© 2023. Published by The Company of Biologists Ltd | Journal of Cell Science (2023) 136, jcs261259. doi:10.1242/jcs.261259

FIRST PERSON

First person – Lu Xu

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Lu Xu is first author on 'Molecular basis of Climp63-mediated ER lumen spacing', published in JCS. Lu conducted the research described in this article while a PhD student in Junjie Hu's lab at Nankai University, Tianjin, China. She is now a postdoc in the lab of Xin Bian at Nankai University, where she performs functional studies of membrane-shaping proteins.

Lu Xu

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

Self-association of Climp63 includes *cis* and *trans* interactions. Because of the heterogeneity of Climp63 oligomers, it is virtually impossible to obtain the crystal or cryo-EM structures of Climp63. To figure out the molecular basis of how Climp63 undertakes its role, we predicted Climp63 structure using RoseTTAFold and AlphaFold. By biochemical and cellular experiments, we confirmed that the predicted 'α0-5HB' model should be the correct conformation for the Climp63 luminal domain (LD). In this conformation, Climp63 uses the tip of 5HB to interact with the C-terminus of another Climp63 in the opposite membrane, thus forming a luminal bridge to maintain a distance of ∼50 nm between two ER membranes. Depletion of Climp63 in cells decreases the ER luminal width to ∼30 nm. Therefore, self-association of Climp63 is important for ER shaping. Our data show that Climp63 acts as an ER luminal spacer at the molecular level and provide a new paradigm for membrane shaping mediated by homotypic interactions.

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

The biggest challenge was to figure out which predicted structures of Climp63 represent the right configuration. To achieve this goal, we constructed more than 20 Climp63 mutant-expressing cell lines and measured the ER luminal width individually by electron microscopy (EM). Fortunately, several mutants have a significant impact on the ER thickness according to the structure predicted by the original RoseTTAFold server, but not that of AlphaFold. In our experiments, EM analysis is very important for us to tell if these residues are involved in *trans* association of Climp63 or not, and the residues that mediate *trans* association help us to clarify the exact configuration information. The verified structural information eventually allowed us to clarify how Climp63 self-associates to form the ER luminal bridge.

Why did you choose Journal of Cell Science for your paper?

In my mind, JCS is a classic journal in the field of cell biology. Articles published here are of high quality, and I learn a lot from many of them. My friends/lab mates reported a gating mechanism of Orai by STIM in JCS a few years ago. I'm very happy that my study is accepted here as well. I hope that our work will offer useful insights to the readers of the journal. I look forward to communicating with researchers around the world through the platform of JCS.

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

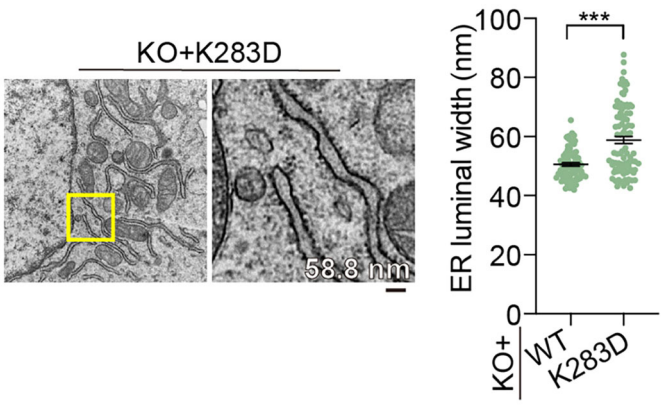
I really appreciate my PhD mentor Dr Junjie Hu. I'm honored that I obtained my PhD degree in the Hu lab. Whenever I'm in trouble, Dr Hu is there to help me. He always inspires me to explore science and teach me how to think critically. He is indeed a role model for me.

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?

Exploration of scientific questions is a very interesting thing for me, although it is usually time consuming and strenuous. In addition, negative results are much more common in my experiments. However, it is really exciting when I get an answer to certain questions after step-by-step troubleshooting, just like a detective who experiences difficulties, but finally finds the truth. I think doing research is a satisfying job for me, and this is my long-term passion.

Lu Xu's contact details: Nankai University, Tianjin, 300071, China.
E-mail: 1120180421@mail.nankai.edu.cn

Journal of Cell Science (2023) 136, jcs261259. doi:10.1242/jcs.261259



The Climp63 mutant K283D destabilizes the salt bridges between K283 and E277/E280. This mutant causes a conformational conversion of the Climp63 luminal domain from being a ‘5HB’ to being a ‘4HB’, and therefore causes a thicker ER lumen.

What’s next for you?

I’m going to start a postdoc in Xin Bian’s lab, where I will focus on the physiological role of Climp63. I think the project is interesting and important, and will lead to more interesting findings about the meaning of ER shaping.

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

When I’m not at work, I like to do exercise, such as cycling and climbing mountains. I also love cooking; I think cooking is just like doing experiments. When I cook, I follow certain steps, procedures and use certain recipes to get the perfect meals. I really enjoy delicious food.

Reference

Xu, L., Xiang, Y. and Hu, J. (2023). Molecular basis of Climp63-mediated ER lumen spacing. *J. Cell Sci.* **136**, jcs260976. doi:10.1242/jcs.260976