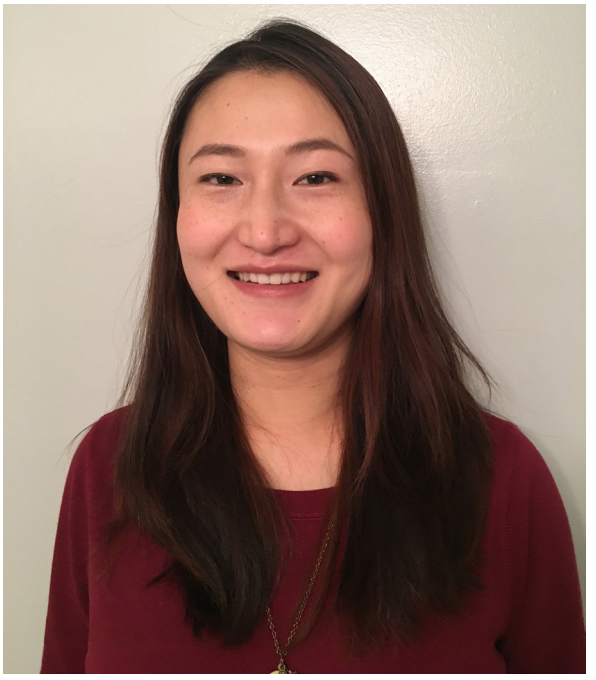
Julia Liu

Breaking Through the Ties That Bind

Pam Goldberg-Smith

Julia Liu, a postdoctoral fellow in the lab of Toren Finkel at the National Institutes of Health (NIH), seeks to discover the underlying connections behind the complicated behavior of biological organisms. She earned her AB in Physics at Princeton University, and a PhD in Biophysics at Harvard University. Julia was recently awarded a NHLBI Career Transition Award (K22), which she considers a privilege but also a promise she needs to fulfill to start her own lab.



Julia Liu

Tell Us About Your Background

My parents are both engineers; my dad is currently a professor of engineering at the University of California, Irvine, while my mom works in geological sciences. My dad tried to get me interested in building machines, but I was drawn to biology because it's so rich and alive. Growing up as an only child in California, I went out exploring in the neighborhood and digging up bugs to observe. I also like animals a lot, so there were times I wanted to be a vet. In undergrad, however, I ended up in the physics department because I enjoyed the classes and problem sets. There's an elegance to physics; everything can be derived from simple laws. I think I owe a lot of that urge, to uncover the underlying principles behind complex phenomena, to growing up with my dad.

What Led You to Study Cardiovascular Science?

For me, it's the excitement of understanding how cells make decisions, for instance, in response to stress, and how we might manipulate the responses. In grad school, I became very interested in how a cell processes DNA damage signals and makes the decision to undergo cell cycle arrest, senescence, or apoptosis. In Galit Lahav's laboratory at Harvard, I studied the response of human embryonic stem cells to DNA damage and how their mitochondria are primed to trigger apoptosis.[1] So that led me to think not only about transcriptional networks in the nucleus but also about mitochondria as important signaling hubs. From there, I found Toren Finkel's interesting research connecting mitochondria, metabolism, and aging, and joined his lab as a postdoc. Now that Toren has moved to Pittsburgh, I'm continuing my project with Tish Murphy who, like Toren, is also a leader in mitochondria and heart research.

What Excites You About Your Current Project?

I'm looking at the role of calcium in regulating mitochondrial function. In simple terms, the mitochondrial calcium uniporter regulates how much calcium enters the mitochondrial matrix, which can stimulate metabolism but in excess can trigger cell death. In Toren's lab, we've developed mouse models with deletions in different proteins belonging to the uniporter and are using them to assess how mitochondrial calcium affects the physiology of mitochondria and different tissues in mice. It's my first time working with mice, so it's cool to see a different phenotype when we've made these genetic perturbations. We found that when MICU1, one component of the uniporter, is deleted, the uniporter loses its gatekeeper ability and lets calcium in even under basal, unstimulated conditions, leading to calcium overload in the matrix.[2] There are a number of different diseases that are characterized by having mitochondrial calcium overload, such as Parkinson's, Alzheimer's, and muscular dystrophy, so understanding how to prevent or mitigate that therapeutically might help us treat these disorders.

What Has Been the Most Exciting Moment in Your Career?

When we constructed the MICU1 mouse model at NIH, we had hypotheses but, of course, didn't know what would happen. I began to see in the litters there was sometimes a tiny,

(*Circ Res*. 2018;122:394-395. DOI: 10.1161/CIRCRESAHA.118.312652.)

Circulation Research is available at http://circres.ahajournals.org DOI: 10.1161/CIRCRESAHA.118.312652

weak pup who often wouldn't survive past a day. When I tested the genotypes of the pups, the runts were always the MICU1 knockouts. As someone who had never worked with mice before, I almost couldn't believe that when we deleted this one gene, I could see with my own eyes a phenotype that affects the whole organism. It brought home to me that this pathway we're studying is important.

What Has Been a Main Challenge for You, and How Have You Overcome It?

The biggest challenge for me was learning to trust my own instinct. There is a lot of doubt when starting an experiment where I wonder if I'm going about it the right way. I tend to overplan and overthink the details to make it the most optimal experiment. Sometimes I have to trust my gut and take the plunge to just get things done. I'm working on building self-confidence and the resolve to follow up on my ideas even when I'm questioning them.

What Qualities Do You Consider Important for Success in Research?

It is important to not be afraid of failing or asking questions for fear of sounding stupid. Stay curious and motivated. Persistence is another big quality to have. Things are probably not going to work for a long time, and you need to keep believing that when plan A doesn't work, plan B or C can still pan out. Scientists need to be resilient. You can't take the failure of one experiment personally. It doesn't mean you're not a good scientist, because we're all constantly running into problems.

What Do You Like and Dislike About Research?

What drives me, and probably most scientists, is the feeling of discovery. Every time you see something new in cells or in a mouse, there's the "wow" factor. We get to be the first to see something cool. Bit by bit we uncover more about the basic scientific questions. There will always be unanswered questions, but on the other hand it's fun always having something new to explore. The drawbacks are that science is a very slow process that sometimes seems incremental. I start to wonder whether I'd be helping more people if, like many of my friends, I'd become a doctor and treated patients every day. I have to hope that my work does eventually have an impact on human health.

How Hard Do You Work?

In science, work doesn't always fit neatly into a schedule—experiments always take longer and need more troubleshooting than you'd predict. Sometimes it feels like we're continually at the beck and call of our cells or mice. There's just no way to escape staying late in the lab or coming in on weekends. I try to work as efficiently as I can, but it comes down to getting results and I'm always prepared to put in as much time as it takes. And honestly, even on the especially long days in lab, my labmates and I are having fun. We're trying new things, talking to smart people and bouncing ideas off each other, and constantly learning. When I feel the work is meaningful and I have goals to accomplish, it's easy to work hard.

What Would You Do to Improve Training in Research?

I've been lucky with my mentors, Galit, Toren, and Tish. Each of them has had a different style, but they have all taken mentoring and training each of their lab members seriously. However, I have seen mentor–mentee relationships go awry, to the detriment of the lab and the individuals involved. Sometimes this happens because the principal investigator (PI) doesn't feel invested in the success of each trainee, and it leads to talented people leaving research and science. I think departments, universities, and grant-funding agencies could do more to put pressure on PIs to prioritize their lab members' scientific and personal well-being. Science should and can be a fun, fulfilling career. Good mentoring contributes so much to fostering a collaborative environment and training the next generation of motivated, thoughtful scientists.

What Do You Do for Fun Outside of the Laboratory?

I've enjoyed classical music since childhood, and I still play cello in a community orchestra. Other than that, I do pretty normal things like hang out with my husband, who works at the National Cancer Institute at NIH. We enjoy traveling, trying different foods, going for hikes with our dog (a Labrador mix named Lilo), going out dancing, and meeting up with friends.

What Worries You Most About Your Future? What Is the Main Obstacle That You Foresee in Pursuing an Academic Career?

I feel that pursuing an academic career is an enormous source of pressure. There's a series of obstacles, each dependent on the previous ones. Looking for a job, getting interviews, starting my own lab, writing grants, acquiring funding, and tenure, are all obstacles where there is not very much room for error in the process. Things may fall in place, but the danger is that any one of those things could potentially go wrong and trigger a downward spiral. And the funding climate is not favorable. There's the NIH Next Generation Researchers Initiative that's meant to help early-stage investigators to get grants, but that's still new, and we'll have to see how that goes. I'm trying to take things one step at a time and not worry about what's down the road.

Disclosures

None.

References

1. Liu JC, Guan X, Ryan JA, Rivera AG, Mock C, Agrawal V, Agarwal V, Letai A, Lerou PH, Lahav G. High mitochondrial priming sensitizes hESCs to DNA-damage-induced apoptosis. *Cell Stem Cell*. 2013;13:483–491. doi: 10.1016/j.stem.2013.07.018.
2. Liu JC, Liu J, Holmström KM, Menazza S, Parks RJ, Fergusson MM, Yu ZX, Springer DA, Halsey C, Liu C, Murphy E, Finkel T. MICU1 serves as a molecular gatekeeper to prevent in vivo mitochondrial calcium overload. *Cell Rep*. 2016;16:1561–1573. doi: 10.1016/j.celrep.2016.07.011.

Circulation Research
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Julia Liu: Breaking Through the Ties That Bind

Pam Goldberg-Smith

Circ Res. 2018;122:394-395
doi: 10.1161/CIRCRESAHA.118.312652
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7330. Online ISSN: 1524-4571