrates Halloween with a parade and costume contest.

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