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FIRST PERSON

First person – Kaiyuan Wu

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. Kaiyuan Wu is the first author on 'GCN5L1 interacts with α-TAT1 and RanBP2 to regulate hepatic α-tubulin acetylation and lysosome trafficking', published in Journal of Cell Science. Kaiyuan is a visiting postdoctoral fellow in the lab of Michael Sack at the National Heart, Lung and Blood Institute, NIH, Bethesda, USA, working on exploring the molecular mechanisms underlying lysosome trafficking in the context of liver function.

Kaiyuan Wu

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

Similar to our daily supplies being delivered by trucks driving on highways, components of cells are transported across the cell by tiny molecular motors along 'molecular highways'. The 'highway' inside the cell is made of protein structures called microtubules, which are composed of a protein called tubulin. The chemical modification of tubulin by a process called acetylation stabilizes microtubules, which in turn promotes the binding and trafficking of the motor proteins that carry the cellular cargo. In our study, we identified a novel mechanism to regulate tubulin acetylation by a protein called GCN5-like protein 1 (GCN5L1). We found that GCN5L1 works with other novel proteins in the acetylation of tubulin; when GCN5L1 is absent, tubulin is less acetylated and the mobility of cargo around the cell is disrupted. We plan to explore this process is more detail because the control of these trafficking pathways in the cell is essential for many cellular and biological processes.

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

The biggest challenge in this project was to elucidate the *in vivo* hepatic effect of GCN5L1-dependent microtubule acetylation. By stabilizing microtubules, GCN5L1 might play a broad role in microtubule-related processes including cell division, cell migration and vesicles trafficking, although these effects remain to be conclusively demonstrated. The reason that phenotypes related to microtubule acetylation are not obvious might reflect the fact that vertebrates may be able to tolerate considerable shifts in the degree of tubulin acetylation. For example, a deficiency in the gene coding for the major α-tubulin acetyltransferase or α-tubulin deacetylase HDAC6 in mice does not lead to significant developmental or homeostatic perturbations. Another possibility is some redundancy in this regulatory pathway. It took a lot of time to read the literature and try several different experiments. Fortunately, the lysosome trafficking assay worked eventually.

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

Journal of Cell Science has a far-reaching audience in the field of cell biology and a great reputation in the scientific community. Our lab has published work in this journal in 2013, which highlighted our work to a broad scientific community. This experience encouraged us to submit our article to this journal again, as we believe that this work will contribute to the understanding of microtubule-related fields, including cell migration, intracellular trafficking and cell signaling.

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

Undoubtedly Dr Michael N. Sack, my postdoctoral mentor. I feel really lucky to work with such a fantastic supervisor. During our studies, Dr Sack not only gave me great support to finish the experiments, but also guidance in my development to become an independent researcher. Under his supervision, I have learned how to ask a scientific question, form a hypothesis and to test and prove it. Furthermore, he also encourages and helps me to practice my English communication, grant writing and academic presentations. His mentorship benefits me now and will be of benefit as my scientific career progresses.

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 curiosity is what drives me. After completing my undergraduate degree, I briefly worked as a lab manager. Compared to this experience, the irreplaceable happiness that comes from finding a novel cellular phenotype or uncovering an unknown molecular

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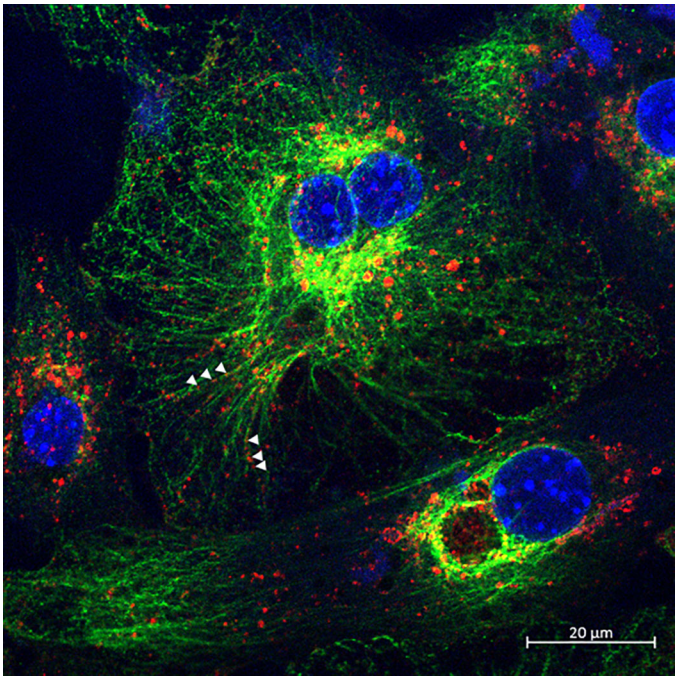

Primary hepatocytes stained for DNA (blue), Lamp1 (red) and acetylated tubulin (green). Lysosomes are distributed along the acetylated microtubule tracks. Arrowheads point to the colocalization of lysosomes with acetylated microtubules.

mechanism is very appealing and rewarding to me. Whenever I learn more about the nature of biology, I feel that we also understand ourselves more. Scientist is not a job to make you rich, but understanding life and the world around us gives me a lot of pleasure and inspired me to pursue an academic career.

“…the […] happiness that comes from finding a novel […] phenotype or […] unknown molecular mechanism is very appealing and rewarding…”

What’s next for you?

At present I am still in my first postdoctoral position. I am currently exploring the role of GCN5L1 in hepatic metabolism, trying to understand lysosome trafficking in the context of liver function.

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

Fishing is my favorite hobby. It is comparable to science: you never know when or if you will have something on the hook, much like discovering something new and interesting in the laboratory. Being patient and giving it your best allows me to enjoy the moment of ‘fishing’ in both situations.

Reference

Wu, K., Wang, L., Chen, Y., Pirooznia, M., Singh, K., Waelde, S., Kehlenbach, R. H., Scott, I., Gucek, M. and Sack, M. N. (2018). GCN5L1 interacts with α-TAT1 and RanBP2 to regulate hepatic α-tubulin acetylation and lysosome trafficking. *J. Cell Sci.* **131**, jcs221036.