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FIRST PERSON

First person – Yasuha Kinugasa

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. Yasuha Kinugasa is first author on 'The very-long-chain fatty acid elongase Elo2 rescues lethal defects associated with loss of the nuclear barrier function in fission yeast cells', published in JCS. Yasuha is a PhD student in the lab of Yasushi Hiraoka at Graduate School of Frontier Biosciences, Osaka University, Japan, investigating the biology of the nucleus and chromosomes.

Yasuha Kinugasa

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

Ceramides act as a crucial skin barrier, and are important for keeping skin moisturised and making our skin look better. Our findings demonstrate that very-long-chain fatty acids, components of ceramides, play an important role in maintaining a barrier at the the cell nucleus. The nuclear barrier is made by nuclear membranes composed of proteins embedded in lipid membranes. We previously showed that cells die when they lose two particular nuclear membrane proteins. In this study, we found that the cell death results from punctures on the nuclear membranes, leading to leakage of contents of the nucleus. A continuous supply of very-long-chain fatty acids rescue the cell lethality, possibly by sealing the nuclear membrane punctures. The nucleus is important for life, keeping the genome (genetic materials) inside. A good metaphor for this would be a bag of your favourite sweets. If the bag was punctured, you would desperately try to seal the punctures so as not to lose your sweets.

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

All of my graduate studies in the laboratory were challenging for me as my major was mathematics in undergraduate school. At the beginning, I made a lot of effort to gain a basic knowledge of biology and acquire experimental skills, such as molecular genetics, biochemistry and imaging. I learned these through experiments and discussion.

During this project, the biggest challenge was to identify the cause of lethal defects. We tried to demonstrate a relationship between nuclear protein leakage and cell death. We needed to follow behavior of nuclear proteins in individual live cells and their fates for a long time, and to explore a method for quantitative interpretation of data. Eventually, we found a correlation between nuclear protein leakage and cell death. Another challenge was that we identified a lipid metabolic enzyme in our study of the nucleus and our laboratory had no experience in lipid metabolism. We wished to determine how the lipid metabolic enzyme rescued nuclear membrane defects. We learned a lot about lipid metabolism, and eventually established a collaboration with an expert laboratory. This project was accomplished by a combination of many techniques including molecular genetics, fluorescence microscopy, electron microscopy, protein biochemistry and lipid composition analysis. I learned the importance of a team work in overcoming challenges in biology.

At the end, submission, and especially revision, of the paper was a challenge and good training for me as a PhD student. I completed my PhD course with this paper.

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

While we previously thought that lethality of *lem2 bqt4* double deletion resulted from chromosome dysfunctions, but the cause turned out to be nuclear membrane disorders, and we found that a single protein, Elo2, suppresses all these phenotypes associated with nuclear membrane disorders, as well as chromosome dysfunctions. This 'eureka' moment stuck with me.

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

We wish to share our marvelous findings with many researchers in cell biology and chose Journal of Cell Science because of its reputation. As expected, I was really encouraged by the constructive comments of reviewers.

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

Professor Hiraoka has strong motivation and a keen sense for science. He provided me with good advice at critical turning points in the project. He and his long-term collaborator,

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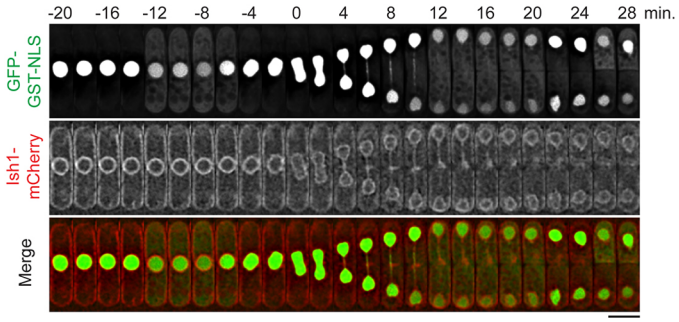

Leakage of nuclear proteins in *S. pombe* cells in the absence of nuclear membrane proteins Lem2 and Bqt4. Time-lapse observations in live cells. Nuclear proteins are visualized with GFP-GST-NLS and nuclear membranes are visualized with Ish1-mCherry.

Professor Haraguchi, taught me how to continue science for the long-term, that is, to enjoy science. "Science is not *a priori* interesting. You make science interesting." When I came across negative results or difficulties in experiments, they often pointed out the positive side and guided me to a more interesting direction.

"Science is not *a priori* interesting. You make science interesting."

Who are your role models in science? Why?

In this laboratory, 60% of the staff are female, and more than 20 babies have been born from mothers working in the laboratory. This is quite exceptional in this country. In particular, Professor Haraguchi is a powerful role model for me as she has made great scientific achievements while raising three children. I definitely want to have both science and my family in my life, so I am trying to keep a work–life balance like her.

What's next for you?

I definitely want to stay in academia so I am looking for a postdoctoral position. I want to continue studies related to fundamental questions of the nucleus and chromosomes.

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

I am a singer and performed in a university a cappella group. I have a powerful voice, so I should try to make my words worthy of my voice.

Reference

Kinugasa, Y., Hirano, Y., Sawai, M., Ohno, Y., Shindo, T., Asakawa, H., Chikashige, Y., Shibata, S., Kihara, A., Haraguchi, T. et al. (2019). The very-long-chain fatty acid elongase Elo2 rescues lethal defects associated with loss of the nuclear barrier function in fission yeast cells. *J. Cell Sci.* **132**, jcs229021. doi:10.1242/jcs.229021