USC Stem Cell NEWS

Scientist Leonardo Morsut is at the top of his game

For USC Stem Cell researcher Leonardo Morsut, the word "set" refers to a collection of scientific data. "Set" is also the prelude to spiking a volleyball over the net—something he used to do for a living as a professional athlete in Italy.

"Professional volleyball was always a side project," said Morsut. "Science was the main thing."

True to his words, Morsut has always put research first. Even while playing volleyball, he attended the University of Padova, where Galileo was once a lecturer. He earned bachelor's and master's degrees in medical biotechnologies, before pursuing a second bachelor's degree in mathematics.

Leonardo Morsut (Photo/Cristy Lytal)

Then, at the peak of his volleyball career, he quit to pursue a PhD at the University of Padova. He focused on gastrulation, the embryonic phase during which a ball of cells organizes itself into distinct layers as a prelude to organ formation. He then picked up a side project: how stem cells behave differently depending upon whether they're on a hard or a soft surface. He and his colleagues found that when stem cells are on a hard surface, they react by producing two signals—YAP and TAZ—that encourage them to become bone cells. He then accepted a postdoctoral fellowship in the laboratory of "synthetic biology" pioneer Wendell Lim, at the University of California, San Francisco.

"Synthetic biology is trying to bring the engineering approach of building things into biology," said Morsut.

He built a synthetic cellular communication system known as "synNotch." SynNotch co-opts a natural communication system, called Notch, in which a cell uses a sensor on its surface to recognize and trigger a response to a signal. Morsut swapped in a new sensor—allowing him to control which signal the sensor recognizes, and what the cell does in response. SynNotch or a similar system could have medical applications, such as engineering cells to attack tumors.

At USC, Morsut plans to use synNotch to direct the differentiation of stem cells into blood vessels that can support engineered organs. He is also developing additional synthetic biology tools, and looks forward to collaborating with researchers at the USC Viterbi School of Engineering and the USC Michelson Center for Convergent Bioscience, slated to open in fall 2017.

"I have high expectations," said Morsut.

About USC Stem Cell

USC Stem Cell is a collaborative and multidisciplinary effort working to translate the potential of stem cell research to the clinical imperative of regenerative medicine.

The initiative brings together nearly 100 research and clinical faculty members from the Keck School of Medicine of USC, Children's Hospital Los Angeles, the USC Viterbi School of Engineering, the USC Davis School of Gerontology, the Ostrow School of Dentistry of USC, the USC School of Pharmacy, and the USC Dornsife College of Letters, Arts and Sciences.

Artist plus researcher equals infinite inspiration

What happens when you pair 14 artists with 14 medical researchers? The answer is on display at the Hoyt Gallery on the Health Sciences Campus of the Keck School of Medicine of USC.

"Artist & Researcher" is the latest in a series of exhibitions curated by the Keck School's artist-in-residence, Ted Meyer.

Barbara Kolo's abstract representation of the kidney hangs beside one of the images from the laboratory of Andy McMahon that inspired the work. Andrea Bogdan's vivid series of colorful glass panels depicts a special type of cartilage cell that plays a vital role in repairing bone injuries, according to recent research from the laboratory of Francesca Mariani. Zeina Baltagi's artwork references lung diseases studied by the laboratory of Amy Firth. Other artworks focus on research about diseases ranging from melanoma to multiple sclerosis.

Artist Barbara Kolo and researcher Andy McMahon (Photo/Richard Carrasco)

Scientists aim to reduce bathroom breaks with stem cells

Having a baby can change a woman's life in one way that she is often too embarrassed to mention. Childbirth can cause urinary incontinence, which affects up to 13 million people and incurs $16.3 billion in annual treatment costs in the US.

To address this problem, this year's winners of the Eli and Edythe Broad Innovation Award are engineering a stem cell-based, biomaterials approach to promote the regeneration of the urethra. The one-year award provides $100,000 of direct research funding and $20,000 to cover services in relevant core facilities at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC.

The project brings together Larissa V. Rodríguez and Rong Zhang from the Department of Urology at the Keck School of Medicine of USC with Eun Ji Chung from the Department of Biomedical Engineering at the USC Viterbi School of Engineering.

They are developing a bioactive hydrogel—a type of water-logged gel made of peptides, which are the building blocks of proteins. They plan to inject this hydrogel around the urethra as a temporary bulking agent to assist with closure. At the same time, the hydrogel will actively deliver fat-derived stem cells and other factors to encourage tissue regeneration and the restoration of muscle tone. Eventually, the hydrogel will completely biodegrade, replaced by a regenerated and fully functional urethra. The team is testing this approach in rats, in hopes of garnering supplementary grant funding to advance this work into clinical trials.

"Urinary incontinence keeps people from enjoying their children, enjoying their grandchildren, going to a movie, doing activities that all of us expect in terms of having a happy life," said Rodríguez, who is also associate provost for faculty and student initiatives in health and STEM, director of Female Pelvic Medicine and Reconstructive Surgery (FPMRS) at the Keck Medicine of USC – Beverly Hills clinic, vice chair of academics for the USC Institute of Urology, and director of the FPMRS Fellowship at the Keck School. "It disproportionately affects women. And I feel a moral sense of really giving back to these women, and giving to a population that I treat by advancing the science."

Middle and high school students realize "pluripotential"

You can be anything you want—just like a stem cell. This was a key lesson for the 500 middle and high school students who attended the USC Stem Cell Day of Discovery in February on the Health Sciences Campus of the Keck School of Medicine of USC.

A day of discovery (Photo/David Sprague)

"It was a true joy to welcome the middle and high school students from our neighboring communities in Boyle Heights, El Sereno, Lincoln Heights, the San Gabriel Valley and throughout Los Angeles," said Rohit Varma, dean of the Keck School of Medicine of USC.

Hosted by USC Civic Engagement and USC Stem Cell, the event introduced the students to stem cell scientists. The students entered labs to get hands-on with microscopes and pipettes. They competed as contestants in the Stem Cell Edition of Family Feud, viewed colorful microscopy at a 3D computer station, and attended a research poster session and resource fair. They also toured the USC Norris Comprehensive Cancer Center and Keck Hospital of USC.

In addition to students, teachers and parents, the event welcomed leaders from the community, business and biotech sector, and local government.

Bone defects inspire perfect union between surgeon-scientist and stem cell researchers

As chair of the Department of Orthopaedic Surgery at the Keck School of Medicine of USC, Jay R. Lieberman regularly sees patients with bone defects too severe to heal. This unmet clinical need inspired him to team up with two stem cell biologists, Gage Crump and Francesca Mariani, to find new solutions.

They kicked off their collaboration in 2013, when they received a $400,000 grant from the Regenerative Medicine Initiative, funded by the Keck School's dean. This enabled the team to explore potential ways to repair human bones through lessons learned from two not-so-distant relatives: zebrafish and mice.

The project also attracted support from the National Institutes of Health (NIH). In 2013, Mariani received an NIH grant to develop a new bone regeneration model in mice. In 2014, Crump secured an additional NIH grant, advancing these investigations in zebrafish.

By studying zebrafish jaw repair, the team discovered that a special type of repair cell, called an "ossifying chondrocyte," is necessary for effectively healing bone. The Crump and Mariani labs published these findings in the journal *Development*.

The team found that similar repair cells also enable mice to heal large-scale rib injuries. To study these injuries further, Mariani recently secured a new $2.4 million NIH grant. Lieberman and Crump will remain key collaborators as they advance their findings.

"By using our new bone regeneration model, we can identify the stem cells needed for bone healing," said Mariani. "We are investigating a promising biological factor that stimulates these cells to mediate repair."

"Collaborative clinician-scientists such as Dr. Lieberman contribute exponentially to the success of any basic research effort," said Andy McMahon, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC. "They understand the clinical requirements needed to translate stem cell research into the future of patient care."

New Grant and Research Highlights

Yang Chai and a multi-institutional research team, called C-DOCTOR (Center for Dental, Oral and Craniofacial Tissue and Organ Regeneration), is one step closer to developing products that facilitate tissue regeneration, thanks to a grant from the National Institute of Dental and Craniofacial Research.

Denis Evseenko is using stem cells to regenerate cartilage as a treatment for osteoarthritis, with support from a grant from the California Institute for Regenerative Medicine (CIRM).

Amy Firth is using gene-edited stem cells to study rare mutations in cystic fibrosis, thanks to a Cystic Fibrosis Million Dollar Bike Ride pilot grant from the Penn Orphan Disease Center.

Justin Ichida is studying how genetic mutations affecting a type of immune cell, known as microglia, might increase the risk for developing Alzheimer's disease, with support from the John Douglas French Alzheimer's Foundation.

Rong Lu is studying how aging affects hematopoietic or blood-forming stem cells, thanks to a grant from the National Heart, Lung, and Blood Institute.

Francesca Mariani is examining the role of cartilage in healing large-scale bone injuries, supported by a Research Project Grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Joseph T. Rodgers is investigating how healing becomes impaired during aging, with support from a grant from the American Federation for Aging Research (AFAR).

Zea Borok is advancing our understanding of how lung cells regenerate, thanks to a grant from the National Heart, Lung, and Blood Institute. The research could translate into new treatments for common lung diseases, such as pulmonary fibrosis or chronic obstructive pulmonary disease.

Ching-Ling (Ellen) Lien, from Children's Hospital Los Angeles, is exploring the molecular and cellular mechanisms of the heart's circulatory system, thanks to a grant from the National Heart, Lung, and Blood Institute. The research will lead to a better understanding of cardiac development, as well as regeneration after injuries such as heart attacks.

Featured Image

On the Surface: This painting by Amanda Kwieraga, an alumna from USC's master of science in stem cell biology and regenerative medicine program, depicts a close-up look at the surface of a cell. Embedded in the surface are receptors, or proteins that receive the molecular signals, such as hormones, neurotransmitters, and nutrients, that allow for cell-cell communication.

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