Eli and Edythe Broad Center
for Regenerative Medicine and Stem Cell Research at USC

Stem Cell

IMPACT REPORT 2018/2019

Keck School of Medicine of USC

contents

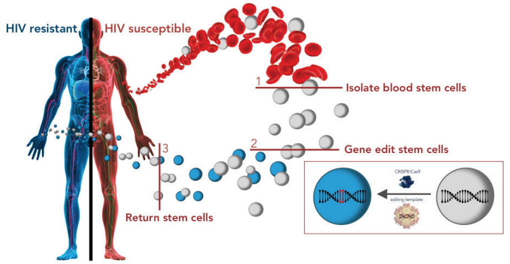
Letter from Director Andy McMahon

In a relatively brief time at USC, we have built a thriving new department, expanded stem cell research across the university in new collaborative partnerships, and set up cutting-edge support facilities to underpin these research efforts.

We have also initiated new educational programs that use the concepts and paradigms of stem cell research to explore how our body systems are built, maintained and repaired, and to train the next generation of stem cell researchers.

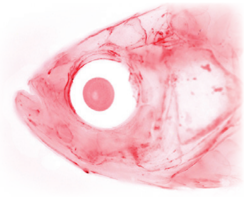
None of this would be possible without the creative scientists who have joined USC within the past few years to establish their independent research careers and the mentoring and example provide by several long term faculty with distinguished careers at USC. In the pages that follow, I would like to introduce you to some of the people behind the science and the personalities that drive our work. I am also pleased to share the story of Anna Kuehl, whose vision has been partly restored following her participation in a USC-led clinical trial for macular degeneration. Lastly and very importantly, meet the talented students and postdoctoral trainees who will propel stem cell research into the future.

Highlights
2018/2019

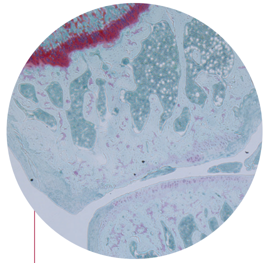


The **Cannon** lab discovered that in latent cases of HIV infection, the virus is still present in the brain.

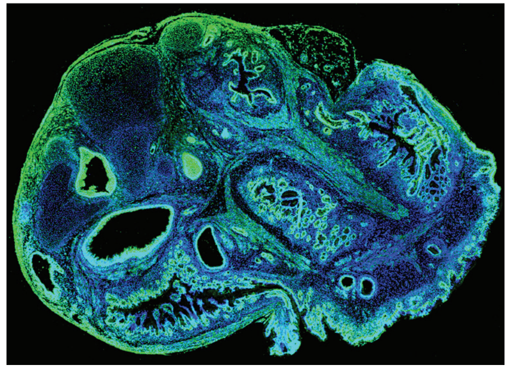
Yang **Chai** was elected to the National Academy of Medicine. His lab also demonstrated an approach in mice for preventing a serious birth defect called craniosynostosis, in which sections of the skull fuse prematurely and restrict brain growth.



Researchers from the **Crump** and **Maxson** labs created a way to study craniosynostosis in zebrafish. The Crump Lab also revealed the roles of specific genes in the development of the jaw and face.



The **Evseenko** Lab provided insights into how gene activity drives the development of cartilage, and described a molecule that he and his company **CarthroniX** are working to develop into a treatment for arthritis.

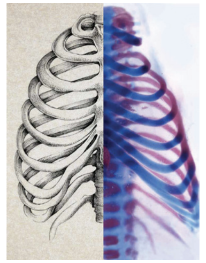


The **Ichida** Lab described how a gene mutation leads to toxicity in nerve cells, causing many cases of ALS and frontotemporal dementia. Ichida and his company **AcuraStem** are working towards a clinical trial for ALS.

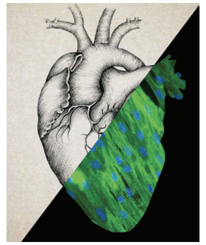
The **Fraser** Lab used a 3D time-lapse imaging technique to better understand skeletal formation.

New recruit Thomas **Lozito** is exploring how to improve skeletal regeneration in humans through lessons learned from lizards and salamanders, which can regrow severed tails.

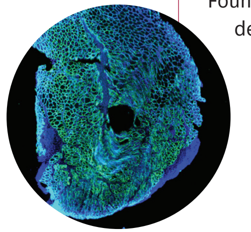
The **Lu** Lab published research detailing how radiation affects the behavior of blood stem cells. The lab also showed how individual blood stem cells compensate for each other's deficiencies, overproducing whichever specific type of immune cell is lacking.

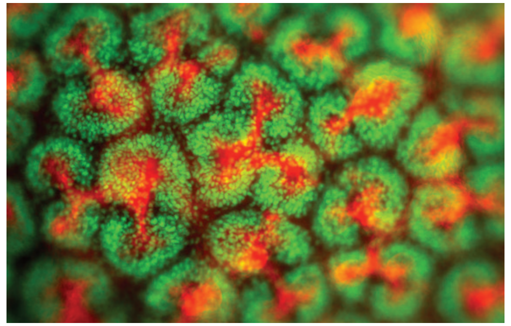


The **Mariani** Lab proposed a model for how mammals repair large bone injuries, and identified key cell types essential to the healing process.

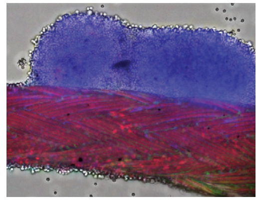


The **McCain** lab delineated how the body's microenvironment affects the proper contraction of the heart.





The **McMahon** Lab will receive $4M in funding over the next five years for the NIH Director's Transformative Research Award, a collaborative project with top scientists at Harvard and Stanford universities. The lab also detailed significant differences and similarities between mouse and human kidneys during development and acute kidney injury.

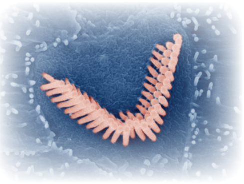


The **Morsut** Lab demonstrated the ability to program cells to self-organize into multilayered structures, reminiscent of simple organisms or the first stages of embryonic development.

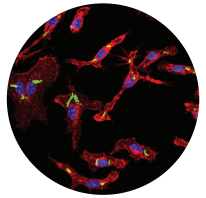
Joseph T. **Rodgers** co-founded a company, Fountain Therapeutics, dedicated to discovering and developing treatments for aging-associated diseases.

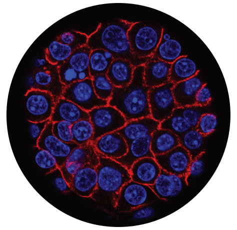
Generous gifts from The Eli and Edythe Broad Foundation and multiple benefactors have provided vital support to expand research and education efforts.

The **Segil** Lab pioneered how to grow and study intact portions of the mammalian inner ear in a Petri dish in order to advance our understanding of hearing loss and balance disorders.

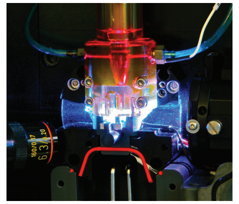


Qi-Long **Ying** launched a startup called **OCgene Therapeutics Corporation** to advance cell therapies to treat bacterial infections and cancer.





The **Yu** Lab reduced lung metastases in mice with breast cancer by inhibiting a specific protein.



USC Stem Cell's Flow Cytometry Core acquired two new machines, including the most sophisticated cell sorter in Southern California.

150

The master's program in Stem Cell Biology and Regenerative Medicine graduated its fifth class, bringing the total number of alumni to 150 as of Summer 2019.

Q&A

USC Stem Cell junior faculty balance babies with biotech research

By Cristy Lytal

Growing stem cells isn't just something junior faculty do in the lab. Eight of the junior faculty in the Department of Stem Cell Biology and Regenerative Medicine recently welcomed new babies into their families—more than half of them within the past year. Here, our junior faculty parents share their joy and wisdom about balancing career and family.

Senta Georgia

Assistant Professor, Endocrinology and Metabolism, Children's Hospital Los Angeles; Pediatrics, and Stem Cell Biology and Regenerative Medicine, USC

Who's in your family?
Four children! My oldest is my daughter Nola. She's eight, and my son Felton is six. My daughter Alexandra is three, and I have a newborn, Marshall. I had my son Felton two months before I became an assistant professor, and I had the youngest two kids while I've been an assistant professor. My husband is a lawyer, and he works for a law firm, and he has law firm hours. Both of us have pretty demanding careers.

How do you balance work and family life?
The most important thing is our support network. And so I have a babysitter, who is just a friend of mine's mom, and she has taken care of all of my kids from the time I finished maternity leave and went back to work until they were ready for preschool at two-and-a-half years old. So I've been really lucky to be able to keep them in a home environment with just one person, who's really like a grandmother to them, because my parents aren't here, and my husband's parents aren't here.
We also have an afternoon nanny, and so that person starts working for our family at 3 p.m. and picks my kids up from the bus stop. She takes them home, gets some lunch, does homework with them, takes them to whatever activities they have, picks up my daughter from preschool, makes sure everybody takes a bath and such. The hard stuff of the day is done, so I can spend quality time with them between 6:30 to 8:30 p.m. when they go to bed. And that's really the only way that this ship keeps sailing!

What do you wish you had known before you started?
You should think about what you're going to do, but you still just have to do it. Don't get paralyzed by the possibilities. If you want to have kids, you have kids. If you don't want to have kids, don't have kids. Allow yourself the freedom to change your mind. It's up to you to decide what you want to do and design your whole life such that it all fits. And so my goal is to master the moment. From 8:30 in the morning to about 5:15 p.m., I am the master of my lab. Monday through Friday from 5:15 to about 9:15 p.m., I have to be the master of my home. And then in that time after, before I try to sleep, I try to have a relationship with other adults. And so I just try to design my life to work.

Min Yu

Richard N. Merkin Assistant Professor,
Stem Cell Biology and Regenerative Medicine

Who's in your family?
My husband and I moved here when I became faculty in February of 2014. My son Nathan was born in May 2016

How do you balance work and family life?
I try my best to be more efficient at work, and get up early in the morning to catch up on work, so I can spend some time with my family during the weekend.

What do you wish you had known before you started?
I would have kids much earlier! It is busy once you have a growing family, but it is a lot of fun. But having a small baby is difficult for faculty to plan travel easily. So maybe having a baby earlier would have been a bit helpful.

Rong Lu

Richard N. Merkin Assistant Professor,
Stem Cell Biology and Regenerative Medicine,
Biomedical Engineering, Medicine

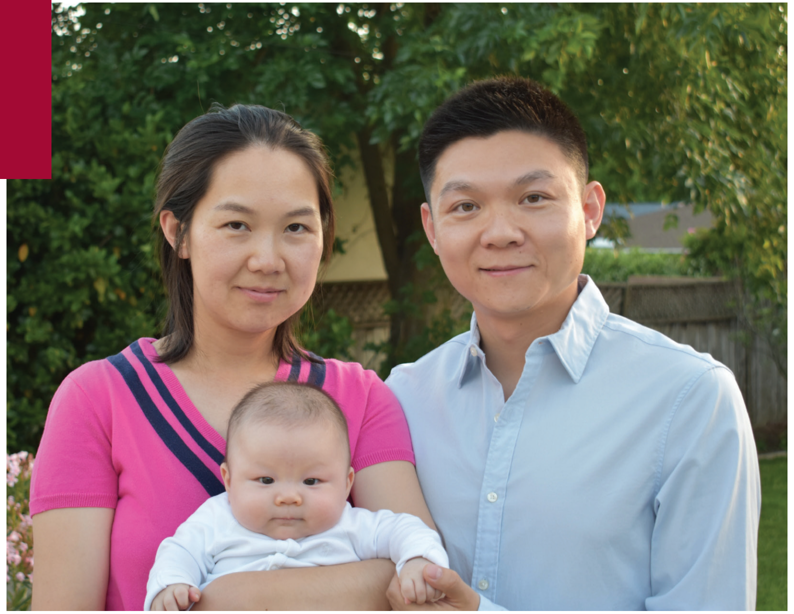
Who's in your family?
I became a junior faculty member at USC in January 2014. My husband and I married when we were in graduate school, but I gave birth to my daughter in September 2014 and my son in March 2017. We are currently a family of four!

How do you balance work and family life?
To achieve some sort of balance, I try to reduce my standards on relatively unimportant things, and I outsource the house/lab work on the less critical parts. For example, I don't have time to cook. I eat at Keck Hospital café or order restaurant food. I don't have time to keep the house neat. I hire people to do the gardening and clean the house periodically. I don't have time to keep an eye on the daily running of the lab. I hire a lab manager to train people and help me keep the lab running. All these are to save my time for important things, such as spending time with my kids when they are little, helping lab members at the critical stages of their projects, etc.

What do you wish you had known before you started?
I wish I had known how much work the two kids require. Maybe if their ages were a little further apart, then family life could be less challenging.

Zhongwei Li

Assistant Professor, Medicine,
Stem Cell Biology and Regenerative Medicine



Who's in your family?
I joined USC in September 2017. I got married to my wife Jingying Yu in 2012, and we just had our first baby boy, Nelson Li, in February 2019.

How do you balance work and family life?
I think it is difficult to balance work and family life. Usually, it is just a sacrifice of one for the other, depending on which one has the priority, case by case. I am glad to have a very supportive wife who takes care of a lot of home duties for our family, so I can put more effort in my work. I also feel that the flexibility of time, being a PI, helps balance work and family life. We can work at home sometimes if we need to be at home with some home duties, such as babysitting. In this case, work and family life are balanced very well.

What do you wish you had known before you started?
Everything looks good. I would do the same if had a chance to do it over again.

Megan McCain

Assistant Professor, Biomedical Engineering,
Stem Cell Biology and Regenerative Medicine

Who's in your family?
I began my faculty appointment in January 2014, married my husband Leo in March 2017, and gave birth to my son Clayton in July 2018.

How do you balance work and family life?
It is really hard! I have a lot less time at work than I used to, so I am forced to say “no” more to ensure that I have enough time for research and teaching, and to manage my stress. I also have to spend more time carefully backwards-planning from deadlines, because I don't have the same flexibility to stay late at work if I fall behind. I also have to rely on my postdocs and students to be more independent now, which is probably good for them in the long-term anyways. Whenever I have an invitation to travel, I also have to decide if it is a really important trip and make sure my husband is able to take care of Clayton, since my husband also works full-time.

What do you wish you had known before you started?
When I came back from maternity leave, I felt overwhelmed and a little lost! When I was pregnant, I did a lot to prepare for leaving for maternity leave, but I didn't prepare for what I would do when I returned. I wish I had set up some achievable tasks for myself during that time so that I had more direction when I came back to work.

Giorgia Quadrato

Assistant Professor, Stem Cell Biology and Regenerative Medicine

Who's in your family?
My family is composed of three people now: my husband Sergio, and my daughter Matilda. I started working at USC in this department in June 2018, and then after two months, I had my baby.

How do you balance work and family life?
There is no such thing as balance. It's a matter of coping with the pressure of doing both. But the most important thing to succeed and keep some sanity as a mom in science is having a supportive partner. And the daycare close by definitely helps. I also feel quite supported in the institute. There are many other faculty with kids, so I feel that everybody understands what I'm going through. I also tried to assemble a team of people that I trust in my lab, and being able to delegate is very helpful. And then, one just needs to accept that you cannot be perfect at pretty much anything anymore!

What do you wish you had known before you started?
Somehow, I thought that the first months would be kind of slow when you start the lab. But I mean, it's overwhelming at the beginning. So I don't know if there could have been a better time to start a family. Maybe there is never a better time. I thought it was going to be probably easier. But at the end of the day, maybe it's better not knowing. Otherwise, you may end up waiting forever!

Leonardo Morsut

Assistant Professor, Stem Cell Biology and Regenerative Medicine

Who's in your family?
I got married in 2009 when I was a graduate student in Italy, and then we moved to San Francisco in 2012 for my postdoc. And in 2013, we had Gabriele in San Francisco. And then in 2017, I started here at USC as an assistant professor, and we had Aurora that summer.

How do you balance work and family life?
The money component is kind of critical, as with different amounts of money, you can get different lengths of care of different quality. So I'm grateful that we have the resources to pick what we think is the best. So Gabriele goes to pre-school and is starting kindergarten next summer, and we have a nanny that comes to our place for Aurora. I feel like we have good people taking care of them. So knowing that they are with people that are helping them—even better than I could do—that's important, and then that allows me to be focused on the job.

What do you wish you had known before you started?
It's like life. I mean, you can post-rationalize about everything. But there's nothing that I don't like about the situation as it is right now.

Michael Bonaguidi

Assistant Professor, Stem Cell Biology and Regenerative Medicine

Who's in your family?
I got married during graduate school. My first child was born towards the end of my postdoc, so I was basically on the job market when he was a year old. Fun times! We had our second son about two years after starting at USC. The older one is Xavier, and the younger is Adrien. My wife Marika and I both work full time, so the kids are in daycare during the day. But then we have family time nearly every day from about 5:30 to 8:30 p.m. And unless there's something that's absolutely urgent that I need to deal with, everything's blocked out.

How do you balance work and family life?
There's an interesting article about the four "burners" of life. It's essentially saying that there is no such thing as perfect work-life balance. So one burner is work, one burner family, third burner is your own health, and the fourth your friends. And to really be successful in life, you can really have two burners going at any one time. I try to balance my life by having two burners go strong, and I divide it up by week. And so I know certain weeks I'll be able, for example, to do better exercising while traveling, but maybe I don't spend quite as much time on work. Or a week after that, I see my family more, and I don't really see my friends at all. I try to rotate those burners or oscillate them, and a lot of it just depends on the priorities for that period of time.

What do you wish you had known before you started?
Being faculty here, you have to prioritize, because there are so many different things that are thrown your way that there's no way to do it all. And so it's essentially saying that I have limits, realizing what my limits are, and working to the strengths. Efficiency is delegating, prioritizing and improving your productivity.

Amy Ryan (Firth)

Assistant Professor, Medicine, Stem Cell Biology and Regenerative Medicine

Who's in your family?
I joined USC in January 2016, so I have been a tenure-track assistant professor for a little over 3 years now. To say life has changed over the past 3 years may be an understatement! I got engaged and married Dan in August 2017. We bought our first home in December 2017 in anticipation of extending our family, which shortly followed with the birth of our baby girl Madelyn Annie on Independence Day 2018! Life is changing every day.

How do you balance work and family life?
I have always prided myself on having a healthy work life balance. Dan and I are both avid athletes: in fact, we met while training for triathlons. Having cycling, running, hiking, swimming, climbing and any other adventurous outdoor activities leaves us with no shortage of ways to maintain a healthy and active lifestyle while spending time together. Since having Maddi, priorities have changed a little!

Balancing being a PI and running my own lab with a healthy family life has definitely become more and more challenging. I often have to spend time on evenings and weekends writing grants or reviewing manuscripts and chatting to collaborators. I am incredibly lucky to have the most amazing husband, who stays home to raise Maddi. I miss her when I am not home, but I am able to come to work and focus, knowing she is in the best hands; he is a fantastic father to her.

Time management is key to trying to maintain balance. One thing that has helped tremendously is commuting to USC by train. This gives me an hour of travel time in each direction to have quiet time to get as much "busy" work done as possible. This frees up time at work for interacting with my research team.

What do you wish you had known before you started?
I attended seminars and courses about the transition to PI. Nothing can quite prepare you. Mastering the art of science is possibly the easiest part of the transition for a postdoc; networking, business, finance, management, travel and teaching are all essential things we are less prepared for, especially all at once!

OUT OF THE WOODS

USC alumna and nature lover Anna Kuehl finds hope to restore her vision

By Breanne Grady

Once upon a time, there was a little girl named Anna Kuehl who loved exploring the nature surrounding her home in the Bavarian Forest. Located northeast of Munich not far from the German-Czech border, this verdant landscape, called Bayerischer Wald, is a wooded, low-mountain region. Kuehl's childhood took place in this idyllic setting, a beautiful playground where she spent many happy hours. Oftentimes, Kuehl would pick wild blackberries and hazelnuts in the foothills that birthed characters like Red Riding Hood, Rapunzel and Snow White.

As an adult, Kuehl moved to the United States and settled in Los Angeles in the early 1960s. At 22, she landed a job as an administrative assistant to USC engineering legend Zohrab Kaprielian. She met and married Hans Kuehl, a dapper and earnest electrical engineering professor, and had two children. While Hans continued his teaching and research, Anna completed her bachelor's degree in accounting at USC and earned her CPA.

Yet Kuehl remained that same girl from the now-faraway forest who found time to appreciate nature. She took frequent hikes in the Palos Verdes Hills of Southern California. On the trails, her favorite plant was the Santa Catalina mariposa lily, a colorful native flower that is white on the outside with a brightly hued interior. On clear days, she saw all the way to Santa Catalina Island, just south in the cobalt blue waters of the Pacific.

Little Girl Lost

As Kuehl grew older, she couldn't marvel at nature's beauty in the same way. Unfortunately, her sight began to deteriorate.

In her mid-30s, Kuehl was diagnosed with dry macular degeneration, an age-related condition that results in the loss of central vision over time. The condition is characterized by the loss of a single-cell layer in the back of the eye called the retinal pigment epithelium (RPE).

At the onset, Kuehl didn't notice anything, but her eye doctor observed an early sign of dry macular degeneration—yellow deposits in the eye called drusen. These deposits form under the retina and are one of the first signs of the condition, often occurring years or decades before the onset of visual symptoms.

Her eye doctor recommended that Kuehl monitor her vision at home using an Amsler grid, a tool ophthalmologists use to detect vision problems resulting from damage to the macula, the central part of the retina. Instead of seeing one black dot in the center of the grid, patients with macular degeneration see an unfocused, larger black area with no distinct shape—essentially a large blind spot.

Eventually, Kuehl found it impossible to see the black dot in the center of the grid.

While her peripheral vision remained intact, she realized she was losing the central vision in her left eye. She could no longer make out people's faces clearly, drive a car or read the time on her watch. Even her beloved hiking excursions became cumbersome.

"I couldn't read the trail names on the posts anymore," said Kuehl, now 78. "I always had to take so many things with me—my magnifying glass, my reading glasses—and I always printed out a big map."

A New Hope

In the Brothers Grimm's fairy tale *Rapunzel*, the sight of a blind prince is a restored by the heroine's tears.

Fortunately, Kuehl's eye doctor at the time, Lisa Olmos, had a different idea: the first human trial of a novel stem cell-based retinal implant that would bring Kuehl all the way back to the doors of her alma mater.

"The loss of one's vision can be extremely devastating."

Mark Humayun

In fact, the USC Roski Eye Institute, part of the Keck School of Medicine of USC, had collaborated for more than a decade with other California institutions to develop a stem cell-based retinal implant for people with advanced dry age-related macular degeneration.

Funded in part by the California Institute for Regenerative Medicine (CIRM), the phase I/IIa study treatment involved implanting an ultra-thin scaffold layered with stem cell-derived RPE cells into the patient's eye. The hope was that implanting RPE cells would halt the progression of the disease. In the best-case scenario, the patient's vision could even improve.

Led at USC by Mark Humayun, a University Professor of ophthalmology, biomedical engineering and integrative anatomical sciences; Amir Kashani, an assistant professor of clinical ophthalmology at the Keck School; and David Hinton, a professor of pathology also at the Keck School, the research involved collaboration with other engineers and scientists including Dennis Clegg, co-director of the Center for Stem Cell Biology and Engineering at the University of California, Santa Barbara.

According to Humayun, a renowned eye doctor and USC Viterbi biomedical engineer, macular degeneration affects 14 million people worldwide. The condition can be inherited or age-related, typically showing up in patients aged 55 or older. Age-related macular degeneration has two primary forms: neovascular, meaning the creation of new blood vessels, called "wet" form; and non-neovascular, meaning no new blood vessels, also called "dry" form.

Humayun had watched his grandmother go blind due to diabetes. She, like Kuehl, had loved nature and all the roses in her garden. That experience helped inform his life's work: restoring sight to the blind.

"The loss of one's vision can be extremely devastating," said Humayun, holder of the Cornelius J. Pings Chair in Biomedical Sciences. "And it can rob one of his or her independence."

In 2013, the Food and Drug Administration approved a device that Humayun co-invented. The Argus II, a retinal implant, was the world's first commercially available "bionic eye" designed to help patients with genetic retinitis pigmentosa, a condition that causes vision loss as the light-sensing cells of the retina gradually deteriorate.

In wet macular degeneration, bleeding and swelling occur in the retina due to the formation of new blood vessels. Treatment consists of injecting drugs into the eye that prevent the new blood vessels from growing. In effect, the medicine alone has the power to stop the disease progression and even reverse vision loss.

On the other hand, 80 percent to 90 percent of age-related macular degeneration patients have the dry form, which doesn't create new blood vessels. According to Kashani, a retinal specialist, the dry form is characterized by the loss of mature RPE cells that support the photoreceptors in the eye responsible for light sensing. Since the RPE cells die primarily in the macula, the retina's mid-region responsible for the sharpest vision, a patient's central vision would worsen over time.

"That led to the idea that we can make these mature RPE cells from stem cells and put them back in under the retina," Kashani explained. "The idea is to replace this single-cell layer early enough in the disease process so that the overlying retina isn't damaged and hopefully you can restore some vision, or at least prevent it from getting worse."

Placement Is Everything

Even more challenging, this layer of RPE cells has to be oriented properly for specific placement in the eye. Past treatment efforts have involved injections of stem cell-derived RPE cells into the macula, a scattershot approach lacking an exact target.

Humayun stressed that placement was a crucial factor for the implant to heal specific, damaged regions of the macula. He made the polymer-based carrier for the RPE cells in collaboration with engineers at Caltech.

The engineering platform itself was another first-of-its-kind, according to Humayun. The substrate was made from parylene, a biocompatible piece of plastic that can be machined in extremely thin form. To engineer this sort of carrier, it needs to behave at the cellular level and seamlessly integrate with the tissue, yet it can't dissolve or erode in the eye.

"In certain areas, it's as thick as only two human hairs and needs to be very thin to allow the diffusion exchange of nutrients, but it also has to be strong enough to carry the RPE cells, so we can fold it and get it in through small, surgical incisions," Humayun said.

Added Kashani, "It's amazing that we can differentiate the RPE cells from human embryonic stem cells and get them to lay flat in a single sheet, which is the same way they exist in the retina. That's a marvel of not only stem cell biology, but also engineering."

Kashani, the eye surgeon for the trial, knew he would have to maneuver the carrier, only four to six microns thick, into the exact spot of the retina where RPE cells had already atrophied or died. After locating the damaged area, he would need to come up with a surgical plan to insert the implant without damaging the surrounding tissue.

After surgery, the RPE cells would need to be monitored, checking how they integrate and function in the patient's eye over time.

Visible Results

Kuehl was selected as one of four patients for the clinical trial. She underwent the surgery for her left eye at Keck Medicine of USC on Oct. 10, 2017. Kashani performed the operation.

For outpatient care, Kuehl slept with a shield on her eye and went back to the doctor's office the following morning. After the shield was removed, she was given a thorough vision test for about an hour, in both bright and dark conditions.

"I got my independence back, and I'm just so happy about it."

Anna Kuehl

"I knew that [my vision] was getting better," Kuehl said. "Using the Amsler grid, I could tell right away. I have used it every day of every year for both of my eyes, and I could tell the shape of the black area had changed after the implant and that [the black area] was getting smaller over time."

Because the trial was part of a phase I/IIa study, Kashani admits the research team wasn't prepared for the exceptionally positive results they saw.

"We weren't really expecting anything significant since most of these patients had such severe disease," Kashani said.

One patient's vision was notably better when tested with an eye chart and measured an ability to read an impressive 17 more letters than before the implant. For two others, tests continue to show that their sight is improving, even if they aren't able to see well enough to read yet.

For the next phase of the clinical trial, researchers will need to conduct a multi-centered trial with a larger cohort of subjects with more visual potential and less severe disease.

Extrapolating beyond the study, Humayun, also the director of the new USC Ginsburg Institute for Biomedical Therapeutics, hopes that one basic idea will have been proven: that stem cells can create replacement parts, organs, tissues and even cells.

"With the right kind of environment and support, you can actually treat very specific regions or diseases down to the cellular level," Humayun said. "One aspect of that could be called precision medicine, and another aspect is that stem cell-based therapies are coming of age. This will be one of the first studies to land that point."

Since the surgery, Kuehl notices little changes in her vision all the time. For example, she can make out the time on her watch again, and reading in general has become much easier. Often, she calls Kashani out of sheer excitement about something new she saw during the day. An avid fan of the opera, Kuehl says she can now read part or all of the subtitles during Metropolitan Opera screenings at local theaters. Remarkably, she can even see the whole faces of people again, whether in person or on television.

"I could only see half of people's faces before on TV and couldn't tell the characters apart," Kuehl said. "But now that I can see better, I can follow the story."

And with sparkling blue eyes filled with joy, she describes how excited she is to go hiking.

"I got my independence back, and I'm just so happy about it," Kuehl said. "Now I don't use a map on the trails, and I can read the trail names on the posts. I don't need anything! I'm much more liberated."

Disclosures:
Regenerative Patch Technologies LLC was founded by Mark Humayun, MD, PhD, and David R. Hinton, MD, from the University of Southern California, and Dennis O. Clegg, PhD, from the University of California, Santa Barbara. The technology to produce the stem cell-based retinal implant is exclusively licensed to Regenerative Patch Technologies LLC from the University of Southern California, the California Institute of Technology and the University of California, Santa Barbara. Humayun and Hinton have an equity interest in and are consultants for Regenerative Patch Technologies LLC.

From professional volleyball to stem cell biology, Leonardo Morsut is at the top of his game

By Cristy Lytal

For USC Stem Cell researcher Leonardo Morsut, the word "set" refers to a collection of scientific data. "Set" is also the prelude to spiking a volleyball over the net—something he used to do for a living as a professional athlete in Italy.

"In my mind, professional volleyball was always a side project," said Morsut, who played for seven years for the professional teams in his hometown of Padova and in Trentino. "It was science that was the main thing."

True to his words, Morsut has always put research first. Even while playing professional volleyball for seven hours a day, he found the time and energy to attend the University of Padova, an institution where Galileo was once a lecturer. He earned bachelor's and master's degrees in medical biotechnologies, before pursuing a second bachelor's degree in mathematics.

Then, at age 25, at the peak of his volleyball career, he quit. He walked away from fame and a generous salary to lead the humble life of a PhD student at the University of Padova. His decision made national headlines in Italy.

"People ask me if I regretted it," he said. "I don't even think about leaving that way. There wasn't really a turning point. There was just one path."

Bioscience and Biology

As a PhD student, he pursued research in bioscience, genetics and the molecular biology of development. He spent years focused on mouse gastrulation, the early embryonic phase during which a ball of cells organizes itself into distinct layers as a prelude to organ formation.

> “For me, this is the realization of a dream and a first step that demonstrates a new way of building biological structures.”
>
> ***Leonardo Morsut***

In the midst of this research, he picked up an unrelated side project: how stem cells behave differently depending upon whether they’re on a hard or a soft surface. Specifically, he and his colleagues found that when stem cells are on a hard surface, they react by producing two signals—called YAP and TAZ—that encourage them to become bone cells. The side project quickly became his main project, and Morsut and his team published their discovery in the journal “Nature.”

“It was really a rush and a blast,” said Morsut. “And it was what launched my career, because then it was easier to get a postdoc in a bigger lab.”

After receiving his PhD and spending an additional postdoctoral year at the University of Padova, he became increasingly fascinated by the emerging field known as “synthetic biology.”

“Synthetic biology is pretty much trying to bring the engineering approach of building things into biology,” said Morsut. “You think about the biological system not as something that you want to learn about, but as something that you want to use to achieve a goal.”

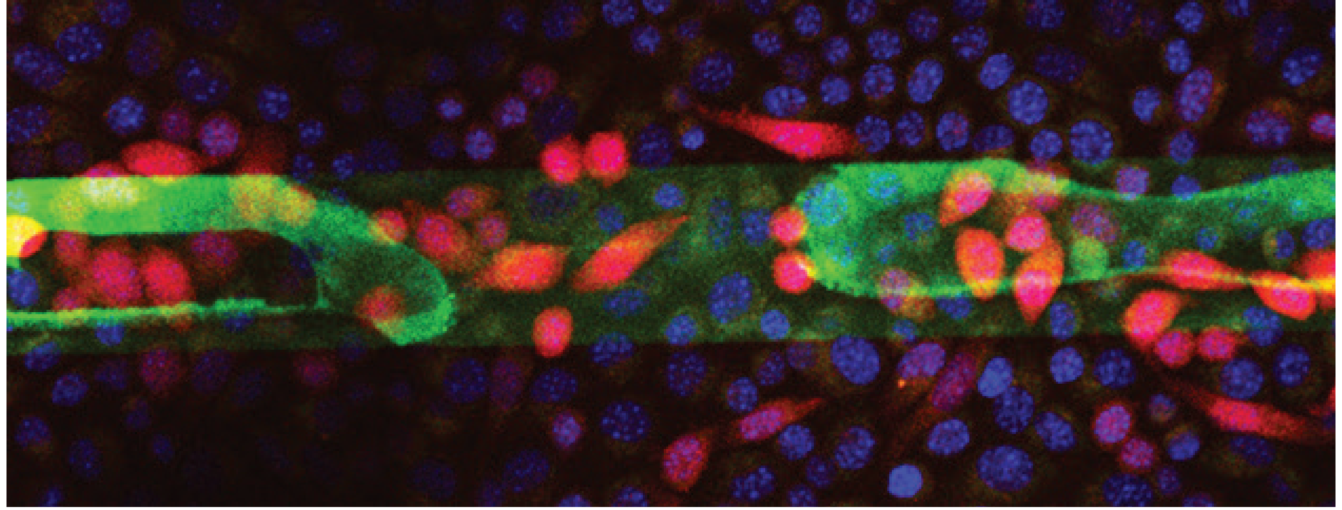
Cellular Communication

Inspired by this approach, he accepted a postdoctoral fellowship in the laboratory of one of the founders of synthetic biology: Wendell Lim at the University of California, San Francisco.

“Wendell and I didn’t even know what I was going to work on, but we liked each other,” said Morsut.

After some initial experimentation, Morsut settled on his main project: building a synthetic cellular communication system known as “synNotch.” This system enables scientists to direct the behavior of cells in useful ways.

Morsut created synNotch by co-opting a relatively simple natural communication system, called Notch, in which a cell uses a sensor on its surface to recognize and trigger a particular response to a specific signal. In Morsut’s synthetic version of Notch, he swapped in a new sensor—allowing him to control which signal the sensor recognizes, as well as what the cell does in response.



In a study published in *Science,* Lim, Morsut and their colleagues used synNotch to guide cells to self-organize into layered spheres, for example, not unlike rudimentary tissues or very early embryos.

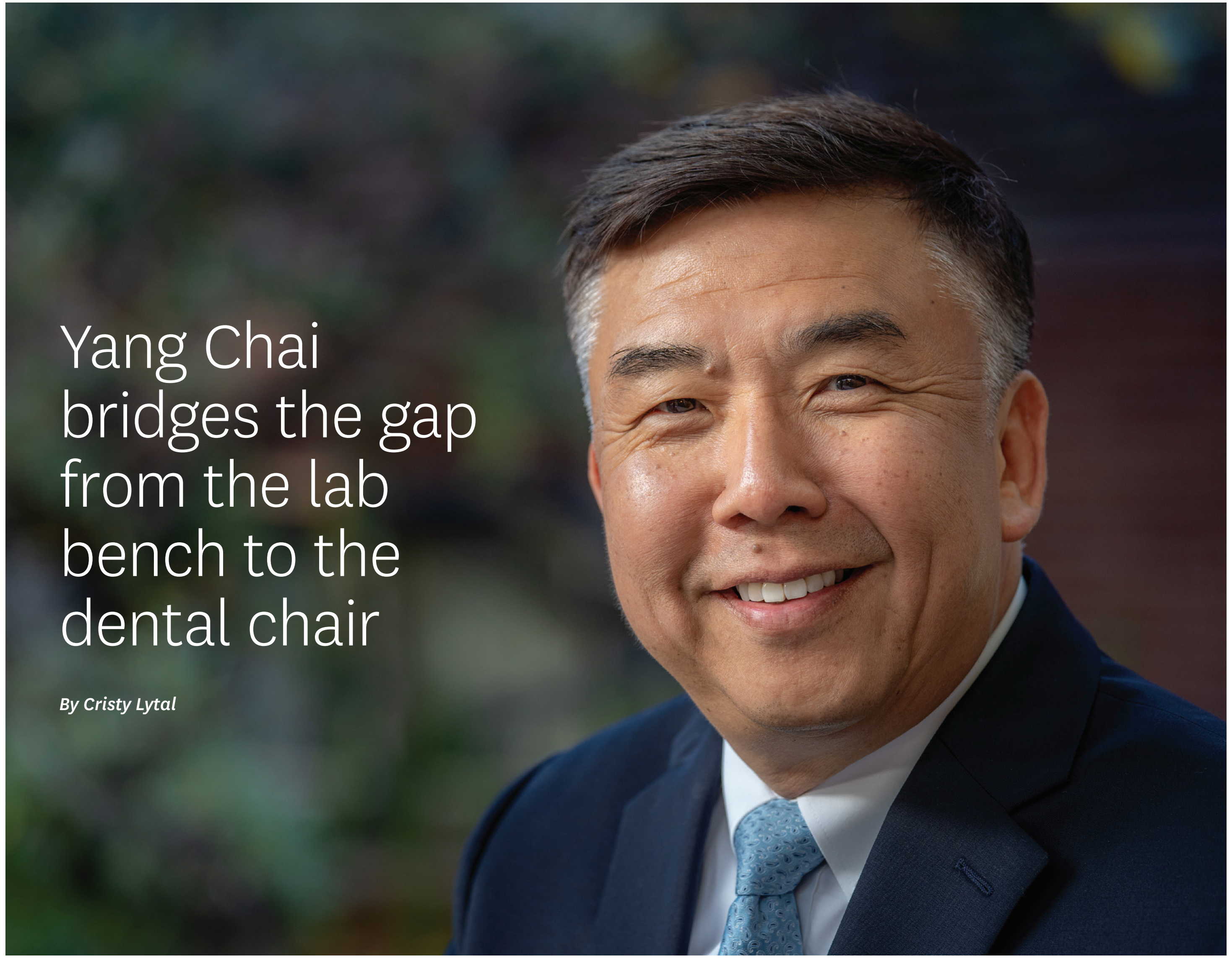
“For me,” said Morsut, “this is the realization of a dream and a first step that demonstrates a new way of building biological structures.”

SynNotch or a similar system could have many potential medical applications. For example, scientists could swap in a sensor that enables an immune cell to recognize a signal from a tumor, and respond with an attack. Alternatively, researchers could use this technology to prompt cells to differentiate and organize into tissues with special properties, such as enhanced injury resistance or regenerative capacity.

This breakthrough earned Morsut a position as an assistant professor of stem cell biology and regenerative medicine at USC. At the same time, his wife Sabina accepted a postdoctoral fellowship in art history at USC. Other big changes were on the horizon: the couple, who originally met when they were 12 years old in their hometown of Padova, expanded their family with the arrival of their second child shortly after starting at USC.

As one of the first projects in his new lab at USC, Morsut is using synNotch to direct the differentiation of stem cells into blood vessels in collaboration with Megan McCain at the USC Viterbi School of Engineering.

“The stem cell department is very exciting, and it has a lot of potential and a lot of forward thinking,” said Morsut. “Engineering is also a strength of USC, and there is interest on both sides to grow more at that interface. That is definitely something that will benefit my research program and vice versa. I have high expectations.”



Yang Chai bridges the gap from the lab bench to the dental chair

By Cristy Lytal

As a young oral surgeon in China, Yang Chai often operated on babies born with cleft lips or palates.

"You talk to the parents, and they were very emotional and trying find out why their kid got this cleft palate or other malformation in the face," he said. "You can tell them all the statistics—one out of 700, one out of 1,500—but to them, it's 100 percent because their kid has this disease. At that time, the whole field didn't really have that much idea about what causes these congenital birth defects."

This was the motivation for Chai's lifelong dedication to the study and practice of craniofacial biology.

A Born Doctor

Chai was born into a family of cardiothoracic surgeons, orthopedic surgeons, pediatricians and other medical professionals in Beijing. His grandmother, a nurse, brought Chai to the hospital where she worked, and he was inspired by doctors' ability to help patients recover from disease. He decided to pursue medicine with a specialty in the craniofacial region.

"I've always been interested in the face," he said. "It's really our identity, and we recognize each other largely by our facial features. And in China, craniofacial surgery or neck surgery is part of dentistry."

Chai earned his undergraduate and professional degrees in oral medicine, also known as stomatology, at Peking University. Upon graduation, he treated many patients with craniofacial birth defects, such as cleft lip and palate, when he was a resident in Oral and Maxillofacial Surgery.

Committed to uncovering the underlying causes of these birth defects, Chai came to the States and pursued his PhD and postdoctoral training in USC's craniofacial biology program, one of the oldest in the world, and his wife joined USC's population research program. He also repeated his clinical training so that he could practice dentistry and oral surgery in the U.S., earning his DDS degree from USC. After his dental school graduation in 1996, he joined the USC faculty and now serves as the George and MaryLou Boone Professor of Craniofacial Molecular Biology, Associate Dean of Research, and Director of the Center for Craniofacial Molecular Biology (CCMB) at the Herman Ostrow School of Dentistry of USC. In 2018, Chai was elected to the National Academy of Medicine in recognition of his ground-breaking and influential research.

Stem Cells, Scaffolds and More

As a faculty member, his first project was a study of the cellular and molecular mechanisms underlying cleft palate. Today, he continues this line of research with a study of how two special populations of cells, called neural crest and muscle progenitors, interact to form the soft palate. In collaboration with USC Stem Cell

Cleft lip and cleft palate are among the most common birth defects, affecting approximately one or two in a thousand babies.

> “If I can help one or just a few patients to make their lives better, I think that’s worth it.”
>
> *Yang Chai*

scientist Megan McCain at the USC Viterbi School of Engineering, Chai’s lab is exploring potential clinical applications of this research by crafting 3D scaffolds to aid muscle regeneration and enhance the surgical repair of soft palate defects.

Using a similar 3D scaffold seeded with stem cells, Chai’s team is also forming strategies for improving the treatment of craniosynostosis, a dangerous birth defect that restricts brain growth due to the premature fusion of various sections of the skull. And a similar scaffold approach, using stem cells derived from dental pulp, has shown equal promise for treating skull injuries that are too large to heal on their own.

All of these scaffolds have produced promising early results in lab animals, and Chai hopes they will eventually advance to clinical trials for patients with these conditions.

As a dentist and oral surgeon, Chai is also committed to understanding tooth root formation, which could have applications for improving dental implants. Although implants have a success rate exceeding 90 percent, patients with multiple implants lack the natural ligaments and nerves to help gage the amount of force to use when biting into foods of different textures. As a result, some patients eventually fracture their implants. Chai hopes to discover and harness cellular and molecular mechanisms that could enhance the regeneration of these ligaments and nerves to create better biological implants.

His lab also studies the molecular and cellular mechanisms involved in forming everything from the tongue to the teeth to the skull, in the hopes of enhancing our understanding of normal craniofacial development as well as birth defects.

To bridge the gap between these laboratory discoveries and patient cures, Chai recognizes the importance of collaborations between biologists, engineers, clinicians and many others.

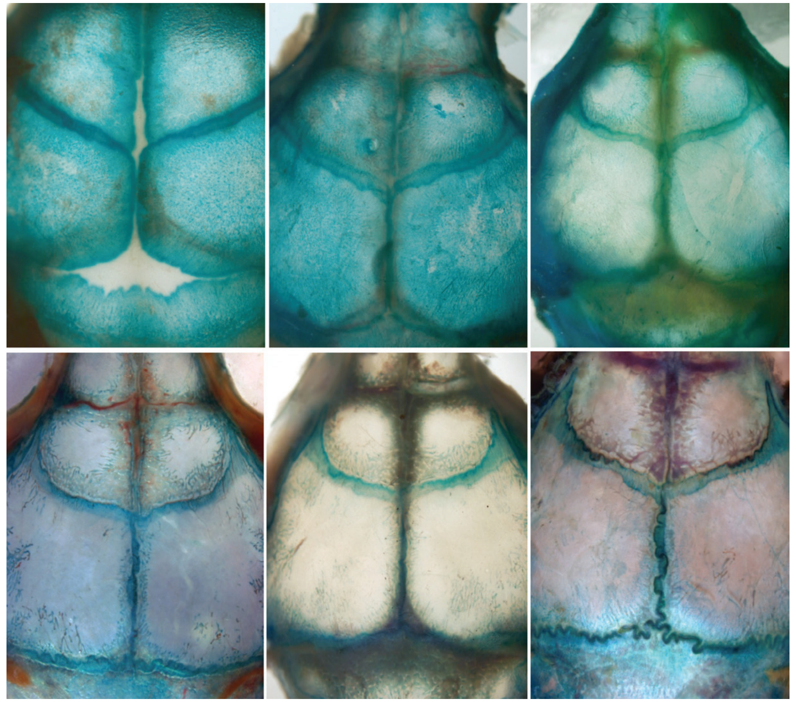
“Over the years, the most exciting thing is to work with a lot of smart people,” he said. “I’m just humbled to see the colleagues that we have at USC and also, of course, the interactions I’ve had with people from all over the world.”

As one example, he’s currently collaborating with colleagues at UCLA, UC San Francisco, UC San Diego, UC Davis, UC Berkeley, Stanford University and City of Hope to form an NIH-funded Center for Dental, Oral and Craniofacial Tissue and Organ Regeneration, or C-DOCTOR for short. This center aims to accelerate tissue engineering and regenerative therapies into clinical trials to treat dental, oral and craniofacial conditions.

Another multi-institutional collaboration, called FACEBASE, is essentially “crowd-sourcing” a large, NIH-funded and publicly available database related to craniofacial development. The massive amounts of resulting data are maintained by Carl Kesselman, director of the Biomedical Data Center at the USC Viterbi School of Engineering.

Despite his busy and productive research portfolio, Chai still devotes his Thursdays to seeing patients as a general dentist and oral surgeon.

“I’ve continued that throughout my career, because I really love the interaction with patients, and it’s a very rewarding process,” he said. “If I can help one or just a few patients to make their lives better, I think that’s worth it.”



A series of mouse skulls (Image by Hu Zhao/Chai Lab)

Justin Ichida reprograms cells and redefines ALS research

By Cristy Lytal

Upon meeting USC Stem Cell professor Justin Ichida, you get the impression that he's a pretty laid-back dude. A third-generation Hawaiian, he'll take the time for a leisurely chat about anything from NFL football to science fiction to the challenges of growing tropical fruit trees in his Los Angeles backyard. What might not be immediately obvious is the work ethic that drives him to toil late into the night as the head of a busy laboratory and a biotechnology startup seeking new treatments for ALS.

Ichida has always been drawn to the laboratory. Growing up on Oahu, he was fascinated by science in all of its many guises—whether it was the experiments in his high school biology class or descriptions of dinosaur DNA in Michael Crichton's *Jurassic Park*.

As an undergraduate at UCLA, he majored in molecular genetics and pursued a series of research experiences. He studied the brains of fruit flies during a summer internship at the University of Iowa, the genetics of cancer at the Danish Cancer Society, and HIV's integration into the genome at UCLA. He also maintained his Aloha spirit as the president of the Hawaii People's Club, and he frequently performed hula and even flew in an island-roasted pig as the main dish for a campus luau.

After graduation, he obtained his PhD in genetics from Harvard Medical School, where he studied how life emerged from the primordial soup in the lab of Nobel Laureate Jack Szostak, and moonlighted as a guitarist in the rock bands Maniatis Maniatis and Holding Room.

"The bands were a bunch of scientists," said Ichida. "But our drummer in Maniatis Maniatis was amazing, actually. He used to be a professional drummer before he became a neuroscientist."

From Primordial Soup to Human Cells

For his postdoctoral training, Ichida remained at Harvard, but joined the laboratory of Kevin Eggan, and shifted his focus from the primordial soup to something further along on the evolutionary timescale: human cells.

Ichida helped identify better ways to make induced pluripotent stem (iPS) cells, and also made a breakthrough that paved the way for new approaches to studying diseases involving motor neurons, including the fatal neurodegenerative disease ALS. In the past, studying patients' motor neurons was nearly impossible, because removing these cells from the body inflicts serious nerve damage. To surmount this obstacle, Ichida pioneered a technique for directly reprogramming patients' readily accessible skin or blood cells into motor nerve cells, which can be used not only to study ALS, but also to test potential treatments.

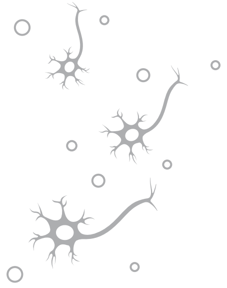
In 2013, Ichida joined USC as an assistant professor of stem cell biology and regenerative medicine, and he has already made tremendous progress in the quest to find new treatments for ALS.

Using reprogrammed patient cells, Ichida's group recently published a study in *Nature Medicine* describing how a gene called *C9ORF72* leads to toxicity in nerve cells—causing 10 percent of all cases of ALS, as well an additional 10 percent of a related disease called frontotemporal dementia.

Ichida's team is also identifying previously undiscovered mutations that trigger ALS in the 90 percent of patients who have no known relatives with the disease.

To translate their discoveries into patient cures, Ichida's team is screening more than 40,000 potential drugs to see if any can stop the degeneration of reprogrammed cells from patients with ALS. They are performing this screening in collaboration with biotechnology company Icagen Corporation and machine learning company DRVision Technologies, supported by $1.5 million in federal funding from the U.S. Department of Defense. The partners have already found several promising drug leads. In addition, Ichida and collaborators co-founded of a local biotechnology company, Acurastem, Inc., to seek to further develop therapeutic strategies.

"There's a real need for discovering something that's going to prolong the lives of these patients," said Ichida. "And that's why we do what we do."



ALS causes progressive paralysis and usually results in fatal respiratory failure within three to five years of diagnosis.

From babies to senior citizens, Denis Evseenko is working for better outcomes

By Cristy Lytal

When Denis Evseenko was a still a student at Novosibirsk State Medical University in southern Siberia, he began pondering the meaning of life.

"I was reading a lot of philosophic things [saying that] everything is pointless because you will die," he said. "And the only one thing that makes it not completely pointless is that you can have a next generation. Kids will be born. Life will continue. So for me, this was such a big thing."

The process of pregnancy and fetal development fascinated Evseenko not only from a philosophical perspective, but also from a biological one. So after earning his medical degree in 1999, he joined an embryology laboratory at the Scientific Center of Clinical and Experimental Medicine, also in his hometown of Novosibirsk. He studied how the human placenta regulates oxygen supply to the fetus and influences lifelong cardiac health.

In 2004, Evseenko moved to New Zealand, where he pursued his PhD in pharmacology at the University of Auckland's Liggins Institute. At the same time, he and his wife welcomed the first of two daughters into their family.

Throughout this time, Evseenko continued to study the placenta, detailing how certain drugs interfere with fetal development.

"I realized that when something goes wrong in development," he said, "there's very little you can do to actually change the outcomes."

He wanted to change outcomes, and stem cell science offered a possibility to leverage his expertise to help patients. So he delved into the stem cell field as a postdoctoral researcher in the laboratory of Gay Crooks, first at Children's Hospital Los Angeles, then at UCLA. He then started his own laboratory at UCLA focused on stem cell-based cartilage repair in 2011, and moved to USC as an associate professor of orthopaedic surgery, and stem cell biology and regenerative medicine in 2015.

It Requires Patients

"For me, it's not science for science," said Evseenko. "I need to see it going somewhere."

To this end, the Evseenko laboratory is advancing some of its recent scientific discoveries towards clinical trials.

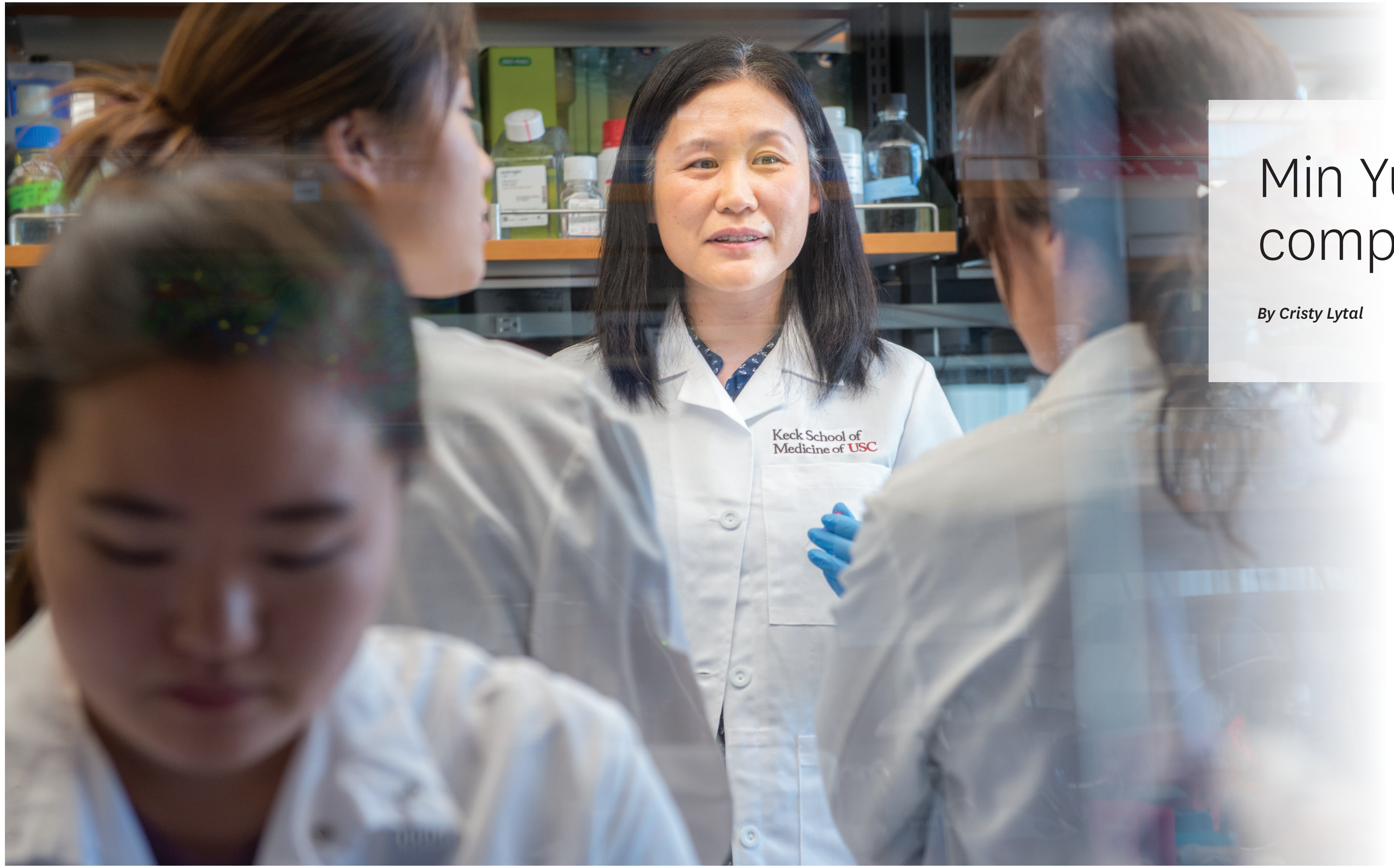
With funding from the California Institute for Regenerative Medicine (CIRM), the lab is working to develop cartilage implants made from stem cells. Surgeons could use these cartilage implants to repair sports-related knee injuries, which affect more than 10 percent of people under 50 years old. Evseenko aims to start clinical trials for this stem cell-based cartilage implant by late 2020.

Evseenko and his company CarthroniX are also working to develop new drugs based on a molecule called HX-1, which can curb inflammation and promote regeneration. A topical form of HX-1 is already on the market as a cosmetic anti-aging serum, named Heraux. Cosmetics proceeds will support the further development of potential medical applications for HX-1. One of these potential medical applications is slowing the progression of jaw arthritis, caused by problems with the temporomandibular or TMJ joint. In collaboration with USC Stem Cell scientist Yang Chai and researchers at the University of Guelph in Canada, Evseenko is involved in the pre-clinical NIH-funded testing of an injectable form of one of the potent and selective HX-1 analogs called CX-011 to reduce inflammation related to TMJ arthritis. The group is also conducting a Department of Defense-funded pre-clinical trial of CX-011 for osteoarthritis of the knee. Recently, animal studies showed that CX-011 is a very safe drug. The scientists intend to launch a clinical trial in 2021.

Evseenko and collaborators at several universities are also exploring the potential of CX-011 to help patients with autoimmune diseases. If CX-011 can achieve this, Evseenko's early embryology studies will come full circle.

"These diseases are so painful, especially a form of rheumatoid arthritis called juvenile arthritis and lupus," said Evseenko. "They need to take drugs that are Category X or D, which means these drugs cause birth defects in their babies. So my main patient passion is about these young females—making pregnancy healthier and helping to deliver healthy babies. If we can do anything to help them, I'll feel good."

Arthritis and other rheumatoid conditions are the leading cause of disability in the U.S.



Min Yu brings curiosity and compassion to cancer research

By Cristy Lytal

In her new lab, Min Yu observed the eerie predictability of a line of breast cancer cells. First in one mouse, then in many, the cells metastasized again and again to the same vital organ: the brain.

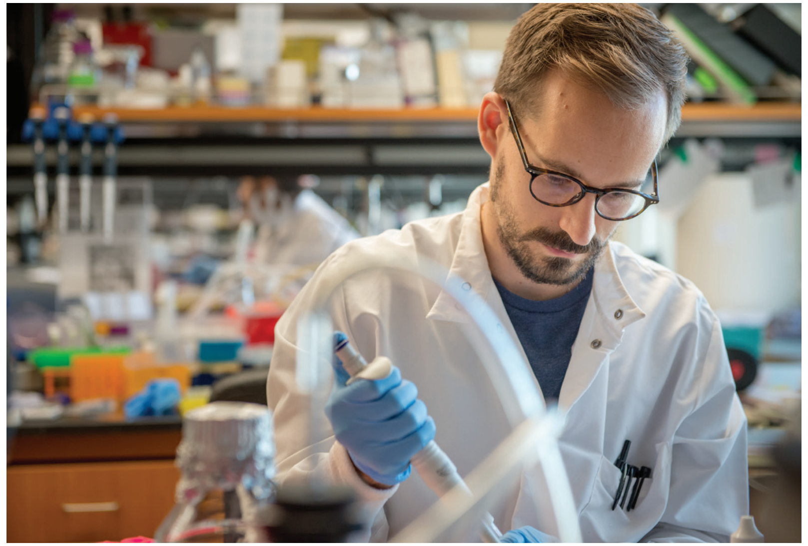
Alarmed, Yu telephoned the oncologist who had collected the cells from a patient. Yu learned that the patient had already succumbed to brain metastasis.

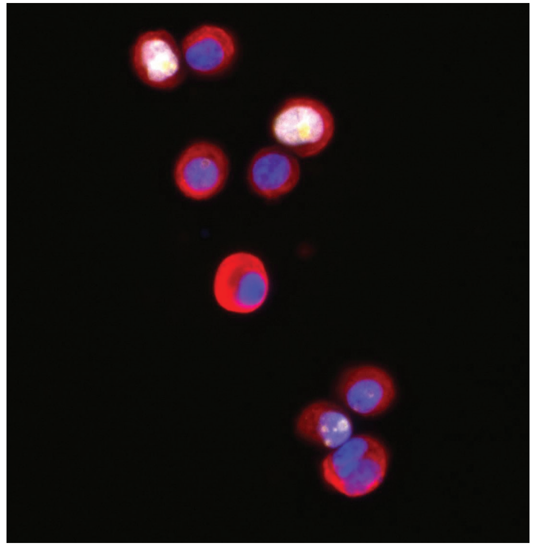
Yu's strong combination of curiosity and compassion has inspired an intensely personal scientific journey.

Yu was born and raised on China's northeastern coast in the city of Qingdao, famous for its beer. She was a curious child, with a strong interest in computer science as well as many other subjects. Ultimately, she chose to follow her mother's example and become a physician.

Yu earned her MD at Shandong Medical University and her master's degree in neurology at Peking University Health Science Center. Working in the neurology field, Yu saw many patients who had inherited diseases with no cures. It was heartbreaking for her to run up against the limitations of current medical practice—so she decided to devote herself to discovering new treatments as a scientific researcher.

Yu left her home country and ventured to the United States, where she joined the PhD program at SUNY Stony Brook University/ Cold Spring Harbor Laboratory and turned her attention to breast cancer—which affects one in eight women and leads to 40,000 deaths annually.





Above, right: Circulating tumor cells isolated from the blood of a patient with breast cancer (Image by Min Yu)

"The lab was creating what we call 3D cell cultures, which are systems to grow mammary cells in the laboratory," she said. "These small structures resemble actual mammalian mammary glands that even secrete milk. And then if you introduce cancer genes, you can transform the normal structure into a cancer-like structure."

For her postdoctoral training, she moved to the Massachusetts General Hospital lab of Daniel A. Haber, who was collaborating with clinicians and bioengineers to study circulating tumor cells, which enter the bloodstream and metastasize at distant sites. Yu was able to collect rare circulating tumor cells and expand them in her newly developed 3D cell cultures—creating a critical mass of cells that could be studied longterm in the laboratory.

"During that time, I lost my dad, because my dad had liver cancer," said Yu. "So that made it clear to me that we need to bridge the basic research to the clinical. That's something very, very important."

With the Patient in Mind

When it came time to start her own research laboratory, Yu was attracted to USC's dynamic, multidisciplinary research environment that encouraged collaborations. Yu is a member of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, and her laboratory is located in the USC Norris Comprehensive Cancer Center, facilitating her collaborations with clinicians who provide her with "liquid biopsies," blood samples containing circulating tumor cells from individual patients with metastatic breast cancer.

Min Yu turned her attention to breast cancer—which affects one in eight women and leads to 40,000 deaths annually.

Yu is always keenly aware that the cancer cells that she studies contain not only important scientific clues, but also the destinies of individual patients with breast cancer. Her team is working hard to learn everything they can about these patient-derived tumor cells, which they can grow using Yu's pioneering 3D cell cultures.

Several of their projects involve probing genetic and molecular profiles to discover which factors promote drug-resistant disease, which cells are the most aggressive "cancer stem cells" and how these cells metastasize.

Through this research, Yu's team has pinpointed specific genes that drive the cells' predictable tendencies to colonize specific organs—whether it be the brain, lungs or bones. Their goals are to use these specific genes as biomarkers to predict the course of an individual patient's disease, or as targets for developing new personalized drug therapies.

Another project involves a collaboration with USC engineer Pin Wang, who developed a nanoparticle to effectively deliver a drug called 5Z-7-Oxozeaenol or OXO to tumor cells. This drug inhibits a protein called TAK1, which in turn reduces lung metastases in mice with the most deadly form of breast cancer—the triple negative strain.

Looking ahead, Yu has already made discoveries with relevance not only to breast cancer, but also to lung cancer. She hopes to continue to expand her research into other types of cancer, maximizing the number of patients who could potentially benefit.

"Since I've been involved in both basic research and clinical practice, I understand the urgency of translating our discoveries into new treatments for patients," she said. "The patient is never far from my mind."

Qi-Long Ying shoots the moon as a cancer researcher

By Cristy Lytal

If you knew that a $10 billion check was hidden in your office building, and that 10 million people had searched for it for more than 10 years without finding it, would you continue the quest? For USC Stem Cell scientist Qi-Long Ying, the answer is a resounding yes.

"If you can cure cancer, that's worth $10 billion, more than that," he said. "We also know that 10 million people already tried, and they failed. So you really need to be very strong. You need to believe in yourself to try this."

Ying's lab is continuing the quest to develop cancer immunotherapy by using a type of immune cell called a macrophage, which can be genetically modified to target solid tumors.

Ying has taken on long odds before. 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.

"At that time, as a kid, I was always curious about everything," he said. "So the older generation told me when I was small that I was always asking many different questions, always asking, 'Why, why, why?' "

Despite his natural curiosity, Ying had had little chance of obtaining a higher education. Chinese universities admitted students based on political and family connections, not academics, throughout most of his childhood. This changed with the death of Chairman Mao in 1976, and the subsequent reinstatement of the "Gaokao," China's merit-based college entrance exam. Ying earned a top score.

"At that time, the test was very important and changed your life forever," he said. "That's why many people, when they learned the results, they always cried. My mother [was so happy that she] also cried."

Although he originally dreamed of becoming a detective or a civil engineer, charismatic recruiters from the First Military Medical University persuaded him to choose a different path. What he didn't fully appreciate at the time was that attending one of China's military medical universities carried an obligation of 25 years of army service.

After Ying graduated in 1987, the army decided that he would work at a remote missile base near the Chinese border with North Korea—a three-day train ride from his hometown, his parents and his three sisters. For a salary of $14 per month, he was charged with treating colds, headaches and minor ailments, and triaging more serious patients to a larger hospital elsewhere.

"We were in the mountains," he said. "It was very, very cold—minus 30 degrees Celsius in the winter. We were not allowed to contact outside people. It took two hours of driving to go to the nearest town. And there were no women, and there was no hope, and life was very boring. We had no future. Sometimes during the weekends, the young officers drank, and they were crying, because there was no hope."

Ying's lab is continuing the quest to develop cancer immunotherapy by using a type of immune cell called a macrophage, which can be genetically modified to target solid tumors.

But Ying was determined to elude his seemingly sealed fate. 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.

During his graduate training in the early 1990s, he and his mentor, a famous Chinese neurosurgeon, injected human embryonic neural tissue into the brains of 18 patients with Parkinson's disease. Some regained the ability to walk, but only temporarily. The procedure also carried a high enough risk of fatal infection that the researchers halted the experiments.

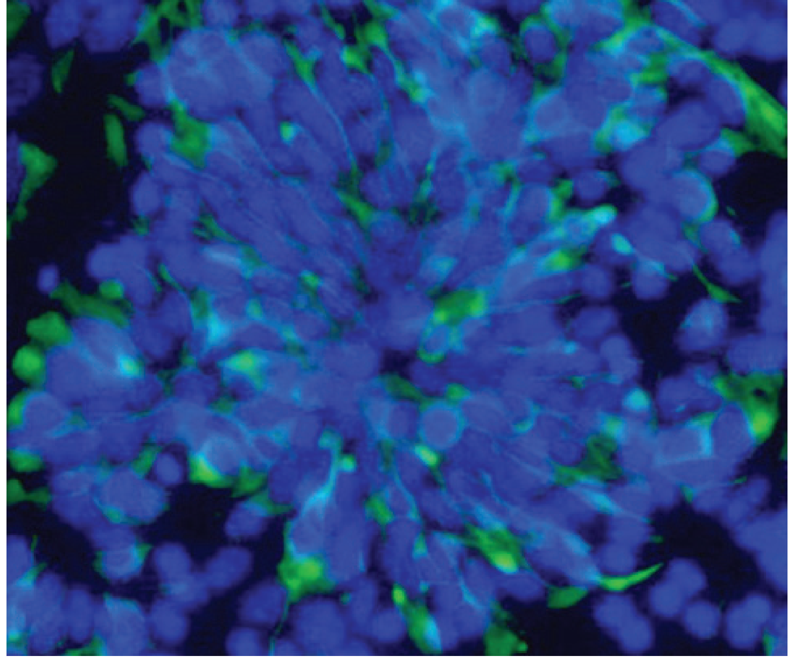
Ying happily pursued these educational and research endeavors for nearly a decade. Then the army noticed his absence and summoned him back to his missile troop—now relocated to the country's remote central region. He realized that to get out of the army, he had to get out of China.

Opportunity Abroad

Ying applied to at least 50 jobs all over the world. It was his unique experience with Parkinson's disease that landed him a two-year postdoctoral position in Austin Smith's laboratory, then at the University of Edinburgh in Scotland. Through six months of dogged persistence and better-than-average luck, Ying secured a passport to embark on his new life.

New to both stem cells and the English language, Ying made a series of breakthroughs: He observed the first proof of ES cells spontaneously fusing with neurons, and developed a more efficient way to turn ES cells into neurons. He also discovered how to inhibit ES cells from differentiating into specialized cells by exposing them to two molecules—dubbed 2i.

Beyond these scientific successes, Ying is keenly aware of how profoundly Smith changed his life.



Neural stem cells (Image by Qi-Long Ying)

"Without Austin, I would not have my daughters. In China, I cannot have more than one child, [my eldest son]," he said. "I would still be in the army as a family doctor, and the only diseases I could treat would be colds, headaches and diarrhea. So I said [to Austin], 'Your offer letter changed everything, changed me.' "

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.

Shortly after his arrival at USC, Ying and a team of researchers made one of *Science* magazine's "Top 10 Breakthroughs of 2010" by using ES cell-based gene targeting to produce the world's first knockout rats, modified to lack one or more genes.

"The rat is not only bigger than the mouse," said Ying. "Physiologically, they are much closer to humans. So many diseases, such as many neurological diseases, can only be mimicked in the rat, but not in the mouse."

He hopes that his story will provide inspiration for the next generation of biologists.

"I started my stem cell career maybe 19 years ago," he said. "At that time, I had no experience whatsoever with stem cells, but I believed I could make contribution to this field, and I worked hard. So to be successful in this very competitive scientific career, you have to have confidence that you can achieve something."

Students and Trainees

The master's program in stem cell biology and regenerative medicine graduated its fifth class, bringing the total number of alumni to 150 as of Summer 2019.

POSTDOC

Jorge Contreras

Rong Lu Lab

What inspired you to get involved in stem cell research?
Being a first generation Latino, a male, growing up in South Los Angeles with two parents who didn't have a high school education, I had no idea what it meant to take science forward. I came across a lot of science professors at community college that kept me encouraged, and Cal State Dominguez Hills was actually the place where I came across a professor, Dr. Helen Chun, who became my mentor in this program called the MARC U-STAR Program, and a second program called the MBRS-RISE Program—two programs that promote diversity in the sciences. It was there that I actually got exposed to the greater scientific community that I didn't know existed.

What is your current research?
Here at USC in Dr. Rong Lu's lab, we are studying how normal stem cells of the blood develop. Studying how the normal stem cell develops in the blood will give us some answers, possibly, to what eventually gives you a disease.

What are your future goals?
My dream job would have been always, and continues to be, to be a professor at a university and teach. I grew up in Los Angeles. And so one part of my goal is to eventually go back to the community that I grew up in and help guide people towards a greater diversity in science.

PHD STUDENT

Albina Ibrayeva

Bonaguidi Lab

What inspired you to get involved in stem cell research?
As an undergraduate student back in Kazakhstan, during my sophomore year, I interned at the National Center for Biotechnology in Astana. This experience enabled me to work with some of the brightest minds dedicated to scientific research in my country and showed me the meaningfulness of a career in biomedical research. Since then, I knew that I wanted to be a scientist. I won a scholarship and was accepted to graduate school at USC, first to study biomedical engineering as a master's student, then the biology of aging as a PhD student.

What is your current research?
I'm studying neural stem cell (NSC) aging. It's already known that NSC activity diminishes during aging, but we know much less about the cellular and molecular mechanisms underlying this decline in the hippocampus, which is a region of the brain involved in learning and memory.

What are your future goals?
After graduating from the USC PhD program, I would like to work as a professor and researcher at a U.S. university. It is one of my dreams to be able to share my knowledge, and being a professor would allow me to do so, while continuing my research to benefit U.S. health care and the science of aging.

PROGRESSIVE MASTER'S STUDENT

Natasha Natarajan

Crump Lab

What inspired you to get involved in stem cell research?
My dad is a surgeon at the Keck Hospital, and my mom works at Kaiser, and she's a pathologist. So I definitely see my initial interest in medicine stem from how much I was inspired by the two of them. But for me, I really wanted to start being a doctor when I first learned about stem cells. It happened when I was 15, and I was in AP Biology, and Cedars-Sinai, the hospital nearby, came to our class and presented us with an opportunity: it was the first ever stem cell writing competition. I wrote the research paper, and I ended up winning, which is really cool. And the prize was getting to work at a lab on stem cells at UCLA.

What is your current research?
What we're looking at is how do zebrafish regenerate cartilage, and looking at the mechanism behind that in hopes of finding a valuable treatment for osteoarthritis. So it's really fascinating.

What are your future goals?
Being a physician is a priority to me, and stem cells are a passion. I want to be a doctor that uses these innovative stem cell therapies and actually implements them in patients.

HIGH SCHOOL STUDENT

Richard Lopez

McMahon Lab

What inspired you to get involved in stem cell research?
I wanted to go into the field of stem cells because my grandma has issues with arthritis in the knees, and so seeing her struggle through that daily is something that hurts me and influences me. So I wanted to go into the field of science, because I know that it can change things like that, especially with the field of stem cells. When I'm older, if I can take part in coming up with not a cure but a treatment for osteoarthritis, which is arthritis in the knees, that'd be cool, to say the least.

What is your current research?
I've been working a lot with Lisa Rutledge. She's mostly studying the different signaling between the stalk of the uteric bud and the tips of the uteric bud in the developing kidney. And Jill McMahon showed me a lot about how to image the urogenital system. I also got to do PCR, and then also gel electrophoresis with Rosa Sierra.

What are your future goals?
I'm starting my college applications!

Meetings

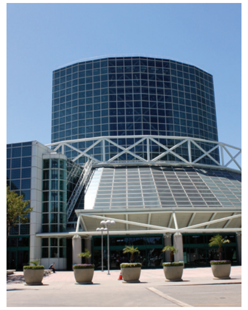
USC Stem Cell and BCRegMed Virtual Symposium
It didn't require plane tickets to bring together scientists from USC Stem Cell in Los Angeles and BCRegMed in Vancouver. During the October 2018 Virtual Symposium, videoconferencing technology enabled these scientists to share ideas as if they were sitting in the same conference room—even though they were more than 1,200 miles apart.

During the day-long event, eight scientists from each institution gave presentations about their latest research. Dual screens in each conference room projected researchers along with their slides. During the Q&A sessions, presenters fielded questions from audiences in both locations—as well as from remote spectators following the event online. Topics ranged from development to disease to tissue engineering.

The symposium ended with a virtual poster session: scientists presented their research as videos rather than on printed paper, and fielded questions on an online platform.

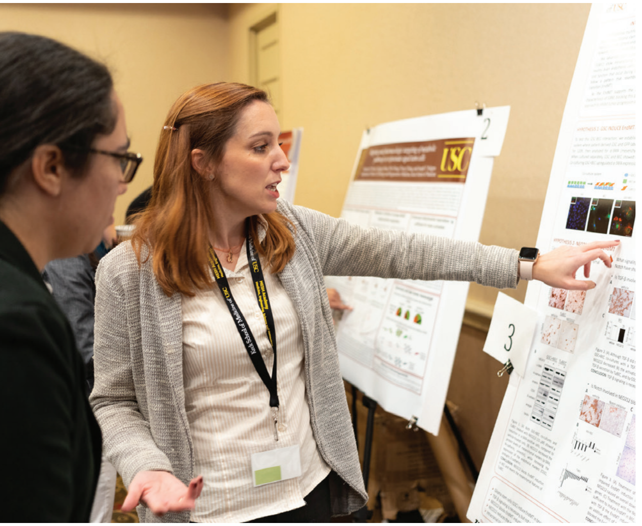
"We hope that this is the first of many virtual symposia," said Andy McMahon, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC.

International Society for Stem Cell Research (ISSCR) Conference
In recognition of its growing stature as an incubator for the biosciences, Los Angeles was chosen as 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 co-hosted the conference, and the city-owned Los Angeles Convention Center served as the venue.



Previous host cities include Barcelona, Boston, San Francisco, Stockholm, Toronto, Vancouver, Yokohama, Philadelphia and 2018's meeting in Melbourne.

"L.A. is the latest and most innovative bioscience hotspot in the state," said Mayor Eric Garcetti, "and ISSCR's choice is a reflection of the scientific advances occurring in our city today."



Interdisciplinary Stem Cell Symposium

“The field of stem cell biology is one of our great convergence opportunities,” said USC Provost Michael Quick, addressing an audience of biologists, chemists, physicists, engineers, clinicians and many others. This diverse group came together for the Interdisciplinary Stem Cell Symposium, hosted by USC Stem Cell and the USC Medicine, Engineering, Science and Humanities (MESH) Academy in November 2018.

Throughout the symposium, scientific talks demonstrated convergence in action through collaborations between researchers from different disciplines. Talks addressed everything from imaging technologies, to gene editing, to tissue engineering, to new approaches to treating disease.

Attendees also connected during a poster session and presentations, and had the opportunity to chat with potential collaborators during lunch, coffee breaks and a reception.

USC Stem Cell

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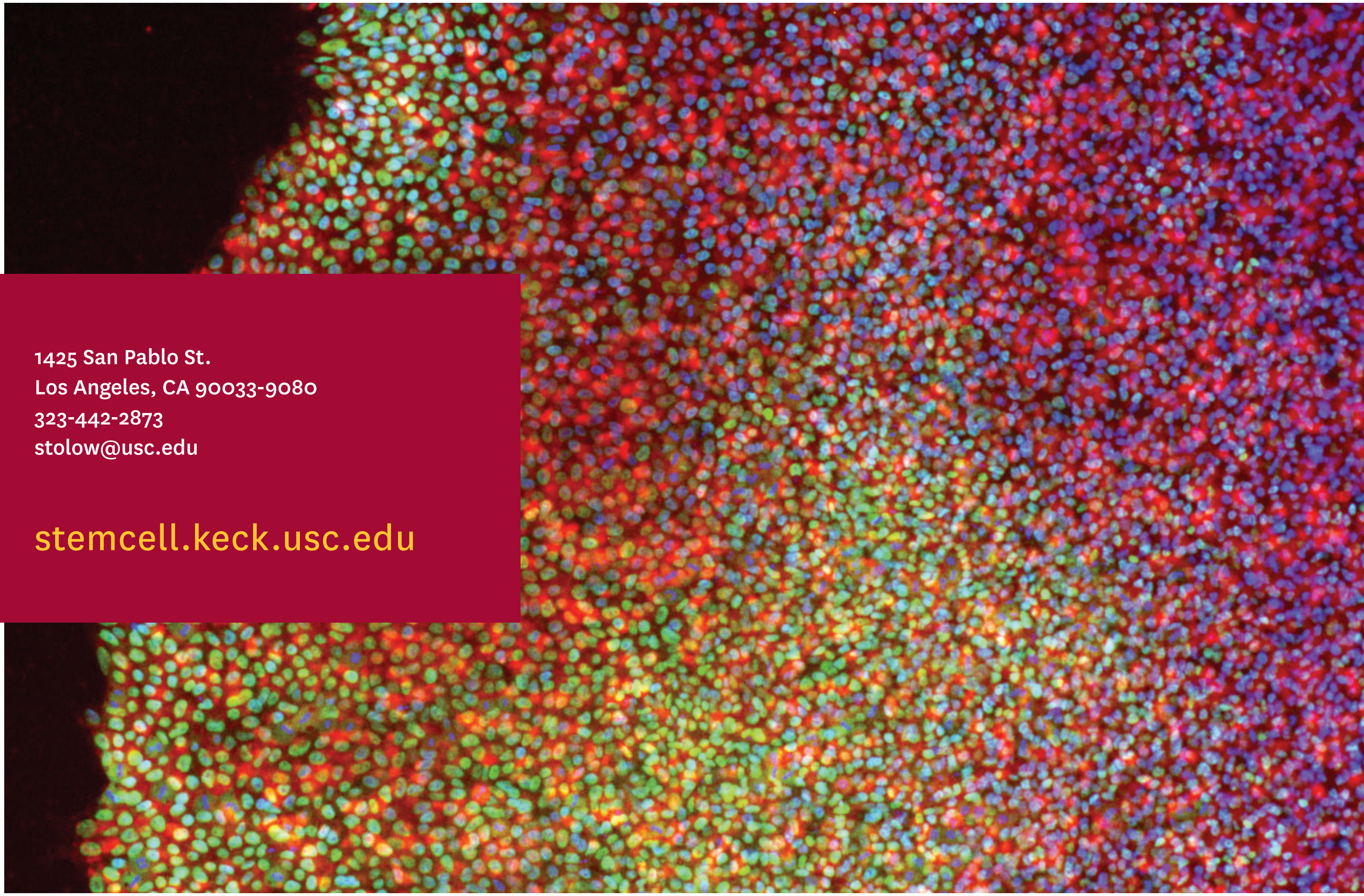

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