

USC Stem Cell NEWS

USC and Amgen launch dialogues to drive discovery

Without collaboration between universities and pharmaceutical companies, scientists might never have developed essential medicines ranging from the antibiotic streptomycin in the 1950s to HIV medications in the 1990s. In recognition of the ever increasing importance of these academia-industry partnerships, USC and Amgen are jointly offering two new opportunities: a 10-week biotechnology lecture series for students and postdoctoral researchers, and a monthly seminar series open to all.

“We look forward to deepening our collaboration with Amgen for the benefit of patients,” said Andy McMahon, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC.



Amgen's Bill Richards visited USC.
(Photo by Cristy Lytal)

Rohit Varma, dean of the Keck School of Medicine, added, “Our close connections with Amgen and other industry partners support the medical school's larger mission of promoting education, research and clinical care in the context of a world-class research university.”

To provide an introduction to Amgen, Qing Liu-Michael, program director of USC's stem cell research center, invited Bill Richards, the company's

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.

executive director of Discovery Research, to USC. Liu-Michael and Richards have been instrumental in building bridges between USC and Amgen.

“We're pleased to partner with USC to provide Amgen and USC scientists with opportunities to learn more about the innovative science happening at our respective institutions,” said Richards.

The monthly seminars alternate between USC speakers at Amgen, and Amgen speakers at USC. Amgen scientists are also leading a 10-week biotechnology lecture series for USC students and postdoctoral fellows. The series covers the process of bringing a drug into clinical use, and culminates with a tour of Amgen's headquarters in Thousand Oaks.

USC and Amgen also recently signed a three-year master agreement for future research collaborations with the goal of accelerating scientific discoveries into clinical therapies.

Hearst Fellow Adnan Chowdhury studies how stem cells respond to infection

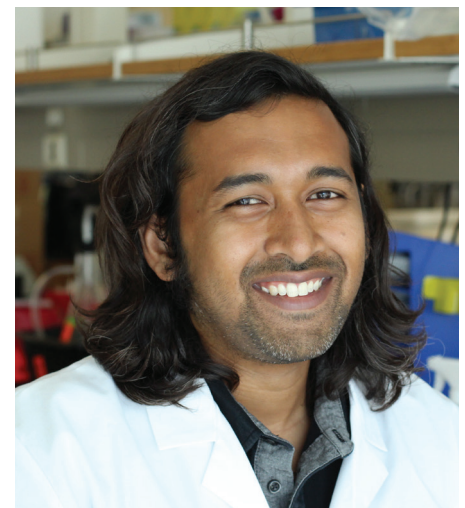
Few researchers have studied how hematopoietic stem cells (HSCs) respond to infection—even though these stem cells give rise to the full battery of specialized immune cells, such as T cells and B cells. Adnan Chowdhury is venturing into this uncharted territory as the winner of the Hearst Fellowship, which will launch his early scientific career with a generous startup package including salary and benefits for a year.

“None of the immunologists think about the hematopoietic stem cells, and none of the hematopoietic stem cell people think about the immunology,” he said.

Chowdhury has always had a tendency to cross disciplinary boundaries. After growing up in Chicago, he not only pursued a major in cell and structural biology, but also minors in chemistry and computer science at the University of Illinois Urbana-Champaign. He then obtained a master’s degree in developmental neuroscience from Saint Louis University. As a PhD student at the Saint Louis University School of Medicine, he studied how the HIV virus cannot effectively replicate in patients who are also infected with GB Virus C (hepatitis G virus), a pathogen that causes no deleterious symptoms. He dedicated his PhD to his grandfather, who was a biology professor and textbook author in Bangladesh.

During his postdoctoral studies, he is studying HSCs in the USC Stem Cell laboratory of Rong Lu. For his Hearst Fellowship project, he will examine the response of individual HSCs during acute and chronic viral infections in mice. He will tag and track individual HSCs, and then evaluate the molecular mechanisms that enable certain HSCs to promote a quick and/or robust immune response. His research could offer clues about how to supplement or stimulate a patient’s HSCs to produce more immune cells faster during a hard-to-beat infection, such as influenza in the elderly or HIV.

“I would like to thank the Hearst Foundations for the opportunity to continue my research,” said Chowdhury, who hopes to become a principal investigator. “This is an idea that no one is looking at, and I really want to blow this field open.”



Adnan Chowdhury (Photo by Cristy Lytal)

Trio of researchers awarded \$3.3 million NIDCR grant

Three USC Stem Cell researchers have been awarded a \$3.3 million grant from the National Institute of Dental and Craniofacial Research (NIDCR) to study craniosynostosis, a birth defect in which the skull fuses together prematurely, leaving little room for the growing brain. This can cause developmental delays, hearing loss, blindness and death.

“This showcases what great collaborations can do,” said Yang Chai, one of three principal investigators on the study. Chai is a professor of stem cell biology and regenerative medicine, as well as George and MaryLou Boone Professor of Craniofacial Molecular Biology, director of the Center for Craniofacial Molecular

Biology, and associate dean of research at the Ostrow School of Dentistry of USC. Joining Chai are Rob Maxson, professor of biochemistry and molecular biology, and Gage Crump, associate professor of stem cell biology and regenerative medicine, both at the Keck School of Medicine of USC.

The researchers will leverage their complementary expertise and study two genes—TWIST1 and TCF12—mutated in craniosynostosis. By better understanding the genetic and molecular processes underpinning craniosynostosis, the researchers hope to one day develop biological interventions to help babies and children with this common birth defect.

Lindsey Barske wins National Institutes of Health (NIH) Pathway to Independence Award

Years ago, Lindsey Barske pulled on a pair of tall rubber boots and began a journey that led from her college research experience on the muddy Alaskan tundra to her current postdoctoral studies in the USC Stem Cell lab of Gage Crump.

Now, she's arrived at a key turning point, having received a National Institutes of Health Pathway to Independence Award (K99/R00) to help transition from the postdoctoral to faculty stage. She'll study facial development in zebrafish



Lindsey Barske (Photo by Cristy Lytal)

and mice, to elucidate human birth defects, such as cleft palate and prematurely fused skull sutures.

After growing up in Connecticut, Barske pursued a biology major at Pomona College. For two summers, she studied with an ecological research team working on Alaska's North Slope. Squishing across the sponge-like ground

in a land of permafrost, caribou and grizzlies, she knew that science was her calling.

She then explored biology during two technician jobs: in the cancer epigenetics lab of Peter Jones at the USC Norris Comprehensive Cancer Center, and in the developmental biology lab of Alvaro Sagasti at UCLA.

"I love embryos," she said. "There seems to be no end to how much they can teach us about biology and evolution."

She obtained her PhD in developmental biology and embryology from Duke University, where she performed research on sex determination and ovary development in mice and turtles. During these years, Barske published five first-author manuscripts and three review articles in top scientific journals, including *Nature*.

In 2012, she accepted a position as a postdoctoral fellow in the USC Stem Cell laboratory of Gage Crump, who calls her "an enthusiastic and insightful researcher who has an eagle eye for the embryo."

To support her research, she was awarded a T32 Hearing and Communication Neuroscience Postdoctoral Fellowship from the National Institute on Deafness and Other Communication Disorders, enabling her to use zebrafish to identify genes shaping bones of the middle ear.

In 2013, she received a prestigious postdoctoral fellowship from the A.P. Giannini Foundation. As a fellow, she has explored how key genes regulate both the timing and spatial arrangement of stem and progenitor cells in the developing face, resulting in publications in journals such as *PloS Genetics* and *Developmental Cell*.

Working with Crump and USC Stem Cell researcher Yang Chai, she co-authored a book chapter about craniofacial research in zebrafish for *Current Topics in Developmental Biology*.

In 2015, Barske and Michaela Patterson, a postdoctoral scholar from the USC Stem Cell laboratory of Henry Sucov, won a Doerr Stem Cell Challenge Grant. Together, they used zebrafish to investigate the role of a gene, known as *Tnni3k*, in heart regeneration.

Her K99/R00 project will focus on how two groups of genes, Fibroblast Growth Factor 20 (*Fgf20*) and the Nuclear Receptor 2f family, restrict the maturation of skeletal progenitors in the developing facial skeleton in both zebrafish and mice—and the implications for other species, including humans. Crump will mentor and Chai will co-mentor the project. USC Stem Cell researchers Rob Maxson and Ruchi Bajpai will be members of her advisory committee, and Stanford University's Joanna Wysocka will serve as a consultant.

Moving forward, she is open to pulling on her rubber boots and following the science wherever it takes her: "I love what I do, and I want to keep being a scientist as long as I can. It's a privilege to get to do this."

Research Highlights

Neil Segil's lab examined how a key gene, called Atoh1, underpins the development and potential regeneration of the inner ear's sensory cells, which are known as hair cells. In the first of two related studies, researchers explored how Atoh1 is either "turned on" or "turned off" through a process called epigenetic regulation during development and postnatal life in mice. In the second study, researchers showed that a group of genes called Hes/Hey directly interact with and repress Atoh1 to sculpt the developing structure in the inner ear called the organ of Corti into a complex mosaic of different cell types that ultimately enables hearing. (*Development*)

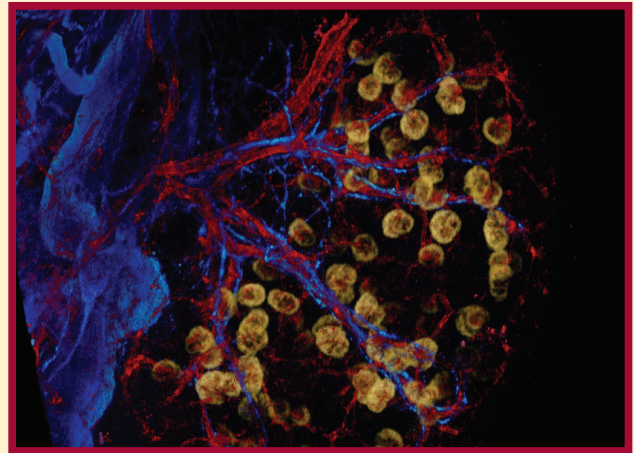
Valter Longo and colleagues demonstrated that a fasting-like diet, when used with chemotherapy drugs, turns the immune system against breast cancer and skin cancer cells in mice. This fasting-like diet raises the levels of bone marrow stem cells that generate immune cells, such as T cells, B cells and natural killer cells that infiltrate tumors. In addition, the fasting-like diet weakens an enzyme called heme oxygenase (HO-1) in T regulatory cells, which protect cancer. All of these changes enhance the effectiveness of chemotherapy drugs. (*Cancer Cell*)

Berislav Zlokovic and collaborators found a protein called 3K3A-APC that may help with the brain's recovery from a stroke. The researchers used 3K3A-APC to produce neurons from human stem cells, and then grafted these neurons into the brains of mice that had sustained strokes. This led to measurable improvements in both motor and sensory function. (*Nature Medicine*)

Tracy C. Grikscheit and collaborators used adult human stem and progenitor cells to generate tissue-engineered liver (TELi). The TELi contained normal structural components, such as hepatocytes, bile ducts and blood vessels, and provided some function when transplanted into mice with liver failure. However, the cellular organization differed from native liver tissue. (*Stem Cells Translational Medicine*)

Jae Jung and collaborators examined three strains of Zika in second trimester human fetal neural stem cells. They discovered that the Zika virus contains 10 proteins, but only NS4A and NS4B matter when it comes to microcephaly. These two proteins stunted the growth of fetal neural stem cells. (*Cell Stem Cell*)

Featured Image



In this embryonic day 15.5 kidney, blood vessels are red, neurons are blue, and podocytes are yellow. The image was created using a staining procedure called iDISCO. (*Image by Riana Parvez and Seth Ruffins*)

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