USC Stem Cell NEWS

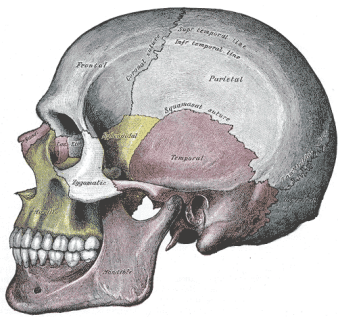
USC, UCLA and UCSF seek craniofacial cures

One in every 2,000 babies is born with a skull that can't grow normally. Various sections of these babies' skulls are fused together at joints called sutures, constricting the brain and disrupting vision, sleep, eating and IQ. For these patients, skull-expanding surgeries become an almost annual event.

Now, three leading universities for stem cell research — USC, UCLA and UCSF — have joined forces to find better solutions for craniofacial defects.

All three institutions have stem cell research centers established with support from Eli and Edythe Broad, and top scientists and clinicians in craniofacial biology.

"It's going to take a group of scientists across these different places with different expertise to make progress towards helping these patients," said Andy McMahon, director of USC's stem cell research center.



Human skull with sutures
(Image courtesy of *Gray's Anatomy*)

Mark Urata — a surgeon at USC, Children's Hospital Los Angeles and Cedars-Sinai Medical Center — underscores the need for less painful treatments. "The operation we perform is state-of-the-art," he said, "yet it's not good enough."

Yang Chai — director of the Center for Craniofacial Molecular Biology (CCMB) at the Ostrow School of Dentistry of USC — sees tremendous value in teaming up with clinicians such as Urata. "When someone has a craniofacial malformation, it really presents a significant challenge to that individual," said Chai. "By working closely with the clinicians, researchers can do more for these kids."

The group has already convened for two day-long faculty retreats, with funding from USC's CCMB, the UCSF Program in Craniofacial and Mesenchymal Biology, and the UCLA Clinical and Translational Science Institute. The next meeting will include postdoctoral fellows, graduate students and others.

They've also established a Craniofacial Anomalies Registry, a collection of DNA, tissue samples and information from patients with these relatively rare disorders. This enables researchers to more easily access these important materials.

Amy Merrill, assistant professor in the CCMB and Department of Biochemistry at USC, explained: "The ultimate goal is to help these children and come up with a therapy that reduces the stress they have to endure to correct these devastating disorders."

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 more than 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. USC Stem Cell is also creating new educational opportunities with the USC Marshall School of Business and the USC Roski School of Art and Design.

USC and CIRM celebrate stem cell awareness day

Please join USC and the California Institute for Regenerative Medicine (CIRM) in celebrating Stem Cell Awareness Day on October 8, 2014 from 4 to 6 p.m. in the lobby of the Eli and Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at USC.

Guests can view research posters and mingle with USC Stem Cell researchers and affiliated faculty from across the university. Light refreshments will be served, and parking will be available.

For more information, contact Kelli-Ann Nakayama at knakayama@med.usc.edu.

Min Yu targets the "seeds" of breast cancer metastasis

For breast cancer patients, the era of personalized medicine may be just around the corner, thanks to recent advances by USC Stem Cell researcher Min Yu and scientists at Massachusetts General Hospital and Harvard Medical School.

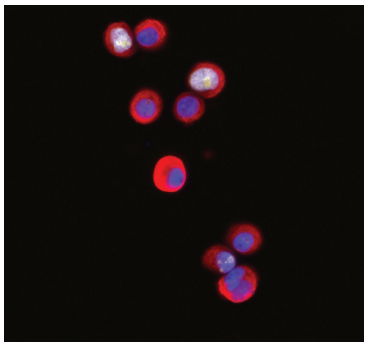
In a July 11 study in *Science*, Yu and her colleagues report how they isolated breast cancer cells circulating through the blood streams of six patients. Some of these deadly cancer cells are the "seeds" of metastasis, which travel to and establish secondary tumors in vital organs such as the bone, lungs, liver and brain.

Yu and her colleagues managed to expand this small number of cancer cells in the laboratory over a period of more than six months, enabling the identification of new mutations and the evaluation of drug susceptibility.

If perfected, this technique could eventually allow doctors to do the same: use cancer cells isolated from patients' blood to monitor the progression of their diseases, pre-test drugs and personalize treatment plans accordingly.

In the six estrogen receptor-positive breast cancer patients in the study, the scientists found newly acquired mutations in the estrogen receptor gene (ESR1), PIK3CA gene and fibroblast growth factor receptor gene (FGFR2), among others. They then tested either alone or in combination several anticancer drugs that might target tumor cells with these mutations and identified which ones merit further study. In particular, the drug Ganetspib — also known as STA-9090 — appeared to be effective in killing tumor cells with the ESR1 mutation.

"Metastasis is the leading cause of cancer-related death," said Yu, assistant professor in the Department of Stem Cell Biology and Regenerative Medicine at the Keck School of Medicine of USC. "By understanding the unique biology of each individual patient's cancer, we can develop targeted drug therapies to slow or even stop their diseases in their tracks."



Circulating tumor cells from a breast cancer patient (Image by Maria C. Donaldson and Min Yu)

Additional co-authors include Aditya Bardia, Nicola Aceto, Francesca Bersani, Marissa W. Madden, Maria C. Donaldson, Rushil Desai, Huili Zhu, Valentine Comaills, Zongli Zheng, Ben S. Wittner, Petar Stojanov, Elena Brachtel, Dennis Sgroi, Ravi Kapur, Toshihiro Shioda, David T. Ting, Sridhar Ramaswamy, Gad Getz, A. John Iafrate, Cyril Benes, Mehmet Toner, Shyamala Maheswaran and Daniel A. Haber.

This work was supported by grants from the Breast Cancer Research Foundation, Stand Up to Cancer, the Wellcome Trust, National Foundation for Cancer Research, National Institutes of Health CA129933, National Institute of Biomedical Imaging and Bioengineering EB008047, Susan G. Komen for the Cure KG09042, National Cancer Institute–MGH Proton Federal Share Program, the MGH-Johnson and Johnson Center for Excellence in CTCs, and the Howard Hughes Medical Institute.

Michael Bonaguidi contributes brain power to USC

As a child, Michael Bonaguidi dreamed of shaping cities as an architect or engineer. Now, he dreams of shaping brains as the newest principal investigator to join USC's Department of Stem Cell Biology and Regenerative Medicine.

"Growing up on Legos and Lincoln Logs, I was very fascinated with building things," he said. "As I took more biology courses and was exposed to other facets of science — from chemistry to physics — I became more interested not in the outside but within. And that's what got me into bioengineering versus structural engineering."

When it comes to brains, Bonaguidi already has his building blocks. His team studies individual neural stem cells within the adult brain. These stem cells have the potential to spawn more stem cells, or to form new neurons and their critical supporting cells.

Bonaguidi found these neural stem cells in part of the brain known as the hippocampus, involved in learning, memory and emotions. These stem cells offer possibilities for treating symptoms associated with Alzheimer's disease and mood disorders.

He's also on the quest to discover whether cells in other parts of the brain can regenerate following head trauma, stroke or various types of brain damage.

"In terms of repair and regeneration, my approach is to learn the lessons of what the brain can do, identify what it can't do and overcome those limits," he said.

Michael Bonaguidi (Photo by Joseph Shin)

One way to push these limits could be by finding potential drugs and chemicals that encourage neural stem cells to either last longer or make particular types of cells. This could usher in new treatments for physically and mentally debilitating conditions.

Bonaguidi has the ideal training to tackle these problems. A native of Chicago, he completed his undergraduate studies in bioengineering at Marquette University. He then pursued a PhD in neuroscience from Northwestern University and postdoctoral training in stem cells at Johns Hopkins University.

"Michael brings an engineer's view of systems and a biologist's view of function to the rare stem cell populations that continue to make new nerve cells throughout our lives," said Andy McMahon, director of USC's stem cell research center. "His research will enhance the existing strength in regenerative neuroscience in our center and synergize with the strong USC neuroscience community."

Bonaguidi is eager to continue his research as a new principal investigator at USC's stem cell research center and the Zilkha Neurogenetic Institute in January 2015.

"For me, I think the sky is the limit at USC," he said. "It's in a tremendous growing phase right now, and that's made very obvious by the substantial investment in stem cell research, neuroscience and imaging."

As a half-marathon runner, hiker and cyclist, he's also looking forward to Southern California's spectacular mountains and year-round sunshine. For him, this is the best way to recharge and "regenerate" his own brain, so he can better work towards regenerating the brains of the patients that will eventually benefit from his research.

"Running is very liberating, especially when so much time is spent in a lab," he said. "You can block out everything and be more in touch with yourself, or you can sort through scientific problems and go to the place where you want to go in your mind."

Research Highlights

Gage Crump's lab published a study on the mutation that causes the facial deformities, immune deficiencies and other birth defects associated with DiGeorge syndrome. The lab showed that the gene in question, called TBX1, regulates cell differentiation and migration through the "Wnt signaling pathway," an important group of molecules that work together to control cell functions. *(Development)*

Francesca Mariani and colleagues showed that the dense connective tissue that surrounds cartilage might contain stem cells that are important for cartilage repair. *(Journal of Bone and Mineral Research)*

Valter Longo and colleagues showed that cycles of prolonged fasting not only protect against immune system damage during chemotherapy, but also induce immune system regeneration by shifting stem cells from dormancy to self-renewal. *(Cell Stem Cell)*

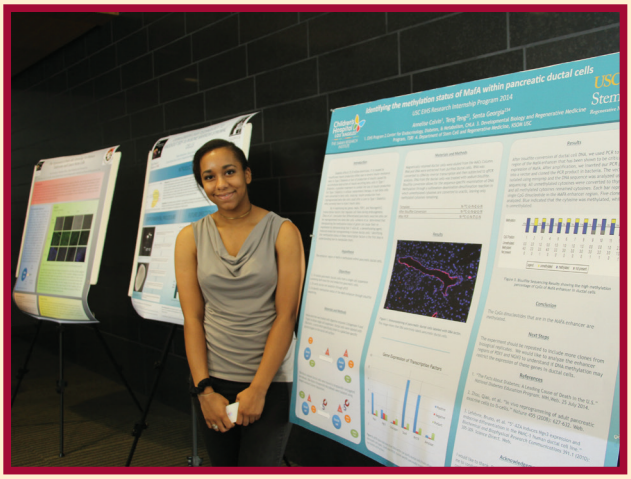
Andy McMahon and collaborators from the University of Queensland grew and expanded stem cell-like cells from the adult mouse kidney's collecting duct, a tube structure that catches urine. These expanded cells, when injected into young mice, can form more collecting duct, suggesting a potential role in kidney repair. *(Journal of the American Society of Nephrology)*

Tracy Grikscheit and colleagues tested a new way to preserve small pieces of intestine for later use. They found that vitrification, a method of freezing tissues without forming ice crystals, is a better way to preserve live tissue than the conventional freezing technique. *(Journal of Surgical Research)*

Fatih Uckun and colleagues identified a potential drug that inhibits a protein called "spleen tyrosine kinase (SYK)," which regulates cell death. Their nanoparticle formulation of this potential drug proved safe and effective in killing human leukemia implanted in mice — an important first step in moving the drug into clinics. *(Journal of Cancer Therapy)*

Cheng-Ming Chuong and colleagues transplanted skin from old to young mice, showing that old skin can restore nearby hair growth. This could be due to several factors, including a reducation in the amount of a molecule called follistatin in the skin as mice age. *(Journal of Investigative Dermatology)*

Featured Image



Annelise Colvin from Harvard-Westlake School was one of 23 students to celebrate their graduations from the USC Early Investigator High School (EiHS) and USC CIRM Science, Technology and Research (STAR) programs. *(Photo by Cristy Lytal)*

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