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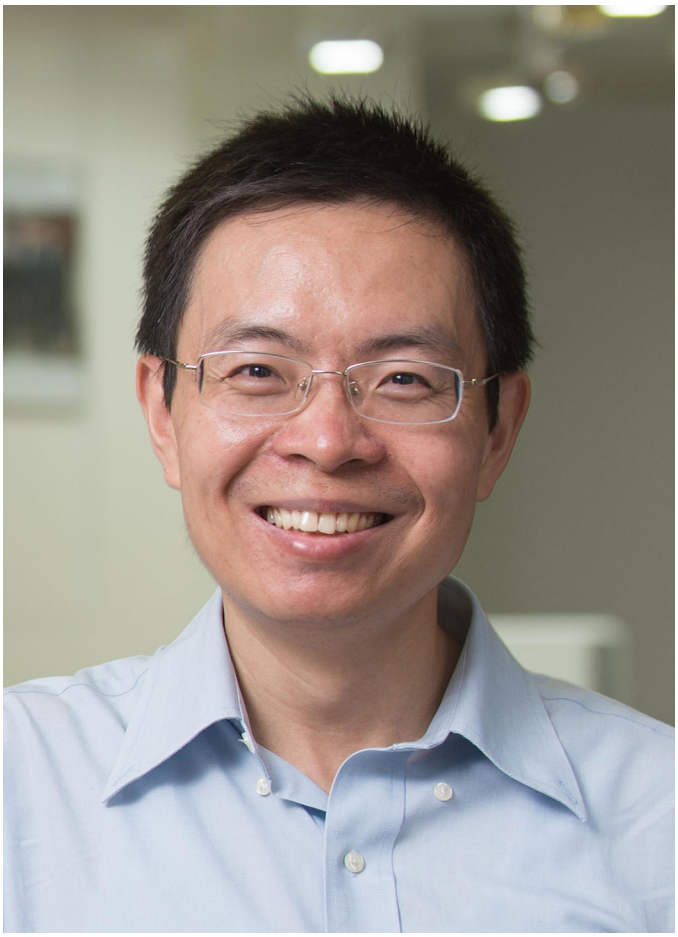
CELL SCIENTISTS TO WATCH

Cell scientist to watch – Guangshuo Ou

Guangshuo moved from China to the USA in 2001 for his PhD at the University of California, Davis. There, he worked on motor proteins in ciliogenesis in *C. elegans* in the laboratory of Jonathan Scholey. He then joined the laboratory of Ron Vale at the University of California, San Francisco, and started to develop tools to investigate the mechanisms of neuroblast division, migration and differentiation in *C. elegans* larvae. Guangshuo returned to China in 2011 to establish his own research group at the Institute of Biophysics at the Chinese Academy of Sciences with a Junior One Thousand Talent Plan Award. Two years later, he moved to the School of Life Sciences at Tsinghua University in Beijing, and he became a principal investigator of the Joint Center for Life Sciences at Tsinghua and Peking Universities. Guangshuo became a Journal of Cell Science Editor in 2017. His laboratory continues to investigate the mechanisms regulating neural progenitors in *C. elegans*, using live-imaging, biochemical and genetic tools.



Guangshuo Ou

What inspired you to become a scientist?

My father worked at the Institute of Geophysics and Geodesy at the Chinese Academy of Sciences. This institute was only two or three minutes' walk away from our apartment, so I could easily go to his office. My father convinced me that biology would be the future; there were a lot more unaddressed, unresolved questions in biology than in his field of geodesy. I definitely agree that there's so much empty space to explore in biology, compared with other disciplines, these days.

What questions are your lab trying to answer just now?

We are answering how extracellular cues are transduced into the cell to remodel the cytoskeleton during asymmetric divisions of the neuroblast, specifically the 'Q' neuroblast, and its directional migration and differentiation in *C. elegans*. We are using imaging techniques, genetics and biochemical approaches. My lab has also set up a conditional knockout technique for neuroblast development in order to address the underlying molecular mechanisms. Recently, we've been exploring some new questions; for example, what kind of cellular behaviour or cellular change will occur under starvation conditions? We have already performed a full genetic screen and we got some unexpected insights into the cell biology underlying stress conditions, such as starvation.

You worked with *C. elegans* for your PhD with Jonathan Scholey. As a post-doc with Ron Vale, you first turned towards planarians. What brought you back to the roundworm?

With Ron, we decided that I'd work on planarian regeneration. I wanted to generate transgenic planarians to follow stem cell behaviour during regeneration, but generating transgenic flatworms just didn't work. One day, I was reading papers and came across the manuscript on *C. elegans* cell lineages by John Sulston and Bob Horvitz in 1977. I realised that this Q cell can do so many things – undergo asymmetric division, migration, differentiation, etc. – so I decided to go back from planarian to *C. elegans* to study this cell. It was not the result of careful career planning, more of surprise and curiosity.

It's a great example of what to do when one faces an experimental roadblock

At that time, Ron was doing his sabbatical in India, so we didn't meet for about ten months during my first year and a half in his lab. I guess that was the most difficult time in my scientific career, figuring and sorting something out by yourself. Everyone around me in the lab at the time was very supportive, and quite open-minded. I read a lot of old literature while my other project wasn't working, trying to see what we can do with modern techniques to solve an older problem. It's an approach to make discoveries.

It's a good message for students and post-docs to look at classic papers in cell and developmental biology that have beautiful descriptive data but might lack mechanistic insights

Exactly! And I'm advising my students to read this work – after all, you should know your field, right? There's a lot of fun to be had

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The Ou lab at Tsinghua University.

reading all these electron microscopy (EM) papers published in the 1950s or 1960s.

What has been the most influential publication or work in your field recently?

It has to be all the genome-editing papers. As a cell biologist, I believe that genetics is a crucial element to understand the underlying molecular mechanism. My lab immediately caught up to the trend, and made conditional knockouts based on somatic CRISPR-Cas9 for neurodevelopment in *C. elegans*. We can make a conditional single knockout or multiple-gene knockouts from experimental design to examining the phenotype in just one week. I think these sophisticated genetic tools have been extremely influential for our ambitions to discover things.

“There’s a lot of fun to be had reading […] EM papers published in the 1950s or 1960s.”

What challenges did you face when starting your own lab that you didn’t expect?

The most challenging thing that I learnt was how to balance being a micro-manager and a macro-manager. Ron was managing in a macro way when I was a post-doc there, so that everyone was motivated to develop their own niche under a big unifying umbrella theme. Naturally, I thought that I should introduce the same mechanism to my own group – everyone has the freedom to decide to come to the lab whenever, and decide themselves which project to choose. But I immediately realised that I was probably too naive, because most people that I recruited were just starting their scientific careers. So I learnt that I should try to understand every student, every person in my lab, and to offer both detailed suggestions, as well as some freedom for their projects.

How are the challenges that you’re facing now different?

They’re very different. Early in my career, I aimed to solve an interesting problem in cell biology, get the results published in a decent journal, and then recruit good people and raise funds. The overall funding situation in China is good, so hopefully I won’t have to overly worry about it for the next few years. Nowadays, the first question that I ask myself about a project is whether this work is going to make a real difference in the field. Therefore, the challenging part that I’m facing now is to identify the most fundamental questions that can be resolved in the near future. I’m quite open-minded to tackle any question in cell or developmental biology, but we have to find a balance: it has to be a fundamental question, and it must also hold a promise to be resolved in the near future. And for that, I’m happy that we’re in a golden age of biological research, or even life science. All the new tools just make many, previously impossible, experiments now possible.

Are you still doing experiments yourself?

I’m not experimenting anymore. These days, I’m trying to understand the sequencing techniques that we use to study cell-biology-related questions, like RNA- or ChIP-sequencing, or 3D-genome data. It’s somewhat of a challenge, but I’m quite happy to learn these techniques. Another research direction that I’m highly involved in is our EM subgroup; we are trying to use focus ion beam scanning EM and cryo-EM tomography to understand protein structures or subcellular structures in cells.

What is the most important advice you would give to someone about to start their own lab?

The most valuable advice is that no boundaries should exist. A big aspect of doing science is the unexpected results. For example, in our forward genetics or RNAi screens, we found some totally bizarre genes that seemed to regulate what we were interested in, and this is going to lead you to a completely unknown field. We should always remind ourselves to move out of our comfort zone and learn something new. It might be initially challenging but is highly rewarding in the end.

How do you achieve a work/life balance when you’re trying to establish yourself as an independent investigator?

I think my job probably goes beyond other jobs; I enjoy every minute when I’m in the lab. To chat with a student or a colleague about a project is really fun. I don’t count how many hours a day or a week I spend in my lab or at work. But I also set out priorities in my daily life. I try to find a timeslot around noon to swim for one kilometre or run for five kilometres. This makes me extremely happy every day. I don’t know whether this is work/life balance, but it definitely helps me.

“We should always remind ourselves to move out of our comfort zone and learn something new.”

You’ve been an Editor for Journal of Cell Science since 2017. How has it been for you?

It’s a wonderful experience to be an editor at JCS, and I appreciate that the journal chose me. During the past year, I learned how to be constructive and also critical as an editor. This is also something I teach my students in the lab; to be constructive and, at the same time, scrutinize every detail when it comes to doing experiments and preparing a manuscript.

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How do you get the most out of the meetings you attend, particularly in the early stages of your career?

The poster sessions can be even more exciting than the talks because there are so many things going on. I gradually realised that a really fun part of any meeting actually starts with the drinks after all the talks are concluded, so after 10 pm, especially in small-scale meetings. I think that's always a good moment to meet and talk to new people, and to go through projects and ideas with them.

Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?

I like to try my own recipes to make fusion cuisine. For the Chinese New Year dinner, I devised a garlic sauce, whose flavour I remembered from an Italian restaurant in San Francisco. I had used the sauce to serve with a Chinese dish of traditionally braised meat. The people in my family really liked it – they finished both the meat and the garlic sauce! I think following an existing protocol with some added creativity at crucial steps is a common strategy for being innovative in both cooking and research. I often joke that after I've retired, I will happily get back to the bench – in my own kitchen. It will happen – but I'll have to wait for another twenty or so years, I guess!

Guangshuo Ou was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.