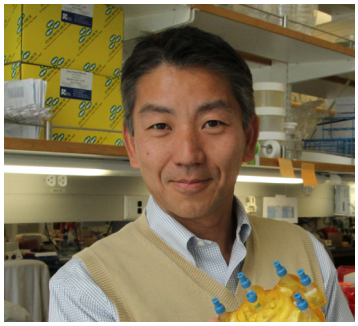
USC Stem Cell NEWS

Calif. stem cell agency awards $4.5 million to USC

Three scientists from Keck Medicine of USC have won grants exceeding $4.3 million from the California Institute for Regenerative Medicine (CIRM) for research into creating a temporary liver, finding novel ways to treat immune and blood diseases, and developing animal models for heart failure, diabetes and neurodegenerative diseases. The grants, received by USC Stem Cell researchers Paula Cannon, Toshio Miki and Qi-Long Ying, are part of the CIRM Tools and Technologies initiative.



From top, Paula Cannon, Toshio Miki and Qi-Long Ying (Photos/ Cristy Lytal and Don Milici)

Miki's team is developing an "extracorporeal liver support system (ELS)" for patients with liver failure. The ELS will house human liver cells, produced from stem cells, in a device outside of the body but connected to the circulation, allowing patients to recuperate without undergoing liver transplantation. The project is an international collaboration with Katrin Zeilinger at Charité University, Berlin, and Frank Shubert at Stem Cell Systems GmbH with support from Germany's Federal Ministry for Education and Research.

Cannon is improving the precision and safety of "targeted nucleases," which she describes as "scissors" used to edit specific genes in blood-forming stem cells. Cannon hopes to develop the next generation of targeted nucleases to treat severe immune deficiencies and blood diseases, such as sickle cell disease.

Ying is using stem cell-based technology to create new laboratory rats for research on heart failure, diabetes and neurodegenerative diseases. Transgenic rats will provide a more powerful tool than transgenic mice, because rats are more similar to humans in their physiology. Ying is collaborating with USC colleagues Justin Ichida, Bangyan Stiles and Ching-Ling Lien, also affiliated with Children's Hospital Los Angeles.

According to Andy McMahon, chair of the executive committee of USC Stem Cell, "We are committed to developing the critical tools and technologies for the broader scientific community to translate stem cell discoveries into patient therapies."

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 Hearst Foundations establish fellowships at USC

It takes more than materials and methods to be a successful young scientist — it also takes means. With this in mind, the Hearst Foundations have given a gift of $250,000 to support junior postdoctoral fellows pursuing stem cell research at USC. As Hearst Fellows, these postdoctoral researchers will launch their careers with a startup package, including a year's salary and benefits. They will access world-class facilities and equipment — including the William Randolph Hearst Foundation Imaging Laboratory, supported by a previous $100,000 gift from the Hearst Foundations. The fellows will also connect with faculty and colleagues across the university through the USC Stem Cell Initiative, a university-wide collaboration bringing together nearly 100 researchers. As part of this vibrant community, the fellows will have the resources to acquire the preliminary data needed to compete for nationwide awards and fellowships.

This gift from the Hearst Foundations comes on the heels of a gift from The Broad Foundation in support of senior postdoctoral fellows. These gifts enable USC to recruit today's promising stem cell scientists to usher in tomorrow's stem cell-based therapies.

Justin Ichida, Sanofi and DRVision fight ALS

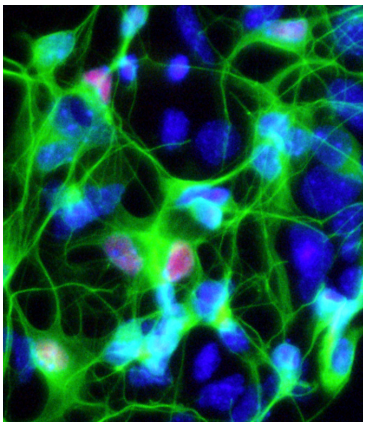
Justin Ichida has marshaled the expertise of Sanofi and DRVision Technologies along with $1.5 million in federal funding to find drugs to fight amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. In ALS, patients suffer from the death of the cells that transmit signals from the brain to the muscles, called motor neurons, leading to paralysis and usually resulting in fatal respiratory failure within three to five years of diagnosis.

This grant comes not from the typical sources at the National Institutes of Health (NIH), but from the Department of Defense (DoD). Each year, the DoD funds two ALS Therapeutic Development Awards, because veterans are more likely than civilians to suffer from this disease for reasons that are not understood.

An assistant professor in the Department of Stem Cell Biology and Regenerative Medicine and the director of the Choi Family Therapeutic Screening Facility, Ichida has pioneered a way to pre-screen drug-like compounds in the laboratory on cells from patients with the most common form of ALS. To accomplish this, Ichida directly reprograms patients' skin cells into motor neurons, which exhibit the disease's signature degeneration. He then puts these reprogrammed motor neurons into a robotic screening machine, which exposes them to drug-like compounds and captures microscopic movies of the results. In his pilot screening of 800 compounds, he found four that kept these motor neurons alive in the Petri dishes — and could eventually do the same in patients.

With his new grant and industry partners, Ichida will scale up his efforts. He'll screen 2,000 FDA-approved drugs in his laboratory. Sanofi will screen an additional 40,000 drug-like compounds. DRVision Technologies will design software to analyze the resulting microscopic images for signs of improved motor neuron survival. If the study reveals viable "hits," expert chemists at Sanofi may develop these compounds into safe, effective drugs that are stable in the blood and possess other prerequisites to testing in a clinical trial.

Ichida believes that partnerships between academia, industry and government can accelerate the development of new treatments for patients with ALS and other fatal diseases.



Top, Justin Ichida (Photo/Cristy Lytal); bottom, motor neurons derived from a patient with ALS (Image/Ichida Lab)

USC Stem Cell Symposium creates scientific synergy

Provost Michael Quick convened the inaugural USC Stem Cell Symposium with a truth about the future of regenerative medicine: "it will take a dedicated community of scholars across the disciplines to have maximum impact."

The January symposium brought together precisely such a community, with speakers from USC's schools of medicine, dentistry, gerontology and engineering and The Saban Research Institute of Children's Hospital Los Angeles. Held at the Keck School of Medicine of USC, the event was hosted by USC Stem Cell.

Andy McMahon, chair of the USC Stem Cell executive committee, shared his vision of engaging even more scholars from beyond the scientific realm. He also unveiled two new opportunities: The USC Stem Cell Hearst Fellowship will support junior postdoctoral fellows pursuing stem cell research at USC. The Doerr Stem Cell Challenge Grants will fund projects uniting graduate students or postdocs in two or more labs.

The USC Stem Cell Regenerative Medicine Initiative Awards enable additional multi-investigator research collaborations among USC-affiliated faculty members. Three winning teams presented their progress.

Another highlight was the keynote address by Fred H. Gage from the Salk Institute for Biological Sciences and the University of California, San Diego. Gage introduced "mobile elements," genetic material that that can move from one part of the genome to another.

At the end of the day, USC's stem cell scientists left the symposium informed and inspired to translate discoveries into new treatments for diseases.

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 assistant professor 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, that's what got me into bioengineering versus structural engineering."

Michael Bonaguidi (Photo/Cristy Lytal)

When it comes to brains, Bonaguidi already has his building blocks. He studies individual neural stem cells within the adult brain. These stem cells can spawn more stem cells, or form new neurons and supporting cells.

"We've been exploring what neural stem cells can do, both under normal conditions and after injury," he said.

One way to promote regeneration could be by finding potential drugs that encourage neural stem cells to last longer or make particular cell types. This could usher in new treatments for debilitating conditions.

Bonaguidi has the ideal training. A native of Chicago, he did his undergraduate studies in bioengineering at Marquette University, his PhD in neuroscience at Northwestern University and his postdoctoral training in stem cells at Johns Hopkins University.

He is eager to continue his research as a principal investigator: "For me, the sky is the limit at USC."

Research Highlights

Cheng-Ming Chuong and collaborators demonstrated that by plucking 200 hairs in a specific pattern and density, they can induce up to 1,200 replacement hairs to grow in a mouse. *(Cell)*

Neil Segil and collaborators created a mouse strain with the mutations responsible for Cockayne syndrome, a DNA repair disorder with symptoms including hearing loss. This will enable researchers to test how DNA damage in the inner ear cells contributes to hearing loss. *(The Journal of Neuroscience)*

Yang Chai and collaborators uncovered biological mechanisms controlling the stem cells that contribute to the continuous growth of the rodent incisor. Their discoveries may inform future strategies for tooth regeneration. *(Developmental Cell)*

Yang Chai's group also identified stem cells responsible for craniofacial bone growth in mice — a finding that advances the understanding of craniosynostosis, a birth defect in which a fused skull constricts the developing brain. *(Nature Cell Biology)*

Tracy Grikscheit and collaborators showed that small intestine grown from human cells replicates key aspects of a functioning human intestine, including elements of the mucosal lining and support structures. *(American Journal of Physiology: GI & Liver)*

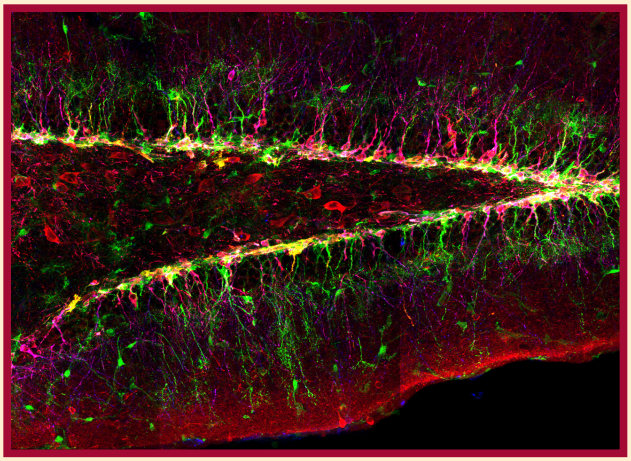
Henry Sucov and colleagues discovered that rodents, like humans, have fat called epicardial adipose tissue in their hearts. They also uncovered the origin and molecular signals that induce the formation of this tissue — enabling the study of its possible role in heart disease. *(Proceedings of the National Academy of Sciences)*

Ellen Lien and collaborators revealed that neonatal mouse hearts can recover normal function after mild injury. If researchers can extend this capacity from newborns to juveniles or adults, it could usher in new treatments for heart disease. *(Developmental Biology)*

Fatih Uckun and collaborators developed a new protein, called CD19L-sTRAIL, that proved effective at killing drug-resistant acute lymphoblastic leukemia cells in mice. *(Journal of Clinical Investigation)*

Chong Pyo Choe and Gage Crump described how molecular cues regulate zebrafish head development. This can shed light on how this important process works and why it sometimes goes awry. *(Development)*

Featured Image



A slice of adult mouse brain containing neural stem cells and newborn neurons *(Image by Michael Bonaguidi)*

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