

FIRST PERSON

First person – Chunchu Deng

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Chunchu Deng is co-first author on 'Dynamic remodeling of ribosomes and endoplasmic reticulum in axon terminals of motoneurons', published in Journal of Cell Science. Chunchu is a PhD Student in the lab of Professor Michael Sendtner at the Institute of Clinical Neurobiology, University Hospital Würzburg, Germany, investigating the dynamics of the endoplasmic reticulum and local translation in motoneurons, and their involvement in motoneuron diseases.

How would you explain the main findings of your paper in lay terms?

The endoplasmic reticulum (ER) is a highly dynamic organelle that plays important roles in cellular functions through protein production, its involvement in lipid and Ca^{2+} metabolism, and regulation of other organelles. During neuronal development, distal axons respond rapidly to extracellular cues, and these responses, including correct pathfinding, require rapid protein production. However, axons are generally thought to harbor only smooth ER, which is not involved in protein synthesis. Previous evidence suggests that ER movements in axons mainly depend on microtubules. In this article, we showed that ER movements in axon terminals not only rely on microtubules, but also on actin and its motor myosin VI, especially in axonal growth cone filopodia. These findings reveal the mechanisms underlying dynamic ER regulation. Moreover, we provided evidence that in axon terminals, extracellular brain-derived neurotrophic factor (BDNF) stimulation activates ribosome assembly and induces ribosome localization to the ER on a timescale of seconds. This fast response to extracellular cues allows rapid protein production in axon terminals. These actin-dependent ER dynamics and BDNF-induced ribosomal changes could be impaired in motoneuron diseases and lead to defective functions of axons and subsequent cell death. These findings may help in developing novel treatment strategies for motoneuron diseases.

Were there any specific challenges associated with this project? If so, how did you overcome them?

To study the association between the ER and actin in axonal growth cones using live-cell imaging, the ER and actin needed to be visualized at the same time. To overcome this challenge, I tried transduction of different constructs into motoneurons. This included transduction of a lentivirus expressing both mCherry–KDEL and GFP–actin using IRES, which is used to co-express heterologous gene products, as well as co-transduction of a lentivirus that expresses mCherry–KDEL and another lentivirus expressing GFP–actin. Previously, I had also tried the 2A protein co-expression system, which allows co-expression of multiple genes. After a lot of effort, I found that the IRES construct resulted in the best



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expression of both mCherry–KDEL and GFP–actin in cultured motoneurons.

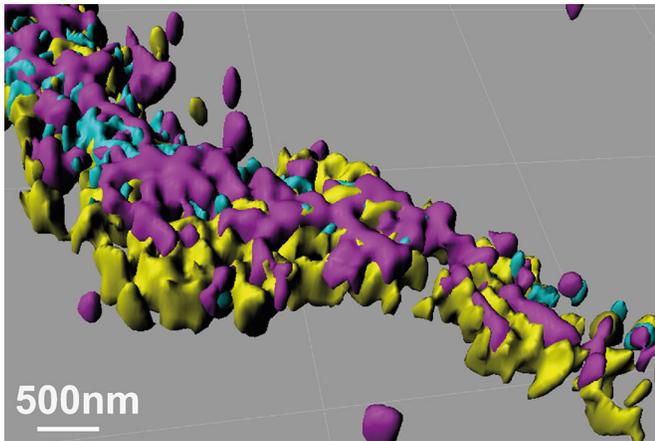
When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

The most striking results for me were the movement of the ER into growth cone filopodia and its interaction with actin. Previous work had shown that the ER barely moves beyond microtubules. The moment when I saw that the ER extended its finger-like structures into filopodia, I was super excited, because filopodia are rich in actin and lack microtubules. Then came the hypothesis that ER movements in filopodia could predominantly depend on actin. I continued to prove this hypothesis with great passion and enjoyed the research very much.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

Yes. My PhD supervisor is Professor Michael Sendtner. He gave me this great opportunity to work as a PhD student in his lab, even though I didn't have a lot of previous experience in bench work. Professor Sendtner is open-minded and has patience and passion for science that helps to create a nice environment in the lab. I also greatly appreciated supervision from Dr Mehri Moradi, co-first author of our article, in the past three years. She taught me lab techniques and gave me a lot of good advice for my project. Their support for both my lab work and daily life helped me to overcome

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Three-dimensional reconstruction of a structured illumination microscopy (SIM) image of axonal growth cone filopodia immunostained to visualize F-actin (yellow), ER (purple) and α -tubulin (cyan).

difficulties in my PhD period. I will also follow their examples when I supervise students.

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?

I studied clinical medicine and handled patients before my PhD. Four years ago, I decided to step into science as a PhD student at the

Institute of Clinical Neurobiology. An interesting reason for this decision was my curiosity about life as a scientist. But a major reason was that I felt it was very important to understand the mechanisms behind diseases and treatment strategies, as for lots of neurological diseases treatments are very limited. It is of great importance that we combine basic and clinical research more closely and bring basic science to public health applications. This was the motivation for me to pursue a career in science.

What's next for you?

I plan to go back to China after my PhD and find a job as a physician in the field of neurology at a university hospital. In the meantime, I also plan to combine clinical and basic research and contribute to the application of neuroscience research in clinical therapies.

Tell us something interesting about yourself that wouldn't be on your CV

When experiments are not working, I like to watch movies to get myself out of the lab work for a while and jump into a fantasy world, or listen to some piano music to relax. After this, I will begin to think about my experiments and search for problems and solutions again. For holidays, I like traveling, especially to the Alps to enjoy nature.

Reference

Deng, C., Moradi, M., Reinhard, S., Ji, C., Jablonka, S., Hennlein, L., Lüningschrör, P., Doose, S., Sauer, M. and Sendtner, M. (2021). Dynamic remodeling of ribosomes and endoplasmic reticulum in axon terminals of motoneurons. *J. Cell Sci.* **134**, jcs258785. doi:10.1242/jcs.258785