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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Lei Stanley Qi

Originally from China, Lei (Stanley) Qi obtained his first degree in physics and mathematics at the Tsinghua University. He then moved to University of California, Berkeley, where he graduated with an MA in physics and worked in the laboratory of Steven Chu, Noble Laureate in Physics (1997), before switching fields to pursue a PhD in bioengineering in the laboratories of Adam Arkin and Jennifer Doudna. Stanley's work earned him the National Institutes of Health Director's Early Independence Award, which allowed him to start his own laboratory at the University of California, San Francisco, as a Systems Biology Fellow without a postdoctoral training period. In 2014, he moved to Stanford, where he is now Assistant Professor at the Department of Bioengineering and of Chemical and Systems Biology, and is affiliated with Stanford Chemistry, Engineering and Medicine for Human Health (ChEM-H). He invented the use of the CRISPR–dCas9 system for transcriptional modulation and genome imaging. His current research is focused on developing new tools and technologies for genome editing and transcriptional modulation, manipulating molecular networks to understand fundamental principles of biology and engineering cells to exhibit desired behaviors, such as teaching immune cells to recognise and eliminate cancers.

What motivates you to be a scientist?

It's a combination of factors. One is being curious about the world, especially life science. This century is the century for life science, and we have already made so many breakthroughs in other disciplines, but we still know so little about many details related to life. The second is my personality. I like the lifestyle of a scientist, because it gives me the freedom to think about questions at will. The third is the feedback – I found myself being able to answer questions and develop technology that people like, and I was encouraged knowing I can do it well enough.

Your background is in physics, so how did you become a bioengineer?

I grew up in China, learned a lot of science in school, and fell in love with physics and mathematics. I liked it because it allowed me to think in a rational way, and simplify the rules to explain very complex stuff – it's just beautiful! So that's why, when I went to college, I got a degree in physics and then in mathematics. Then I felt somehow limited, because the graduate education in China doesn't provide the freedom to encourage grad students to explore like they do in the US. So I came to Berkeley. I was in the physics program but at that moment I started to realize that for bigger breakthroughs I have to combine physics with something else. My first advisor at Berkeley was Steven Chu, who was later the Secretary of the Department of Energy in the US. After he left I needed to change to a different lab, and I also wanted to try something different. I asked Steve, and he said "there are a lot of new fields coming out, and one is called synthetic biology". I hadn't heard of synthetic biology until then.

What is the research focus of your lab right now?

Work in my lab is currently focused on three areas. First is technology development. We developed CRISPRi technology to rationally engineer the transcription process, and to control how individual or multiple genes are expressed by either activating or repressing them. We also developed another method based on CRISPR to image genomic DNA in living cells, and we are now working on new technology to make it easier to image, hopefully everywhere in the genome, on a large scale. The second area is how to use technology to understand biology better. We can use tools to perturb gene expression, and other labs have developed powerful tools to analyze expression levels or their interactions. Can we combine them together to map out the dynamic image of transcription control during a process like a development? The third area is therapeutics, and I really hope that somehow, after maybe five or ten years, our work will become a real world-changer. The whole CRISPR field opens up a big new field for gene therapy. So we are now thinking how we can utilize our tools to implement new therapeutic methods, for *in vivo* gene therapy or cancer immune therapy. Using cells as therapeutic reagents is becoming very popular and promising in treating certain types of cancer. We want to use our engineering methods to create such cells, like adding an extra safety level to moderate their activity, because those cells are sometimes too effective.

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The winner of the Qi lab Grand Photoshop Contest. 'The Delaware'. [Photo courtesy of Yuchen (Tony) Gao.]

What is the biggest roadblock that you face in your research?
Our roadblock occurs when we try to think about how we can use technology to cure cancer. My background is in physics, synthetic biology and bioengineering, and I actually don't know much about cancer. It's a learning curve to be able to really talk with cancer biologists and physicians to realize what the real problem is, what problem is worth pursuing and what the next feasible target is.

And how do you get around that?
I talk with different experts and collect different opinions, because cancer and cancer therapy are really big fields, and for every particular cancer there's a whole different world. I encourage people from my lab to work closer with people from other labs and it really helps because they have a question they want to solve, and we have tools but we are wondering where we can use them.

"My advice [on collaborations] is to be effective in communication."

What is your advice on establishing good collaborations?
My advice is to be effective in communication. This is obvious but can be quite hard, because a lot of times people don't know what others are expecting or can offer. I'm usually just very frank and ask: "what do you want us to do?", and I find that those collaborations are much better.

What challenges did you face when you were establishing your own lab that you didn't expect?
There were two major challenges. For the first, I would just use the word 'complexity'. A lab really has to have all the factors come together. Science is of course very important, but there is also coordination between people and the dynamics of the lab. For example, people join and leave, and how do you pass knowledge from senior to junior people? In the beginning it wasn't easy to think of so many factors. The second challenge was that I'm the kind of person that always wants things to happen faster, and setting up a lab is not fast. I can't work 24 h without sleep and get it done. I spoke to senior faculty, and they always told me "be patient". So… be prepared for that process; for me it was a challenge! [laughs]

What new challenges are you facing now?
Now people in the lab work on different projects, but as a PI, one immediate thing that comes to mind is the scientific direction. Do these projects solve a problem in the field? That's why, as the lab becomes more established, I make sure we are working on the most important thing, because our resources – money we got from the public and our time – are limited. The second thing is that science evolves very fast and so questions keep changing. The challenge is to move the lab into a more productive stage, and when those changes happen, ensure that it's a smooth transition.

" (…) define a question that you will have a passion for for twenty years."

What was the best advice you ever received?
For two years at UC Berkeley I lived with Professor Donald Glaser. He was a Nobel laureate in physics in 1960, and he passed away several years ago. I helped with some office work in exchange for the free apartment. Once I asked him what the biggest obstacle to becoming a scientist is, and his answer was "don't get bored". It's quite simple, but if you think about it, it's really universally true; most people stop working in science because they get bored. Another important piece of advice I got from my PhD advisor Adam Arkin. I really wanted to have my own lab, and I asked what was important? And he said "you have to define a question that you will have a passion for for twenty years. Think about that big goal that you cannot possibly work out in a short period of time, and you will find yourself always moving and making progress". To me, being a scientist means being a dreamer and having a dream about something really fascinating, even if it may never be accomplished.

How important is it for you to attend scientific meetings?
Firstly, they provide a totally new environment to think about questions. Instead of being locked in your office, looking at same laptop everyday, you go to a new place, meet new people, hear about new ideas that sometimes can be quite irrelevant, but stimulating. A lot of thoughts that I believe to be brilliant are generated from scientific meetings. The second reason is that at a scientific meeting you can go to a session where you know what to expect but end up hearing something new. For example, the reason that I got into the CRISPR field was really through a short meeting in 2010, when most people didn't even know what a CRISPR was. I went to a meeting called 'Bay area RNA meeting'. You'd expect all kinds of RNA talks, and there were talks about RNA structure, non-coding RNA, regulatory RNA, tRNA, but then there was Jennifer Doudna's student giving a talk on CRISPR, which is an RNA-related system, so that's why it was in that meeting! I thought 'this is something really amazing, I should look into that'.

What are your hobbies outside science?
My hobby is to spend some time doing nothing. Just trying to feel like I don't have a goal, I don't have a purpose for a day. I do that because I feel it's the best way to generate some thoughts and philosophy, for me to realize why I'm doing something. Being in science means there is so much purpose, there are so many goals, but it's just one side of life; there are so many things that you don't need a purpose for, and I try to explore that part by just doing something random without a goal.

Lei Stanley Qi was interviewed by Anna Bobrowska, Editorial Intern at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.