

USC Stem Cell NEWS

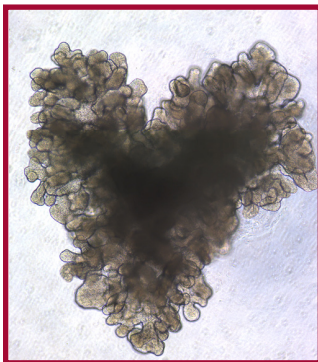
A Message from Director and Chair Andy McMahon

I hope that this message finds you safe and well. As we return to our labs, I thought this would be a good time to let you know about what has been happening in USC's stem cell research center.



(Photo by Christina Gandolfo)

In March, we received instructions to wind down non-COVID-19 research projects in our labs, to minimize the spread of the novel coronavirus. We donated our gloves and goggles to front-line health care providers, and redirected some scientific energies to address the pandemic.



Lung organoid (Image by Lu Tian/Chen Lab)

Stem cells provide an ideal way to generate human lung cells, a primary site of COVID-19 infection. Lung researchers from our department, including Drs. Ya-Wen Chen and Amy Ryan, are directing human stem cells to produce lung and airway cells and organoids—simplified lung-like structures. These human models are critically useful for studying infection and screening large numbers of drug-like molecules, to identify promising leads.

Two other researchers in our center are exploring the antiviral potential of drug-like molecules, originally identified as promising treatments for diseases unrelated to COVID. Dr. Denis Evseenko

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.

Centered at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research, the initiative brings together researchers and clinicians from USC and Children's Hospital Los Angeles.

is studying whether a potential arthritis treatment could also serve as an anti-inflammatory for patients with self-destructive immune reactions to the novel coronavirus. With support from the California Institute for Regenerative Medicine, CIRM, Dr. Justin Ichida is collaborating with Dr. Chen to test whether an ALS drug candidate could block coronavirus infection.

For those engaged in non-COVID research, the time outside the laboratory has been an opportunity to learn new skills, pursue funding, analyze data, write prolifically, teach remotely, and forge collaborations, through Zoom courses, seminars and symposia.

In the coming weeks, we will be resuming non-COVID lab experiments, using social distancing, protective equipment, and safety protocols.

We also look forward to welcoming our master's students in the fall for an entirely online educational experience. Faculty are swapping ideas and experiences, with a shared goal of providing as engaging a learning experience as possible.

While there have been many challenges and pressures for our community, this unprecedented time away from our laboratories and classrooms has allowed us to reflect, regroup and prepare for what lies ahead.

Ya-Wen Chen grows miniature lungs with maximum potential

As the SARS-CoV-2 coronavirus outbreak escalated into a pandemic, USC lung researcher Ya-Wen Chen expected to be spending a lot of time at home, sheltering in place.

“At the beginning of the quarantine, I was going to focus on writing grants,” said Chen, who joined USC as an assistant professor of medicine, and stem cell biology and regenerative medicine in 2019. “I also wanted to spend time cleaning my house, cleaning my backyard, getting everything on track.”

Instead, Chen realized that her laboratory possesses a key resource to advance the fight against COVID-19: mini human lungs grown from stem cells. These lab-grown lung structures, known as organoids, provide a way for scientists to test potential anti-viral treatments.

While this is Chen’s first foray into coronavirus research, it’s not her first quarantine. When SARS-CoV broke out in 2003, Chen was living in Taiwan, where she grew up. She spent her childhood in a small rural village, playing in rice fields with her three siblings and more than 20 cousins. In high school, she had an inspiring teacher who encouraged her to pursue biology.

“After I graduated, my teacher passed away while he was collecting samples for the class. He got hit by a car and fell off a cliff,” she said. “We were actually very close. I knew a lot of students who became interested in biology because of him. For me, that’s the sign of a truly successful teacher—one who inspires students to love what he or she teaches.”

Chen earned a bachelor’s degree in biology at Tunghai University in Taiwan, a master’s degree in tumor biology from Georgetown University, and a PhD in molecular medicine from the University of Maryland, Baltimore.

For her postdoctoral training, she joined the stem cell laboratory of Hans-Willem Snoeck at Columbia University, and developed human lung organoids. Chen also collaborated with a large research team to develop a technology to maintain donor lungs outside of the body.

In January 2019, Chen started her own lab at USC.

“I’m gay, and to live comfortably, without worrying about being discriminated against, was an important factor in choosing where to start my faculty career,” she said. “USC is a prestigious school, and the Pulmonary



Ya-Wen Chen (Photo/Ya-Wen Chen)

Division and stem cell department cultivate junior faculty and encourage interdisciplinary collaborations. The idea of being able to pursue what I’m truly passionate and curious about made me join USC.”

Chen’s lab uses human stem cells to study lung development, injury and disease. One of the lab’s major goals is to find a method for mass producing large numbers of identical lung organoids. These organoids could be used to screen thousands of potential drugs to treat pulmonary fibrosis, as well as infectious diseases.

One of these diseases is COVID-19. The lab is working to develop an antiviral to prevent the virus from entering the cells that line the lungs, called the epithelium. These cells contain a receptor called ACE2, and an enzyme called TMPRSS2. The virus uses this enzyme as a key to “unlock” ACE2, which becomes an entry point into the cells. Chen’s team is using lung organoids to test whether an antibody can block the enzyme, locking out the virus. To test a potential antiviral to protect lung cells involved in gas exchange, Chen is collaborating with USC Stem Cell scientist Justin Ichida. The California Institute for Regenerative Medicine, CIRM, awarded them \$150,000.

Other projects involve everything from growing blood vessels for lung organoids, to regenerating the trachea and airway for patients with congenital tracheal stenosis.

“For me,” said Chen, “I always want to fulfill my curiosity to find the answer.”

Alumna Kalya Stanten follows the science

By following her love of science, USC master's program alumna Kalya Stanten has found herself in some very interesting places—



Kalya Stanten (Photo/Kalya Stanten)

including a virology lab at the outset of the COVID-19 pandemic.

“I was in Paula Cannon’s lab,” said Stanten, who graduated with a Master of Science in Stem Cell Biology and Regenerative Medicine in May 2020. “Through my own work there, not

only did I get more of a look at the gene editing process, but I also gained a greater knowledge of virus biology. And it was really inspiring to see the lab transition to try to tackle the COVID-19 situation.”

Stanten joined the Cannon Lab during her junior year as a biochemistry major at USC. When she was accepted into USC’s progressive degree program, which allows students to earn their undergraduate and master’s degrees simultaneously, she was able to continue working in the Cannon Lab while pursuing specialized course work in stem cell biology and regenerative medicine.

“Even though biochemistry is notoriously one of the hardest biology majors, the reason that I was in these classes was because I love science,” said Stanten, “which set me up well to make the transition into the stem cell master’s program and keep choosing to follow science.”

Stanten began following science from a young age. She credits her father, a jet engine engineer, with being the first person who inspired her to think like a scientist. She credits her mother, who works at the sustainability office at Clorox, with imparting a joy for biology. As early as middle school, Stanten recalls being “blown away”—in a good way—when her class had the

opportunity to dissect a cow eye.

As a high school student at Sacred Heart Cathedral Preparatory, Stanten attended her first lecture about stem cells during a global youth summit on the future of medicine hosted by Brandeis University.

“That blew my mind,” she said. “Right there was really what solidified my desire to pursue the research route.”

She knew that USC would offer excellent opportunities to continue learning about new scientific findings and to pursue her passion for research. As an undergraduate, she participated in the Freshman Science Honors Program, an advanced curriculum in the natural sciences for high-achieving students.

She made the most of her undergraduate years: participating in a study abroad program in Athens, a sorority, the Rugby Team, and the Ski & Snowboard Team. She also began volunteering at Camp Kesem for children with parents or guardians affected by cancer.

One of her favorite undergraduate courses was Regenerative Medicine: Principles, Paradigms and Practice, taught by Andy McMahan, the director of USC’s stem cell research center. The comprehensive and challenging course provided an ideal segue into the stem cell master’s program.

As a master’s student, Stanten enjoyed working hands-on with stem cells. She gained broad exposure to current research, learned how to design better experiments, and grew as a scientific thinker. The program cemented her desire to work in the biotech industry, before applying to PhD programs.

“After my three years in the Cannon Lab, I’m coming out of it wanting to contribute to regenerative therapy development and still feeling excited to do laboratory bench work,” said Stanten. “Even though bench work can come with some tediousness and some frustration, I find the problem-solving satisfying, whether it is at the bench or musing over therapeutic strategies. So I’m excited to go into industry, because I want to experience what research looks like there.”

Award Highlights

Andy McMahon has been elected as a new member of the National Academy of Sciences in honor of his outstanding contributions to developmental biology. The National Academy of Sciences brings together nearly 3,000 leading researchers to provide objective, science-based advice on critical issues affecting the nation.

Rong Lu earned a \$6.6 million Emerging Investigator Award from National Heart, Lung, and Blood Institute (NHLBI). She is using this grant to study the unique properties of individual blood forming stem cells and how they contribute to aging, leukemia and other medical conditions.

Min Yu received the Era of Hope Scholar Award from the U.S. Department of Defense. This \$4.95 million award supports gifted early-career scientists making extraordinary contributions in the fight against breast cancer. Yu is leveraging the award to understand and target the rare circulating tumor cells that seed metastasis.

Megan McCain won a National Science Foundation CAREER Award for innovative and novel research in the area of cellular systems and molecular bioengineering. The award is supporting research on the uterus and how its smooth muscle cells respond and adapt to mechanical forces.

Led by **Yang Chai**, the Center for Dental, Oral and Craniofacial Tissue and Organ Regeneration (C-DOCTOR) has been granted \$30 million from the National Institute of Dental and Craniofacial Research (NIDCR). C-DOCTOR is a consortium of California academic institutions with a mission of becoming a sustainable, comprehensive national

resource center to enable regenerative therapies to replace dental, oral and craniofacial tissues or organs lost to congenital disorders, traumatic injuries, diseases and medical procedures.

Peter Fabian is the recipient of a National Institutes of Health Pathway to Independence Award for his research on craniofacial development in zebrafish. Known as the K99/R00, the award will help him transition from the postdoctoral to the faculty stage of his career.

Ebony Flowers has been named a Postdoctoral Enrichment Fellow by the Burroughs Wellcome Fund and an A.P Giannini Foundation Fellow for her research on breast cancer metastasis.

Featured Image



Staying the Course: During the remote work period, USC Stem Cell launched new Zoom courses to enhance manuscript writing and bioinformatics skills for postdocs and graduate students across the Keck School of Medicine of USC. (Screenshot/Cristy Lytal)

Your Support

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