

## CELL SCIENTISTS TO WATCH

# Cell scientist to watch – Fei Xavier Chen

Fei Xavier Chen received his Bachelor's degree from Shandong University, China, and his Master's degree from Fudan University, where he worked on the structure and function of the histone demethylase LSD2. He then moved to the USA to join Ali Shilatifard's group for his PhD, first at the Stowers Institute for Medical Research, Kansas City, and then at Northwestern University, Chicago. During this time he identified the transcription regulator PAF1 as a crucial player in the pausing-elongation step of transcription and its role in enhancer activation. He then did a short postdoc with Joan Massague at the Memorial Sloan Kettering Cancer Center, New York, to study transcriptional and epigenetic dysregulation in cancer progression. In 2019, Fei established his independent research group at the Fudan University in Shanghai; his lab uses a wide range of approaches to study the mechanisms of transcriptional regulation in health and disease, with a special focus on cancer.

### What inspired you to become a biologist and work on transcription regulation?

What really drew me to biology was the large number of unknowns – I felt that there were many more unanswered questions in biology than in other sciences. I trained as a structural biologist, and then during my Master's got into the transcription field through a collaboration with Dr Yujiang Shi's group at Harvard. The fundamental mechanisms of transcription really fascinated me; I attended a Cold Spring Harbor Conference in China and got to talk to Ali [Shilatifard]. We had a couple of follow-up chats online and he invited me to join his lab for a PhD, then at the Stowers Institute for Medical Research in Kansas City.

### What are the main themes your lab is working on?

Our lab is very much interested in uncovering the principles of communication between the transcriptional machinery and chromatin, but also how transcription is dysregulated in diseases such as cancer. Actually, wanting to combine these two fields, transcription and cancer biology, was the reason that I joined Joan Massague's lab, who is a pioneer in cancer metastasis, for my postdoc. I think transcriptional or epigenetic dysregulation is likely to play a major role in metastasis, because when people have compared primary and metastatic tumours, they haven't found any key mutations that are driving this process.

### Is combining different cutting-edge technologies, from cryo-EM to genomics methods, central to your research?

Yes, but I'd also say that I never think of myself as a technology person. My research has always been very question driven, so we just try to establish or use any technology that can help us best address our questions, and it's also the reason why we collaborate a lot. I think combining various techniques is very powerful – since



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transcription is a highly dynamic process, structural biology can often provide you with a perspective that you wouldn't be able to get from other technologies. Conversely, given that transcription occurs on a genome-wide level, genomics can provide the global view that structural biology can't give you.

### If you had to pick a favourite method, what would that be?

At the moment this would be combining a protein degradation system, dTAG, with a genomics method called PRO-seq, which enables us to measure the nascent transcriptome at really high resolution. Because of the complex nature of transcription regulatory networks, if you perturb one factor you often affect hundreds of genes and therefore, it becomes very tricky to identify the direct function of a given transcriptional regulator. However, by using a protein degradation system we can deplete any protein within hours and therefore really investigate direct effects of various factors.

### Do you read a lot of papers? How important is reading to you?

Reading is basically one of my hobbies (smiles). I think it's very important to know the scientific literature well, because the aim of science is to explore the unknown – therefore, you really need to know what is known already. Reading older papers, for example from the 80s or 90s, also gives you an understanding of the history of a field and the progress in knowledge. Now that I have more time again compared to when I started up the lab, I also regularly read papers from other fields.

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The first lab trip at Disneyland in Shanghai in 2020, just after opening the lab.

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**Do you have a favourite recent paper?**

It’s really hard to pick just one. I think something that the transcription field has overlooked or underestimated for quite some time is the process of premature transcriptional termination. A recent paper from Matthew Simon’s lab that I found particularly striking showed that 80% of paused RNA polymerase II molecules are actually prematurely terminated, instead of going into productive elongation. This would also explain some of our unpublished data of knocking down the Integrator–PP2A complex, which we recently identified and which plays a key role in early termination of transcription.

**You established your lab at the end of 2019. What did you find the most challenging aspect of being a new PI?**

I found it quite challenging to balance my time between training students, pushing the projects by doing some experiments myself, applying for grants and keeping up with the progress in the field. Now that my students have become more independent and can often do the wet lab work better than me, I have mostly stepped away from experiments and have more time for expanding projects, going to conferences and reading papers.

**Your lab has very rapidly grown to over 20 people. What have you learned from your PhD and postdoc advisors regarding successfully managing such a big team?**

If you would have told me two years ago that I’ll have a lab of 20 people, I would have been very surprised! Actually, it was

never my plan from the start to have such a big group. One of the reasons this happened was that we’re doing both basic research and translational research that involves collaborations with clinicians, so I co-mentor a lot of their students. What I’ve learned from both Ali and Joan is that the important thing is to simply put most of your effort into your lab. Even though Ali was the chair of the department and Joan was the director of the institute, they spent most of their time in the lab and kept on thinking about projects even after they went home from work. So, I make sure to be at the lab a lot and keep track of the progress of projects.

**And what is the best piece of scientific advice that you ever received?**

To follow my curiosity and always have the big picture in mind, instead of getting too stuck on the details.

**Shanghai has been in strict lockdown for the past two months [at the time of the interview], which I imagine was quite a difficult situation to manage**

One challenging and unfortunate part was that we were just wrapping up a couple of papers and still had a few experiments to finish when we went into full lockdown. I managed to do a lot of writing, so I feel I spent this time really fruitfully, but it was also very important that I motivated the students and talked to them regularly, as staying at home for such a long time can be quite tough! I also encouraged them to read and we discussed several recent publications – I often tell them that spending time to accumulate knowledge and think deeply about the project is important, also when pushing the projects. Overall, perhaps one positive side of the pandemic has been that there were many more online meetings than before, which was a great opportunity for students to hear excellent talks by scientists from all over the world.

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**Finally, what is something people wouldn’t know about you by looking at your CV?**

I used to play a lot of video games with friends when I was at university. Then as a graduate student, I always worked long hours and stayed late in the lab, and my evening hobby while running experiments became watching how young people play video games. Unfortunately, nowadays I don’t really have the time to follow these sports games anymore.

Fei Xavier Chen was interviewed by Máté Pálffy, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.