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FIRST PERSON

First person – Tak Shun Fung

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. Tak Shun Fung is first author on 'Two distinct actin filament populations have effects on mitochondria, with differences in stimuli and assembly factors', published in JCS. Tak Shun is a graduate student in the lab of Prof. Henry Higgs at Geisel School of Medicine at Dartmouth, USA, investigating the relationship between actin cytoskeletal dynamics and mitochondrial dynamics.

Tak Shun Fung

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

Mitochondria are the powerhouse of the cell. To generate energy used for cellular processes, they must maintain a gradient of hydrogen ions and protons across their inner membrane. Unhealthy mitochondria do not generate this gradient and are ultimately destroyed by a process called mitophagy. Our work focuses on the consequences of the loss of the mitochondrial proton gradient, which is known as depolarization. We show that depolarization results in the rapid assembly of a thick 'cloud' of actin filaments around mitochondria. Actin is a polymerizable protein that can dynamically assemble for various cellular functions and uses a number of assembly factors depending on the context; our work identified the specific assembly factor in this context.

We also followed up more closely on the effects of depolarization-induced actin. It is generally accepted that mitochondrial depolarization can break up the organelle into smaller units (fragmentation), but we were very surprised to find that mitochondria did not fragment in the initial stages (~30 min after depolarization). Rather, the inner membrane underwent extensive shape changes, which we refer to as 'circularization'. In addition, the actin cloud seems to inhibit circularization, which is the opposite of what we expected. Our current hypothesis is that the actin cloud serves a protective role, allowing mitochondria a chance to recover from depolarization before being permanently eliminated by mitophagy.

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

We faced many small problems throughout the project instead of a major one - the journey was analogous to climbing up a mountain split into different stages. What I learnt was that scientific research is really a teamwork-heavy endeavor, and at every stage, our team came together to lay out honestly where we were and what the immediate concerns were to keep the focus. I think that communication was crucial in the whole buildup of this project. One impasse I remember was trying to preserve the mitochondrial 'circularization' in fixed samples, we had to systematically tinker with various fixation conditions (time and concentration etc.) before we figured out ways to do it.

Sharing some other experience, I found that testing simple but meaningful things (like understanding why experiments went wrong or fail) can pay dividends in the long run. Also, talking about what puzzled us and explaining our work and hypotheses to other scientists helped a lot. Many times, they point out our blind spots and tell us glaringly obvious problems that need addressing (obvious to them, not us).

Lastly, practice makes perfect. When I worked on live cell imaging, I did tons of repetition in order to familiarize myself with the instruments and obtain high quality and quantifiable images. The microscopes really became my best friends because of the amount of time I spent with them.

> "…the journey was analogous to climbing up a mountain split into different stages"

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

The first time I saw depolarization-induced mitochondrial rearrangement 'live' with dual-color imaging (inner and outer mitochondrial membrane markers) on the Airyscan microscope. The entire process remains to this day a vivid memory in my mind. I am still puzzled and amazed at how differently the two membranes on the same organelle respond; and how dynamic they still are, after depolarization.

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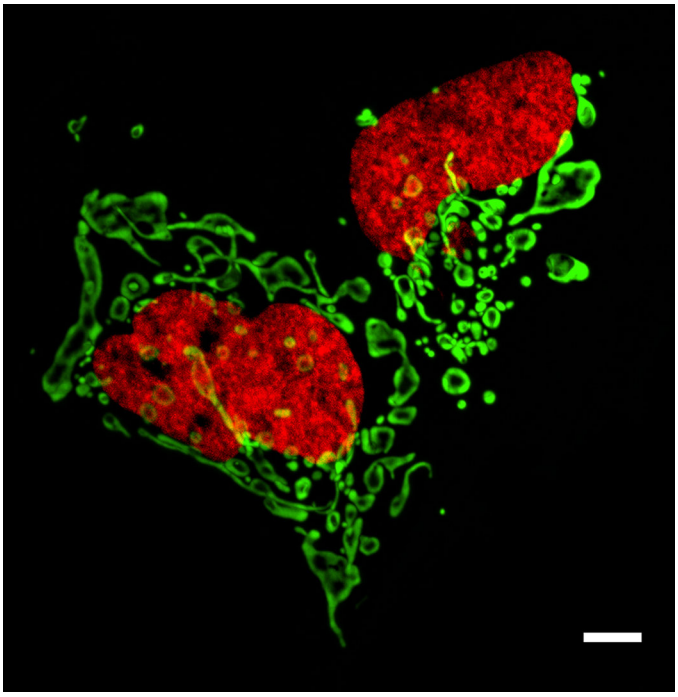

Mitochondrial matrix (green) after depolarization-induced circularization in U2OS cells. Red, nucleus. Scale bar: 10 µm. 20 min CCCP treatment.

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

Journal of Cell Science is a lovely journal. It retains a broad readership and it publishes relevant and thoughtful articles. Articles that challenge our preconceptions and pre-existing ideas in cell biology. For these reasons, I hold Journal of Cell Science in high regard.

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

I am thankful to my current PhD mentor Prof. Henry Higgs. He was always ready to discuss experimental results and talk about future experiments. He taught me how to be critical of my own work, keep an open mind and have the courage to go after interesting hypotheses. Besides the science, Prof. Higgs is a fine writer. Having his help in writing (correcting my many howlers and spelling/grammatical errors) has been invaluable. The other person I am grateful to is Dr Rajarshi Chakrabarti. He is not only an intelligent and skillful scientist but a true friend both in and out of the lab, and I feel very fortunate that I can work with him on this project.

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?

During my time in college, I experienced scientific research in different fields. In the end, I found cell biology to be the area that I am most motivated by and where results excited me the most. On top of that, the cell biologists and mentors I knew then were very supportive people. They shared their honest experience with me, the joys and anguishes, and I decided to take the next step into cellular research.

Who are your role models in science? Why?

I don't have a specific person in mind. I think that colleagues, postdocs, lab technicians and undergraduate students who are self-driven, scientifically rigorous, hard-working and display an independence of mind are all people I can learn from. I also respect scientists who are willing to admit their mistakes and learn from them. Lastly, I think there is far too little credit given to researchers who spend time and effort to teach others who are new to a technique or the subject, but I really appreciate those who do.

What's next for you?

I will be continuing my graduate studies. There is much work still to be done.

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

I can spend hours reading and exploring second-hand bookstores and public libraries. If I travel to a new city or town, I will try to take time to visit these places.

Reference

Fung, T. S., Ji, W.-K., Higgs, H. N. and Chakrabarti, R. (2019). Two distinct actin filament populations have effects on mitochondria, with differences in stimuli and assembly factors. *J. Cell Sci.* **132**, 234435. doi:10.1242/jcs.234435