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FIRST PERSON

First person – Ziyan Fang

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. Ziyan Fang is first author on 'The *Salmonella* effector SifA initiates a kinesin-1 and kinesin-3 recruitment process mirroring that mediated by Arl8a and Arl8b', published in JCS. Ziyan conducted the research described in this article while a PhD student in Stéphane Méresse's lab at Centre d'Immunologie de Marseille-Luminy (CIML), Marseille, France. She is now a postdoc in the lab of Elina Zúñiga at Division of Biological Sciences, University of California, USA, where her research interests lie in studying the cellular and molecular aspects of the host immune responses during viral or bacterial infection.

Ziyan Fang

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

Salmonella are food-borne pathogens. Although the human immune system has several physical and chemical barriers against infection, *Salmonella* are able to cross the intestinal barrier and eventually reach organs such as the liver or spleen, causing, depending on the strain, inflammatory diarrhoea and/or typhoid fever. These bacteria replicate inside cells. There they establish a membrane-associated replication niche, called vacuoles, and induce the formation of tubules from their vacuoles along the microtubule cytoskeleton. These membrane structures divert nutrients, ensuring the proliferation of *Salmonella*. In this study, we focused on understanding the molecular mechanisms involved in the formation of the *Salmonella* replication niche. We found that kinesin-3, a human protein, is present on *Salmonella* vacuoles and is involved in niche establishment. Previously, our team showed that kinesin-1, another human protein of the same superfamily, is also present on *Salmonella* vacuoles. In this project, we show that kinesin-3 uses a different recruitment mechanism than kinesin-1 and that they may have a cooperative function in *Salmonella* virulence. Finally, we provide an example of the adaptation of intracellular bacteria and their ability to mimic certain cellular functions in order to make use of them.

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

The main challenge in working on this topic was to find the necessary resources. This was complicated by the fact that few scientists have worked with our molecule of interest. There were few or no tools available to scientists and even fewer commercial products. So we had to start from scratch and produce antibodies, expression vectors, etc. Another difficulty was the very low level of expression of the endogenous protein, which made it impossible to detect by immunofluorescence at the cellular level. We therefore had to work with an overexpression system throughout the study. Working with this system was not an easy task, especially for large proteins, such as kinesin-3, for which we were often confronted with low transfection efficiency. In particular, when overexpression meets infection, the difficulty is exacerbated – it is not easy to find enough overexpressing and infected cells. We therefore spent a lot of time consulting the literature and conducting pre-experiments to establish protocols.

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

One of the most impressive moments in this work was when we first observed the presence of kinesin-3 on *Salmonella* vacuoles. Before this study, we only knew about kinesin-1; no other kinesin had been detected there. This result aroused our interest and prompted us to continue this study. Another important moment was the discovery that kinesin-3 interacts with proteins secreted or recruited by *Salmonella*, which allowed us to demonstrate that this molecular motor is in fact actively recruited by the bacteria. Finally, I think it was the effect of knocking down this protein in *Salmonella*-infected cells and the important consequences of the absence of this protein that amazed me the most because it gave meaning to this research.

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

Journal of Cell Science is a well-known journal in the field of cell biology, which is the focus of my work. I have read many articles published in JCS during my thesis. It is therefore very natural that JCS came to the fore when it was time to choose the journals to which we could propose this work.

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

Stéphane Méresse has been an excellent supervisor. He guided me to speak and write English properly. He has always encouraged me

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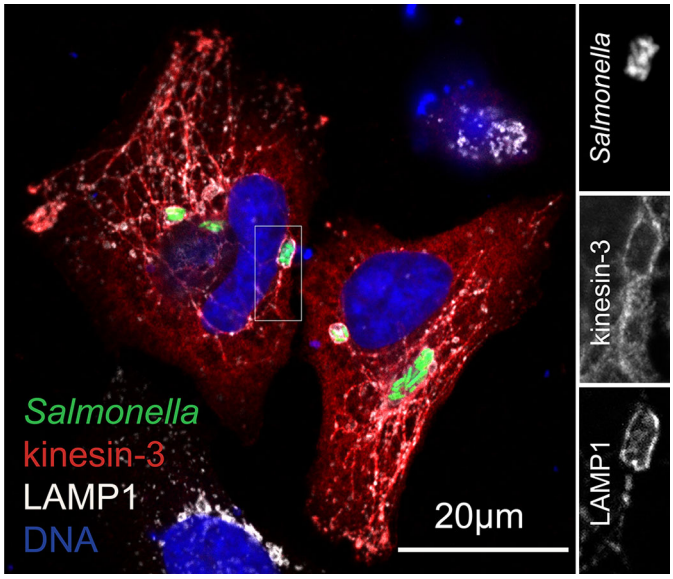

Cultured human cells infected with the pathogenic bacterium *Salmonella* and overexpressing kinesin-3. These cells were immunostained to visualize *Salmonella* (green), the *Salmonella* replication vacuole (LAMP1 in white) and the nucleus of the infected cell (DNA in blue). This illustrates the ability of *Salmonella* to induce the formation of a network of membranous tubules, connected to its replication vacuole and on which we discovered the presence of kinesin-3 (FLAG–KIF1Bβ; red).

to learn new experimental and other skills. In the lab, thanks to his guidance, I never felt like I was alone in this project. His curiosity, interest and attitude towards science have inspired me a lot. It was a great challenge for me to study abroad. With Stéphane's help, I quickly adopted the working environment and made progress every year. I have good memories of my PhD studies.

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 child, I wanted to become a scientist exploring the unknown, so I chose biology as my major at university. I almost stayed away from the front lines of scientific research for a year before I started my PhD study. Because of this experience, I have realized that I should continue doing research and at that time I had the opportunity to apply for a PhD position in the team of Stéphane Méresse. This PhD study has motivated me the most to pursue a career in science. Not only does my supervisor's, my colleague's and my husband's passion in science impact me, but I also found my interests in scientific research and meaning in doing science. Scientific research is an infinite loop of asking and answering questions. Every question that is raised and answered are tiny steps, and although I cannot see their application or significance immediately, they might benefit humanity in the future. I like asking and answering questions. I think this is why I enjoy the scientific research field.

Who are your role models in science? Why?

My role model in science is Marie Curie, who won the Nobel Prize twice. I appreciate her unwavering dedication to science. Her portrait and her scientific career are on display in the corridors of the CIML, where I did my PhD work. I feel that every time I pass by her portrait I am inspired and encouraged to go forward. I like one of her quotes: 'Be less curious about people and more curious about ideas'.

What's next for you?

After four years of PhD in the south of France, I moved to San Diego in October 2021 with my cat Soja and my husband Xing (now a postdoc at Scripps Research). Thanks to Elina Zúñiga, I will be working as a postdoc in her lab at UCSD starting mid-December. My postdoc research will focus on studying the cellular and molecular aspects of host–immune responses upon viral infections. This postdoc research is a new challenge for me and a great opportunity for me to bloom.

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

I am developing some new hobbies, like swimming and tennis. There are many tennis courts, apartment swimming pools and beautiful beaches in San Diego.

Reference

Fang, Z., Fallet, M., Moest, T., Gorvel, J.-P. and Méresse, S. (2022). The *Salmonella* effector SifA initiates a kinesin-1 and kinesin-3 recruitment process mirroring that mediated by Arl8a and Arl8b. *J. Cell Sci.* **135**, jcs259183. doi:10.1242/jcs.259183