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FIRST PERSON

First person – Hsin-Yi Lee

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. Hsin-Yi Lee is the first author on 'Misfolding-prone proteins are reversibly sequestered to an Hsp42-associated granule upon chronological aging', published in Journal of Cell Science. Hsin-Yi is a postdoctoral fellow in the lab of Jun-Yi Leu at the Graduate Institute of Life Sciences and the Institute of Molecular Biology in Taipei, Taiwan, investigating the dynamics of protein complexes and the phosphoproteome in yeast.

Hsin-Yi Lee

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

Yeast resembles human cells in many ways. They share many common processes in cell growth, division and even aging. That is why we used yeast as a model organism to investigate the aging process. By studying yeast, we hope that we can provide new insights and eventually the knowledge can help us understand, or even control, the aging process in humans, so that ultimately we all can be forever young! We observed how yeast regulates the location of proteins in their little cells upon aging, because proteins are very important for cell health. Interestingly, a group of proteins (~7.5%) are differentially stored in aged cells as distinct small dots (which we call granules), while most other proteins are evenly distributed throughout the whole cell. We believed that there must be some good reasons for yeast cells to form these granule structures specifically upon aging. Therefore, we designed a series of experiments to examine the functions of one of the biggest granules. Surprisingly, we found that cells with the granules live longer. The granules can collect damaged proteins to regulate their activities and can also release some good proteins for cells to fight environmental stresses. Furthermore, our evidence showed that the granules are an ancient innovation that evolved more than 100 million years ago. Our results suggest that the granule structure may be a common machinery that regulates protein location and functions to help cells survive during the aging process.

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

After the completion of the screen, a big challenge was to search for a suitable functional assay to determine the consequence of granule formation of the Hsp42-stationary phase granule (Hsp42-SPG). It is not easy to find a well-studied enzyme that has readily available assays and which also depends on Hsp42 for granule formation. We took more than a year to read the literature and try every possible experiment. Fortunately, the luciferase activity assay worked eventually.

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

Yes. It was when we found that heat-shock proteins can be released from Hsp42-SPGs upon heat stress and reassemble after further incubation in normal temperature. To observe the response of living organisms is always a lot of fun to me.

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

Journal of Cell Science is one of my favorite journals and is also where I keep checking for new articles. During the literature search, I found many interesting papers related to my study from the journal. I am also impressed with the quality of research articles from the journal, and that is the main reason I selected Journal of Cell Science.

"…doing science is more exciting after every discussion."

Have you had any significant mentors who have helped you beyond supervision in the lab?

Yes. My mentor Dr Jun-Yi Leu gave me great freedom to try what I wanted to do. When I was discouraged by negative data, he kept pushing me and trying to give me valuable suggestions. He seldom gets angry, so it is helpful to discuss things with him. Through the discussion, I can clearly see his passion for scientific research. That mindset is infectious and I feel that doing science is more exciting after every discussion.

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?

When I was a senior high-school student, my biology teacher gave brilliant lectures. She not only explained textbooks well, but also

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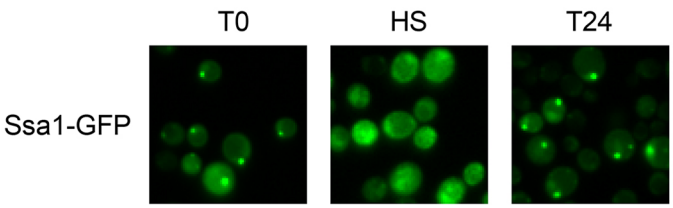

Heat-shock proteins (Ssa1–GFP) can be released from Hsp42-SPGs upon heat shock and reassemble after further incubation (T24, 24 h) at normal temperatures.

discussed philosophy with me and other questions a young boy has. She was so inspiring and I think that is when I started to love biology and decided to do biological studies in the future.

What's next for you?

I am working on other projects about the dynamics of protein complexes and the phosphoproteome in yeast. After finishing these projects, I plan to apply for a postdoctoral fellowship in another country and continue doing biological research.

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

I love traveling. Seeing beautiful things and people around the world opens my minds and gives me great inspiration.

Reference

Lee, H.-Y., Chao, J.-C., Cheng, K.-Y. and Leu, J.-Y. (2018). Misfolding-prone proteins are reversibly sequestered to an Hsp42-associated granule upon chronological aging. *J. Cell Sci.* **131**, jcs220202.