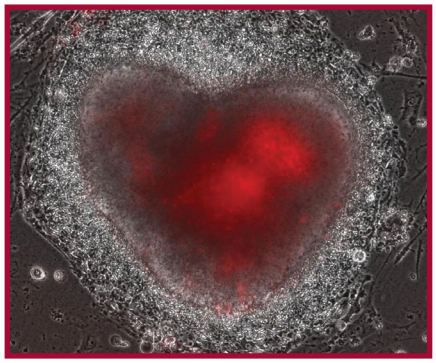
USC Stem Cell NEWS

LA wins bid to host major stem cell conference

In recognition of its growing stature as an incubator for the biosciences, Los Angeles will be the host city for the 2019 International Society for Stem Cell Research (ISSCR) Conference. With the generous support of the Choi Family, USC Stem Cell will co-sponsor the conference, and the city-owned Los Angeles Convention Center will serve as the venue.

"We are extremely excited to welcome the International Society for Stem Cell Research to Los Angeles for the first time ever and look forward to their 17th annual meeting in 2019," said Mayor Eric Garcetti. "L.A. is the latest and most innovative bioscience hotspot in the state, and ISSCR's choice is a reflection of the scientific advances occurring in our city today."

Previous host cities include Barcelona, Boston, San Francisco, Stockholm, Toronto and Yokohama.



Stem cells labeled with red fluorescent protein (Image/Wen-Hsuan Chang)

Rohit Varma, interim dean of the Keck School of Medicine of USC and director of the USC Roski Eye Institute, underscored the meeting's significance.

"We are honored to welcome the international community of leading stem cell researchers to the 2019 ISSCR Conference in Los Angeles," he said. "By bringing together these exceptional scientific minds, the conference will serve as an incubator for new ideas and research collaborations, which will eventually translate into better, more creative therapies for patients."

USC Stem Cell supporter KC Choi extended his "thanks to USC for giving me this rare opportunity to support stem cell researchers from all over the world."

As chair of USC Stem Cell's executive committee, Andy McMahon thanked Mayor Garcetti and the Chois and extended his "warmest welcome to the visionaries and leaders who will attend this event, highlighting research at USC and sister institutions."

Eli Broad, who with his wife Edythe has funded three stem cell centers that bear their names at USC, UCLA and the University of California, San Francisco, added: "California has become the world leader in stem cell research, with some of the most promising research being conducted in Los Angeles. Edye and I look forward to the increased knowledge and scientific collaborations that will come out of the 2019 International Society for Stem Cell Research."

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.

Second cohort of Broad Clinical Research Fellows chosen

The second cohort of Broad Clinical Research Fellows is making strides towards finding stem cell-based therapies for lymphedema in cancer patients, large bone fractures and short bowel syndrome. To support full-time research related to stem cell biology and regenerative medicine, each fellowship provides $65,000 for salary, $7,500 for supplies and $1,500 for meetings, and is potentially renewable for a second year.

In Tracy C. Grikscheit's lab at Children's Hospital Los Angeles, surgeon-scientist **Christopher Schlieve** will work to create stem cell-derived intestines for patients with short bowel syndrome (SBS), which leaves them unable to absorb adequate nutrition after losing part of the intestines. Grikscheit's lab has already succeeded in taking the first step in growing human stem cell-derived tissue-engineered small intestine (TESI) in a mouse. However, this TESI lacks the proper nerves to contract the intestines and move food through the system. Schlieve's goals are not only to add nerves to the stem cell-derived TESI, but also to do so in a pig—so that the intestines will be the correct size to transplant into a human newborn baby with SBS.

A general surgery resident at the Keck School of Medicine of USC, **Gene K. Lee** will explore a stem cell-based treatment for lymphedema, limb swelling after cancerous lymph node removal. He'll reprogram rat skin cells into stem cells, and implant them onto a scaffold in lymphedematous rat limbs. He hopes that the stem cells will form lymph nodes and channels to carry fluid out of the limbs. He'll work under Young Kwon Hong and Alex Wong in the Department of Surgery.

Keck School orthopaedic surgery resident **R. Kiran Alluri** will focus on ways to use stem cells to treat critical bone defects, or fractures too large to heal on their own. He plans to deliver human stem cells that produce a protein that encourages bone growth, called BMP-2, to rats with critical bone defects to promote healing. He will work under Jay R. Lieberman, professor and chair of the Department of Orthopaedic Surgery, and professor of biomedical engineering at the USC Viterbi School of Engineering.

Researchers receive inaugural Broad Innovation Awards

Two teams of scientists have won the inaugural Eli and Edythe Broad Innovation Awards in Stem Cell Biology and Regenerative Medicine at USC. This year's competition provides $120,000 each to the teams for engineering and studying miniaturized organs.

One team brings together Justin Ichida, assistant professor of stem cell biology and regenerative medicine; Megan McCain, assistant professor of biomedical engineering, and stem cell biology and regenerative medicine; and Dion Dickman, assistant professor of biological sciences. They will create a new approach for studying amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. This fatal disease damages the intersections between motor nerve cells and muscle cells, called neuromuscular junctions (NMJs). Normally, motor nerve cells release chemicals into these NMJs, signaling to the muscle cells to contract, and enabling movement. The team will use samples of skin or blood cells from patients with ALS to generate NMJs on a gelatin "chip." They will then study these patient-specific NMJs to determine why they degenerate and how to rescue them.

The other team unites Keyue Shen, assistant professor of biomedical engineering, and Rong Lu, assistant professor of stem cell biology and regenerative medicine. The team will pioneer an approach for studying the stem cells in bone marrow that replenish the blood and immune systems. These stem cells, called hematopoietic stem cells or HSCs, adjust their behavior according to molecular signals, such as oxygen and proteins in their environment, or niche. The team will recreate these various aspects of the HSC niche in a Petri dish as a way to study and improve bone marrow transplantation, a common cancer treatment.

Justin Ichida named New York Stem Cell Foundation - Robertson Investigator

Some people see an award as remuneration for work well done. Upon being named a New York Stem Cell Foundation (NYSCF) – Robertson Investigator, ALS researcher Justin Ichida sees his award as motivation for work still left to do.

"If you just look at the people who have won this award before, these are people who have really revolutionized the field of stem cell research and disease research," said Ichida, assistant professor of stem cell biology and regenerative medicine at USC. "So this award not only speaks to the potential that our lab's research has shown, but also motivates us to do some big science, like fellow winners."

Justin Ichida (Photo/Cristy Lytal)

The NYSCF Stem Cell Investigator Program provides $1.5 million, five-year awards to creative young scientists pursuing high-risk, high-reward stem cell research with the potential to accelerate cures for major diseases. The program received initial support from The Leona M. and Harry B. Helmsley Charitable Trust, and expanded through a Robertson Foundation grant.

Ichida is using his prize to find new ways to treat amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. Patients suffer from the degeneration of their motor neurons, which communicate between the brain and muscles. This usually results in paralysis and fatal respiratory failure within three to five years of diagnosis.

Ichida is using stem cell technology to reprogram skin and blood cells from ALS patients into motor neurons, which exhibit the disease's signature degeneration. Ichida's lab previously discovered that these degenerating motor neurons fail to do something critical for their own survival: dumping waste products. In contrast, healthy cells employ tiny compartments called vesicles to transport and get rid of cellular garbage, such as toxic proteins. The researchers found these defective vesicles in motor neurons derived from patients with several different genetic mutations known to cause ALS. This suggests that these various mutations might all result in the same vesicle problem, potentially treatable by a single drug.

The Ichida Lab also used patient-derived motor neurons to pinpoint a previously unidentified mutation that causes sporadic cases of ALS in patients with no relatives known to have the disease. This mutation impairs vesicles—as in other forms of ALS. With support from the NYSCF – Robertson Investigator Award, Ichida's group will continue to identify mutations that cause sporadic cases, which account for nearly 90 percent of ALS. To determine this, Ichida's team performs genome sequencing on cells from patients with sporadic ALS, as well as from their unaffected parents. In each patient, out of hundreds of mutated genes, one to two usually contain the code to make proteins with the potential to cause disease. The scientists then use genome editing tools to correct each suspicious mutation, and check if this rescues the cells.

In a complementary project funded by the U.S. Department of Defense, the Ichida Lab has teamed up with industry partners to discover drugs to help patients with ALS. USC and Sanofi are putting patient-derived motor neurons into robotic screening machines, which are exposing them to 43,000 drug-like compounds and capturing microscopic images of the results. DRVision Technologies is providing software to analyze the resulting microscopic images. So far, the team has found three chemical families that affect vesicle trafficking and survival in cells from patients with the most common form of ALS.

"Dr. Ichida's research into slowing or stopping ALS is groundbreaking," said USC Provost Michael Quick, "and is a tremendous example of the industry-leading research directed by the University of Southern California."

Research Highlights

Gage Crump and collaborators revealed that arthritis is much more widespread in the animal kingdom than previously suspected—afflicting zebrafish and related ray-finned fishes. Given that fish and humans diverged hundreds of millions of years ago, when bony vertebrates first evolved, this indicates that both arthritis and the susceptible type of joint, known as "synovial," are at least as ancient as bone itself. *(eLife)*

Gage Crump and collaborators also used zebrafish to show how two types of molecular signals, called Jagged-Notch and Endothelin1, work in tandem to control where and when stem cells turn into facial cartilage. This plays a major role in making the upper and lower regions of the face distinct. *(PLoS Genetics)*

Gage Crump, Francesca Mariani and colleagues used zebrafish to elucidate the role of cartilage in bone repair. Upon injury, a gene called indian hedgehog a (ihha) instructs a thin lining of stem cells, which surround the surface of bones, to make cartilage that helps healing. *(Development)*

Francesca Mariani and collaborators demonstrated the role of a gene called Prkci in organizing cells into balls and tubes during early embryo and organ formation. *(Developmental Biology)*

Rong Lu's lab found that transplantation dose affects the behavior of blood-forming stem cells in the bone marrow of mice. This provides clues about how transplantation dose affects patients undergoing this treatment for cancer and blood diseases. *(Cell Reports)*

Megan McCain and colleagues grew well-developed muscle fibers on a tiny scaffold or "chip" molded from a type of water-logged gel made from gelatin. *(Scientific Reports)*

Valter Longo and collaborators discovered that a fasting-mimicking diet may improve multiple sclerosis in mice and humans. The diet triggers the release of the hormone cortisone, which initiates the killing of autoimmune cells and production of healthy new cells. *(Cell Reports)*

Andy McMahon and colleagues revealed how bone formation in vertebrates is linked to a shared gene, called Sp7 or Osterix, that acts early in establishing bone-forming cells or osteoblasts. *(Developmental Cell)*

Neil Segil and colleagues showed that the chemotherapy drug cisplatin causes more acute hearing loss in mice with the equivalent of Cockayne syndrome, which can cause hearing loss and other symptoms. *(The Journal of Neuroscience)*

Featured Image

USC's May 2016 Commencement Ceremony marked a beginning, not only for its two-year-old master's program in the nascent field of stem cell biology and regenerative medicine, but also for this program's second graduating class. *(Photo/USC)*

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