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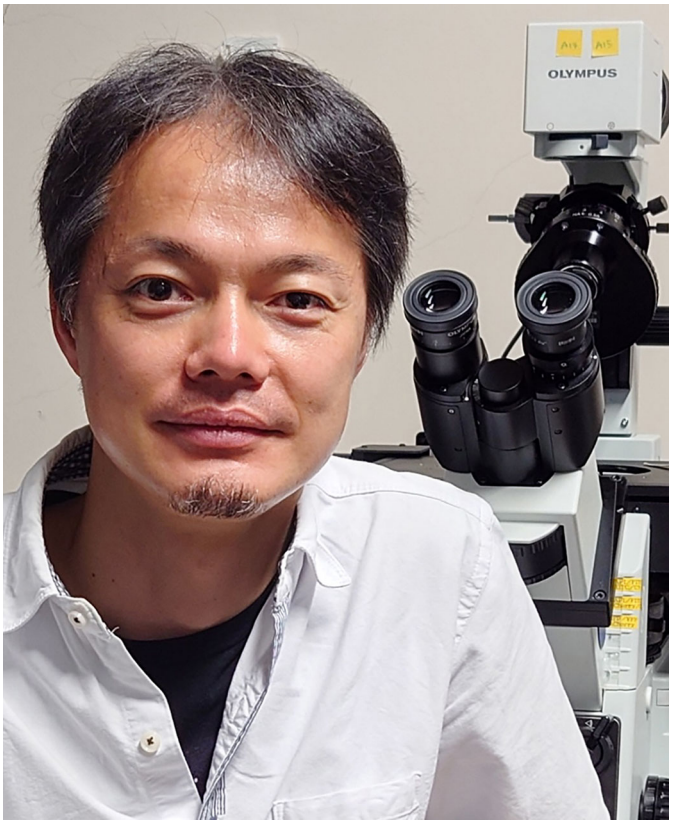
FIRST PERSON

First person – Yasuhiro Hirano

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. Yasuhiro Hirano is first author on 'Ceramide synthase homolog Tlc4 maintains nuclear envelope integrity via its Golgi translocation', published in JCS. Yasuhiro conducted the research described in this article while a lecturer in Professor Yasushi Hiraoka's lab at the Graduate School of Frontier Biosciences, Osaka University, Suita, Japan. He is now a lecturer in the lab of Professor Tatsuo Fukagawa at the Graduate School of Frontier Biosciences, Osaka University, investigating the maintenance of nuclear membrane homeostasis by inner nuclear membrane proteins.



Yasuhiro Hirano

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

The genome is enclosed in the nuclear envelope (NE) to protect it from damage. Maintaining NE integrity is important to health because breakage of this barrier can lead to DNA damage, cellular senescence and cancer. Interestingly, we previously reported that the loss of two (only two!) NE proteins, Lem2 and Bqt4, causes lethal NE rupture in fission yeast. In this study, we found that overexpression of the ceramide synthase homolog Tlc4 rescued this effect. Tlc4 localization in the Golgi was regulated by Lem2 and Bqt4. The Golgi localization of Tlc4 was tightly linked to ceramide levels in the cell. Ceramide species are essential lipids for skin barrier formation, suggesting that regulating the balance of ceramide levels between the NE and other membranous organelles is necessary for maintaining integrity of the NE.

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

The hardest challenge of this project was to find key factors associated with the rescue effect of Tlc4. Although sequence alignment indicated that Tlc4 is a homolog of ceramide synthase, we could not detect any ceramide synthase enzymatic activity of Tlc4 experimentally, meaning that its function is not related to ceramide synthase activity. As one of the specialties of our laboratory is fluorescence microscopy, we thoroughly observed various genetically modified fission yeast strains and eventually found that the intracellular localization of Tlc4 correlated with the phenotype.

Another challenge arose during revision of the article. I had an accident and broke my right clavicle (affecting my dominant hand!) before the last experiment. Thus, I had to finish the experiment and write the manuscript with the broken bone fixed by a metal plate and bolts.

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

The moment was when I realized that the Golgi localization of Tlc4 is greatly reduced in the *lem2*-shut-off *bqt4*Δ cells. Although I had noticed that the strong fluorescent foci in the cytoplasm of Tlc4–GFP-expressing *lem2*-shut-off *bqt4*Δ cells decreased upon shut-off, I wasn't confident whether it was significant, because the loss of Lem2 and Bqt4 results in membrane disorder. To address this, I first identified the foci as Golgi structures. Next, to confirm that the Golgi structures remain after shut-off, I introduced a Golgi marker into the cells and finally confirmed the link between the Golgi localization of Tlc4 and Lem2/Bqt4.

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

We chose Journal of Cell Science because most of our data are based on microscopic analyses and genetics, which are used in cell biology. In addition, as our previous study on this topic was published in Journal of Cell Science in 2019, we expected that this study would be interesting to readers of the journal.

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

My supervisor, Professor Yasushi Hiraoka. He not only supervised me throughout this project, but also showed me how one should behave as a scientist with a great sense of humor and fun. He showed us, by his example, that it is important to do science freely.

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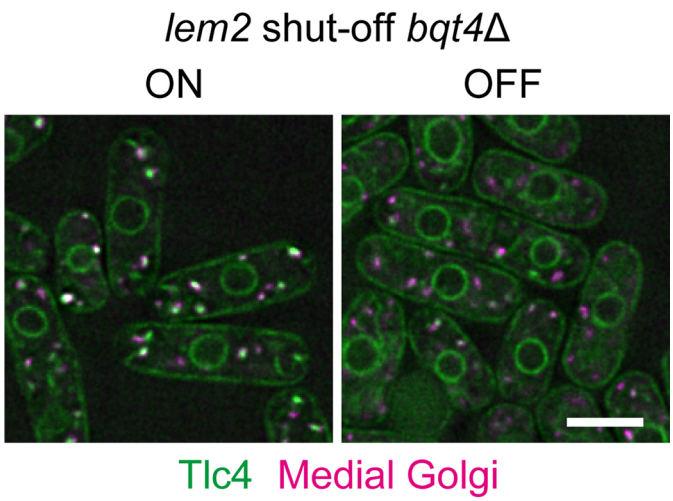

Lem2 and Bqt4 are required for the Golgi localization of Tlc4. The *lem2*-shut-off *bqt4Δ* cells expressing Tlc4–GFP and a medial-Golgi marker, Mnn9–mCherry, were cultured under 'on' and 'off' conditions of *lem2* expression. Under the *lem2* shut-off condition, Golgi localization of Tlc4 (seen as overlapping green and magenta signals) was almost completely absent.

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?

My origin as a scientist lies in a chemistry experiment that I saw in elementary school. My teacher magically turned clear colorless water bright red in an instant. That was an earth-shattering moment for little me (I believe there was no earthquake in Japan at that moment). Since then, I can't stop chasing the moment when something new becomes visible and my old world is completely changed.

Who are your role models in science? Why?

My role models are my friends at our institute. They are highly motivated and enjoy science from the bottom of their hearts. If I see them around, it is time for discussion. We can share our 'omoroi' (fascinating) science anytime, sometimes with coffee, beer and Japanese sake. I am really lucky to have met them at this institute.

What's next for you?

Our work is still only halfway to understanding the mechanisms of how the NE, especially the nuclear membrane, is maintained in the cell. I would like to uncover more in the near future.

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

I love to precisely record things that I see or observe using a digital camera or a microscope. Thus, I am tenacious in using the best lenses. The beauty of the point spread function always calms me down.

Reference

Hirano, Y., Ohno, Y., Kubota, Y., Fukagawa, T., Kihara, A., Haraguchi, T. and Hiraoka, Y. (2023). Ceramide synthase homolog Tlc4 maintains nuclear envelope integrity via its Golgi translocation. *J. Cell Sci.* **136**, jcs260923. doi:10.1242/jcs.260923