

FIRST PERSON

First person – Sei Yoshida

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. Sei Yoshida is the first author on 'Dorsal ruffles enhance activation of Akt by growth factors', published in Journal of Cell Science. Sei completed this work in the lab of Joel Swanson, University of Michigan Medical School, USA. He is currently an assistant research scientist in the lab of Ling Qi, also at the University of Michigan Medical School.

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

We are interested in the physiological functions of macropinocytosis, a large-scale form of endocytosis, or 'cell drinking process'. Our recent papers show that macropinosomes, vesicles that are formed within a cell during macropinocytosis, participate in cell growth. In this paper we observe that a growth factor protein induces crater-like cell membrane structures, which are called circular dorsal ruffles (CDRs) in our research field. We also find that CDRs serve as signal platforms to recruit and/or activate Akt, an essential molecule of growth factor signaling. In other words, the cell uses the crater-like structures as 'buckets' for important signaling molecules and uses this system for growth. We hypothesize that signaling molecules elicit changes in cell morphology that in turn regulate the signal pathways, thereby creating a feedback process between signaling and morphology to modulate cell function.

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

"He taught me how to enjoy science as well as life."

I was excited when my live-cell imaging showed the phosphoinositide PIP3 localized just inside circular dorsal ruffles. This finding led us to hypothesize that the ruffle structure is used as a signal platform for Akt phosphorylation. This idea was later supported by our western blot data showing that preventing circular dorsal ruffle formation blocked growth factor-induced Akt phosphorylation. I was surprised when I saw the western blot film in the darkroom.

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

Journal of Cell Science is a premier journal for cell biologists. I would be satisfied with my research career if I could regularly publish papers in Journal of Cell Science.

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

I have worked with Dr Joel Swanson, who is a co-corresponding author of this paper, for 10 years. He taught me how to enjoy science

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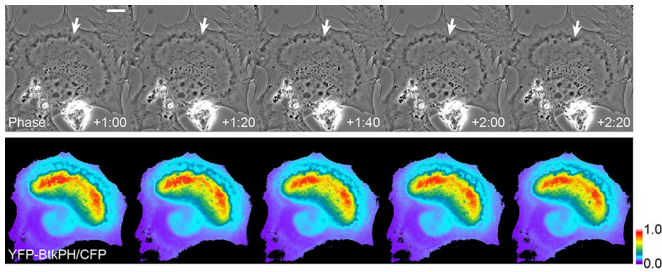
as well as life. I have many memories of discussing our favorite science topic, macropinocytosis.

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?

Several discoveries convinced me to pursue a career in academic science. When I was a graduate student in Japan, I observed that a protein secreted by *Shigella flexneri* induced macropinocytosis, suggesting that the protein modulates signal transduction in host cells. Because of this finding, I pursued my PhD. The second discovery happened when I was a postdoctoral fellow in Dr Swanson's lab. I stimulated mouse bone marrow-derived macrophages with macrophage colony-stimulating factor to induce macropinocytosis. Fluorescence resonance energy transfer microscopy of live cells showed transient activation of Rac1 at macropinocytic cups. We published those findings in Journal of Cell Science (Yoshida et al., 2009). A third discovery occurred during the project for this paper. I observed a strong PIP3 signal accumulating inside macropinocytic cups and found that the process is involved in the Akt signal pathway. These findings inspired me to pursue my career as an independent researcher.

What's next for you?

I want to explore how this research applies to clinical science, as macropinocytosis has been recognized as being important in cancer and infectious diseases. I have been trying to establish an independent research program, but it is challenging. I will keep trying.



Live-cell imaging of a fibroblast expressing YFP-Btk-PH, a probe for PIP3, and CFP, a reference protein, after stimulation by platelet-derived growth factor. Time after addition of growth factor is indicated at the bottom of the phase contrast images (minutes: seconds). Comparison of phase contrast and YFP-BtkPH/CFP ratio images shows sustained high ratio values inside circular dorsal ruffles (arrow). Scale bar: 10 μ m.

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

I came to the USA from Japan as a single father of an 8-year-old daughter. Ann Arbor, Michigan, has been a good place for our family. With support from Dr Swanson and other lab members, I somehow managed the 'research and kid' situation. My daughter now lives away from home as a college student, and I believe I am ready to leave this comfortable nest.

References

- Yoshida, S., Hoppe, A.D., Araki, N. and Swanson, J.A. (2009). Sequential signaling in plasma-membrane domains during macropinosome formation in macrophages. *J. Cell Sci.* **122**, 3250-3261.
- Yoshida, S., Pacitto, R., Sesi, C., Kotula, L. and Swanson, J.A. (2018). Dorsal ruffles enhance activation of Akt by growth factors. *J. Cell Sci.* **131**, jcs220517.