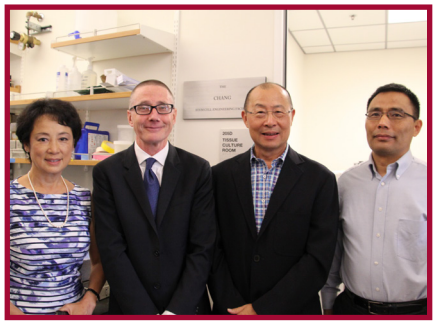
USC Stem Cell NEWS

USC opens Chang Stem Cell Engineering Facility

USC Stem Cell faculty and staff welcomed their supporters, the Chang and Choi families, and nearly 100 of their friends to celebrate the grand opening of the Chang Stem Cell Engineering Facility, located in the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC. Established with a generous gift from the Chang family, the new facility serves researchers at USC and elsewhere.

"My hope for this facility is to change people's lives and make people live longer and better," said alumnus Daniel Chang, who gave the gift with his wife Cai Li, son Jorlly, and daughter and USC freshman Carrisa.

The new facility genetically modifies embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), which can be derived and propagated by the existing CIRM Stem Cell Core Facility. Genetically modified ESCs and iPSCs provide a way to investigate disease mechanisms and develop treatments. With these genetic modifications, investigators can also expose some of the cells to thousands of potential drugs at the existing Choi Family Therapeutic Screening Facility.



From right, Qi-Long Ying, director of the Chang Stem Cell Engineering Facility; Daniel Chang; Andy McMahon, director of USC's stem cell research center; and Cai Li Chang (Photo/Cristy Lytal)

"USC's stem cell research center is a one-stop-shop where scientists can have iPSCs derived, genetically modified and screened for therapeutic drugs," said Andy McMahon, director of USC's stem cell research center.

"This is a unique pipeline that no other institution has."

Qi-Long Ying, director of the Chang Stem Cell Engineering Facility, added: "By combining the power of genome editing and stem cell technology, this facility provides a versatile and efficient stem cell engineering platform to help investigators from USC and beyond create disease models in a dish and develop treatments."

McMahon is already using gene editing to create tools for studying kidney development, and USC Stem Cell's Justin Ichida is using it to create models of amyotrophic lateral sclerosis and hearing loss. And this is only the beginning.

"Genome editing is one of the most powerful tools to study the genetic control of organ development and biological processes, to explore disease mechanisms, and to treat genetic disorders," said McMahon. "This facility enables every scientist to access the technical expertise to support and accelerate their quests for treatments for human disease."

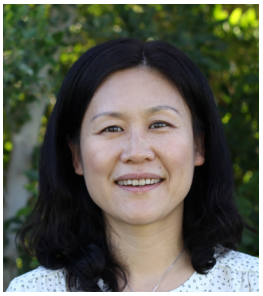
About USC Stem Cell

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. 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.

The Baxter Foundation awards grants to USC scientists

It takes a special doctor to push beyond existing patient treatments and engage in the quest for new ones. That's why the Donald E. and Delia B. Baxter Foundation selected three assistant professors involved in innovative medical research to receive $100,000 awards.



Min Yu from the Department of Stem Cell Biology and Regenerative Medicine will use her award to make progress towards new approaches to treating patients with breast cancer. Yu's approach involves drawing blood from a cancer patient, filtering out the rare circulating tumor cells (CTCs) and allowing these cells to multiply in the lab. She is now making progress towards identifying what she believes are the most lethal subset of CTCs, called metastatic cancer stem cells (MCSCs). Some of these MCSCs show a propensity for establishing metastatic tumors in one organ as opposed to another. To better understand these patterns, Yu is studying MCSC genes and the "on-off switches" for their genes, called epigenetic regulators.

Jon-Paul Pepper, a facial plastic surgeon and USC Stem Cell principal investigator, is addressing nerve injuries that cause weakness or paralysis in collaboration with 2014 Baxter Foundation Fellow Justin Ichida, assistant professor of stem cell biology and regenerative medicine. Knowing that muscles can permanently atrophy without a nerve supply, Pepper is injecting stem cell-derived nerve cells into mice with sciatic nerve injuries to provide input and support to the muscles while the native nerves heal.

A neuroradiologist, **Kevin S. King** from the Department of Radiology is studying dementia and cognitive decline. King will use functional Magnetic Resonance Imaging to assess the responsiveness of blood vessels in the brains of 160 people inhaling low levels of carbon dioxide. For three years, he'll follow up with the patients to determine if unresponsive brain blood vessels predict cognitive decline and dementia.

USC selects Broad Clinical Research Fellows

The Broad Clinical Research Fellowships are enabling physician-investigators to explore stem cell-based approaches related to four very different medical conditions. Each one-year fellowship provides $74,000 of support, and is potentially renewable for a second year.

Andre Luis de Castro Abreu is studying a mechanism of kidney repair regulated by the organ's macula densa cells, which sense and communicate salt concentration and fluid flow. He is using imaging to confirm that this mechanism is present in human kidneys, and to learn how to stimulate it to enhance kidney repair.

Victoria Forte is investigating if cancer stem cells (CSCs) are present in the blood of tumor-free cancer patients at least one-year post-treatment. By detecting and analyzing these CSCs, she hopes to determine if CSCs can be targeted post-treatment to prevent cancer recurrence.

Rodrigo Martínez Monedero is studying why adult mammals cannot repair deafness. To do this, he hopes to explore epigenetic regulation, or the genetic switch that might trigger an important population known as adult supporting cells to regenerate the inner ear.

Kathy Schall is exploring intestinal regeneration. She'll investigate the molecular signals — including the Wnt signaling pathway — that trigger intestinal regeneration in zebrafish, and identify stem and progenitor cells within the intestines. Her goal is to develop new treatments for patients with short bowel syndrome.

Stem Cell retreat brings together Calif.'s Broad centers

Working alone, a scientist or university can only make so much progress in finding answers or new treatments for diseases ranging from HIV to cancer to diabetes. That's why nearly 300 scientists from USC, UCLA and UCSF gathered for a Tri-institutional Stem Cell Retreat. Held in Santa Barbara in May, the retreat showcased innovative projects from the universities' stem cell research centers, all of which were established with support from Eli and Edythe Broad and the California Institute for Regenerative Medicine.

"If we want a true measure of success for the meeting, it won't simply be that we've had a good time, but that our scientific interchange provides new insights and collaborative opportunities," said Andy McMahon, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC.

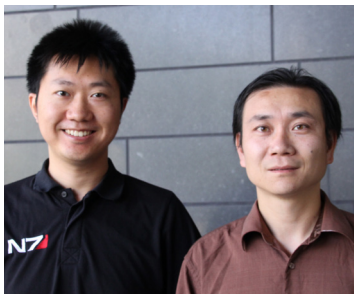
Keynote speaker Amy Wagers from the Harvard Stem Cell Institute detailed an experiment in which she connected the circulatory systems of an old mouse and a young one. The old mouse experienced youthful benefits, including a decrease in heart enlargement and an increase in the regeneration of muscle, neurons and the insulin-producing beta cells of the pancreas. Conversely, the young mouse suffered ailments of age, including a decrease in the regeneration of muscle, neurons and beta cells. Her goal is to use these youthful blood-borne factors to treat age-related dysfunction.

In all, about 30 principal investigators, postdoctoral scholars and PhD students discussed advances relevant to many diseases. An additional 100 scientists presented their research on posters, with 10 giving brief poster highlight talks.

"I've learned so much from this meeting," said McMahon. "It's a rapidly moving field, so I think we need a retreat next year as well."

USC postdocs win Doerr Stem Cell Challenge Grants

Just as there are times when two heads are better than one, there are times when two labs are better than one. Thanks to the new Doerr Stem Cell Challenge Grants, teams of postdoctoral researchers from different USC labs have each received up to $10,000 in funding to pursue interdisciplinary one-year projects.



From top left, Lindsey Mork and Michaela Patterson; from bottom left, Ang Li and Yuwei Li (Photos/ Cristy Lytal)

One winning team brings together two postdocs that work miles apart. Ang Li studies feather development in Cheng-Ming Chuong's lab on the Health Sciences Campus, and Yuwei Li researches imaging techniques in Scott E. Fraser's lab on the University Park Campus. Together, they will use pioneering imaging tools to study cell behavior during feather development. They will monitor how cells move and organize in response to bioelectric cues, or the electric currents that occur within all living organisms.

The other award went to two postdocs in the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC — Lindsey Mork from Gage Crump's lab and Michaela Patterson from Henry Sucov's lab. They'll use zebrafish to investigate the role of a gene, known as Tnni3k, in heart regeneration. When activated, this gene appears to lower the number of cells called mononuclear diploid cardiomyocytes, which form new cardiac muscle after heart attacks.

"The program's goal is to stimulate new interdisciplinary stem cell research projects initiated and proposed by students and postdocs," said Andy McMahon, chair of USC Stem Cell's executive committee. "This will enhance their creativity and independence, as well as their ability to compete for future grants supported by agencies such as the NIH."

Research Highlights

Andy McMahon and colleagues demonstrated how a protein called Sox9 regulates the production of cartilage. The study clarifies Sox9's role in causing a condition of bent bones and respiratory failure called campomelic dysplasia. *(Cell Reports)*

Berislav Zlokovic, Justin Ichida and collaborators revealed how the risk for Alzheimer's disease increases when the activity of a gene called PICALM decreases, dimishing the ability to clear toxic amyloid-beta proteins from the brain. *(Nature Neuroscience)*

Neil Segil's lab revealed that more than 3,000 genes in the cells of the inner ear are affected by drugs called aminoglycoside antibiotics, which cause hearing loss in up to one-fourth of patients. The knowledge gained may provide potential targets to alleviate similar hearing damage. *(Frontiers in Cellular Neuroscience)*

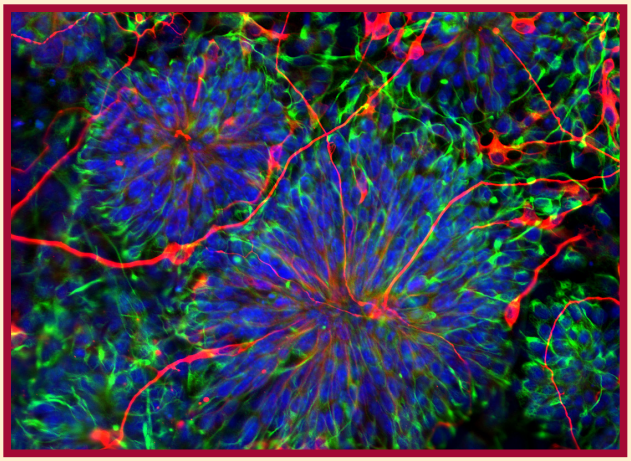
Valter Longo and collaborators showed that cycles of a four-day low-calorie diet that mimics fasting cut visceral belly fat, elevated the number of progenitor and stem cells in several organs, boosted neural regeneration, and improved learning and memory in mice. A pilot clinical trial in humans showed decreased risk factors for aging, diabetes, cardiovascular disease and cancer without major adverse effects. *(Cell Metabolism)*

Scott Fraser and collaborators presented an imaging technique, incorporating 2-photon light sheet microscopy, that captures the dynamic three-dimensional beating motion of the live embryonic zebrafish heart at subcellular resolution. This enables more detailed observation of how genetics shape heart development. *(Biomedical Optics Express)*

Henry Sucov, Ellen Lien and colleagues published two studies detailing a new source for cells that can develop into blood vessels and identifying the signaling protein, called CXCL12, which guides this process in zebrafish. They also described how CXCL12 promotes the maturation of immature blood vessels in mice. *(Developmental Cell)*

Tracy Grikscheit and collaborators described how zebrafish provide a fast and inexpensive way to study the role of intestinal stem cells in recovering from short bowel syndrome, a condition that also afflicts humans. *(American Journal of Physiology: Gastrointestinal and Liver Physiology)*

Featured Image



Embryonic stem cells differentiated into neurons (green: stem cells, red: neurons) *(Image by In Kyoung Mah/Mariani Lab)*

Your Support

To learn how you can transform medicine by supporting USC Stem Cell, contact:

Keck School of Medicine of USC
(323) 442-1013
stemcelldev@usc.edu
stemcell.usc.edu/donate

USC Stem Cell