© 2018. Published by The Company of Biologists Ltd | Journal of Cell Science (2018) 131, jcs223842. doi:10.1242/jcs.223842

FIRST PERSON

First person – Yiliu (Charlie) Zhang

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. Yiliu is the first author on 'The unusual flagellar-targeting mechanism and functions of the trypanosome orthologue of the ciliary GTPase Arl13b', published in Journal of Cell Science. Yiliu is a Research Fellow in the lab of Sudipto Roy at the Institute of Molecular and Cell Biology (IMCB), Singapore, investigating the development and functions of multi-ciliated cells in vertebrates.

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

Cilia and flagella are important structures of the eukaryotic cell. In humans and animals, cilia perform important sensory and motility functions and have been associated with many developmental diseases. For the parasite (*Trypanosoma brucei*) responsible for the deadly African sleeping sickness, the flagellum is crucially required for motility and cell survival. For cilia to grow and function normally in both animals and the parasite, an important protein – Arl13b – needs to specifically localize to the cilia. However, whereas the animal version of Arl13b is equipped with an array of 'gadgets' to travel to the ciliary membrane, the parasitic version (TbArl13) utilizes a single small 'tool' to dock to the ciliary cytoskeleton. Think of the cilium as a city, and all the animal Arl13b would fly and land at the airport, but the parasitic Arl13 would hit the harbor on a fast boat. We found that, despite the difference in transportation, they end up networking with the same 'people' and do similar business in the city. For the parasitic Arl13, the unique transportation choice may just be a matter of 'heritage' and is not a prerequisite for its functions. We have shown this by forcing the parasitic Arl13 to 'travel by air' and proved that it could still do its job. Because TbArl13 is crucially required in the parasite flagellum, its unique way of transportation makes a novel target for therapeutic intervention.

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

For the first two-thirds of this project, I was not sure whether my hypothesized Arl13b orthologue had anything to do with Arl13b – it was too different in many ways. Of course, the protein was showing enough interesting features to be worth pursuing in and of itself. But if it was, indeed, a divergent Arl13b ortholog found in the protozoan flagellate, the differences and commonalities together could reveal something interesting about the evolution of Arl13b and the cilia. This question pushed me to study the protein as comprehensively as I could, in order to reach a conclusion that at least I myself could sit well with. It took quite some time, but I believe it benefited the research and I was able to learn new things and collaborate with many talented scientists along the way.

Yiliu Zhang's contact details: 61 Biopolis Drive, Proteos #08-12, Singapore 138673, Singapore.
E-mail: ylzhang@imcb.a-star.edu.sg

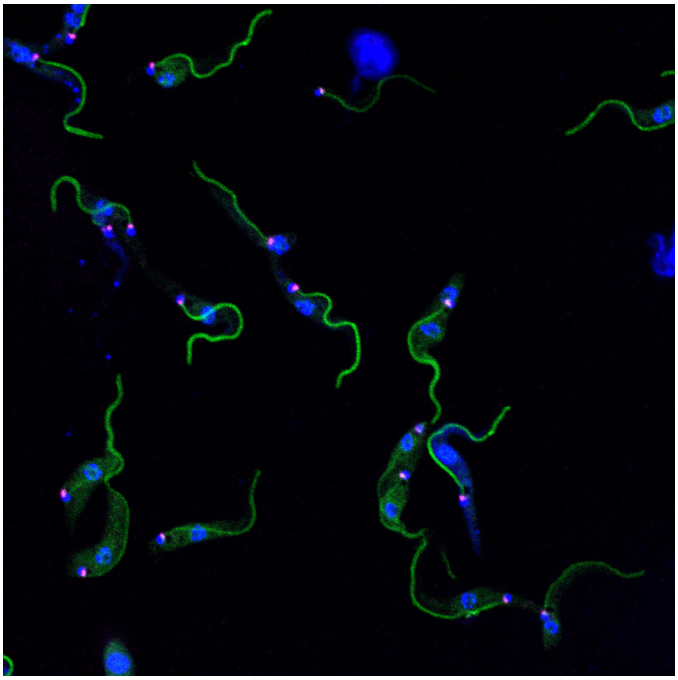
Yiliu (Charlie) Zhang

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

"I have always been fascinated by how 'life' works."

There were several exciting moments, but the first one is often the most memorable. It was an evening when I decided to take a deeper look at a 'peculiar-looking' GTPase I had just came across in an unrelated genomic dataset. Blast and alignment results suggest the GTPase domain is similar to that of Arl13b, but my protein lacked many features and had an extensive N-terminal domain that I had not seen in any other GTPases I could find. After quickly ploughing through the literature, I learned that (a) the N-terminal extension is a PKA D/D domain, (b) the D/D domain is a targeting domain and is also found in non-PKAs and (c) the missing elements on the trypanosome protein are mostly related to protein targeting. The 'eureka' moment was when I connected these dots and said to myself: "The N-terminal domain must be a targeting device 'standing in' for the missing targeting elements – if this protein localizes to the flagellum, it sure looks like an Arl13b in disguise!" There was some luck, but that turned out to be quite a good guess.

Journal of Cell Science (2018) 131, jcs223842. doi:10.1242/jcs.223842



Differential localization of the two Arl3 homologues in *T. brucei*. TbArl3A (green) is highly enriched along the flagella, while TbArl3C (magenta) is specifically located at the flagellar base. Cells were imaged live, with cell-permeable DAPI to mark the nuclei and kinetoplasts.

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

A large proportion of papers I read during my PhD were from Journal of Cell Science, so I have a feeling of familiarity and trust towards this journal. Journal of Cell Science is highly reputable and has very high standards for scientific excellence. Furthermore, it welcomes and appreciates studies of a wide range of model organisms, which – in my opinion – is critical in biology as, more often than not, discoveries come from the study of irregularities.

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

I was fortunate to have Dr Cynthia He as my PhD supervisor. She cares deeply for her students and went far and beyond to help them either in or out of the lab. She has very high standards for science, and always encourages everyone to achieve higher. At the same time, she trusts and empowers people to take responsibilities. She always encouraged new ideas and was extremely supportive when we wanted to act on them. Without her insight and guidance, this paper would never have come to fruition and I, definitely, would not have had such an enjoyable PhD journey.

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 been fascinated by how 'life' works. I remember reading about the anatomy of the cell somewhere when I was just a primary school kid, and was in utter disbelief – how is it possible that all these molecules just 'know' where to go and how to assemble by themselves? I studied life sciences as an undergraduate but was really tempted to make my own discoveries and contribute to the collective knowledge even just a tiny bit. That's why I chose to pursue a PhD.

What's next for you?

After completing my PhD last year, I joined the lab of Dr Sudipto Roy. I don't have a detailed roadmap for the next 5 to 10 years yet, but I am learning many cool new things now that I have availed myself of multicellular creatures (i.e. zebrafish!). There is also some continuity, as my current projects focus around ciliated tissues and their differentiation.

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

I am a music fan. Whenever I learn that I will travel for conferences or other reasons, usually the first thing I do is to check if there is a good band touring nearby.

Reference

Zhang, Y., Huang, Y., Srivathsan, A., Lim, T. K., Lin, Q. and He, C. Y. (2018). The unusual flagellar-targeting mechanism and functions of the trypanosome orthologue of the ciliary GTPase Arl13b. *J. Cell Sci.* **131**, jcs219071.