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FIRST PERSON

First person – Yukako Nishimura

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. Yukako Nishimura is co-first author on 'The formin inhibitor SMIFH2 inhibits members of the myosin superfamily', published in JCS. Yukako conducted the research described in this article while a research fellow in Virgile Viasnoff and Alexander D. Bershadsky's lab at the Mechanobiology Institute, National University of Singapore. She is now an assistant professor in the Division of Developmental Physiology, Institute for Genetic Medicine, Hokkaido University, Sapporo, Japan, investigating the functions of cytoskeletal networks in mechanobiology.

Yukako Nishimura

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

The 'structural scaffold' of the cell is the actomyosin network, consisting of actin fibers, with numerous actin-associated proteins, and myosin II filaments, which are the major generators of traction forces exerted by cells on their surroundings. Importantly, this actomyosin network is highly dynamic – meaning it can change shape and size depending on cellular processes. Regulating this dynamic network is crucial for many cellular and developmental processes, such as cell migration, cell division and cancer metastasis. One of the essential regulators is the formin family of proteins, which are involved in nucleation and elongation of actin filaments. A small molecule inhibitor, termed SMIFH2, has been shown to potently inhibit a broad range of formins in cells and has been widely used in hundreds of studies since its discovery. In this study, we used cellular and *in vitro* assays to demonstrate that SMIFH2 inhibits not only formins but also various members of the myosin superfamily, including class II, V, VII and X myosins. This finding reveals that SMIFH2 is not a specific inhibitor of formins and suggests that the compound should be used with caution in future studies of actomyosin-dependent processes that might involve both formins and myosins.

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

We did not have any specific difficulties in terms of science, because all our team members are specialists in either cell biology or biochemistry. We collaborated smoothly before the COVID-19 pandemic. Unfortunately, the pandemic hit us during our submission and revision period; experiments and data analysis were interrupted because of lockdown of labs in both the USA and Singapore. It was a hard time for us to wait until labs were reopened. During this time, we tried to overcome the situation and focus on advancing our project with frequent Zoom meetings and chats via email.

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

We had two exciting moments during this project. First, we found that fibroblasts treated with SMIFH2 exhibited reduced traction forces, similar to when myosin was inhibited, even though their actin cytoskeleton, including stress fibers, seemed intact. This result was puzzling but also exciting, because it suggested that formins may be involved in force generation by regulation of actin turnover. After this finding, we proceeded to run an *in vitro* actomyosin contraction assay using permeabilized cells containing no G-actin to see if SMIFH2 directly inhibited myosin II-based contraction. In this specific assay, we were able to track ATP-dependent cellular contraction in actin filament bundles stabilized with phalloidin. Surprisingly, SMIFH2 partially inhibited contraction after addition of ATP, suggesting that SMIFH2 could inhibit myosin activities! We immediately contacted Dr James R. Sellers to suggest a collaboration, and he and his group members checked SMIFH2 functions for several myosins using biochemical assays.

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

Journal of Cell Science is the one of the longstanding journals for cell biologists and covers important fields and interests. The journal was the first choice for our paper, because we believe our work is of interest for the broad readership of Journal of Cell Science.

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

Even though I have had many mentors who helped me in my scientific career, I have to mention Dr Alexander D. Bershadsky (Sasha) and Dr Virgile Viasnoff here. They have been supportive of

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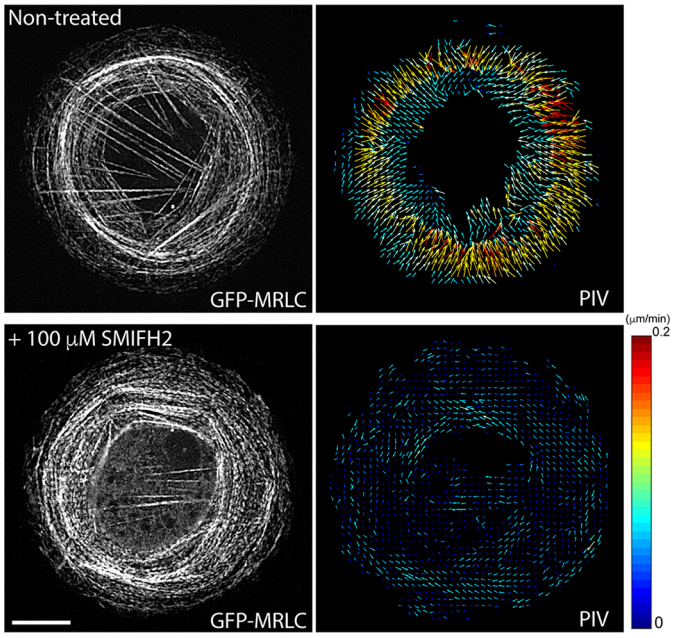

SMIFH2 (100 µM) inhibits centripetal movement of myosin II mini filaments (left panels) induced by ATP in permeabilized HFF cells. Arrows in right panels represent the direction and velocity of myosin II filaments, with colour code shown in the right. Scale bar: 10 µm.

my career even after I left their labs. They were patient and encouraged me and other colleagues when our project was stuck. My discussions with them were always helpful and exciting, since they like to share their extensive scientific knowledge to inspire new directions. Sasha is a cell biologist and Virgile is a physicist by training, so it was a great combination to discuss our project deeply from multidisciplinary perspectives. It was a wonderful time for me to work with them 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?

I wanted to be engaged in biology-related jobs when I was a child. After entering university to learn more about biology, I had a chance to join a series of lectures and practical training in developmental biology at a marine laboratory. While doing experiments, meeting and talking with several scientists in such a special place impressed me a lot. This experience motivated me to pursue my career in academic science.

Who are your role models in science? Why?

I would like to mention two women scientists, Dr Taiko Noumura (Ochanomizu University, Japan) and Dr Clare M. Waterman (National Institutes of Health, USA) as my role models. Dr Taiko Noumura was my first supervisor in science when I was an undergraduate. Dr Clare M. Waterman was my mentor when I was a postdoc in the USA. During my time in their labs, I was impressed with their science, specifically their motivation to ask straightforward investigative questions. They took risks to answer their questions and loved discussions and communications with their lab members. I also learnt from them how to stay alive in a scientific career as a woman. My goal is to become such a ‘strong’ woman scientist.

What's next for you?

Recently, I moved to Hokkaido University in Japan as an assistant professor. My next challenges involve setting up a new lab, continuing my science and supervising undergrads and graduate students in the university. I look forward to working together with younger scientists.

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

I like to eat and drink! I enjoyed barbecues, crabs with Old Bay seasoning, and drinking bourbon and Californian wines when I was in the USA. I enjoyed a lot of hawker foods in Singapore, such as chicken rice, bah kut teh (pork ribs in broth), satay (skewered and grilled meat) and hokkien mee (stir-fried egg noodles). I was also a big fan of Tiger beer. I am now enjoying fresh seafood in Japan and Japanese sake, and I will explore more local foods and drinks in Hokkaido.

Reference

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