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FIRST PERSON

First person – Sherman Foo

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. Sherman Foo is first author on 'Diacylglycerol at the inner nuclear membrane fuels nuclear envelope expansion in closed mitosis', published in JCS. Sherman conducted the research described in this article while a PhD student in the labs of Snezhana Oliferenko (The Francis Crick Institute, London, UK, and Randall Centre for Cell and Molecular Biophysics, King's College London, UK) and Markus R. Wenk (Singapore Lipidomics Incubator, National University of Singapore). He is now a postdoc in the lab of Buzz Baum at Medical Research Council Laboratory of Molecular Biology, Francis Crick Avenue, Cambridge, UK, where he is currently studying cellular organization of hyperthermophilic archaea, with a particular focus on the surface layer and cell cycle of *Sulfolobus acidocaldarius*.

Sherman Foo

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

The nucleus of eukaryotic cells is made up of chromosomes enclosed by the double-membrane nuclear envelope. The genome, encoded on chromosomes, serves as a set of instructions for the proper functioning and survival of the cell. For cell proliferation, the genome must be faithfully duplicated and segregated by a microtubule-based molecular machine called the mitotic spindle. In turn, the nuclear envelope must be remodeled to allow chromosome segregation and the formation of two daughter nuclei. A range of strategies for managing the nuclear envelope during mitosis has arisen in evolution, ranging from 'open' mitosis, when the nuclear envelope breaks down at mitotic entry and reforms around the segregated genomes, to 'closed' mitosis, when the duplicated chromosomes are segregated within an intact nuclear envelope. For the latter to occur, the nuclear envelope must expand to maintain nuclear volume throughout the division – but where does the extra membrane material come from? In this work, I developed tools to observe changes in the levels of two lipids that are used to produce the rest of the membrane, phosphatidic acid and diacylglycerol, with high spatiotemporal resolution. My results show that two membrane lipid biosynthetic pathways, one that starts with phosphatidic acid, and another with diacylglycerol, collaborate to enable the expansion of the nuclear envelope during closed mitosis. Cells that lack either pathway have troubles dividing their nuclei, but when both pathways are absent, nuclear division fails completely.

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

Lipids are usually detected through conventional biochemical methods, such as mass spectrometry-based lipidomics. Although powerful, such methods fail to provide accurate spatial and temporal information on the distribution of specific lipids within the cell. We and others knew that the conversion of phosphatidic acid into diacylglycerol was an important regulatory point in the mitotic surge in the synthesis of membrane lipids, but we did not know where in the cell these lipids were enriched, or where membrane lipids destined for the nuclear envelope were synthesized. By approaching this problem from another perspective, using fluorescent genetically encoded lipid biosensors, we were able to visualize both phosphatidic acid and diacylglycerol throughout the process of closed mitosis in the fission yeast *Schizosaccharomyces pombe*. This breakthrough led to surprising observations, allowing us to generate and test a new set of ideas on the regulation of membrane biosynthesis for mitotic nuclear envelope expansion. Optimization of these fluorescent probes, from determining the best architecture to choosing expression levels to verifying the usability, was an arduous process. I dealt with it by designing a clear strategy to follow from early on. For each step, I made and tested several modifications of the basic design. Checking several designs in parallel saved time and provided encouragement, since at least one of them was bound to work better than others!

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

Figuring out the contribution of the Kennedy pathway to glycerophospholipid synthesis required the expansion of the nuclear envelope during mitosis – this was the 'eureka' moment for me. During the process of optimization of my lipid biosensors, I was performing imaging experiments in various yeast culture media to investigate whether there were differences in background fluorescence, cellular autofluorescence, etc. It was then that I realized that *S. pombe* cells lacking the diacylglycerol kinase Dgk1 could grow reasonably well in the rich medium but

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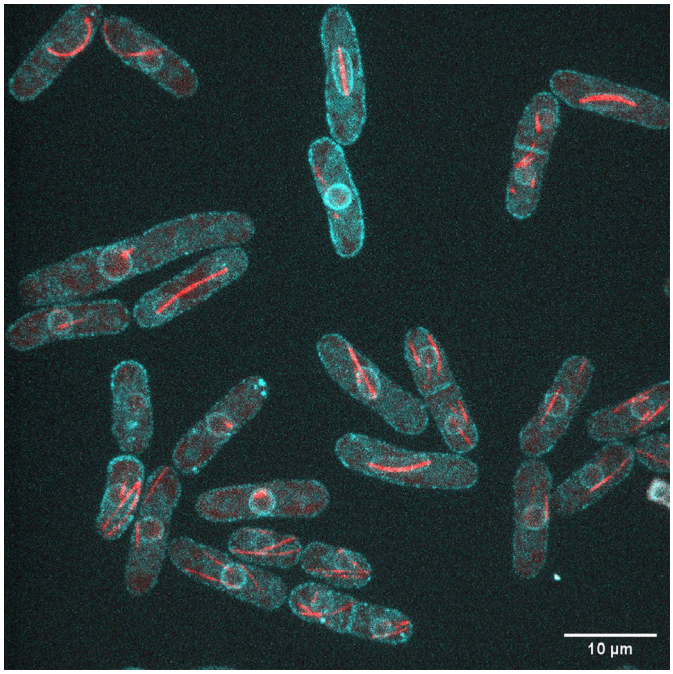

A field of view showing the heterogenous population of *dgk1*Δ *Schizosaccharomyces pombe* cells expressing the NLS-DG sensor–GFP (cyan) and mCherry–α-tubulin (red).

were extremely sick and diploidized in a defined minimal medium. Thinking 'what could be different between rich and minimal media?', I considered choline and ethanolamine, the precursors for the Kennedy pathway that uses them, together with endogenous diacylglycerol, as the factors that produce major membrane lipids. I did a very straightforward experiment where I added these precursors to the minimal medium. Strikingly, this alone rescued the extreme mitotic phenotypes of my *dgk1* mutants. This simple observation led us to the discovery that the Kennedy pathway is an important contributor to mitotic nuclear envelope expansion.

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

The Journal of Cell Science is a highly reputable journal that enjoys a wide readership. We believe that our results will be of interest and relevance to many cell biologists and hope that this story will reach its target audience through JCS.

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

Professors Snezhana Oliferenko and Markus R. Wenk, my PhD supervisors, have contributed significantly to my development as a scientist. Besides their constant guidance and supervision of my research work, they were unwavering in their support of my personal development, encouraging critical thinking and helping me to acquire important skills for my academic career, including writing, giving talks and imbuing research with the spirit of collaboration.

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 have always had a keen interest in the sciences since my school and university years. In particular, it was the positive and enjoyable experience during my undergraduate summer and final year research projects in the labs of Professors Helge Ewers and Lina Lim, respectively, which motivated me to pursue a scientific career. My Master's project in the lab of Andrew Beavil, which allowed for greater control of the direction of my research, further bolstered my decision to pursue a career in science.

Who are your role models in science? Why?

I have been fortunate to have excellent research advisors throughout the course of my undergraduate education and PhD training. Their expertise, professionalism and joy at pursuing research have inspired me over the years to constantly better myself scientifically.

What's next for you?

I have recently started a postdoc in the lab of Buzz Baum at the MRC Laboratory of Molecular Biology, working on archaeal cell biology.

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

I enjoy cooking, as it reminds me of the process of following an experimental protocol, except that you have the freedom to deviate from the protocol as you wish (for better or worse), not measure any of the reagents accurately, and still end up with something edible (usually) at the end of the process.

Reference

Foo, S., Cazenave-Gassiot, A., Wenk, M. R. and Oliferenko, S. (2023). Diacylglycerol at the inner nuclear membrane fuels nuclear envelope expansion in closed mitosis. *J. Cell Sci.* **136**, jcs260568. doi:10.1242/jcs.260568