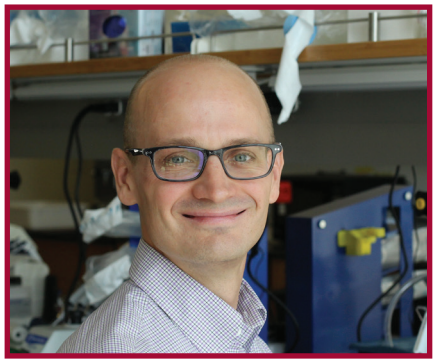
USC Stem Cell NEWS

Scientist Joseph T. Rodgers interprets stem cell signals

For Joseph T. Rodgers, the path to becoming an assistant professor of stem cell biology and regenerative medicine at USC began in the woods of Ohio.

"My dad is a chemical engineer, and he's an outdoorsy person," said Rodgers. "You just go off in the woods and all that goes along with that — fishing, catching frogs and turtles. That was how everything started."

Rodgers attended Catholic schools, and double majored in biology and chemistry at the Jesuit-run John Carroll University. To this day, the philosophy of the Jesuits influences Rodgers, who is no longer formally religious: "The main philosophy of the Jesuits is service. My interpretation of service is expanding knowledge through research and education. That's a driving force of why I'm here today."



Joseph T. Rodgers (Photo/Cristy Lytal)

He continued to expand knowledge by attending graduate school at The Johns Hopkins University School of Medicine, where he earned a PhD in biochemistry, cellular and molecular biology. Rodgers was the first graduate student in the laboratory of Pere Puigserver, who was just starting out. They published a slew of papers about metabolism. When Puigserver moved his laboratory to Harvard Medical School, Rodgers followed and completed his first postdoc. He then did a second postdoc in the laboratory of Tom Rando at the Stanford School of Medicine, where he studied the signals the body uses to regulate stem cells' metabolism and how this affects stem cells' ability to make and repair tissue.

Recently, Rodgers' team found that injury triggers the release of a molecule into the blood stream that puts stem cells throughout the body into a "high-alert" state, primed to repair and heal as needed. Eventually, doctors could prescribe some version of this molecule to patients before surgery, soldiers before combat or others.

As a new assistant professor, Rodgers is excited to continue uncovering the signals that instruct stem cells to build and repair tissue: "This is a research area that's ripe for somebody to tackle this question. But also, I really hope to be an inspiring professor — whether it's inspiring the students to enter research, or to be teachers themselves, or to be authors, or to go on to do whatever they want. There are a lot of really interesting things about science, and I just love this. And I hope to convey that to the students."

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.

Q&A: USC Stem Cell Ambassador Richard Merkin

Richard Merkin, founder of Heritage Provider Network, member of the Keck School Board of Overseers and USC Stem Cell Ambassador, is known for his philanthropy and leadership in the health care field. The Merkin Family Foundation recently established four assistant professorships in regenerative medicine at USC.

Q: Why do you support the Keck School?

A: My entire career has focused on my desire to ensure that, as a society, we are able to provide high-quality health care to all of our citizens. I believe that, through my support for the Keck School, we will be able to advance the discovery of cures to advance this effort.

Q: What interests you about regenerative medicine?

A: Regenerative medicine offers the greatest promise to move beyond the same solutions we have used for years. USC's research centers are making strides in tomorrow's clinical advances and innovative research projects.

Q: Why did you choose to support junior faculty?

A: Some of the greatest breakthroughs come from younger individuals because they have not been taught that there is only one way to think about a problem. Einstein was 26 years old when he published four papers that changed our views of space and time. The lifeblood of innovation is the fresh views that come from young, passionate, hardworking, talented scientists.

Mini-symposium introduces next-generation researchers

The next generation of scientists is turning to stem cells to advance our understanding of systems ranging from the blood to the brain, from the liver to the lungs. Six of these scientists presented research at the Junior Faculty Candidate Mini-symposium hosted by USC's Department of Stem Cell Biology and Regenerative Medicine.

Alexander Pollen from the University of California, San Francisco (UCSF), addressed the evolution of the human brain. He discussed how neural stem cells contribute to brain development and how a genetic variation may be responsible for increasing brain size and improving learning in humans.

Sergei Doulatov from Boston Children's Hospital and Harvard Medical School explained how to use stem cells to model anemia in a petri dish. He exposed these cells to drug-like compounds, one of which suggested a way to treat Diamond-Blackfan anemia.

Hsiang-Ying (Sherry) Lee from the Whitehead Institute for Biomedical Research offered an equally sanguine view of treating anemia. She described how environmental and molecular signals trigger blood progenitor cells to self-renew or differentiate.

Joan Font-Burgada from the University of California, San Diego, discussed a group of highly regenerative liver cells, dubbed hybrid hepatocytes, with great potential for transplantation to treat liver disorders. He also illuminated the genetic signals that unleash cholangiocarcinoma, an aggressive bile duct cancer.

Purushothama Rao Tata from Massachusetts General Hospital highlighted how lung cells maintain their ability to become other cell types in health, injury, and cancer development, also known as tumorigenesis.

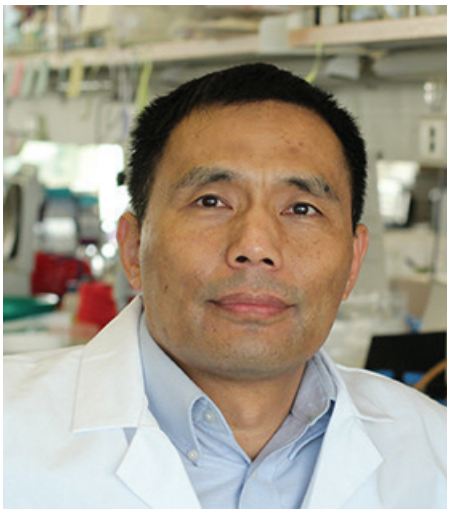
Leonardo Morsut from UCSF introduced "synNotch," a group of synthetic signals that can direct cell behavior. Eventually, synNotch or a similar system could enable the engineering and study of tissues with properties such as enhanced injury resistance or regenerative capacity.

Andy McMahon, chair of the Department of Stem Cell Biology and Regenerative Medicine, thanked these top candidates for junior faculty positions at USC for sharing their inspiring work.

"I'd just like to thank all of our speakers," he said. "It's been a spectacular day."

Scientists Qi-Long Ying and Austin Smith win 2016 McEwen Award for Innovation

Researchers Qi-Long Ying from USC and Austin Smith from the University of Cambridge have won the 2016 McEwen Award for Innovation, the highest honor bestowed by the International Society for Stem Cell Research (ISSCR). Supported by the McEwen Centre for Regenerative Medicine, the award recognizes groundbreaking stem cell discoveries that open new avenues to explore or treat human disease.



Qi-Long Ying (Photo/Cristy Lytal)

Ying originally joined Smith's laboratory as someone who knew next to nothing about stem cells. The third child of a farmer and a factory worker, he grew up in Yongkang, a small city in China's Zhejiang province, during the Cultural Revolution. After the death of Chairman Mao in 1976 and reinstatement of China's merit-based college entrance exam, Ying earned a top score and chose the First Military Medical University. What he didn't fully appreciate at the time was that attending a military medical university carried an obligation of 25 years of army service.

After Ying graduated, the army decided that he would work at a remote missile base near the Chinese border with North Korea. While there, he spent two years studying for the highly competitive exam to attend graduate school in China and earned admission to Shanghai Medical University, where he pursued his master's and PhD degrees.

Then the army noticed his absence and summoned him back to his missile troop. He realized that to get out of the army, he had to get out of China. Ying landed a postdoctoral position in Smith's laboratory, then at the University of Edinburgh in Scotland.

New to both stem cells and the English language, Ying began trying to "rewind" mouse neural stem cells into embryonic stem (ES) cells — and thought he had succeeded. Months later, he realized that that the neural stem cells had spontaneously fused with ES cells in the same petri dish, producing abnormally large ES cells — the first proof of spontaneous fusion.

Still under Smith's mentorship, he began exploring new and better ways to induce ES cells to self-renew or differentiate in the laboratory. He found a more efficient way to turn ES cells into neurons.

Next, he and Smith made the breakthrough that would eventually earn the McEwen Award. They discovered that they could inhibit ES cells from differentiating into specialized cells by exposing them to two proteins — called leukemia inhibitory factor (LIF) and bone morphogenic protein (BMP) — and published the results in *Cell* in 2003. Subsequently, in a 2008 paper in *Nature*, they used two inhibitory molecules — dubbed 2i — to mimic this effect.

"We can use embryonic stem cells to generate different cell types," said Ying. "And these cell types can be used for cell replacement therapy, for drug screening and for many other purposes."

After seven productive years, Ying left the Smith Lab to accept a faculty position at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, where he also serves as the director of the Chang Stem Cell Engineering Facility. Ying's team made one of *Science* magazine's "Top 10 Breakthroughs of 2010" by using stem cell-based gene targeting to produce the first knockout rats, modified to lack genes.

In recognition of their accomplishments, Ying and Smith will accept the McEwen Award and shared $100,000 prize at ISSCR's meeting in San Francisco.

"To be successful in this very competitive scientific career," said Ying, "you have to have confidence that you can achieve something."

Research Highlights

Andy McMahon's group discovered that while the gene *Six1* plays a fleeting and early role in mouse kidney development, it may have a more substantial role in human kidney development. The team hopes this will advance understanding of normal development and Wilms' tumor, associated with *SIX1* mutations. *(Development)*

Neil Segil and colleagues published two studies describing the regulation of the gene *Atoh1* during the development of the inner ear. This gene may provide a target for encouraging the regeneration of the inner ear to treat deafness or damage. *(Development)*

Paula Cannon and collaborators described a more efficient way to edit genes in blood-forming or "hematopoietic" stem and progenitor cells (HSPCs). Gene therapy using HSPCs has potential for treating HIV and other diseases of the blood and immune systems. *(Nature Biotechnology)*

Gage Crump and colleagues found roles for the Iroquois (*Irx*) genes in protecting joint cartilage cells. The loss of these cells causes arthritis, the leading cause of disability in the U.S. *(Developmental Cell)*

Henry Sucov's group learned that when a type of cellular signaling called TGF beta goes awry, this leads to developmental defects in the channel leading blood out of the heart. *(Developmental Biology)*

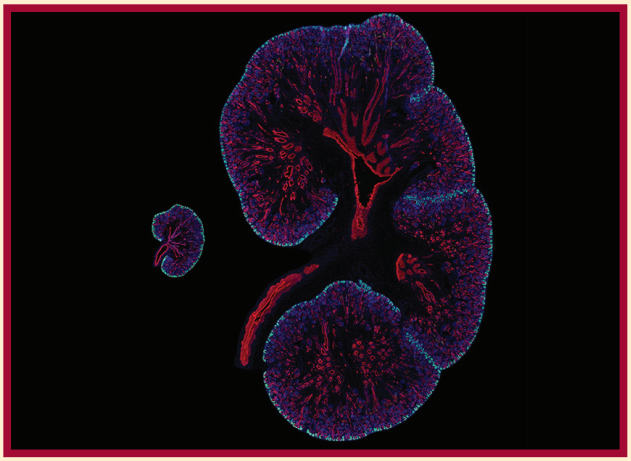
Keigo Machida and collaborators revealed the gene *NANOG* as a potential target for disrupting the chemo-resistant stem cells that become liver tumors. *(Cell Metabolism)*

Francesca Mariani and collaborators identified *Prkci* as a key gene in maintaining the balance between producing too many and too few stem cells. The gene influences whether stem cells self-renew to produce more stem cells, or differentiate into more specialized cell types, such as blood or nerves. *(Stem Cell Reports)*

Wange Lu and colleagues uncovered key genes involved in prostate cancer onset and progression. *(Scientific Reports)*

Qi-Long Ying and collaborators used the technology CRISPR/Cas9 to edit genes in mouse embryonic stem cells and create transgenic mice, which can advance the understanding of genetic diseases. *(Scientific Reports)*

Featured Image



Embryonic day 15.5 mouse kidney next to a 15.5 week human fetal kidney with SIX2 (cyan) marking nephron progenitor cells. The collecting duct system is red; nuclei are blue. *(Image by Lori O'Brien/McMahon 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

© 2016 Keck Medicine of USC